

EPINEPHRINE CONTENT OF THE SUPRARENAL GLANDS IN ANAPHYLAXIS.

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PLATE 89.

(Received for publication, June 5, 1920.)

Since the discovery of the pressor action of the internal secretion of the suprarenal glands by Oliver and Schäfer (1) many attempts have been made to assign to these glands a function of considerable importance, that of maintaining the normal tone of the vascular system in combating agencies which tend to lower the blood pressure and produce shock-like phenomena. The suprarenal glands were examined histologically in different conditions of shock with somewhat variable results. Bainbridge and Parkinson (2) found by staining methods that epinephrine entirely disappeared from the suprarenal glands in cases of death from acute infections, and in postoperative shock. Hornowski (3) likewise found, by staining methods, that the epinephrine disappears from the suprarenals in postoperative shock, and he believes the latter to be due to epinephrine depletion. Corbett (4) states that the epinephrine store of the suprarenals is depleted to the extent of from 75 to 3 per cent of the normal by various experimental procedures leading to shock. Cramer (5), on the other hand, using histochemical methods, found the suprarenals actually loaded with epinephrine granules, and actively secreting them into the central vein in cases of postoperative shock, at a time when the blood pressure was low and the temperature subnormal.

The epinephrine output of the suprarenals in various conditions of experimental shock has been investigated by Bedford (6), who found that the epinephrine content of adrenal blood was greatly augmented during shock, and this he believes to be associated with an increased activity of the glands, a mechanism to save the animal from shock and low blood pressure. Stewart and Rogoff (7), making quantitative estimations of the rate of output of epinephrine from the suprarenal glands in a given unit of time, found that this was not influenced by low blood pressure such as occurs after various procedures to induce shock.

The condition of the suprarenal glands in anaphylactic shock and during the state of sensitization does not seem to have been examined, either as regards pathological changes therein, or from the standpoint of their functional activity, although pathological changes in the liver, kidney, muscle, myocardium, spleen,

and blood vessels have been described in experimental acute and chronic anaphylaxis (Gay and Southard (8), Longcope (9), and Boughton (10)). In view of the alleged alterations of the epinephrine content and output of the suprarenal glands in various forms of surgical shock, it seemed probable that the suprarenal glands of animals in anaphylactic shock might show similar changes, especially so since the experiments of Hirschfeld and Hirschfeld (11) suggest the presence of a vasoconstricting substance in the blood of animals in anaphylactic shock. Furthermore, a more or less beneficial effect has been shown to be produced by the administration of epinephrine to animals in anaphylactic shock (Galambos (12)).

We therefore undertook to determine the epinephrine content of the suprarenal glands in animals sensitized to a foreign protein, as well as in those subjected to varying degrees of anaphylactic shock. Guinea pigs and rabbits were used in the experiments. The animals were sensitized by a subcutaneous or intraperitoneal injection of ox serum, and after an incubation period of at least 2 weeks they were reinjected with the antigen intravenously. Immediately after death or at the height of shock the suprarenal glands were removed,¹ weighed, and their epinephrine content was determined. We have also determined the epinephrine content of the suprarenals of sensitized, but not shocked animals. In the latter group the animals were killed at the height of sensitization by a blow on the neck. All the control animals were treated in the same manner.

The epinephrine estimations were made, for the most part, by the colorimetric method of Folin, Cannon, and Denis (13). We have not, however, used their uric acid standard, but have employed instead a freshly prepared solution of epinephrine hydrochloride made from the adrenalin of Parke, Davis and Company.

The results of the experiments are summarized in Table I, from which it will appear that the epinephrine content of the suprarenal glands in sensitized and in shocked animals does not materially differ from that of normal animals. The average epinephrine content of the suprarenals of normal guinea pigs was 0.073 mg. per 100 mg. of gland, that of sensitized guinea pigs 0.066 mg. per 100 mg. of gland, while that of guinea pigs dying in anaphylactic shock was 0.072 mg. per 100 mg. of gland. The epinephrine content of the suprarenals of normal rabbits averaged 0.30 mg. per 100 mg. of gland, that of a

¹ All operations were performed under ether anesthesia.

fully sensitized rabbit was found to be 0.27 mg. per 100 mg. of gland, while the average epinephrine content of rabbits in anaphylactic shock for periods varying from 2 minutes to 3 hours appeared to be 0.28 mg. per 100 mg. of gland.

TABLE I.

Epinephrine Content of the Suprarenals in Normal, Sensitized, and Shocked Animals Determined by the Colorimetric Method.

Experiment No.	Weight.	Condition.	Weight of suprarenals.	Epinephrine.	
				Total.	Amount per 100 mg. of gland.
Guinea pigs.					
	<i>gm.</i>		<i>mg.</i>	<i>mg.</i>	<i>mg.</i>
1	410	Normal.	270	0.19	0.070
2	460	"	350	0.29	0.083
3	465	"	230	0.15	0.065
4	455	Sensitized.	290	0.18	0.062
5	468	"	270	0.19	0.070
6	385	Anaphylactic shock; died in 4 min.	160	0.13	0.081
7	450	" " " " 3 "	230	0.17	0.074
8	355	" " " " 4 "	180	0.09	0.050
9	455	" " " " 3 "	250	0.16	0.064
10	425	" " " " 4 "	280	0.20	0.072
11	378	" " " " 3 "	230	0.21	0.091
12	442	" " " " 4 "	220	0.16	0.073
13	363	" " " " 4 "	320	0.24	0.075
14	445	" " " " 4 "	330	0.22	0.067
Rabbits.					
	<i>kg.</i>				
15	1.9	Normal.	320	1.27	0.39
16	1.9	"	150	0.33	0.22
17	2.0	Sensitized.	230	0.63	0.27
18	1.5	In anaphylactic shock 20 min.; killed.	100	0.37	0.37
19	1.5	Anaphylactic shock; died in 2 min.	100	0.25	0.25
20	1.7	" " " " 3 hrs.	280	0.63	0.23

The chemical method for estimation of epinephrine such as we employed in the above experiments may be open to objection, since substances other than epinephrine, notably uric acid, give similar color reactions. It was thought desirable, therefore, to confirm the

above findings by some other method, and a few experiments were made to determine the epinephrine content of the suprarenals of normal, sensitized, and shocked guinea pigs by the segment method of the surviving rabbit intestine after the method of Cannon and de la Paz (14) and Hoskins (15). The suprarenal glands were extracted with normal saline solution, and assayed for their epinephrine content against a freshly diluted solution of adrenalin hydrochloride 1:1,000 of Parke, Davis and Company. In some of the experiments (Nos. 26 to 29, Table II) the suprarenals were extracted, as for the

TABLE II.

Epinephrine Content of the Suprarenals in Normal, Sensitized, and Shocked Guinea Pigs Determined by the Biological Method.

Experiment No.	Weight.	Condition.	Weight of suprarenals.	Epinephrine.	
				Total.	Amount per 100 mg. of gland.
	gm.		mg.	mg.	mg.
21	400	Normal.	250	0.10	0.04
22	400	"	250	0.20	0.08
23	425	Sensitized.	270	0.10	0.04
24	425	"	300	0.12	0.04
25	404	In anaphylactic shock.	350	0.15	0.04
26	445	Anaphylactic shock; died in 4 min.	330	0.10	0.03
27	363	" " " " 4 "	320	0.10	0.03
28	442	" " " " 4 "	220	0.15	0.07
29	378	" " " " 4 "	230	0.08	0.03

colorimetric method, with 1 cc. of 0.1 N hydrochloric acid in 8.5 cc. of water, and heated to boiling. 0.5 cc. of 10 per cent sodium acetate was then added, and the whole filtered. The standard for these experiments was made in the same manner; *i.e.*, a solution was made to contain 1 mg. of epinephrine in 10 cc. containing 1 cc. of 0.1 N hydrochloric acid and 0.5 cc. of 10 per cent sodium acetate. This was further diluted with water, as required. The segment of rabbit intestine was always suspended in the same volume of Tyrode solution, oxygenated and kept at a constant temperature of 38°C. Fig. 1 illustrates the method.

The results of these experiments are presented in Table II. It will be seen that the epinephrine content of the suprarenals, as in the preceding experiments, runs practically the same in the sensitized and shocked animals as in the normal controls.

It is not desired to draw too far reaching conclusions from these experiments. They show clearly that the epinephrine store of the suprarenal glands is not materially altered by sensitization or by varying degrees of anaphylactic shock. Neither the epinephrine output nor the activity of the suprarenal medulla in sensitized and shocked animals, however, can be judged from these experiments, as Stewart, Rogoff, and Gibson (16) have pointed out that there is no necessary relation between the store of epinephrine in the suprarenals and their output; and Kuriyama (17) has also recently come to the conclusion that the secretory activity of the suprarenal medulla cannot be judged by its epinephrine content. Nevertheless, with the epinephrine content of the suprarenals remaining practically normal during sensitization and anaphylactic shock, it is highly improbable that there is any relation between these phenomena and the chromaffin substance of the suprarenals, such as has been claimed by some authors for surgical shock.

CONCLUSION.

The epinephrine store of the suprarenal glands remains unaltered in guinea pigs and rabbits which have been sensitized to ox serum, or subjected to varying degrees of anaphylactic shock by the reinjection of the foreign protein.

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EXPLANATION OF PLATE 89.

FIG. 1. Epinephrine content of the suprarenal glands determined by the biological method. *B* was a solution of adrenalin chloride, 1 cc., containing 0.01 mg. *C* contained 0.001 mg. per cc. The suprarenals of Guinea Pig 115 (Experiment 26, Table II) were extracted as for the colorimetric method, and diluted 10 and 100 times respectively.

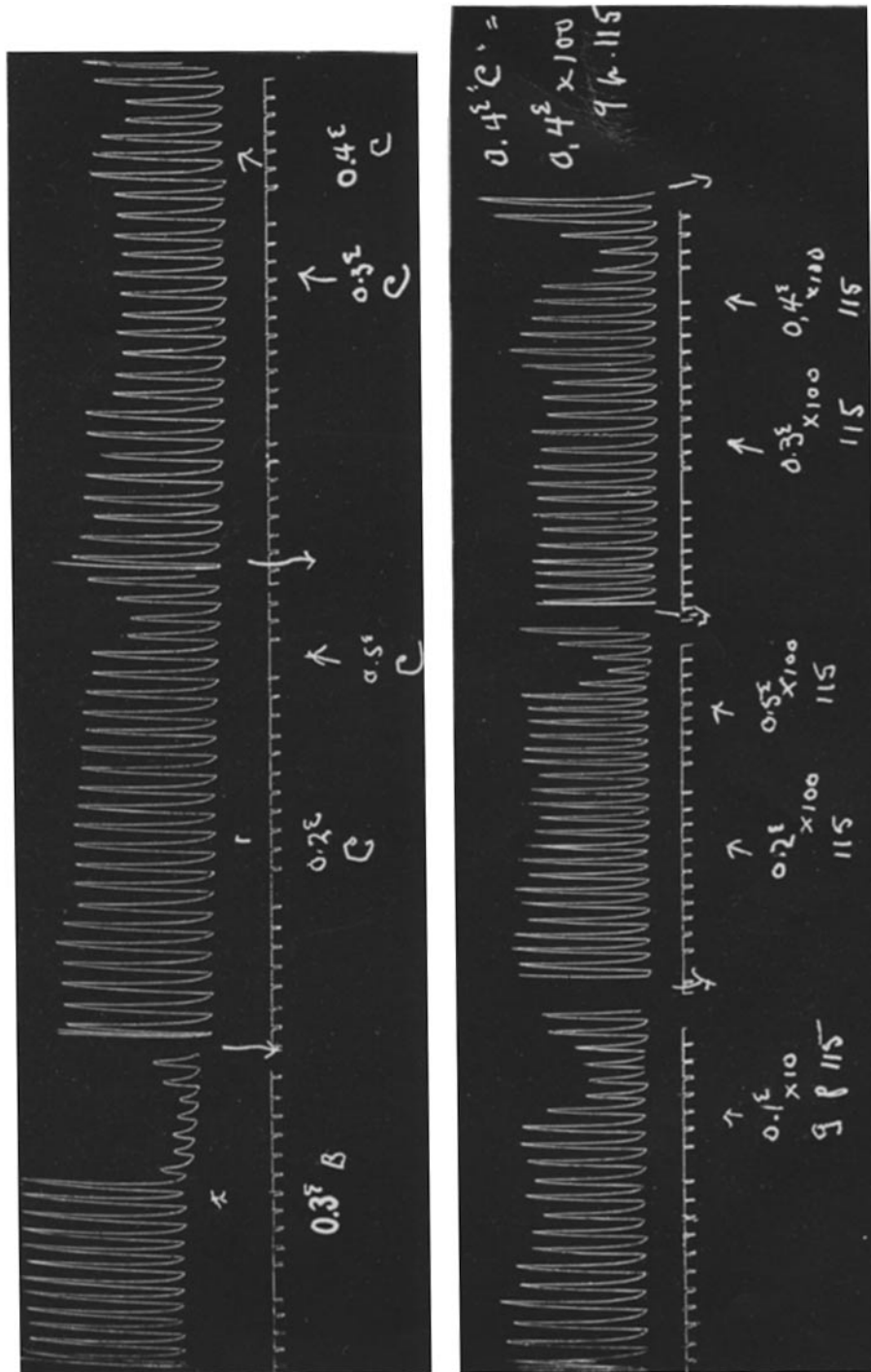


FIG. 1.

(Smith and Ravitz: Suprarenal glands in anaphylaxis.)