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ULTRASTRUCTURE OF THE ADRENAL MEDULLA AND BLOOD CATECHOLAMINE LEVEL DURING BURN TRAUMA

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The results of an electron-microscopic analysis of the adrenal medulla were compared with those of biochemical investigation of the blood catecholamine level during burn shock. In the erectile phase of burn shock adrenalin and noradrenalin stored in the depots is released, whereas in the torpid phase further liberation of the contents of the granules is accounted for entirely by adrenalin. A distinguishing feature of this period is the intensification of synthesis. After burning a holocrine type of secretion predominates and leads subsequently to exhaustion of the adrenal medulla. Reparative processes are characteristic of burns, but the synthesis and secretion of catecholamines take place less intensively than in healthy animals.

KEY WORDS: burn trauma; sympathico-adrenal system; catecholamines; secretory granules.

There is no question of the urgent importance of the study of the role of the sympathico-adrenal system (SAS) in the response to burns. However, the available information does not give a complete picture of the functional state of the adrenal medulla [2, 4, 7, 15]. There have been few light-optical investigations of the adrenal medulla during burn trauma [3, 8] and no information on ultrastructural changes in the medulla is to be found in the literature.

The object of this investigation was to make an electron-microscopic analysis of the adrenal medulla and to compare the results with those of biochemical determination of the blood catecholamine level in the course of burn shock.

EXPERIMENTAL METHOD

Burn shock was produced in experiments on 30 dogs by the method described earlier [1]. The blood pressure was recorded by a mercury manometer in the common carotid artery.

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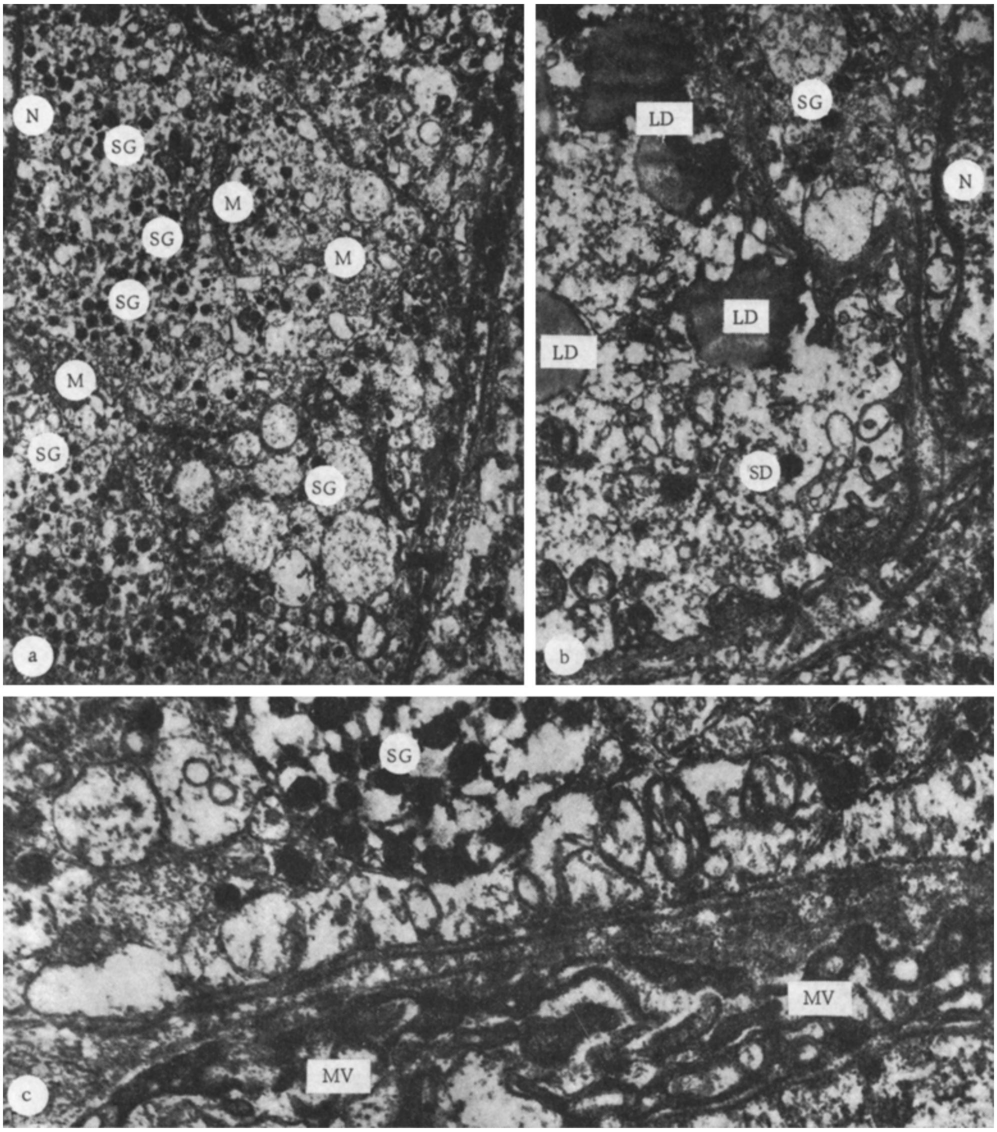

Fig. 1. Adrenal medulla in the erectile phase of burn shock: a) group of pale and dark chromaffin cells whose cytoplasm contains few secretory granules near the basal layer of a capillary. 7400×; b) lumen of capillary with numerous lipid drops. 13,300×; c) formation of numerous microvilli. 18,000×. SG) Secretory granules; M) mitochondria; N) nucleus; LD) lipid drops; MV) microvilli.

Material for electron microscopy was taken 5 and 60 min later and also on the 6th day. The control group consisted of five intact dogs. Pieces of adrenal medulla were fixed in 1% osmium tetroxide solution, dehydrated in acetone, and embedded in a mixture of Epon and Araldite. Ultrathin sections, stained with lead citrate and uranyl acetate, were examined in the UÉVM-100K electron microscope. The catecholamine concentrations in the peripheral blood and caudal vena cava were determined by a fluorometric method [5] with modifications [6, 14].

EXPERIMENTAL RESULTS

The ultrastructure of the adrenal medulla in intact dogs was similar in its general features with that of various mammals [9, 12, 13]. Two types of chromaffin cells were distinguished: pale and dark; which differed in their content of ribosomes and of electron-dense secretory granules filled with catecholamines. Blood vessels, characterized by their fenestrated endothelium, ran between the cells.

Histochemical analysis on representatives of various taxonomic groups (rats, golden hamsters, guinea pigs, pigeons, chickens, frogs) indicates that there is no basis for differentiating chromaffin cells into adrenalin-

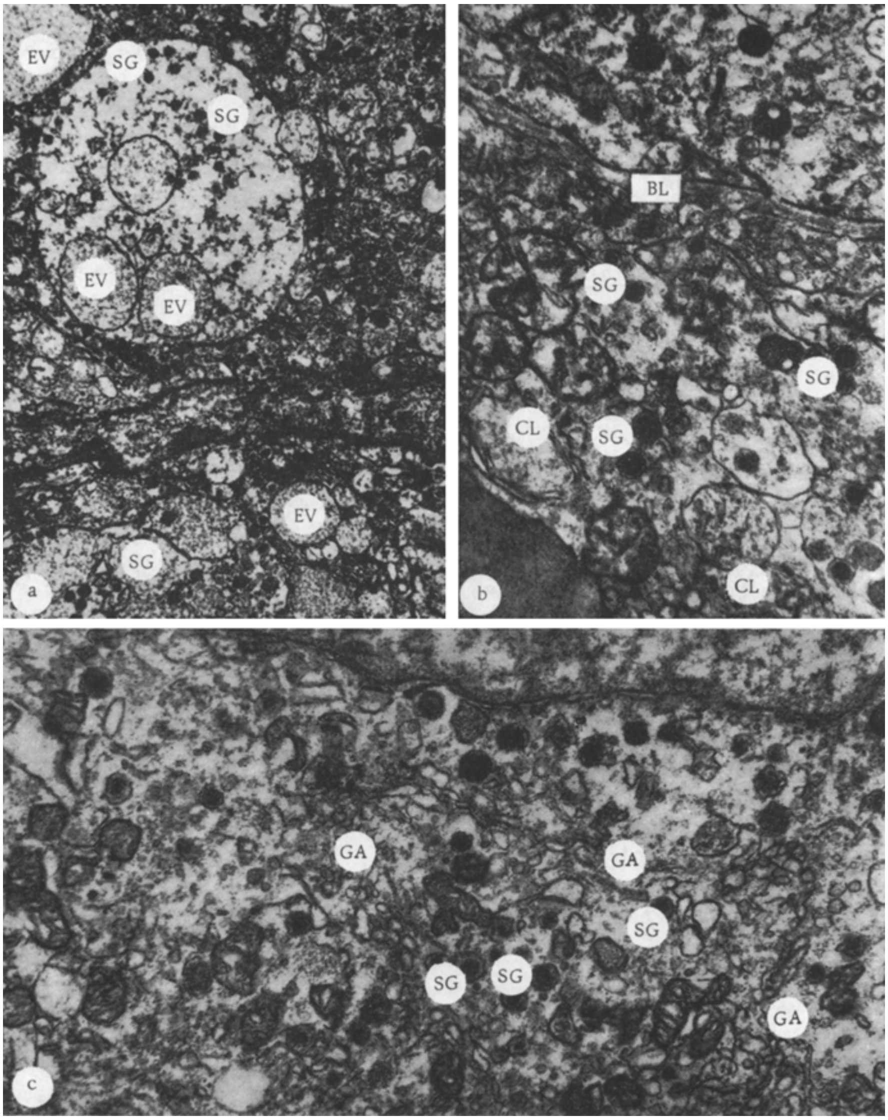

Fig. 2. Adrenal medulla in torpid phase of burn shock: a) appearance of empty vacuoles (EV), formed by liberation of contents of secretory granules (SG). 14,000×; b) appearance of numerous secretory granules (SG) with fragments of cytoplasm in capillary lumen (CL), basal layer (BL) is undamaged. 23,300×; c) formation of new SG in Golgi apparatus (GA). 14,000×.

and noradrenalin-producing cells [10]. Differences in the structure and histochemical properties of the medullary cells are evidently determined by predominance of the processes of synthesis or secretion of the hormone.

In the erectile phase of shock the discharge of catecholamines was intensified, and all stages of liberation of the contents of the granules could be traced. Their membrane gradually stretched and increased in diameter, the osmiophilic material was dissolved, and an empty vacuole remained at the site of the granule. Whereas in intact animals transport takes place by transendothelial pinocytosis, in burns the hormonal products are discharged en masse mainly by a holocrine form of secretion (Fig. 1a). It will be clear from Fig. 1a that in the direction from the center of the cell, where the nucleus lies, toward the pole adjacent to the capillary, the quantity of secretory material gradually diminishes.

Not only secretory granules but also fragments of the cytoplasmic matrix together with lipid drops were found in the capillary lumen (Fig. 1b). Micropinocytotic vesicles and microvilli also appeared in the endothelium (Fig. 1c), evidence of increased permeability of the tissue–blood barrier. In the erectile phase of

TABLE 1. Changes in Blood Pressure (in mm Hg) and Catecholamine Level (in μg/liter) in Caudal Vena Cava during Burn Shock

Statistical index	Background			Erectile phase of shock			Torpid phase of shock		
	BP	A	NA	BP	A	NA	BP	A	NA
M	162,6	1,61	4,00	243,6	3,29	4,83	108	9,76	0,71
$\pm m$	5,2	0,31	0,53	9,3	0,59	0,66	4,0	1,66	0,33
P				0,001	0,03	0,3	0,001	0,001	0,001

Note. Here and in Table 2: BP) blood pressure, A) adrenalin, NA) noradrenalin.

TABLE 2. Changes in Blood Pressure (in mm Hg) and Catecholamine Level (in μg/liter) in Peripheral Blood during Burns

Statistical index	Background			During burns		
	BP	A	NA	BP	A	NA
M	155,0	1,04	1,27	110,0	0,6	1,02
$\pm m$	4,8	0,26	0,42	4,2	0,2	0,38
P				0,001	0,1	0,6

shock increased discharge of catecholamines was thus observed, and was confirmed by the results of biochemical investigations which showed that the blood adrenalin and noradrenalin levels in the dogs were increased (Table 1). Under clinical conditions, an increase in the catecholamine excretion with the urine has been observed immediately after burns [15].

In the torpid phase of shock typical residual profiles were recorded in the cytoplasm of the medullary cells (Fig. 2a), the presence of which is equivalent to the forced liberation of the contents of the granules; these structures varied in their electron density and were particularly numerous in the lumen of the capillaries (Fig. 2b). Activation of secretion formation was reflected in intensive formation of granules in the zone of the lamellar complex, and also in the presence of many mitochondria (Fig. 2c). In this period the blood adrenalin concentration was increased sixfold, whereas the noradrenalin level fell significantly (Table 1). This last fact can probably be explained by the utilization of noradrenalin as a substrate for adrenalin synthesis. To some extent this reaction was compensatory and protective in character, for it is well known that adrenalin has a stronger glycolytic effect than noradrenalin, i.e., the liberation of adrenalin is advantageous from the point of view of the metabolic situation. The hyperadrenalinemia after severe burn trauma is evidently a standard response and is observed in animals of different species (rabbits, rats) and in man [2, 7, 15].

Comparison of the results of electron-microscopic and biochemical investigations in the torpid phase of shock thus indicates activation of the synthesis of adrenalin and of its strongly progressive liberation into the blood stream. A noteworthy fact is that the excessive concentration of the amine did not restore the normal blood pressure, which was considerably reduced during this period (Table 1). This effect must probably be attributed to a decrease in the sensitivity of the adrenoreceptors and also to marked inhibition of both the central and the peripheral nervous apparatuses controlling vascular tone [8].

During the development of burns the rate of excretion of catecholamines was considerably reduced. Structures of the endoplasmic reticulum and lamellar complex were hardly distinguishable in the cells. The tiny mitochondria were few in number and were arranged either relatively uniformly in the cytoplasm or mainly in the perinuclear region. The most striking feature from the point of view of the present investigation was the character of distribution of the secretory granules. Whereas in the erectile and, in particular, in the torpid phase of shock they had virtually disappeared in the region bordering on the capillaries, in the burned animals, on the other hand, the granules were displaced to the periphery of the cells (Fig. 3a, b). It is important to note that they did not pass through the tissue–blood barrier and remained in the cytoplasm. The holocrine form of secretion, responsible for the forced liberation of hormones during the period of shock, was again replaced by the less effective pinocytosis, the intensity of which was low in this period.

Substantial inhibition of secretion thus took place. The biochemical data confirms this conclusion, as shown by the low peripheral blood levels of adrenalin and noradrenalin (Table 2).

The microcirculatory disturbances, manifested as intravascular aggregation of erythrocytes of ameboid shape (Fig. 3b), slowing of the blood flow, stasis, and so on, also are interesting. Essentially sludging, so characteristic of burns and other pathological processes [11], developed.

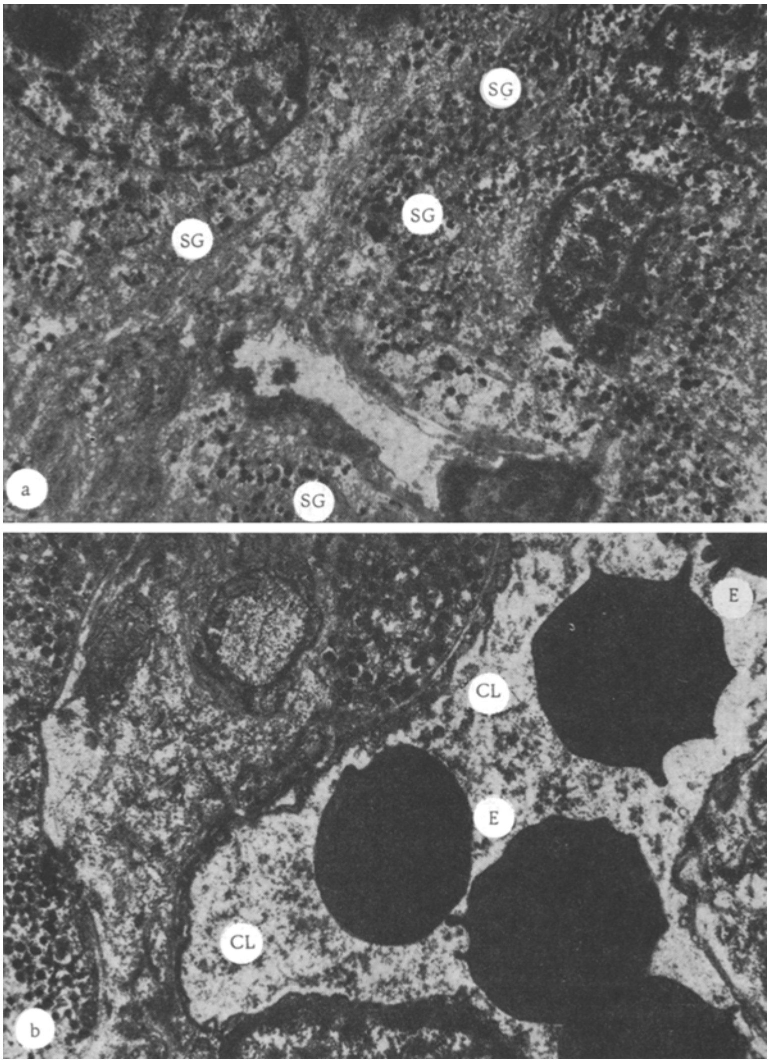

Fig. 3. Adrenal medulla (in burns): a) redistribution of secretory granules (SG) and their displacement toward periphery of cytoplasm of chromaffin cells. 6600 ×; b) appearance of erythrocytes (E) of ameboid shape and their aggregation; capillary lumen (CL) contains no secretory granules. 12,000 ×.

To sum up the results, the phasic character of the response of the SAS, as established by biochemical methods, was confirmed on the electron-microscopic level. After burns a holocrine type of secretion predominates and leads to exhaustion of the adrenal medulla. Repair processes are characteristic of burns, but the synthesis and secretion of catecholamines take place less intensively than in healthy animals.

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