

EFFECT OF ADRENALECTOMY AND NARCOSIS ON THE ANAPHYLACTIC REACTION

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Adrenalectomy in mice increases the sensitivity of the animals to a general anaphylactic reaction of the reversed direct anaphylaxis type, which is abolished by hydrocortisone. The local response of this type in adrenalectomized animals is less clear than in controls, and injection of hydrocortisone reduces the number of positive reactions in intact animals also. Deep ether anesthesia, under which the animals received their injection of anti-mouse serum, had no significant effect on the general and local reactions of the reversed direct anaphylaxis type.

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Studies of reversed direct anaphylaxis (arising under the influence of cytotoxic sera of various types) is of great importance to the new science of immunopathology and to the elucidation of the role of humoral factors in the corresponding pathological processes. On the basis of several features (the character and action of the antibodies, the degree of accessibility of the corresponding antigens, quantitative relationships between the reagents) direct reversed anaphylaxis differs from the classical anaphylactic reactions, not only of direct, but also of reversed induced anaphylaxis.

The object of this investigation was to study the effect of adrenalectomy and anesthesia, with their direct action on the course of active and passive anaphylaxis, on reactions of this type.

EXPERIMENTAL METHOD

Experiments were carried out on albino mice on which adrenalectomy was performed 48 h before the tests. Anti-mouse sera, i.e., sera of rabbits immunized with a mouse spleen suspension in homologous serum, were used. Their titer in the complement fixation test was 1:400 with an antigen dilution of 1:1000. To reproduce the general reaction the sera were injected intravenously, but for local reactions intradermally. Local phenomena were expressed as vascular reactions (hemorrhages), the size of which was measured on the inner surface of the mouse's skin, and the results were assessed by the usual system. General reactions were assessed from the mortality of the animals during the 24 h after injection of serum.

EXPERIMENTAL RESULTS

Effect of Adrenalectomy. The minimal lethal doses of antiserum for the adrenalectomized animals 24 h after the operation were much lower than the doses for the intact control animals (0.005 and 0.1 ml respectively). On the second day they showed a decrease (0.0025) and reached a minimum on the 4th day (0.0012 ml), when the difference between doses for the control and experimental animals reached 80 times. By the 12th day the lethal doses for the control and intact animals had become the same. Unilateral adrenalectomy had no effect on the sensitivity of the mice to anti-mouse serum. However, adrenalectomy did not strengthen, but rather weakened the local reactions to intradermal injection of anti-mouse serum. In adrenalectomized mice the number of negative reactions was 22 in 55 animals (40%), in unilaterally adrenalectomized mice 17 in 60 animals (28%), and in the controls 17 in 89 mice (19%). Some of the animals

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TABLE 1. Effect of Adrenalectomy, Cortisone, and Ether Anesthesia on Manifestation of Skin Reactions of the Reversed Direct Anaphylaxis Type

Animals	No. of mice	Intensity of skin reactions					
		-, ±		+, ++		+++, ++++	
		abs.	%	abs.	%	abs.	%
Control	89	17	19	44	49	28	32
Unilaterally adrenalectomized	60	17	28	32	53	11	19
Bilaterally adrenalectomized	55	22	40	24	44	9	16
Receiving cortisone	63	22	35	22	35	19	30
Anesthetized	62	13	20	23	37	26	43

Note. The antiserum used was diluted 1:4.

TABLE 2. Effect of Cortisone on General Reversed Direct Anaphylaxis

Animals	Dose of anti-mouse serum (in ml)						
	0, 1	0, 075	0, 05	0, 01	0, 005	0, 0025	0, 0012
Adrenalectomized				17/17	13/18	7/17	1/8
Adrenalectomized and receiving cortisone		4/6	2/6	0/18	1/12		
Control, intact	6/6	2/6	1/6	0/9	0/6		

Note. Here and in Table 3, numerator shows number of dying mice, denominator gives total number of animals in experiment.

died after bilateral adrenalectomy, presumably through the entry of the serum into the blood stream, because reproduction of local reactions required administration of the serum in doses causing death of the adrenalectomized mice if the serum entered the blood stream (Table 1).

Effect of Cortisone. Hydrocortisone, when injected into the adrenalectomized mice in two doses, each of 3 mg, 18 and 3 h before intravenous injection of the anti-mouse serum, sharply reduced their sensitivity to the serum, and lethal doses of the serum were then almost identical for the experimental and control animals (Table 2). Injection of adrenalin into the adrenalectomized animals in various doses and at various times had no effect on the course of the general anaphylactic reaction.

The Effect of Cortisone on the Local Reactions Was Studied in Intact Animals. In mice receiving cortisone, the number of negative reactions was increased from 19 to 35% (Table 1).

Effect of General Anesthesia. The effect of ether anesthesia was studied in animals which were deeply anesthetized at the time of receiving the injection of serum and for the next 30 min. Anesthesia reduced the sensitivity of the adrenalectomized mice to the action of anti-mouse serum, and LD₅₀ in this case was increased by about 5 times compared with the dose causing 50% mortality under ordinary conditions (Table 3). So far as local reactions are concerned, anesthesia had no appreciable effect on their manifestation (experiments on intact animals, see Table 1).

These investigations revealed differences as regards the effect of the adrenal system and the action of ether anesthesia on general and local reversed direct anaphylaxis. Local reactions of mice to intradermal injection of anti-mouse serum were weaker than the reactions in the control animals, although after intravenous injection of the same serum, adrenalectomized animals died from much smaller doses than controls. This was observed not only after 18 h, but also earlier: in experiments in which the dye Evans' blue was used to demonstrate the course of development of the local reactions, 2 h after injection the skin reactions

TABLE 3. Effect of Ether Anesthesia on Course of General Reversed Direct Anaphylaxis in Adrenalectomized Mice

Animals	Dose of serum (in ml)						LD ₅₀
	0,06	0,03	0,015	0,007	0,003	0,0015	
Control	8/8	9/10	4/8	4/4	4/7	1/4	0,0048
Anesthetized	5/10	7/12	6/12	3/9	0/4	0/4	0,02

(the size of the blue stain) in the adrenalectomized and control animals were of the same size. Adrenalectomy evidently depressed the development of the hemorrhagic reaction. The results of this experiment were influenced by the mortality among the adrenalectomized mice due to the general toxic action of the antiserum. The absence of effect of ether anesthesia on the local reversed anaphylaxis could be attributed to the short time of its action, for reactions of this type appear later (18 h). Other mechanisms could also lie at the basis of the development of the skin lesions.

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