CHANGES IN COMPONENTS OF FIBRINOLYSIS DURING SHORT-TERM ADAPTATION TO HIGH ALTITUDES

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A study of coagulation of the blood in dogs in the town of Frunze (760 m above sea level) and at Tuya-Ashu (3200 m above sea level) showed that in the "emergency" phase of adaptation (the first 3 days) activation of fibrinolysin and profibrinolysin accompanied by inhibition of antifibrinolysins and of inhibitors of profibrinolysin activators is observed. The concentration of fibrinogen in the plasma falls during this period by 100 mg%, and this could be a factor increasing vascular permeability and improving the tissue oxygen supply. Later, together with an increase in the concentration of fibrinolysin and of profibrinolysin activators, the level of inhibitors of fibrinolysis rises considerably. The ratio between all the components of fibrinolysis is established at a new level.

KEY WORDS: hemocoagulation; fibrinolysis; short-term adaptation.

During adaptation of lowland dwellers to high altitudes of 2000-3600 m above sea level the fibronylsis rises steadily after several phasic fluctuations during the first days of adaptation, It is higher in indigenous inhabitants of high mountain regions than in inhabitants of the foothills [1]. This principle has been established after investigations on man and experiments on animals [4].

This paper describes a study of changes in the various components of the fibrinolytic system at high altitudes.

EXPERIMENTAL METHOD

The state of coagulation of the blood was studied in 28 dogs in the town of Frunze (760 m above sea level) and at the hill station of Tuya-Ashu (3200 m above sea level) on the third and 26th days of adaptation.

The blood clotting power was determined with the N333 coagulograph and on the basis of biochemical tests, the fibrinogen concentration and fibrinolytic activity were determined by Bidwell's method in percent and in units by a technique developed by the present writers [6], and activity of the individual components of fibrinolysis was determined by the method of Astrup and Muller, with calculation of the content of components of the fibrinolytic system by Gritsyuk's method [3].

EXPERIMENTAL RESULTS

The state of the general clotting power of the dogs' blood at different periods of adaptation is given in Fig. 1. As these data show, after the dogs had stayed in the hills for 3 days, the duration of blood clotting was lengthened and its end delayed. On the 26th day of adaptation the same pattern was found but less clearly. The viscosity of the blood was slightly reduced and the density of the clot increased. Changes in

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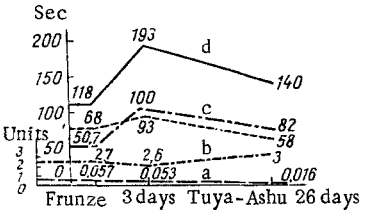

Fig. 1

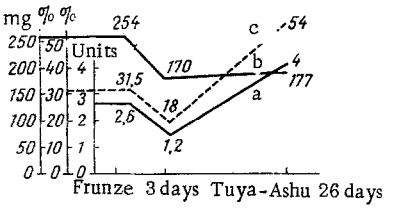

Fig. 2

Fig. 1. General indices of clotting power of blood during adaptation of dogs: a) density of clot; b) viscosity of blood; c) beginning of blood clotting; d) end of blood clotting.

Fig. 2. Fibrinogen concentration and fibrinolytic activity during adaptation of dogs. Fibrinogen concentration: a) in mg %, b) in AFS units; c) fibrinolytic activity (in %).

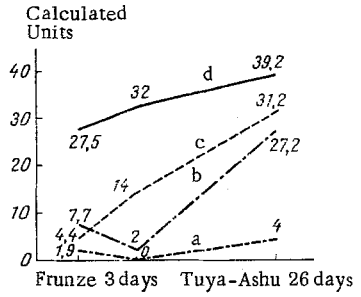

Fig. 3. Activity of individual components of fibrinolysis during adaptation of dogs: a) antifibrinolysins; b) inhibitors of profibrinolysin activators; c) fibrinolysin activators; d) fibrinolysin.

the biochemical indices showed that the delay in thrombin formation could be attributed to a marked increase in the concentration of free heparin (initially 13.2 ± 1.36 sec, on the 26th day 21.8 ± 1.3 sec; $P < 0.01$) and of antithrombins (initial thrombin time 21.5 ± 1.17 sec, on the 26th day 29.5 ± 1.9 sec; $P < 0.01$). The fibrinogen concentration fell during the first days and remained low on the 26th day of adaptation. The fibrinolytic activity fell during the first days but rose considerably later (Fig. 2).

Changes in the individual components of fibrinolysis are shown in Fig. 3. During the first days activation of fibrinolysin and profibrinolysin took place, accompanied by inhibition of antifibrinolysins and of inhibitors of profibrinolysin activators; together with activation of heparin and antithrombins, these changes could be the cause of the observed hypocoagulation.

On the 26th day not only was a marked increase in the levels of fibrinolysin and of profibrinolysin activators observed, but the concentration of antifibrinolysins was increased, and so also, to an even greater degree, was the concentration of inhibitors of profibrinolysin activators. Probably this largely restored equilibrium to the process of activation of fibrinolysis and ultimately led to the establishment of general indices of blood coagulation at a new and optimal level for the conditions created. The characteristic features of this level were hypocoagulation, a decrease in viscosity of the blood, and an intensification of fibrinolysis, resulting in an improvement to the blood supply and of the access of oxygen to the tissues. At the same time, the risk of hemorrhage was prevented by a more rapid onset of blood clotting and an increase in the density of the clot, which were compensated so far as thrombosis is concerned by an increased concentration of components of the fibrinolytic system.

Phasic fluctuations in fibrinolytic activity during the first days of adaptation can probably be explained by utilization of fibrinolysin in the rapid lysis if fibrinogen, the concentration of which fell in the course of 3 days from 271 to 170 mg % on average for the series.

Lysis (reduction) of the fibrin film in an animal adapted to high altitudes is biologically advantageous, for it leads to increased vascular permeability and it facilitates the access of oxygen to the tissues in the initial stage of adaptation, described by Mirrakhimov [2, 5] as the "emergency" phase, when all the efforts of the body are aimed at the "fight for oxygen." This reaction is in harmony with the reactions of other systems responsible for the oxygen supply of the body: increased alveolar ventilation, increased volume and linear velocities of the blood flow, increased circulating blood volume, increased red cell count and hemoglobin concentration (increased respiratory surface of the blood), etc.

In the next, "intermediate" phase the ratio between the components of fibrinolysis changes toward the accumulation of inhibitors during a continued increase in the concentration of fibrinolysin and of profibri-

nolysin activators. The general trend toward hypocoagulation becomes weaker at this time and hemocoagulation is established approximately at the characteristic level for animals adapted for a long time to high altitudes.

The further study of the state of the components of fibrinolysis during long-term adaptation to high altitudes is important, for in the modern view the fibrinolysis system has a direct relationship to the regulation of cell metabolism and the study of its changes must shed light on the mechanisms of tissue adaptation.

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