

EFFECT OF SMALL DOSES OF CORTISONE ACETATE COMBINED WITH AN ANTIHISTAMINIC IN RAGWEED POLLINOSIS*

EARL B. BROWN, M.D., F.A.C.P.,** AND THOMAS SEIDEMAN, M.D.,***
BRONX, N. Y.

EFFECTIVE relief of hay fever by cortisone acetate, given orally in doses ranging from 100 to 150 mg. daily, has been reported in 3 patients by Carryer and associates,¹ and in 8 patients by Friedlaender and Friedlaender.² Gelfand³ observed rapid clinical improvement in 2 patients, and Schwartz and associates⁴ noted excellent results in 21 of 24 patients. However, the high dosage schedule followed by these authors required that their patients be watched carefully. It has been demonstrated⁵ that, in prolonged administration of cortisone in high doses, close supervision of the patients, restriction of sodium, and potassium supplementation are necessary to prevent undesired hormonal effects upon metabolism. These factors, aside from the costs involved, have delayed widespread use of the hormone in clinical practice.

The present study was undertaken to (1) determine the efficacy of small doses of cortisone acetate† administered orally in combination with an antihistaminic agent‡ in relieving ragweed pollinosis; and (2) investigate the possibility of synergism of the hormone and the antihistaminic. As it appeared unlikely that cortisone acetate in daily doses of as little as 15 to 30 mg. would be clinically effective in such cases, it was thought that a possible synergism of the two preparations might enhance the symptomatic relief that follows administration of the antihistaminic. Thus, low-cost treatment requiring little more than routine supervision would be made available to patients with hay fever.

PROCEDURE

Forty patients who had obtained poor results from hyposensitization therapy or had received no previous treatment were studied from Aug. 15 to Sept. 30, 1952. Of this number, 20 were male and 20 female; their ages

TABLE I. DISTRIBUTION OF CASES (NUMBER OF PATIENTS) BY DURATION OF SYMPTOMS AND YEARS OF TREATMENT

	TIME IN YEARS			
	0	1-3	3-10	>10 YEARS
Duration of hay fever	—	3	19	18
Years of treatment	12	16	9	3
	P. N. UNITS			
	0	50-500	550-1,500	1,500-5,000
Total dose of ragweed pollen antigen	0	50-500	550-1,500	1,500-5,000
Number of patients	6	16	10	8

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*The cortisone and Neo-Antergan used in this study were supplied by the Medical Division of Merck and Company, Inc., Rahway, N. J.

**Adjunct Attending in Medicine (Allergy).

***Assistant Attending in Medicine (Allergy).

†Cortone Acetate tablets (Merck).

‡Neo-Antergan Maleate tablets (Merck).

TABLE II
DAILY RECORD OF SYMPTOMS

		DAILY RECORD OF SYMPTOMS																												Year-----											
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31									
Severe Hay Fever																																									
Moderate Hay Fever																																									
Slight or no Hay Fever																																									
Severe Hay Fever		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31									
Moderate Hay Fever																																									
Slight or no Hay Fever																																									

By "slight" hay fever is meant the condition in which sneezing occurs only once or twice daily, chiefly in the morning; "moderate" hay fever, daily attacks which last several hours; "severe" hay fever indicates practically continuous attacks.

ranged from 13 to 65 years. Although hay fever had been present for at least three years in the majority of these patients, 12 had not received treatment prior to admission to the clinic.

The diagnosis of ragweed pollinosis was confirmed by intracutaneous tests in all patients. Ragweed pollen antigen was given subcutaneously in doses that were increased gradually until the maximum tolerance of each patient was reached; 1,550 to 5,000 protein nitrogen units was the highest total dosage given, and this was tolerated by only 8 patients. Distribution of cases by duration of hay fever and years of treatment is summarized in Table I.

In the first week in August, or on their first visit, but not later than August 22, all patients were given a card, a portion of which is illustrated in Table II. There was space to record four full months on this card. It was presumed that by having each patient record his symptoms daily rather than report them at weekly intervals to one of the staff members, more accurate and objective evidence could be collected for evaluation. All cards were collected during the last week in September, when the ragweed season in this area is essentially ended.

During the week of August 15, each patient was given one of the eight combinations listed in Table III, to be taken three times daily for five to eight days. At the end of this period, another combination was substituted without the patient's knowledge. Hyposensitization therapy was continued throughout the study.

TABLE III. DRUG COMBINATIONS

NEO-ANTERGAN	ORAL CORTISONE ACETATE
25 mg.	5 mg.
25 mg.	10 mg.
25 mg.	Placebo
50 mg.	5 mg.
50 mg.	10 mg.
50 mg.	Placebo
Placebo	5 mg.
Placebo	10 mg.

A statistical chart was then prepared. Reports of no or slight hay fever symptoms were arbitrarily rated 0; moderate symptoms, 1; severe symptoms, 2. The rating of each patient was charted against the average pollen count during the period in which treatment was given. The complete chart is shown in Table IV.

In analyzing any study of patients suffering with hay fever, the correlation between pollen count and symptom intensity should be taken into account. This may be done by covariance analysis. The procedure adopted was to calculate the mean of the hay fever symptom ratings recorded for each patient during the five to eight days in which a particular drug combination was administered. The analysis of covariance could then be applied to the mean hay fever symptom ratings and the mean pollen counts of the experimental period. The hay fever symptom ratings thus obtained have been adjusted for the variability in pollen counts, i.e., they represent the ratings of

TABLE IV

PATIENT	NEO-25 + 5 CORTONE		NEO-25 + 10 CORTONE		NEO-50 + 10 CORTONE		10 CORTONE		NEO-25 MG.		5 CORTONE		NEO-50 + 5 CORTONE		NEO-50	
	*123456789	PC	123456789	PC	123456789	PC	12345678	PC	12345678910	PC	123456789	PC	1234567	PC	1234567	PC
M. L.	000001122	65	1110000	81			1111221	37	2211010	81	0110010	47				
G. M.	021011101	65			1111111	47			0001111	81	000000000	65	0000000	25	11211	37
R. F.									2021111	81	0000011	10				
C. S.	1001122	34	2111111	68			0000011	25	2111011	81			0111111	47	1000121	25
J. M.			111111122	65			122122	37			1111221	25			1111111	47
A. P.			2111211	45							0000000	10				
I. S.	022111001	65	1111100	81							2202111	34	0000000	10	1111222	81
C. D.	00001	30	000001001	65							00002	30			2100001	10
	00000	40									0111110	81			0000000	10
S. A.			0011000	68			2111011	47								
C. C.	2111101	68	2211212	81									0001010	10		
E. A.			1000001	34			0111111	68	0001	30	00001111	65			1111111	81
B. A.	01101	96	0000200	34			01111	37								
M. T.			0022002	34	1111111	47	1011101	68	2011111	68	0021101	47			1111100	81
M. C.	2011111	81	0011111	34									0000001	10	1221000	47
A. G.													1110010	25		
S. G.			2222212	81	2122001	47										
A. C.			0022000	45	2122201	81										
M. B.	00000	37														
S. L.	100101100	65														
F. R.	000000000	65	0000000	47	11111	37							1111111	47	00000	47
D. L.					0000000	25										
M. O.	1111000	40														
F. K.	0000000	68														
F. Z.	0000000	47	22222	95			2222222	47								
M. C.	2222222	81														
H. D.	1000000	81														
M. H.	0000000	81														
J. B.			222122	37	2222012	65										
J. Mc.			0000002	47												
C. C.	2221011	68														
H. G.																
D. R.																
R. K.	00000100	68	0000000	47												
L. S.			0000011	75												
L. G.			200000	96			11010000	34					00000000	10		
J. S.																
S. C.	10011111	42			1111111	40									000000	50
L. A.	00012221	73														

*Number of days on drug combination; PC, average pollen count as recorded in the World Telegram and Sun on counts made at Brooklyn Jewish Hospital, Allergy Division, Brooklyn, N. Y.

TABLE V. MEAN HAY FEVER SCORES OF 151 OBSERVATIONS MADE ON 40 PATIENTS RECEIVING THE VARIOUS DRUG COMBINATIONS; MEAN $\pm$ STANDARD ERROR

	NEO 25 + 5 CORT.	NEO 25 + 10 CORT.				NEO 50 + 5 CORT.	NEO 50 + 10 CORT.	
Corrected Mean Score* $\pm$ S.E.	0.52 0.11	0.78 0.12	0.84 0.16	0.48 0.12	0.68 0.09	0.54 0.21	0.84 0.18	0.77 0.12
Uncorrected Mean Score	0.54	0.78	0.82	0.52	0.66	0.43	0.82	0.79
Mean pollen count	58	61	49	64	48	27	50	60
Number of observations	24	22	12	21	35	7	10	20

*Mean score corrected for differences in mean pollen counts during period of study.

patients exposed to a constant pollen concentration. These statistics are entered in line 1 of Table V. For purposes of comparison the uncorrected ratings and pollen counts are also included.

This analysis reveals no significant statistical difference in the improvement of patient's symptoms with the various drug combinations. However, the correlation between scores and pollen count, although small, was noteworthy—($r = +0.169$, Pr. 05).

No signs indicative of undesirable effects upon metabolism were observed during the study, although low-salt diet and extra-dietary potassium were not prescribed for these patients.

SUMMARY

1. Forty patients with ragweed pollinosis were studied from Aug. 15 to Sept. 30, 1952, to evaluate the effects of five-to-eight-day courses of 5 and 10 mg. doses of cortisone acetate administered orally in combination with 25 and 50 mg. doses of an antihistaminic.

2. The results obtained with each course of treatment were evaluated by covariance analysis; the ratings of symptom intensity were adjusted in accordance with the mean pollen count for the period studied so that these represent data obtained from patients exposed to a uniform pollen concentration.

3. Statistically, no significant difference was demonstrated in the results of treatment with the various dosage and drug combinations, but the correlation between records of symptom intensity and pollen count was noteworthy.

4. The metabolism was not affected adversely by the small doses of cortisone used in this study.

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