COURSE OF EXPERIMENTAL PEPTONE SHOCK FOLLOWING PRELIMINARY ADMINISTRATION OF DOCA

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It has been reported in the literature that considerable morphological and functional changes in the adrenal cortex develop during shock reactions [1, 6, 14, etc.]. It has not yet been finally settled, however, what function of the adrenals is mainly affected in these reactions of the animal organism.

Most investigators have found that the glucocorticoid function of the adrenal cortex is mainly disturbed [6, 5, 14, etc.]. Many authors describe the ineffectiveness of desoxycorticosterone acetate (DOCA) in shock and blood loss [5, 10, 11, etc.], and only a few consider that this hormone, when given together with saline solutions, effectively prevents histamine shock.

In the present investigation the action of DOCA on the course of experimental peptone shock was studied.

EXPERIMENTAL METHOD

The investigation was carried out on 20 dogs (10 control and 10 experimental) of both sexes and weighing from 5.8 to 20 kg. Shock was produced by the intravenous injection of 40% peptone solution in a dose of 0.3 g/kg body weight.

As tests for shock in the experiments the blood pressure in the femoral artery and the respiration were studied before injection of peptone, during shock, and 15, 30, and 60 min after injection of the peptone. Besides these indices, the leukocyte and eosinophil counts were taken before injection of DOCA (in the principal series), before injection of peptone, during shock, and 30 and 60 min after injection of peptone.

The eosinophils were stained with Dunger's solution [3, 4].

During the ten days before the experiment the experimental animals received 5 injections of a 0.5% oily solution of DOCA, each in a dose of 2.5 mg/kg [5], on alternate days.

EXPERIMENTAL RESULTS

The results of the control series of experiments showed that after injection of 40% peptone solution in a dose of 0.3 g/kg body weight of the dry substance the arterial pressure fell (Table 1). This fall was accompanied by motor excitation of the animals, replaced by depression and by lowered reactions to nociceptive stimulation. After the injection of peptone solution the arterial pressure remained at a low level for 10 min or longer. As is clear from Table 1, in these experiments the arterial pressure rose in the later periods of the investigation, but it showed a tendency to fall again 60 min after the injection of peptone. This was observed in 4 of the 10 experiments of the control series.

TABLE 1. Changes in Arterial Pressure in Peptone Shock

Statistical index	Series of experiments	No. of animals	Arterial pressure (in mm Hg)				
			Initial	During shock	15 min later	30 min later	60 min later
M ± m	Control	10	118±4	39±5	100±3	110±1.5	105±6.6
	Experimental	10	129±5	34±3	70±13	89±10	78±11
P				>0.05	0.04	0.05	0.05

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TABLE 2. Changes in the Leukocyte Count during Peptone Shock

Statistical index	Series of experiments	No. of animals	Leukocyte count (in thousands/mm^3)				
			Before injection of DOCA	Before experiment	During shock	30 min after	60 min after
M ± m	Control	9	–	13.3 ± 1.1	3.5 ± 0.9	6.4 ± 1.5	4.8 ± 0.6
	Experimental	9	105. ± 0.16	17.0 ± 1.7	3.8 ± 0.5	11.0 ± 1.7	8.7 ± 1.5
P					> 0.05	0.05	0.03

Injection of peptone was accompanied by an increase in the respiration rate, sometimes paroxysmal. Later, i.e., at the time of maximal fall of arterial pressure, in 5 of 8 experiments, respiration became slower and deeper. In the remaining cases, when the respiration rate was unchanged, a marked increase was observed in its depth.

After injection of the peptone solution the leukocyte count showed a decrease (Table 2). A second fall in the leukocyte count 60 min after the injection of peptone was observed in 5 of 9 experiments.

During shock the eosinophil count was reduced considerably and showed little change in the subsequent period of the investigation (Table 3).

After the characteristics of the reaction of normal animals to peptone had been established, the principal series of experiments was carried out.

It is clear from Table 1 that the initial arterial pressure of the experimental animals receiving DOCA fell somewhat lower after injection of peptone solution in the same dose than the pressure in the control animals. The difference, however, was not statistically significant.

After the injection of peptone, the reaction of the animals of the experimental series to nociceptive stimulation showed a more marked depression. The arterial pressure of these animals was restored more slowly. In 6 of 10 experiments it did not reach the initial level even 60 min after the injection of peptone, and only in 3 experiments was there an appreciable increase at the 15th minute of shock. In 8 of 10 cases a second fall of arterial pressure was observed at the 60th minute of shock (see Table 1). One animal died 60 min after the injection of peptone without emerging from the state of shock.

In the principal series of experiments, by comparison with the control series, the arterial pressure thus recovered more slowly and a secondary fall took place more regularly.

After injection of the peptone solution, at the time of the maximal fall of arterial pressure, the respiration rate was increased in 6 of 9 experiments, decreased in two, and remained unchanged in one experiment. In 5 of 9 animals the depth of respiration was increased. Subsequently no consistent changes in respiration could be observed.

Hence, in contrast to the control dogs, in the experimental animals the rate of respiration was increased during shock and its depth was also slightly increased.

It is clear from Table 2 that injection of DOCA raised the leukocyte count by 62% ($P < 0.01$). Injection of peptone in the dose used led to leukopenia of almost the same intensity as in the animals of the control series. In later periods of the investigation, in the principal series of experiments the leukocyte count returned to its initial level 30 min after the injection of peptone. A second fall in the leukocyte count was observed regularly (in 7 of 9 experiments) 60 min after the injection of peptone. The second fall in the leukocyte count in every case coincided with the second fall of arterial pressure. This phenomenon was more marked than in the control series. According to data in the literature [2, 7, 8], it reflects a relationship between the change in the leukocyte count and the character of the reaction of the nervous system.

Investigation of the eosinophil count in the peripheral blood before injection of DOCA and before the experiment (corresponding to the last injection of DOCA) revealed a small decrease, not statistically significant, in their number in the animals of the principal series. In 4 of 9 cases the intramuscular injection

TABLE 3. Changes in the Eosinophil Count in the Peripheral Blood during Peptone Shock

Statistical index	Series of experiments	No. of animals	Eosinophil count (cells/mm^3)				
			Before injection of DOCA	Before experiment	During shock	30 min after	60 min after
M ± m	Control	9	–	105 ± 25	14 ± 7	16 ± 7	23 ± 9
	Experimental	7	134 ± 42	124 ± 24	2 ± 1	46 ± 21	75 ± 21
P				> 0.05	> 0.05	> 0.05	0.04

of DOCA led to an increase in the eosinophil count in the peripheral blood. It is interesting that in 3 dogs the course of the shock was much more severe, and one animal died 60 min after the injection of the preparation without emerging from shock. In these experiments a chemical blocking of the adrenal cortical function probably developed. There are reports in the literature [9] of a chemical blocking of adrenal cortical function, developing after administration of large doses of DOCA, which is interpreted in the light of Sayers' theory [12] of self-regulation of the system of the pituitary and adrenal cortex. This theory is supported by the fact that the eosinophil count in the peripheral blood of the animals in the principal series of experiments, in contrast to the controls, showed a marked tendency to increase after the injection of peptone in the later periods of the investigation (see Table 3). These changes in the eosinophil count were statistically significant ($P < 0.001$).

The preliminary injection of DOCA into the animals thus led to a longer fall of arterial pressure, to an increase in the rate and depth of respiration, to eosinopenia, and to depression of the animals when peptone shock was subsequently produced. In the experimental animals, by comparison with the controls, a second fall of the arterial pressure and in the leukocyte count was consistently observed. A characteristic feature of these experiments was the marked increase in the eosinophil count in the peripheral blood during the stage of recovery from shock.

Hence it may be concluded that when an increased concentration of DOCA is present in the body, the course of experimental peptone shock in animals is aggravated.

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