EFFECT OF ADRENALIN ON ABILITY OF INTACT ERYTHROCYTES TO INCREASE PLASMA THROMBOPLASTIN ACTIVITY

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Investigations in vitro using blood from healthy persons and patients with atherosclerosis showed that under the influence of adrenalin the erythrocytes secrete into the plasma a substance with the properties of platelet factor 3.

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It was shown in 1963 [11] that if the isolated rabbit aorta is perfused with physiological saline, addition of adrenalin causes a rapid appearance in the perfusion fluid of a substance with thromboplastic activity as the result of the reaction of the vascular endothelium.

Giving regard to the common features observed in responses of cell membranes to physiologically active agents and also the high lability of the phospholipids of the erythrocyte membrane, which diffuse relatively easily into the plasma [2, 4, 6-10], in this investigation the ability of adrenalin to influence the transfer of substances with properties of platelet factor 3 from erythrocytes into the plasma was studied in healthy persons and patients with atherosclerosis.

Such an investigation is justified because of the disturbances of lipid metabolism occurring in atherosclerosis and reflected in the state of the erythrocyte membrane and the tendency toward thromboses.

EXPERIMENTAL METHOD AND RESULTS

Isotonic NaCl solution was poured into one of three siliconized test tubes containing oxalated blood, and adrenalin solution (adrenalin bitartrate) in concentrations of 0.001 and 0.01 μg/ml was poured into the other two tubes so that, while the relative volumes of the ingredients remained constant, the concentration of adrenalin in the plasma corresponded in one case to the normal blood level (0.1 μg/liter) and in the other case to 10 times that level (1 μg/liter). Control tests were carried out with plasma rich in platelets [1]. After incubation on a water bath for 5 min at 37°, plasma containing few platelets was obtained from all six samples. The thromboplastin activity (by the prothrombin consumption method [3]) and the hemoglobin concentration [5] in the plasma were determined.

The investigations were carried out on 15 healthy persons aged 20-45 years and on 30 patients with atherosclerosis aged 50-71 years (equal numbers of men and women).

In the control group changes in thromboplastin activity were observed in 8 persons (53.3%): an increase (positive release effect) in 7 and a decrease (negative release effect) in 1. The relationship between the frequency of the positive release effect and concentration of adrenalin added was expressed as follows: in 2 cases the effect was obtained in both concentrations, in 3 at a concentration of 0.01 μg/ml, and in 2 cases only at 0.001 μg/ml. The comparative magnitude of the positive release effect was independent of the adrenalin concentration, and its mean value was 8.7% (an increase in the prothrombin consumption time relative to the control, expressed in percent).

In the group of patients changes in thromboplastin activity were observed in 22 persons (73.3%): an increase in 16, a decrease in 5, and opposite effects for different concentrations of adrenalin in 1. The

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TABLE 1. Effect of Incubation of Blood with Adrenalin on Thromboplastin Activity of Plasma Deficient in Platelets. Prothrombin Time of Serum (in sec; M±m)

Plasma deficient in platelets			
from blood incubated with	from plasma rich in platelets incubated with		
Isotonic NaCl solution	46.7±0.62	Isotonic NaCl solution	40.3±0.33
Adrenalin 0.01 μg/ml	56.0±1.08	Adrenalin 0.01 μg/ml	39.6±0.34
Adrenalin 0.001 μg/ml	51.7±0.48	Adrenalin 0.001 μg/ml	36.6±0.64

slight predominance of cases with a negative release effect is not statistically significant. A noteworthy feature was the relationship between the increase in relative frequency and magnitude of the positive release effect and the increase in adrenalin concentration: with a concentration of 0.001 μg/ml the effect was observed in 6 cases and its mean value was 8.8%, while with a concentration of 0.01 μg/ml the effect was observed in 14 cases and it was quantitatively greater (14.7%). Just as in the group of healthy subjects, no relationship was observed between the change in thromboplastin activity and the increase in hemoglobin concentration in the plasma of individual patients.

The results of an experiment illustrating the development of a positive release effect are given in Table 1.

It follows from Table 1 that plasma deficient in platelets from blood incubated with adrenalin possessed higher thromboplastin activity than plasma obtained from blood after incubation with isotonic NaCl solution. In control experiments in which, instead of blood, plasma deficient in platelets was used, no such effect was observed. So far as the higher thromboplastin activity of plasma deficient in platelets obtained from blood (46.7 sec) compared with plasma deficient in platelets but obtained from plasma rich in platelets and incubated, like the blood, with isotonic NaCl solution (40.3 sec) is concerned, this reflects the release effect in response to dilution of the plasma itself [2].

It is concluded from the results of these experiments that under the influence of adrenalin the erythrocytes can release a thromboplastin factor into the plasma with properties resembling those of platelet factor 3.

The increase in thromboplastin activity is observed relatively more frequently and quantitatively to a greater degree in patients with atherosclerosis when the adrenalin concentration in the blood plasma rises to a level exceeding physiological. The negative release effect is evidently due to the influence of anticoagulant factor.

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