

# EFFECT OF VITAMIN A ON THE DEFENSIVE REACTION OF THE ORGANISM FOLLOWING INJECTION OF THROMBIN INTO THE BLOOD STREAM

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The results of the author's previous investigations [1] showed that vitamin A activates certain humoral agents of the anticlotting system. A number of investigations [2-4] have suggested that the survival of animals following the entry of thrombin into the blood stream depends on the level of functional activity of the anticlotting system. It should be expected, in face of the effect of vitamin A on the anticlotting system mentioned above, that an excess of vitamin A would be reflected on the survival rate of the animals following the entry of thrombin into the blood stream.

## EXPERIMENTAL METHOD

Investigations were carried out on male albino rats weighing from 150 to 250 g and kept on a standard casein-starch diet in accordance with the formula of the Institute of Nutrition, USSR Academy of Medical Sciences. The animals of the control group (52) received no additions to the diet, while the rats of the experimental group (47) received 600 i.u. vitamin A daily. Blood was taken from 10 control animals and 10 experimental animals 30-32 days later. All the remaining rats received an injection of thrombin (activity 6 sec) in a dose of 0.6 ml/100 g body weight. Blood was taken from the jugular vein, into which the thrombin was injected. A blood sample was taken from the animals surviving 30 min after the injection of thrombin. The following determinations were made in the blood samples: the fibrinolytic activity (the euglobulin time by the method of Kowalski, Kopec, and Niewiarowski [7] and from the decrease of fibrin in the clots by Bidwell's method [6]), the free heparin level [5], and the anti-thrombin activity (expressed as the ratio in % between the thrombin time of the plasma of the experimental and intact animals).

## EXPERIMENTAL RESULTS

The study of the tolerance of the animals to thrombin gave the following results. In the control group, 35 of the 52 rats, or 67.3%, died. Of the 37 rats receiving an excess of vitamin A, 17, or 46%, died after injection of thrombin. Statistical analysis of the results using the alternative variation method showed that the difference in the mortality rate (the survival rate) of the animals in the experimental and control groups was significant ( $P = 96.4\%$ ).

The results of the determination of the level of the humoral agents in the blood before and after injection of thrombin are given in the table.

It is clear from the table that, in the animals of the experimental and control groups, after injection of thrombin, the fibrinolysis was activated, and the fibrinogen content fell, the free heparin level rose, and the anti-thrombin activity was increased. In the control rats, the euglobulin time was reduced by 64%, the decrease in fibrin in the incubated clot was increased 2.4 times, the fibrinogen level fell by 63%, the heparin content was increased by 70%, and the antithrombin activity by 20%. In the animals receiving an excess of vitamin A, the euglobulin time was reduced by 73%, the loss of fibrin in the incubated clot was increased by 160%, the fibrinogen content fell by 80%, and the heparin level and antithrombin activity rose by 30%.

Humoral Agents of Anticlotting System in Animals Receiving Excess of Vitamin A and Their Changes after Injection of Thrombin ( $M \pm m$ )

Experimental conditions	Fibrinolytic activity		Fibrinogen content (in %)	Free heparin (in sec)	Anti-thrombin activity (in %)
	Euglobulin time (in h)	Decrease of fibrin (in %)			
Control	Before injection of thrombin				
	2,1 $\pm$ 0,1	20,0 $\pm$ 0,09	0,24 $\pm$ 0,01	7,9 $\pm$ 0,7	95,0 $\pm$ 2,9
	After injection of thrombin	0,76 $\pm$ 0,08	0,09 $\pm$ 0,01	12,5 $\pm$ 1,1	116,0 $\pm$ 4,1
	(100 %)	(100 %)	(100 %)	(100 %)	(100 %)
Excess of vitamin A	Before injection of thrombin				
	1,3 $\pm$ 0,07	32,0 $\pm$ 1,5	0,12 $\pm$ 0,07	12,0 $\pm$ 0,9	117,0 $\pm$ 2,6
	After injection of thrombin	0,52 $\pm$ 0,01	0,024 $\pm$ 0,01	16,0 $\pm$ 0,6	146,0 $\pm$ 1,5
	(100 %)	(100 %)	(100 %)	(99,9 %)	(100 %)

Note: The values of P (given in parentheses below the mean values) were calculated by comparing the indices before and after injection of thrombin.

Hence, in the animals receiving excess vitamin A, activation of fibrinolysis and the accompanying lowering of the blood fibrinogen level after injection of thrombin were more marked than in the control group. The increase in the tolerance to thrombin caused by excessive administration of vitamin A was evidently associated with the ability of vitamin A to increase the preparedness of the anticlotting mechanisms to respond to the threat of thrombosis.

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