THE PHYSIOLOGICAL ANTICLOTTING SYSTEM AFTER ACUTE BLOOD LOSS

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The clotting power of the blood may be lowered as a result of deficiency of one of the various coagulation factors or of excess of inhibitors of blood coagulation. No explanation has yet been suggested, however, for the mechanism of development of increased coagulability of the blood.

In our previous investigations [3-9] we showed that the increased clotting power of the blood after acute blood loss is accompanied by the appearance of active thrombin in the blood, by an increase in the adhesive power of the platelets, and by a decrease in the antithrombin II activity. In all probability, however, these changes are not primary but are the result of certain undiscovered changes in the coagulatory system. The suggestion that these primary changes are associated with increased activity of various procoagulants (factors V, VII, VIII, IX, X, PTA) in the plasma has not been confirmed in our experiments. Since the clotting of the blood may be accelerated not only by an increase in the concentration of the factors stimulating coagulation, but also by a decrease in the concentration of those inhibiting it, it appeared important to study the anticlotting system of the blood. Our preliminary findings [6, 8] showed that after blood loss there is decreased activity of antithrombin II in the plasma and of antithromboplastin in the hemolyzate, the rate of inactivation of heparin in vivo is unchanged, and there is no significant change in the activity of antithrombin III or of antithromboplastin in plasma heated to 60°. According to V. P. Baluda and N. A. Gorbunova [2], the plasma antithromboplastic activity is decreased after blood loss.

In 1958-61, B. A. Kudryashov and his co-workers [10-13] produced experimental evidence in support of the existence of a physiological anticlotting system in animals, both reflex and humoral in nature, and they suggested a method of injecting thromboplastin and thrombin parenterally in order to study the state of this anticlotting system in vivo.

The object of the present research was to investigate the physiological anticlotting system during the development of increased coagulability of the blood following acute blood loss.

EXPERIMENTAL METHOD

Experiments were carried out on 50 Flanders rabbits of both sexes, weighing about 1.6 kg. Blood for analysis was taken from the femoral artery by means of graduated silicone-treated cannulas. The clotting time of the blood was determined by S. Ts. Bazaron's method [1] in an apparatus with automatic regulation of the temperature, and the fibrinogen by means of the biuret reaction after precipitation with thrombin [16] and sodium sulfite [15]. The FEK-M photoelectric colorimeter with a green filter was used for the determinations.

Thromboplastin, prepared from rabbit's brain [17], was injected into the marginal vein of the ear in the form of a 50% suspension in physiological saline, possessing an activity of 11.5 sec in a dose of 0.2 ml/kg.

Blood was withdrawn from the femoral artery to a volume equivalent to 1.25% of the body weight of the rabbit, or about 25% of the total blood volume.

EXPERIMENTAL RESULTS

The first group comprised 20 rabbits with an initial clotting time of the blood of 811.5 ± 103.8 sec. Five minutes after bleeding, when a state of sharply increased coagulability of the blood had developed [the clotting time of the blood fell by 67.35% ($P < 0.001$) and measured 265.0 ± 35.9 sec], thromboplastin was injected intravenously. For the two variants of the control tests, normal rabbits were used, having a clotting time of the blood

of 819.2 ± 160 sec. In one variant, 20 rabbits received an injection of active thromboplastin like the experimental animals, and in the other, ten rabbits were injected with the same preparation after it had been inactivated by heating.

It will be clear from the table that the results did not confirm the hypothesis that during the increase in the clotting power of the blood after acute blood loss the function of the physiological anticlotting system is weakened. On the contrary, after bleeding the tolerance to the intravenously injected thromboplastin was apparently increased.

Effect of Bleeding on the Function of the Physiological Anticlotting System

Experimental conditions	Dose of thromboplastin (in ml/kg)	No. of animals		
		total	survivors	dying from thrombosis
After bleeding	0.2	20	15	5
Without bleeding	0.2	20	10	10
" "	0.3 (inactivated by heating)	10	10	–

Statistical χ^2 studies of the experimental data [14] showed that the range of the observations was too small to allow the confident assertion to be made that acute blood loss stimulates the activity of the physiological anticlotting system. Nevertheless, this conclusion is permissible if it is remembered that a higher concentration of thromboplastin was produced in the experimental rabbits than in the control animals after injection of equal doses of this procoagulant, because their total blood volume was appreciably reduced as a result of the blood loss.

How can we explain the paradoxical result that while the coagulability of the blood is increased, the function of the physiological anticlotting system is not weakened but may actually be stimulated?

Our earlier experiments [5, 7] showed that the increased coagulability of the blood after blood loss is accompanied by the appearance of an excess of thrombin in the circulating blood, which must bring the physiological anticlotting system into action [10-13]. Among the signs of activity of this system, in our previous investigations we noted a decrease in the platelet count and in the antihemophilic globulin, and a lowering of the prothrombin index [3, 4, 6, 8, 9]. In addition to these, in the present research we also found a decrease in the fibrinogen concentration, on the average by 20%. However, these signs were much less marked than after stimulation of the anticlotting system with massive doses of thromboplastin, when there was a sharp increase in the clotting time of the blood to 1-2 h or more, and in two cases the coagulability of the blood was completely abolished. Besides the lowering of the coagulability of the blood, the fibrinogen concentration was lowered by 50-67%, as has been reported by other workers. In two experiments in which the blood completely lost its coagulability after the injection of thromboplastin, no fibrinogen could be detected in the plasma by precipitation with fibrin. By precipitation with sodium sulfite, however, fibrinogen was detected in concentrations of 110.3 and 121.4 mg% (before injection of thromboplastin the fibrinogen concentration was 301.3 and 248.9 mg%, respectively).

It is evident that after the injection of thromboplastin, the slowing of the blood clotting was due to a decrease not only in the concentration of certain coagulants, but also in the affinity of fibrinogen for thrombin. The findings of B. A. Kudryashov and co-workers [10-13] suggest that the slowing of the coagulation of the blood during activation of the physiological anticlotting system may be due to the presence of antithrombin VI.

Hence, a weakening of the function of the physiological anticlotting system in rabbits is not the cause of the increased coagulability of the blood after blood loss.

SUMMARY

The state of the physiological anticoagulation system was studied according to B. A. Kudryashov, during increased blood coagulation. The tolerance of 50 rabbits to the intravenous injection of thromboplastin was determined after an acute blood loss. As revealed, the state of hypercoagulation after blood loss was not provoked by disturbances in the function of the physiological anticoagulation system.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
