*Membr. and Cell Biol.*, 1996, Vol. 10 (2), pp. 211–224
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# A Possible Role of Adenine Nucleotide Metabolism in the Regulation of Human Erythrocyte Volume

F. I. Ataullakhanov, V. M. Vitvitsky, and S. V. Komarova
*Scientific Centre for Hematology, Russian Academy of Medical Sciences, Moscow*

A simplified mathematical model of cell metabolism describing ion pumps, glycolysis, and adenylate metabolism was constructed and investigated in order to clarify the functional role of the adenylate metabolism system in human erythrocytes. The adenylate metabolism system was shown to be capable of functioning as a specific regulatory system stabilizing intracellular ion concentration and, hence, erythrocyte volume upon changes in cell membrane permeability. This stabilization is provided by an increase in the adenylate pool associated with the increase in the activity of ATPases. A proper regulation of the adenylate pool may be achieved only by the regulation of the AMP degradation or synthesis rate. The optimal rate of the adenylate metabolism in erythrocytes ranges from several tenths of a percent to several percents of the glycolytic flux. An increase in this rate results in the deterioration of the cell metabolism stability. A decrease in the adenylate metabolism rate makes the functioning of this metabolic system inefficient, because the time necessary to achieve the stabilization of intracellular concentration of ions becomes comparable with the erythrocyte life span.

*(Received 14 February, 1995)*

Owing to its discoid shape, the erythrocyte has a high cell surface area to volume ratio providing for its high deformability during passage through capillaries. The maximal permissible increase of the erythrocyte volume is 15–20% of the physiological volume. This restriction is determined by conditions of erythrocyte filtration in the spleen [1]. On the other hand, the erythrocyte volume may not be substantially reduced as this involves an unavoidable increase of hemoglobin concentration leading to higher viscosity of the intracellular contents [2]. The existence of volume restrictions requires stabilization of the erythrocyte volume.

The erythrocyte volume is totally determined by the ionic homeostasis of this cell [3, 4]. Numerous factors (pathological processes, oxidizers, antibiotics etc.) are capable of increasing the membrane permeability to erythrocytes that should be conducive to perturbation of their ionic homeostasis and changes in volume. Evidently, erythrocytes must have systems ensuring compensation for changes in cell membrane permeability and stabilizing their volume. Results of a number of studies allowed formulation of model concepts of basic physico-chemical regularities which determine homeostasis in erythrocytes [5, 6], as well as construction and investigation of mathematical models which describe ion homeostasis in combination with energetic metabolism [3, 5, 7–10]. At present, the available experimental data are insufficient for a comprehensive verification of

such models. However, yet now it is clear that they do not describe a number of interesting peculiarities of erythrocyte metabolism, specifically a higher ATP level associated with the increased pool of adenylates ([ATP] + [ADP] + [AMP]) in erythrocytes with enhanced permeability of cell membranes to cations [11–17]. All known models predict the opposite dependence, i.e. drop of ATP concentration with growth of membrane permeability. The increase of ATP concentration at higher ion fluxes could contribute to a better work of ion pumps and stabilization of erythrocyte volume. The aim of the present study was to check the hypothesis according to which metabolism of adenine nucleotides is regulated in a way to provide a more efficient stabilization of erythrocyte volume. In order to check the proposed hypothesis in a simple mathematical model, we investigated the possibility of stabilization of ion composition of erythrocytes through regulation of metabolism of adenylates under changes in permeability of the cell membrane.

## HYPOTHESIS

According to the proposed hypothesis, the pool of adenylates is regulated in a mode under which the increase in membrane permeability leading to activation of ion pumps results in the growth of the pool of adenylates and [ATP]. The increasing [ATP] induces additional activation of $Na^+$,$K^+$-ATPase making possible compensation for the increased influx of ions to the cell that stabilizes the erythrocyte volume.

Our hypothesis is based on the following postulates:

1. Stabilization of erythrocyte volume is realized through stabilization of intracellular concentration of ions.

2. The intensity of operation of ion pumps in the erythrocyte is proportional to the intracellular $Na^+$ concentration and depends on the components of the pool of adenylates.

3. The rate of ATP production from ADP in glycolysis (glycolytic flux) as a function of ATP concentration is a bell-shaped curve with an abrupt slope in the range of physiological ATP concentrations.

4. An essential aspect of our hypothesis is the postulate that the metabolism of adenylates ensures the growth of adenylate pool and, consequently, the intracellular ATP concentration during activation of processes consuming ATP, specifically operation of ion pumps.

The purpose of our study was to elucidate the possible regulatory relations in the metabolism of adenine nucleotides which could provide for the required regulation of the size of adenylate pool.

## MATHEMATICAL MODEL

To check our hypothesis, we devised a mathematical model describing in a simplified mode the interaction of ion transport with the metabolism of energy and adenylates in human erythrocytes. The model includes a transmembrane ion gradient (e.g., $Na^+$ gradient) with a high and invariable extracellular and low intracellular concentrations of ions, an ion pump aspirating ions from the cell, glycolysis as the energy source and a system of adenylate metabolism (Fig. 1). The system of adenylate metabolism in human erythrocytes includes AMP synthesis in the reactions induced by adenosine kinase and adeninephosphoribosyl

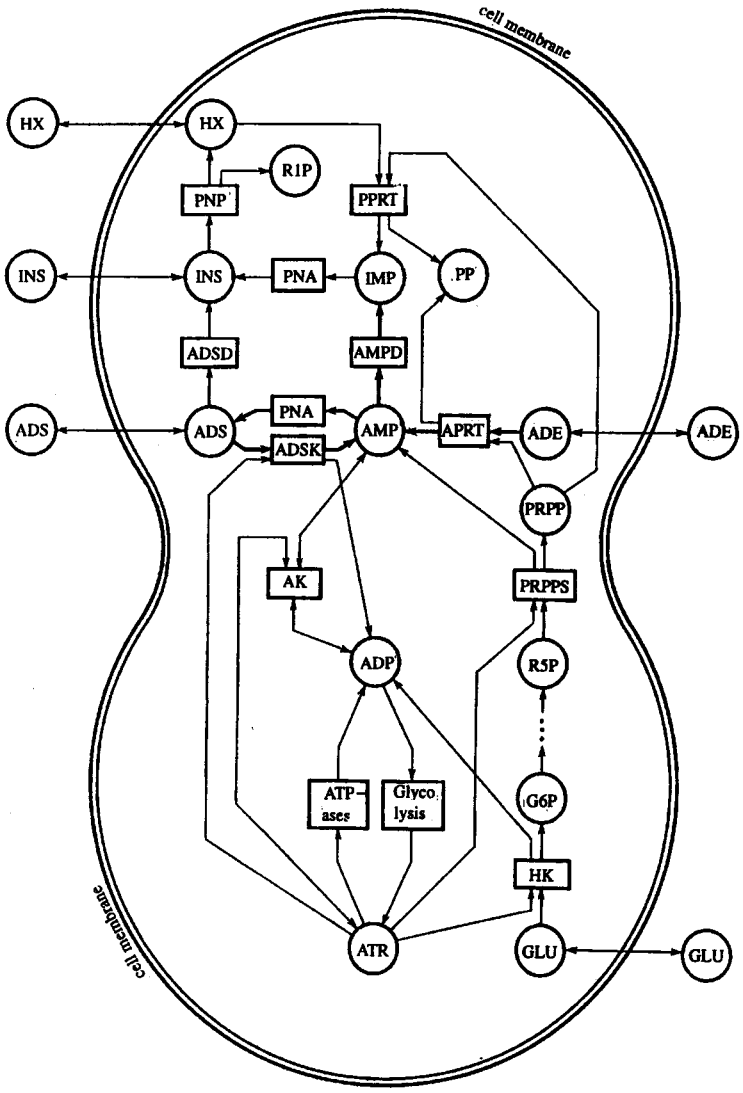


**FIGURE 1.** Linkage of adenylate metabolism to other metabolic systems in human erythrocytes. The dotted line indicates the route of glucoso-6-phosphate transformation into riboso-5-phosphate. ATPases include all ATP-consuming processes which are not shown in the figure. Designations: ADE, adenine; ADP, adenosine-5′-diphosphate; ADS, adenosine; AMP, adenosine-5′-monophosphate; ATP, adenosine-5′-triphosphate; GLU, glucose; G6P, glucoso-6-phosphate; HX, hypoxanthine; IMP, inosine monophosphate; INS, inosine; PP, pyrophosphate; PRPP, phosphoribosylpyrophosphate; R1P, riboso-1-phosphate; R5P, riboso-5-phosphate; AK, adenylate kinase; ADSK, adenosine kinase; ADSD, adenosine deaminase; AMPD, AMP-deaminase; APRT, adeninephosphoribosyl transferase. HK, hexokinase; PNA, purine-5′-nucleotidase; PNP, purinenucleoside phosphorylase; PPRT, purinephosphoribosyl transferase; PRPPS, phosphoribosylpyrophosphate synthase.

transferase, AMP degradation via AMP-deaminase and purine-5′-nucleotidase, redistribution between ATP, ADP and AMP in the adenylate kinase reaction (see Fig. 1).

Changes in the intracellular concentration of ions and the levels of components in the pool of adenylates are described by the following system of differential equations:

$$\dot{I} = U_i - 3U_p, \tag{1}$$

$$\dot{T} = U_{gl} - U_p + U_{-ak} - U_{+ak} - U_{ask} - 2U_{aprt},$$

$$\dot{D} = U_p - U_{gl} - 2(U_{-ak} - U_{+ak}) + U_{ask} + U_{aprt},$$

$$\dot{M} = U_{-ak} - U_{+ak} + U_{ask} + 2U_{aprt} - U_d,$$

where $I$, $T$, $D$ and $M$ are the intracellular concentrations of ions, ATP, ADP and AMP, respectively; $U_i$ is the rate of passive influx of ions to the cell; $U_p$ is the intensity of ion pump operation (transport of 3 ions is supposed to require one ATP molecule); $U_{gl}$ is the glycolysis rate; $U_{+ak}$ is the rate of ATP and AMP consumption and the half-rate of ADP formation in the adenylate kinase reaction; $U_{-ak}$ is the rate of reverse adenylate kinase reaction; $U_{ask}$ is the rate of adenosine kinase reaction; $U_{aprt}$ is the rate of adeninephosphoribosyl transferase reaction; $U_d$ is the total rate of AMP degradation in the AMP-deaminase and purine-5′-nucleotidase reactions.

As we are interested in elucidating the qualitative character of regulatory relationships, the analysis was simplified by describing the rates of all fluxes in the system with power functions. It was shown earlier [18–20] that such approximation provided adequate description of enzymic reactions in sufficiently wide ranges of variation of concentration of metabolites.

We presume that the rate of passive entry of ions into the cell is determined solely by the permeability of cell membrane:

$$U_i = PJ, \tag{2}$$

where $P$ is the cell membrane permeability; $J$ is the extracellular ion concentration.

The rate of operation of ions pumps is proportional to the intracellular concentration of ions. We examine two types of this rate dependence on the concentration of adenylate pool components:

(1) the rate of ion pump operation is proportional to ATP concentration in erythrocytes:

$$U_p = W_1 IT; \tag{3}$$

(2) the rate of ion pump operation is proportional to the ratio of [ATP] to [AMP]. In our opinion, this dependence provides better description of the real kinetics of ATPase in native erythrocytes [18, 21]:

$$U_p = W_1'IT/M, \tag{3a}$$

where $W_1$ and $W_1'$ are the parameters reflecting activity of the ion pump.

The rate of ATP production from ADP in glycolysis

$$U_{gl} = W_2 T^{0.52} M^{0.41}. \tag{4}$$

This expression was obtained earlier in [18] as approximation of the experimental dependence of the glycolytic flux on [ATP] in human erythrocytes [22, 23]. Parameter $W_2$ characterizes the glycolysis activity in the cell.

The total rate of AMP synthesis in the adenosine kinase and adeninephosphoribosyl transferase reactions is expressed as

$$U_a = W_3 T^{n1} M^{k1}, \tag{5}$$

where parameter $W_3$ reflects the total activity of the reactions of AMP synthesis; $n1$ and $k1$ are the parameters reflecting the dependence of AMP synthesis on [ATP] and [AMP], respectively.

The total rate of AMP digestion in the AMP-deaminase and purine-5′-nucleotidase reactions:

$$U_d = W_4 T^{n2} M^{k2}, \tag{6}$$

where $W_4$ is the summary activity of reactions of AMP degradation; $n2$ and $k2$ are the parameters reflecting the dependence of the rate of AMP degradation on [ATP] and [AMP], respectively. In our model the rate of AMP digestion is equally dependent on [ATP] and [AMP], as ATP is known to be a strong effector of both purine-5′-nucleotidase and AMP-deaminase [24–28]; $U_{+ak}$ and $U_{-ak}$ are the rates of forward (ADP synthesis) and reverse adenylate kinase reaction.

The rate of adenylate kinase reaction is considerably higher than those of other reactions [11, 29]. This suggests that the adenylate kinase reaction is always close to equilibrium. Assuming the equilibrium constant to be unity, we pass to new slow variables: energy pool of the cell $E = 2T + D$ and the adenylate pool $A = T + D + M$.

$$\dot{I} = PJ - 3U_p, \tag{7.1}$$

$$\dot{E} = W_2 T^{0.52} M^{0.41} - U_p - CW_3 T^{n1} M^{k1}, \tag{7.2}$$

$$\dot{A} = W_3 T^{n1} M^{k1} - W_4 T^{n2} M^{k2}, \tag{7.3}$$

$$D^2/TM = 1, \tag{7.4}$$

where

$$T = (A + 3E - (6AE - 3E^2 + A^2)^{0.5})/6 \tag{8}$$

$$M = (7A - 3E - (6AE - 3E^2 + A^2)^{0.5})/6. \tag{9}$$

The coefficient $C$ can vary from 1 to 3 depending on the contribution of adeninephosphoribosyl transferase reaction to the total rate of AMP synthesis: when $U_a = U_{aprt}$, $C = 3$; when $U_a = U_{ask}$, $C = 1$. We assumed here that adenosine kinase and adeninephosphoribosyl transferase make equal contributions to the AMP synthesis that makes $C = 2$.

## RESULTS

Investigation of the model was basically reduced to the selection of conditions which provide stabilization of the intracellular concentration of ions through regulation of the pool of adenylates under variation of the cell membrane permeability.

To estimate the quality of stabilization of ionic composition of erythrocytes in our model under variation of membrane permeability, we used the sensitivity coefficient which is reciprocal to the stabilization coefficient. By definition, the sensitivity coefficient $Q$ describes the sensitivity of stationary intracellular concentration of ions $I_s$ to changes in the cell membrane permeability $P$ and is expressed as

$$Q = (d\ln I_s)/(d\ln P) = (dI_s/dP) \cdot (P/I_s).$$

The better stabilization is achieved, the lower is the sensitivity coefficient. The ideal stabilization means that the stationary intracellular concentration of ions $I_s$ is independent of the cell membrane permeability $P$, i.e. $Q = 0$. In our model the sensitivity coefficient $Q$ is described by the following analytical expression:

$$Q = \frac{((n2 - n1)/(k2 - k1))\,(2.46U + (z + 0.41)PJ) + 0.48PJ - 3.12U}{(((n2 - n1)/(k2 - k1))\,0.41 - 0.52)\,(PJ + 6U)}, \tag{10}$$

where $z = 0$ at $U_p$ proportional to [ATP] and $z = 1$ at $U_p$ proportional to the ratio [ATP]/[AMP]; $U$ is the stationary flux in the system of adenylate metabolism.

In our model the sensitivity coefficient $Q$ is a hyperbolic function of the ratio $(n2 - n1)/(k2 - k1)$.

The model was tested for three variants of metabolism of adenylates within the framework of eqs. (5)–(6) with the assumption of linear dependence of the ATPase reaction rate on [ATP] (3): (1) the rate of AMP synthesis is constant ($k1 = n1 = 0$); (2) the rate of AMP

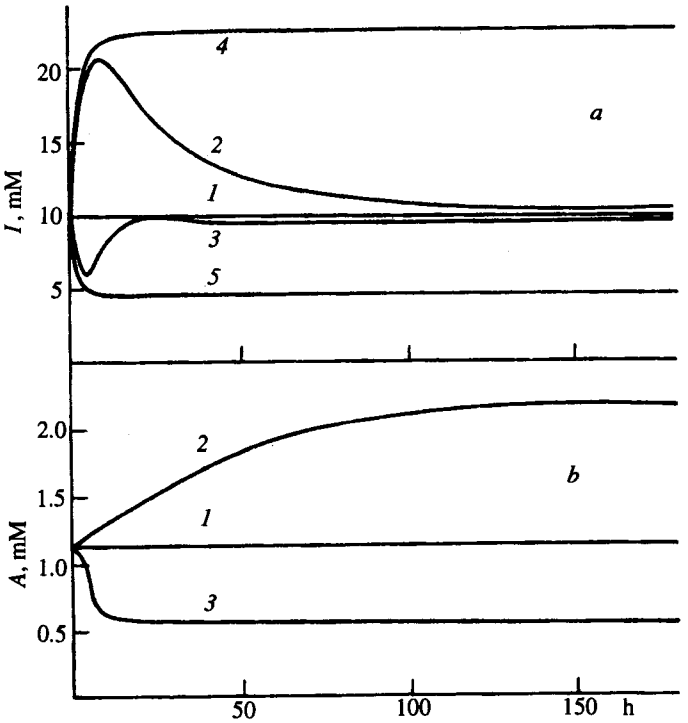


**FIGURE 2.** The time course of changes in the intracellular concentration of ions (*a*) and the pool of adenylates (*b*) obtained from model (7.1–7.4) at a constant rate of AMP synthesis at stepwise changes in the cell membrane permeability. Initial stationary values *I* and *A* (lines *1*) were obtained at values of parameters set by condition (12). Curves *2* were derived upon increase and curves *3* upon decrease (at the initial moment) of parameter *P* (permeability of cell membrane to ions) to values of 0.12 and 0.03 1/h, respectively. Curves *4* and *5* were obtained at the same increase and decrease of parameter *P* for the case of invariable pool of adenylates $A = 1.11$ mM (exclusion of eq. 7.3 from system (7.1–7.4).

digestion is constant ($k2 = n2 = 0$); (3) the rate of AMP synthesis is linearly dependent on [ATP] ($k1 = 0$, $n1 = 1$).

The first version was also examined assuming the dependence of ATPase rate on [ATP]/[AMP] (3a).

(1) When the rate of AMP synthesis is constant and its degradation rate is described by eq. (6), it is convenient to express the activity of AMP-degrading processes as

$$W_4 = W^*U, \tag{11}$$

where $U$ = const is the rate of AMP synthesis and $W$ is the normalized activity of AMP degradation process.

Figure 2 shows the time course of changes in the intracellular concentration of ions and the pool of adenylates derived from the model (7.1–7.4) at a stepwise variation of the cell membrane permeability.

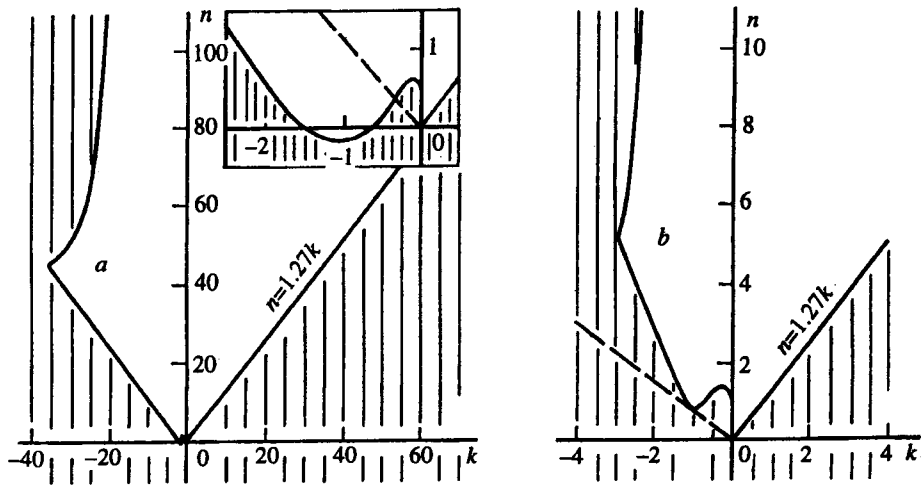


**FIGURE 3.** Range of the existence of stable stationary state of system (7.1–7.4) in the plane of parameters $n$ and $k$ at a constant rate of AMP synthesis (non-hatched area). *a*, $U = U_0 = 0.02$ mM/h. The inset shows the vicinity of the origin of coordinates. *b*, $U = 0.2$ mM/h. Other parameters are determined by condition (12). The dashed line shows the ratio $n/k$ at which the ideal stabilization of intracellular concentration of ions is achieved.

The values of parameters reflecting activities of enzymes and fluxes were as follows:

$$J = J_0 = 100 \text{ mM},$$

$$P = P_0 = 0.06 \text{ h}^{-1},$$

$$W_1 = 0.2 \text{ mM}^{-1}/\text{h}, \tag{12}$$

$$W_2 = 13.48 \text{ mM}^{0.07}/\text{h},$$

$$W = 0.01 \text{ mM}^{-(n+k)},$$

$$U = 0.02 \text{ mM/h},$$

$$n = 1, 2,$$

$$k = -1.$$

At the above selection of parameters the stationary state in this system describes well the physiological values of concentrations and fluxes of ions and metabolites in human erythrocytes [11, 13, 22, 30–33].

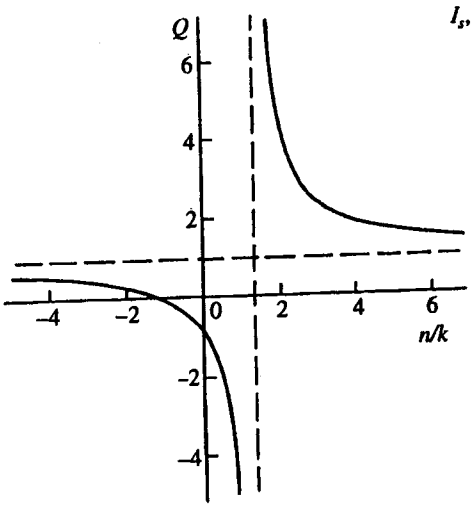


Fig. 4

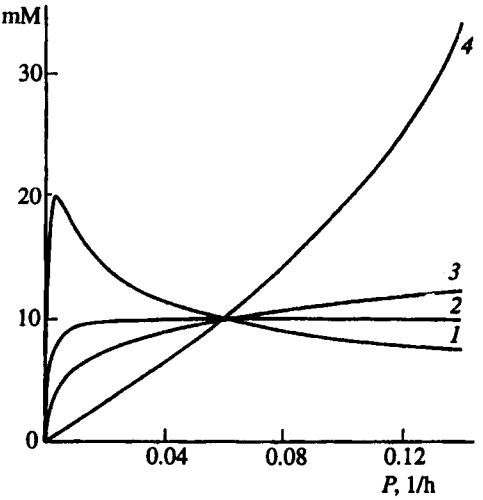


Fig. 5

**FIGURE 4.** The dependence of sensitivity coefficient of stationary intracellular ion concentration to changes in the cell membrane permeability $Q = (d \ln I_s)/(d \ln P)$ on ratio $n/k$ obtained assuming linearity of the dependence of the ATPase reaction rate on ATP (3). Asymptotes $n/k = 1.27$ and $Q = 1$ are indicated with dashed lines.

**FIGURE 5.** Effect of $n/k$ ratio on the dependence of stationary intracellular concentration of ions ($I_s$) on the permeability of cell membrane ($P$). All curves were derived at $k = -1$ and different $n$ values. *1*, $n/k = -0.5$; *2*, $n/k = -1.12$; *3*, $n/k = -2$. Other parameters are determined by eq. (12). Curve *4* was obtained at the invariable pool of adenylates.

$$I_s = 10 \text{ mM},$$

$$T_s = 1 \text{ mM},$$

$$D_s = 0.1 \text{ mM},$$

$$M_s = 0.01 \text{ mM},$$

$$U_{gl} = U_p = 2 \text{ mM/h}.$$

As one can see in Fig. 2, the model is capable of providing very good stabilization of the stationary concentration of ions through variation of the level of adenylate pool (curves *2*, *3* in Fig. 2*a*). In the case of invariable pool of adenylates ($A$ = const) variations in the membrane permeability are conducive to considerable changes in the intracellular concentration of ions (curves *4*, *5* in Fig. 2).

Examination of the model has shown that in a wide range of $n$ and $k$ values there exists a stable stationary state of the system (7.1–7.4) which is always single (Fig. 3). Let us designate all concentrations and fluxes in this state by subscript $s$. Within this range,

stabilization of the stationary intracellular concentration of ions ($I_s$) may be achieved through variation of the cell membrane permeability ($P$). Stabilization is provided for by the growth of adenylate pool upon the increasing rate of ATP consumption.

The dependence of $Q$ on $n/k$ ratio is shown in Fig. 4. The left and right branches of the hyperbola correspond to negative and positive $k$ values, respectively. When values of all other parameters are determined by condition (12), the ideal stabilization of the stationary intracellular concentration of ions $Q = 0$ is achieved at a ratio of $n/k = -1.12$. Stabilization of $I_s$ is deteriorated upon deviation from this $n/k$ value. Negative values of $Q$ in Fig. 4 point to the appearance of ovecontrol when the increase of membrane permeability $P$ leads to the drop of intracellular ion concentration $I_s$. Figure 4 clearly demonstrates that a satisfactory stabilization of $I_s$ cannot be reached at positive $k$ values.

The dependence of the stationary intracellular concentration of ions on the cell membrane permeability at different values of $n/k$ ratio is shown in Fig. 5, where curve *2* reflects the ideal stabilization of $I_s$. Stabilization of $I_s$ is deteriorated upon deviation of $n/k$ ratio from this value (curves *1* and *3* in Fig. 5).

At $n/k = -1.12$, i.e. in the case of ideal stabilization of $I_s$, the pool of adenylates increases proportionally to $P$ (line *1* in Fig. 6*a*). In this case the increase of adenylate pool is basically determined by the growth of intracellular ATP concentration (Fig. 6*b*, line *1*), whereas the energy charge remains virtually invariable (Fig. 6*c*, line *1*).

The rate of adenylate metabolism in the model is determined by parameter $U$. The model shows that the optimal rates of adenylate metabolism in erythrocytes are within the range from a few tenths to several percents of the magnitude of glycolytic flux. The increase of this rate is conducive to a narrower range of the existence of stable stationary states of the system (7.1–7.4) in the plane of $n$ and $k$ parameters. At the same time, this leads to higher values of $n/k$ ratio at which the best stabilization of $I_s$ is achieved. When the magnitude of $U$ increases 10 times compared to its initial value, the ideal stabilization of $I_s$ can no longer be achieved within the range of stable stationary solution of system (7.1–7.4) (see Fig. 3). Further growth of $U$ makes impossible the achievement of a sufficiently noticeable stabilization of $I_s$ in the range where the stationary state is stable. Inhibition of the rate of adenylate metabolism is conducive to inefficient regulation of the adenylate metabolism because the time necessary for a substantial change of the pool of adenylates becomes comparable with the lifetime of erythrocytes in the blood flow. At subsequent stages of work, parameters of the activity of processes involved in the system of adenylate metabolism were selected in a way ensuring that the stationary flux in this system does not exceed 0.02 mM/h.

(2) When the rate of AMP digestion is constant ($k2 = 0$, $n2 = 0$) and the rate of its synthesis is described by eq. (5), in the stationary state it follows from eq. (7.3) that

$$0 = W_3 T^{n1} M^{k1} - W_4 T^0 M^0 = W_3 T^{n1} M^{k1} - W_4,$$

or

$$0 = W_3 - W_4 T^{n-1} M^{-k1}.$$

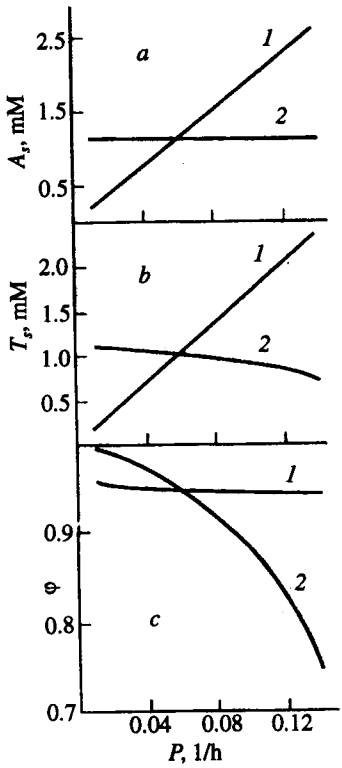


Fig. 6

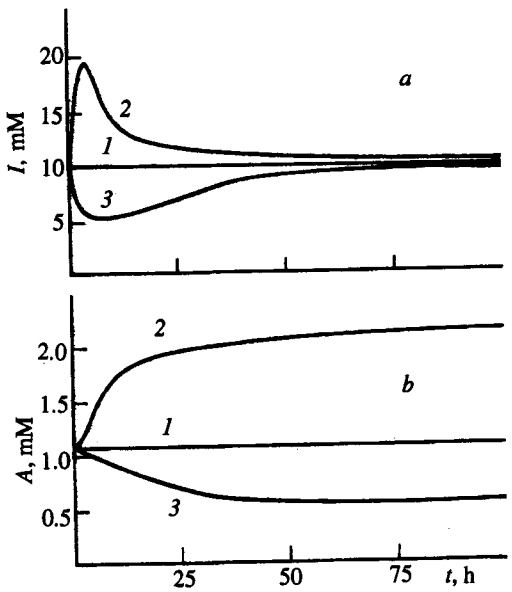


Fig. 7

**FIGURE 6.** Dependence of the stationary value of the adenylate pool (*a*), ATP concentration (*b*) and energetic charge (*c*) on the cell membrane permeability to ions. Curves *1* were derived from model (7.1–7.4) at values of parameters determined by condition (12); curves *2* were obtained at invariable pool of adenylates $A = 1.11$ mM.

**FIGURE 7.** The time course of changes in the intracellular concentration of ions (*a*) and the pool of adenylates (*b*) derived from model (7.1–7.4) at a constant rate of AMP degradation and stepwise changes in the cell membrane permeability. The initial stationary values of *I* and *A* (*1*) were obtained at parameters set by condition (12). *2*, increase and *3*, decrease (at the initial moment) of parameter *P* (cell membrane permeability to ions) to 0.12 and 0.03 1/h, respectively.

After introduction of designations $n = -n1$, $k = -k1$ eq. (7.3) for the stationary state acquires the same form as in the case of constant rate of AMP synthesis. Thus, it may be inferred that the stationary behaviour of the model is the same for the cases of constant rates of AMP synthesis and degradation.

For this model, substantial changes are displayed by the kinetics of transitory processes (Fig. 7). Comparison with the data shown in Fig. 2 indicates that in the case of constant AMP degradation rate the duration of transitional processes diminishes at higher membrane permeability and increases when it goes down.

(3) In the stationary state, the variant, in which the rate of AMP synthesis is linearly dependent on [ATP] ($k1 = 0$, $n1 = 1$) and its degradation rate is determined by eq. (6) as in the version examined in paragraph (2), is expressed in the same mode as in the case of constant rate of AMP synthesis with $n = n2 - 1$, $k = k2$.

In this situation the time course of changes in the concentration of ions and the pool of adenylates upon jumpwise variation of the cell membrane permeability is little different from that shown in Fig. 2.

When the rate of AMP synthesis is constant and the rate of ATP-consuming processes is proportional to [ATP]/[AMP] ratio ($U_p = W_1'IT/M$), the qualitative results of the model examination prove to be identical to those discussed above (see paragraph (1)). The ideal stabilization of the stationary intracellular concentration of ions $Q = 0$ is achieved at a ratio $n/k = -0.33$ and at values of other parameters determined by condition (12) $W_1' = 0.002\ h^{-1}$.

## DISCUSSION

The results obtained indicate that the system of adenylate metabolism may play the role of the stabilizer of ion composition and, hence, erythrocyte volume. Stabilization is achieved due to the growth of the pool of adenylates with the increasing digestion of ATP. Regulation of the operation of ion pumps through variation of ATP level allows a several-fold increase of the range of permissible changes in the cell membrane permeability. To achieve the required regulation of the pool of adenylates, it is sufficient to regulate either only the rate of AMP degradation or only the rate of its synthesis.

In the case of regulation of AMP degradation, ATP should activate and AMP inhibit the reactions in which AMP is digested. The extent of the activation and inhibition is nearly the same within the range of physiological values of parameters.

In the case of regulation of AMP synthesis, AMP should activate and ATP inhibit the reactions of AMP synthesis. It is also noteworthy that realization of regulation, based on the enzymes of synthesis of the system of adenylate metabolism, reduces the duration of transitory processes with the establishment of a new stationary state upon the increase in the membrane permeability.

At a linear dependence of the rate of AMP synthesis on ATP concentration and a regulated rate of AMP degradation the required regulation of the level of adenylate pool is also achieved; however, this necessitates a stronger activating effect of ATP on the processes of AMP degradation.

Analysis of the model showed that the efficiency of stabilization of intracellular ion concentration in the model is deteriorated with the increasing rate of adenylate metabolism. At the same time, the interval in which the system is in the stable state is reduced. Based on this, we presume that low rates of metabolism of adenylates in erythrocytes [30–32, 34] are determined by the requirement of stability of the cell metabolism. The rate of adenylate metabolism virtually determines the expediency of the entire system operation. In this context, the effect of stabilization of ion composition of erythrocytes through regulation of the size of adenylate pool should be manifested during sufficiently long time intervals which are required for the occurrence of substantial changes in the pool of adenylates and may be as long as hours and even days. Most probably, the role of such regulation should consist in the compensation of long-term changes in conditions of the cell existence. These

may include changes in the permeability of cell membrane, activity of glycolysis or ion pumps etc. resulting from the development of a pathological process or cell ageing. Some pathologies, such as chronic renal insufficiency, sepsis, myeloid leukemia, are known to be conducive to a considerable increase of ATP level in the cell. The latter change correlates with the increased cell membrane permeability to ions in such cells [11–16]. We believe that these experimental results provide a good support for the hypothesis discussed above.

In our view, differences in the ATP levels in individual erythrocytes observed in blood of healthy people may also be explained by the differing sizes of the pool of adenylates compensating for the differences in the cell membrane permeability determined by some intrinsic (genetic) or external factors.

This study was supported by the Moscow City Committee on Science and Technology, grant GN-18/94.

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