Effect of Cortisone and Adrenocorticotropic Hormone on Delayed Hypersensitivity to 2,4-Dinitrochlorobenzene in Guinea Pigs.* (19734)

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Cortisone and adrenocorticotropic hormone (ACTH) have been reported effective in suppressing skin reactivity of the delayed type to tuberculin in animals(1-3), and in human beings(4). Varied results have been reported in immediate type of allergic reactions, *e.g.*, anaphylaxis(5-7), Prausnitz-Küstner reactions(8), and Arthus reactions(9). ACTH accelerates the recovery rate of clinical contact dermatitis provided the offending contactant has been withdrawn from the skin (10). No investigations of the locus of the effect of these hormones on delayed reactivity to simple chemical compounds in experimental animals have been reported.

We undertook the present investigations with the purpose of determining: 1) the effect of these hormones in varied doses on guinea pigs previously sensitized to 2,4-dinitrochlorobenzene; and 2) the effect of therapy during the sensitization period on subsequent skin reactivity.

Materials and methods. White and light-skinned guinea pigs weighing 250-350 g and maintained on an *ad libitum* diet of rabbit pellets (Purina) and leafy vegetables were used in all experiments. All animals were sensitized with 2,4-dinitrochlorobenzene using a modification of the method of Landsteiner and Jacobs(11). A 1% solution of 2,4-dinitrochlorobenzene (Eastman) in olive oil was painted on a shaved area of skin at the back of the neck each day for 7 days. After an additional 7 days the animals were tested with the chemical in oil on an area of the back approximately 1 cm square which had been shaved and treated with depilatory cream (Neet). Skin reactions were read at 24 and 48 hours after testing. Reactions were designated arbitrarily as: +++, marked homogeneous erythema; ++, homogeneous erythema; +, erythema; and 0, no reaction.

The hormones (Cortone, Merck, and Acthar, Armour†) were administered intramuscularly in the hip. Cortisone was administered twice daily at 8 A.M., and 3 P.M., and ACTH was given 3 times daily at 8 A.M., 3 P.M., and 10 P.M. All animals were observed frequently for signs of drug toxicity.

Results. Series 1. Three groups of 8 animals which had been previously sensitized and which showed marked skin reactions were used. One group was used as a control, the second received cortisone, 10 mg per day, and the third group received ACTH, 15 mg per day. The animals were treated for 48 hours and the skin was tested. Therapy was continued through the observation period. No difference in skin reactivity was noted between the groups.

Series 2. Groups of 4 animals were treated in this series, the dose of cortisone being increased to 20 mg and 30 mg per day for 2 groups, and the dose of ACTH being increased to 30 mg and 45 mg per day. Again no difference in reactivity was noted between experimental groups.

Series 3. Since the animal tolerated the hormones well, the dose of cortisone was increased to 50 mg per day, and the dose of ACTH to 75 mg per day. A diminution of skin reactivity was not evident. Table I shows extremes in reactions for each group of the first 3 series.

Series 4. Since these hormones proved ineffective in preventing skin reactivity once sensitization had been initiated, it seemed possible that the drugs might in some way affect the course of sensitization. To test this hypothesis 7 groups of 4 animals each were sen-

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TABLE I. Effect of Varied Dosage of Drugs on Skin Reactivity in Previously Sensitized Animals.

Treatment	Dosage/day, mg	Skin reactivity 24 hr	Skin reactivity 48 hr
Control	0	2+ – 3+*	+ – 2+
ACTH	15		
Cortisone	10		
ACTH	45		
Cortisone	30		
ACTH	75		
Cortisone	50		

* 3+ = marked homogeneous erythema; 2+ = homogeneous erythema; + = erythema; 0 = no reaction.

TABLE II. Effect of Treatment During Sensitization.

Group	Dosage/day, mg	Skin test 24 hr	Skin test 48 hr
Control	0	2+ – 3+*	+ – 2+
Cortisone	10	2+ – 3+	+ – 2+
	20	3+	2+
	30	2+ – 3+	+ – 2+
ACTH	15	2+ – 3+	+ – 2+
	30	2+ – 3+	+ – 2+
	45	2+ – 3+	+ – 2+

* 3+ = marked homogeneous erythema; 2+ = homogeneous erythema; + = erythema; 0 = no reaction.

sitized as previously, except that doses of 10, 20, and 30 mg per day of cortisone and 15, 30, and 45 mg per day of ACTH were given to 6 groups with the 7th retained as a control. Treatment was continued during the course of the sensitization process (7 days). At the end of this period the sensitizing sites were carefully washed several times with 95% ethyl alcohol in an attempt to remove any residual chemical. After a period of 7 days the animals were skin tested. Extreme results of each group are presented in Table II. No significant differences were observed.

Discussion. These results indicated that cortisone and ACTH in the doses and manner used played no role in diminishing the skin reactivity to 2,4-dinitrochlorobenzene in guinea pigs. Further, it was shown that these animals are not adversely affected by massive doses (200 mg cortisone, 300 mg ACTH per kg body weight per day), when administered over a period of several days. These drugs also proved ineffective under the conditions employed in preventing sensitization with a simple chemical compound.

Summary. Guinea pigs sensitized to 2,4-dinitrochlorobenzene were treated with small to massive doses of ACTH and cortisone without reducing their skin reactivity to topical application of a solution of the drug. Attempts to prevent sensitization by treatment during the sensitization period were negative.

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