

# MECHANISM OF ACTION OF $\epsilon$ -AMINOCAPROIC ACID ON CAPILLARY PERMEABILITY

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Capillary permeability, when increased by hyaluronidase, trypsin, plasmin, kallikrein, and heparin is reduced by the action of  $\epsilon$ -aminocaproic acid.

\* \* \*

Previous investigations showed that a factor of essential importance in the mechanism of the hemostatic action of  $\epsilon$ -aminocaproic acid (ACA) is its effect on capillary permeability [2]. The present investigation was carried out to study the mechanism of this effect.

## EXPERIMENTAL METHOD

Experiments were carried out on 20 dogs and 30 rabbits. Capillary permeability to liquids and protein was determined by the arterio-venous method, which has proved most adequate [3]. After exposure of the vessels blood was taken from the femoral artery and vein and the initial permeability determined. Next, heparin (350 units/kg body weight) was injected into the artery. Blood was again taken 15 min later and 1.5 mg/kg body weight of 6% ACA solution\* was injected into the artery. A third blood sample was taken 15 min later. The fibrinolysin [5] and fibrinase [1] activity and the fibrinogen [5] and heparin [3] concentration were determined in all three samples.

The rabbits were divided into two groups with 15 animals in each group. Permeability of the skin capillaries in group 1 was determined by the Duran-Reynals method (intradermal injection of 0.08 ml 0.6% trypan blue solution). An increase in permeability was produced by kallikrein (3.4 units) and hyaluronidase (0.36 mg) dissolved in physiological saline (0.06 ml). The area of spread of the dye was measured. The results were calculated in percentages, taking the control value as 100%.

Permeability of the skin capillaries in the rabbits of group 2 was determined by Menkin's method (intravenous injection of 10 ml 0.6% trypan blue solution). An increase in permeability was produced by intradermal injection of fibrinolysin (120 units) and trypsin (0.3 mg), dissolved in physiological saline (0.06 ml). The time taken for the color to appear (limits of variations) and the area of staining were measured.

## EXPERIMENTAL RESULTS

Heparin caused an increase in permeability of the capillaries for liquid in the dogs (Table 1). At the same time, the heparin concentration increased significantly, while the fibrinase activity and fibrinogen content decreased. In most animals (17 dogs) the fibrinolytic activity was increased, although for the group as a whole the changes were not statistically significant. When ACA was injected against this background, the blood heparin concentration rose.

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TABLE 1. Results of Experiments on Dogs (M ± t)

Capillary permeability				Fibrinolytic activity (in %)			Fibrinase activity (in %)			Fibrinogen (in mg%)			Heparin (in units/ml)		
for liquid (in ml)		for protein (in %)		initial index	heparin	ACA	initial index	heparin	ACA	initial index	heparin	ACA	initial index	heparin	ACA
initial index	heparin	ACA	initial index												
3,1±0,6	6,3±1,1	3,2±1,6	4,5±1,6	8,7±2,3	4,8±0,9	14,9±2,2	32,4±8,8	20,4±4,5	78,3±3,7	32,5±7,2	58,7±12,0	>0,05	—	1,7±0,3	1,5±0,2
P	<0,05	>0,05	—	>0,05	>0,05	>0,05	>0,05	>0,05	<0,01	<0,01	>0,05	>0,05	—	<0,05	<0,05

TABLE 2. Results of Experiments on Rabbits of Group 1

Scheme of experiments	Area of staining (in %)
Physiological saline + dye (control)	100
Kallikrein + physiological saline + dye	350 ± 27
Kallikrein + ACA + dye	149 ± 1.6 P < 0.01
Hyaluronidase + physiological saline + dye	400 ± 4.2 P < 0.01
Hyaluronidase + ACA + dye	138 ± 1.5

TABLE 3. Results of Experiments on Rabbits of Group 2

Scheme of experiment	Time of appearance of color in min	Area (in %)
Physiological saline (control)	25—30	100
Fibrinolysin + physiological saline	7—12	499±4,9 P < 0,01
Fibrinolysin + ACA	18—20	253±4,0
Trypsin + physiological saline	3—5	352±1,7 P < 0,01
Trypsin + ACA	13—15	250±2,2

The results of experiments on rabbits (Tables 2 and 3) demonstrate that ACA reduced the capillary permeability when increase by injection of hyaluronidase, fibrinolysin, kallikrein, and trypsin.

The results of these investigations confirm previous findings obtained by the writers and other workers [2, 4] showing that fibrinolysin, hyaluronidase, kallikrein, and heparin have a marked effect on capillary permeability. These substances can be considered to participate in the physiological systems of regulation of capillary permeability in man and animals. The experiments on rabbits also confirm the writer's clinical observations showing the inhibitory action of ACA on capillary permeability. This can be considered to be largely due to the effect of ACA on various enzymes and biologically active substances taking part in the regulation of permeability, and in particular, on heparin, fibrinolysin, kallikrein, fibrinase, and hyaluronidase. The method of this broad action of ACA is not yet clear.

#### LITERATURE CITED

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