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EFFECT OF NALOXONE ON CIRCULATORY CHANGES IN ANAPHYLACTIC SHOCK

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Administration of naloxone improves the state of animals in shock whether induced by pain, hemmorrhage, exotoxins, and endotoxins or of spinal origin [8-10], although the effect achieved depends on the dose of the drug and the stage of the pathological response [1, 7]. Since one cause of shock is blockage of the microcirculatory bed [2] and since it is essential to study the specific features of its different types [4], and since the action of antagonists of opiate peptides in analphylactic shock (AS) has not yet been analyzed, it was decided to study circulatory changes in AS in relation to the effect of naloxone.

EXPERIMENTAL METHOD

Guinea pigs weighing 250 g were sensitized by two subcutaneous injections of horse serum in a dose of 0.1 mg/kg. The reacting dose (0.5 mg/kg) of serum was injected 3 weeks later into the heart. A group of animals was given a subcutaneous injection of naloxone in a dose of 0.5 mg/kg 0.5 h before injection of the allergen. Injection of allogeneic serum led to the development of AS at once or after 1-2 min in all the guinea pigs. Many of them died in the first 10 min of the experiment, others later; the remainder which survived were killed at various times (from 1 h to 30 days) after development of AS. Data on mortality of the animals from AS, depending on the action of naloxone, were subjected to correlation analysis with calculation of the coefficient of cross-correlation [5]. The lungs, liver, kidneys, heart, adrenals, spleen, stomach, and pancreas of the experimental, and also of control (not sensitized, killed after injection of allogeneic serum) guinea pigs were studied histologically in sections stained with hematoxylin-eosin, azure-eosin, and toluidine blue. The microcirculatory bed also was visualized in film preparations of the mesentery by

TABLE 1. Survival Rate of Guinea Pigs from AS Depending on Action of Naloxone

Experimental conditions	Number of animals	
	which died	which survived longer than 1 h
AS induced without naloxone	40	6
AS induced 30 min after naloxone	15	16

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TABLE 2. Diameter of Blood Vessels in Guinea Pig Menentery Depending on Course of AS (M ± m)

Type of course of AS	Arteriole	Precapillary	Capillary	Postcapillary	Venule	Arteriolovenular anastomosis
Control	13,7±1,0	13,5±1,3	5,7±0,6	13,5±1,3	17,5±1,7	13,7±1,0
Death during first 10 min	16,8±1,2*	17,7±1,6*	7,8±0,8*	19,2±1,9*	17,6±1,7	17,2±1,3*
Death on 1st day	18,2±1,8*	15,2±1,5	5,4±0,5	18,8±1,9*	16,6±1,6	15,5±1,3
Survival (killed after different time intervals)	13,7±1,2	10,7±1,0	6,5±0,5	15,5±1,4	16,8±1,6	14,0±1,1

Legend. Asterisk indicates significance different from control at p = 95%.

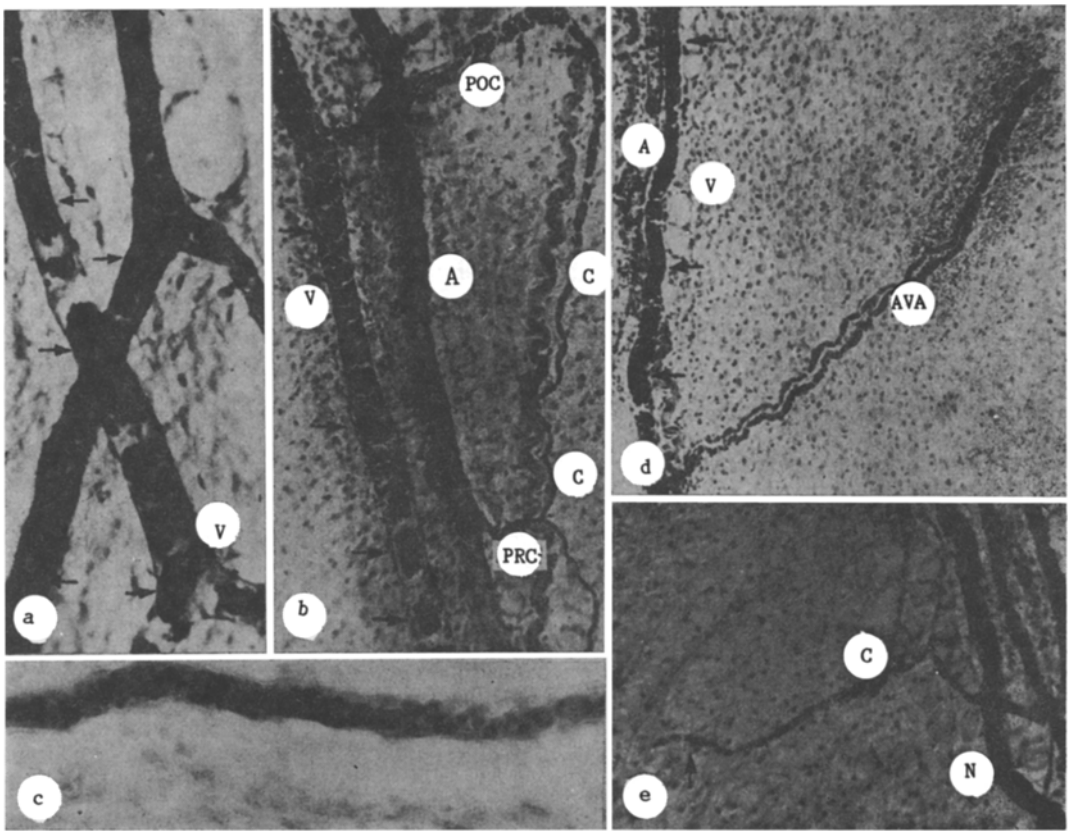

Fig. 1. Changes in vascular bed of guinea pig with AS with different types of course. Stained with Sudan black B (a, b, d, e); demonstration of acid phosphatase by naphthol phosphate AS-TR with Fast blue BB (c). a) Death during first 10 min. Aggregates of erythrocytes in arterioles and venules. 200 ×; b) Slow development of shock. Congestion and aggregates of erythrocytes in venous division of microcirculatory bed, dilatation of postcapillary. 80 ×; c) Slow development of shock. Groups of lymphocytes with high acid phosphatase activity in zone of aggregation of erythrocytes. 200 ×; d) Animal killed 1 day after development of shock. Dilatation of arteriolovenular anastomosis, hemorrhage, aggregates of erythrocytes in venule. 80 ×; e) Sacrifice 30 days after shock. Formation of a new capillary. 80 ×. A) Arteriole; PRC) precapillary, C) capillary, POC) postcapillary; V) venule; AVA) arteriolovenular anastomosis; N) nerve.

impregnation [3] and by modified histochemical methods of determination of glycoproteins and lipids [6], and the diameters of vessels in all parts of the terminal vascular bed were measured in histological preparations. The results of the measurements were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The mortality from AS with and without injections of naloxone is shown in Table 1. The coefficient of cross-correlation between preliminary administration of naloxone and survival of the animals from AS for more than 1 h was 0.389 (X^2 = 11.65), which is greater than X^2_{01} = 6.63. Consequently, significant correlation exists with a probability of 99% between these two features.

Morphological investigation revealed no characteristic changes resulting from injection of naloxone to the animals. No significant differences were found in the morphological picture of AS, with varied degrees of severity, on macroscopic and histological investigation of the internal organs of guinea pigs dying at different stages of the experiment or killed after a mild pathological reaction.

Morphological features of changes characteristic of AS, associated with its different types of course (rapid death, protracted shock, survival) were found only by investigation of film preparations of the mesentery. For instance, in all animals which died during the first 10 min from AS hemmorrhages, dilatation of all components of the terminal vascular bed of the mesentery (Table 2), and the presence of aggregates of erythrocytes, mainly in its venous portion (Fig. 1a), were observed. The erythrocytes in these aggregates stained deeply with Sudan black, and lymphocytes, monocytes, and polymorphonuclear leukocytes with high activity of acid and alkaline phosphatases were found among them.

During the slow development of anaphylactic shock, dilatation of precapillaries and of true capillaries, characteristic of it, was not found in the mesentery (Fig. 1b), but in the zone of aggregation of erythrocytes, there was a marked increase in the number of cells with high lysosomal hydrolase activity (Fig. 1c). If the clinical features of AS were mild, constriction of the precapillaries of the mesentery was found, aggregates of erythrocytes were formed only in venules (Fig. 1d), and many leukocytes with high lysosomal hydrolase activity were found among the aggregated erythrocytes. For many days after AS, the dilatation of the arteriolovenular anastomoses and the presence of aggregates of erythrocytes in the venules, characteristic of it, continued and the frequency of their detection was inversely proportional to the duration of the pathological state. Not until one month after AS could they be found. In addition, they were conspicuous features of the formation of new capillary buds and loops, growing from capillaries and arteriolovenular anastomoses (Fig. 1e).

Thus naloxone inhibits the development of AS in guinea pigs sensitized by allogeneic serum if injected 0.5 h before the reacting dose of the allergen, thereby increasing the number of mild clinical forms of AS. The study of the vascular bed in film preparations not only enables a reliable diagnosis of AS to be made, but the severity of its course and the duration of the process can also be determined.

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