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THE INFLUENCE OF CORTICO-STEROIDS ON THE ALLERGIC SKIN WHEEL REACTION AND THE DELAYED-TYPE REACTION (MANTOUX)

By

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According to Hauge & Vale (3) the immediate skin wheal reaction to the specific allergen is diminished after treatment with triamcinolone. They treated 10 patients suffering from bronchial asthma with triamcinolone 4 mg. 3 times a day for $3\frac{1}{3}$ days. The allergen wheal reactions performed before and after cortico-steroid treatment showed a decrease of 40 per cent of pre-treatment value.

In a previous work (4) we treated 60 grass pollen allergic patients for 6 days with a therapeutic dose of prednisone. Measurement of the size of the grass pollen and histamine wheal reactions before and after treatment gave no change in these patients. Our findings are in agreement with these of *Feinberg, Danneberg & Malkiel* (2).

However, the measurement of the wheals in our previous work was done directly before and directly *after* the cortico-steroid therapy. As usual in steroid-treatment the dose was reduced *gradually*, and it must be admitted that the reason why Hauge & Vale and we arrived at different results may be that Hauge & Vale measured the wheal reactions at the time when the treatment was most intensive, and we measured after gradually reducing the dosis.

Therefore, the present study was performed in order to measure the wheals *during* maximal steroid treatment, and using higher doses of cortico-steroids than in the previous work. Besides, it was intended to study the influence of such cortico-steroid therapy on the delayed-type (tuberculine type) of reaction. It is generally considered that cortico-steroids have an inhibitory effect on delayed-type reactions (1).

MATERIAL AND METHODS

In 50 clinically typical hay fever patients (35 males, 15 females, 16-45 years old) with pronounced allergy towards grass pollen the immediate skin wheal reactions to grass pollen were measured before and during maximal prednisone treatment (Table 1). Before the start of the steroid therapy the patients were questioned about possible contra-indications. During the treatment they were asked not to take any other drugs. The prednisone dosage scheme is shown in Table 1 together with the days and sites of testing. For the immediate skin wheal reaction we used aqueous grass pollen allergen 1:10,000 from the same

TABLE 1
Prednisone Dosage Scheme, Tests and Test sites.

Test day	Prednisone dose (mg)	Test	Test site (median 1/3)
Fridag	0	1. grass pollen	left volar
Saturday	0	1. Mantoux II	right dorsal
Sunday	0		
Monday	0	1. Mantoux read	
Tuesday	10+10	2. Mantoux II	left dorsal
Wednesday	10+10		
Thursday	10+10		
Friday	10+5	2. grass pollen	right volar
Saturday	5+5	Mantoux II read	
Sunday	5+0		

Table 2 shows:

- 1) that there is no statistical difference in the grass pollen skin wheal reactions (immediate type) before and during treatment with prednisone,
- 2) that in the delayed-type reactions (Mantoux) there is a clear decrease in the size of reactions during treatment with prednisone.

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batch, no. 775, produced by Allergological Laboratorium, Copenhagen. For the delayed-type reaction we used purified tuberculin with 1/50,000 mg in 0.1 ml stabilized with 0.05 % Tween 80 and 0.1% chinisol produced by Statens Serum Institute, Copenhagen. The tests were carried out before the hay fever season in March and April 1969 in the same way as all other intradermal tests at the Allergy Clinic of the University, in the median one third of the forearms (Table 1). 0.2 ml of grass pollen allergen 1:10,000 was injected in the first 9 patients, but later only 0.05 ml owing to a strong local reaction after testing with 0.2 ml and the tuberculin tests produced an initial diameter of 5 mm. Disposal syringes calibrated to 0.01 ml were used. The tests were read as scheduled in Table 1. They were measured in mm in two directions at right angles (Table 2). A control group of 24 persons (18 allergic, 6 nonallergic), randomly selected for investigation of the possible variation of the size of the histamine wheal at 7 days' interval, was tested with histamine 1:10,000 0.05 ml without having any kind of treatment within this period. The purpose of this control material was to illustrate the range of variation of the method (Table 2 b).

TABLE 2 a

Size of Allergic Wheal and Erythema plus Tuberculin Test before and on the fourth day of Treatment with 20 mg Prednisone.

no. of patients	Before prednisone treatment			On the 4th day of prednisone treatment		
	Grass pollen			Grass pollen		
	wheal	erythema	Mantoux	wheal	erythema	Mantoux
1	19×16	60×70	7×8	19×17	70×55	7×7
2	17×23	60×40	9×9	17×23	50×40	6×6
3	15×25	55×45	9×9	15×25	45×35	6×6
4	15×25	58×55	6×8	15×17	50×42	6×8
5	14×12	77×60	3×2	13×15	65×65	3×2
6	18×35	80×75	10×13	19×28	42×55	7×10
7	11×11	0	6×5	11×11	0	3×3
8	17×25	55×55	7×8	13×17	45×40	6×7
9	9×11	0	3×3	11×14	0	0
10	12×15	46×47	0	11×16	46×38	0
11	11×13	55×52	10×10	11×14	60×52	6×4
12	11×12	60×45	7×5	11×11	65×45	3×3
13	8×11	30×33	7×7	8×10	35×37	7×6
14	11×18	65×58	12×12	12×20	60×50	4×5
15	11×22	60×55	0	10×19	55×52	0
16	9×10	25×25	5×5	9×10	25×28	5×4
17	10×14	45×45	5×5	11×14	50×45	3×4
18	10×15	45×50	0	10×14	40×50	0
19	10×12	50×45	6×6	10×12	55×55	6×6
20	9×12	45×45	0	10×13	45×45	0
21	10×10	60×48	5×5	10×11	60×50	4×4
22	9×14	45×55	7×9	9×12	40×45	6×7

Table 2 a cont.

no. of patients	Before prednisone treatment			On the 4th day of prednisone treatment		
	Grass pollen			Grass pollen		
	wheal	erythema	Mantoux	wheal	erythema	Mantoux
23	12×13	42×42	0	11×14	45×40	0
24	8×9	45×38	9×11	9×10	50×35	7×6
25	11×20	40×43	8×10	11×20	45×43	8×7
26	9×9	23×22	6×8	9×9	25×23	2×3
27	11×11	35×32	0	11×11	35×30	0
28	9×10	40×40	5×6	9×11	40×35	5×5
29	7×9	0	7×5	8×9	15×15	4×3
30	6×7	20×20	5×6	6×7	20×22	3×4
31	6×11	40×50	8×10	8×8	45×45	7×8
32	9×8	25×26	7×7	8×9	20×25	6×5
33	9×8	40×45	5×5	9×7	40×45	5×5
34	5×5	0	8×8	5×5	0	8×8
35	10×12	40×50	0	9×11	35×50	0
36	10×9	45×40	6×6	9×9	40×35	5×4
37	13×13	80×60	4×3	14×12	60×65	3×3
38	9×9	35×35	5×5	9×9	42×45	5×3
39	9×10	45×45	3×3	9×10	43×45	3×3
40	11×12	55×45	0	11×12	40×42	0
41	11×10	45×50	0	11×10	43×45	0
42	8×11	40×40	4×3	8×11	35×32	2×2
43	6×5	8×8	0	5×5	10×10	0
44	7×8	15×15	9×7	7×6	10×10	7×6
45	10×10	35×40	5×5	9×11	38×40	3×3
46	10×9	50×40	6×8	9×9	50×45	5×6
47	9×7	40×30	6×9	9×7	35×35	5×7
48	8×8	45×40	5×7	8×8	40×38	7×6
49	8×7	18×18	8×10	8×7	18×15	7×8
50	14×14	50×40	5×4	13×13	50×50	5×3

RESULTS

The variation in size of the grass pollen immediate skin wheal reactions and the delayed-type allergy reactions before and during maximal prednisone treatment are shown in Table 2.

The statistical analysis of the figures (Table 2 b3) did not show any significant decrease in size of the grass pollen wheals on the fourth day of steroid treatment after an intake of a total of 70 mg. prednisone, whereas there was found a clear, overall decrease of the size of the delayed-type allergy reactions.

TABLE 2 b

Statistical Analysis of the Size of Allergic Wheals and Tuberculin Tests before and During Steroid Treatment.

Pt.	Grass pollen wheal			Tuberculin test		
	before	after	diff.	before	after	diff.
1.	304*	323	19	56	42	— 14
2.	391	391	0	81	36	— 45
3.	375	375	0	81	36	— 45
4.	375	255	— 120	48	48	0
5.	168	198	27	6	6	0
6.	630	532	— 98	130	70	— 60
7.	121	121	0	30	9	— 21
8.	425	221	— 204	56	42	— 14
9.	99	154	55	9	0	— 9
10.	180	176	— 4	0	0	0
11.	143	154	11	100	24	— 76
12.	132	121	— 11	35	9	— 26
13.	88	80	— 8	49	42	— 7
14.	198	240	42	144	20	— 124
15.	242	190	— 52	0	0	0
16.	90	90	0	25	20	— 5
17.	140	154	14	25	12	— 13
18.	150	140	— 10	0	0	0
19.	120	120	0	36	36	0
20.	108	130	22	0	0	0
21.	100	110	10	25	16	— 9
22.	126	108	— 18	63	42	— 21
23.	156	154	— 2	0	0	0
24.	72	90	18	99	42	— 57
25.	220	220	0	80	56	— 24
26.	81	81	0	48	6	— 42
27.	121	121	0	0	0	0
28.	90	99	9	30	25	— 5
29.	63	72	9	35	12	— 23
30.	42	42	0	30	12	— 18
31.	66	64	— 2	80	56	— 24
32.	72	72	0	49	30	— 19
33.	72	63	— 9	25	25	0
34.	25	25	0	64	64	0
35.	120	99	— 21	—	0	0
36.	90	81	— 9	36	20	— 16
37.	169	168	— 1	12	9	— 3
38.	81	81	0	25	15	— 10
39.	90	90	0	9	9	0
40.	132	132	0	0	0	0
41.	110	110	0	0	0	0
42.	88	88	0	12	4	— 8
43.	30	25	— 5	0	0	0
44.	56	42	— 14	63	42	— 21
45.	100	99	— 1	25	9	— 16
46.	90	81	— 9	48	30	— 18

Table 2 b cont.

Pt.	Grass pollen wheal			Tuberculin test		
	before	after	diff.	before	after	diff.
47.	63	63	0	54	35	-19
48.	64	64	0	35	42	7
49.	56	56	0	80	56	-24
50.	196	169	-27	20	15	-5

	n	50		50
	M	-7.78		-16.68
	s	39.08		23.52
	t	-1.41		-5.01
* mm.	P	0.05		0.001

Pt.	1th	7th	diff.	Pt.	1th	7th	diff.
1.	120	120	0	2.	180	140	-40
3.	100	100	0	4.	150	150	0
5.	130	120	-10	6.	120	110	-10
7.	150	90	-60	8.	120	140	20
9.	130	100	-30	10.	140	140	0
11.	90	100	10	12.	130	140	10
13.	180	180	0	14.	150	150	0
15.	130	120	-10	16.	120	170	50
17.	120	120	0	18.	130	130	0
19.	110	100	-10	20.	130	120	-10
21.	120	120	0	22.	130	130	0
23.	140	120	-20	24.	100	100	0

Histamine wheals

Control group: 11 females,
13 males. Figures: square mm.

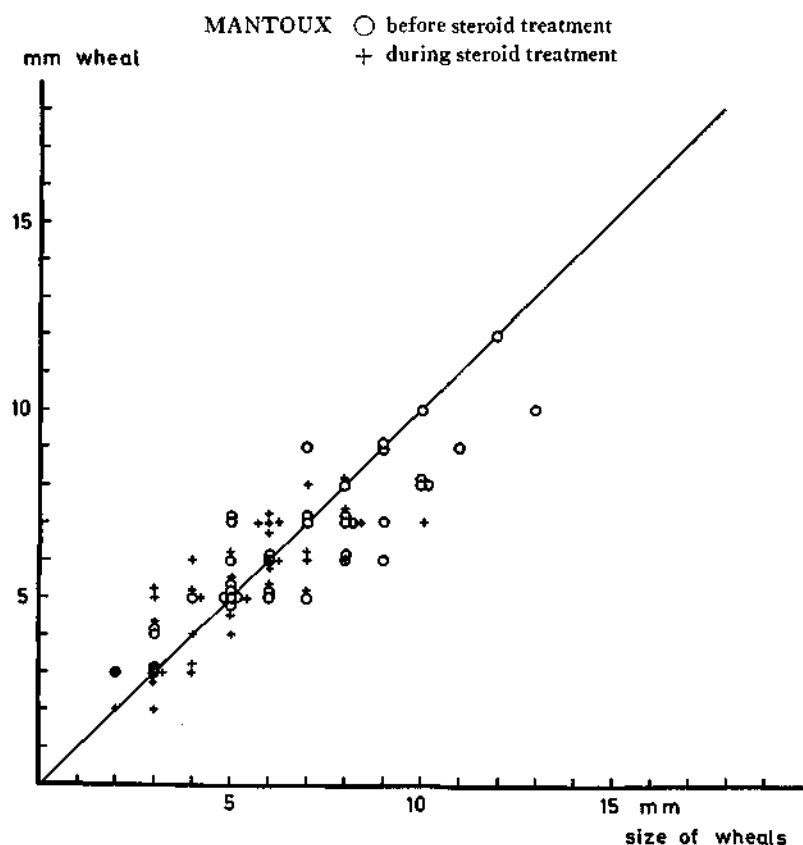
24	24
130	125
	0.20
	1.09

DISCUSSION

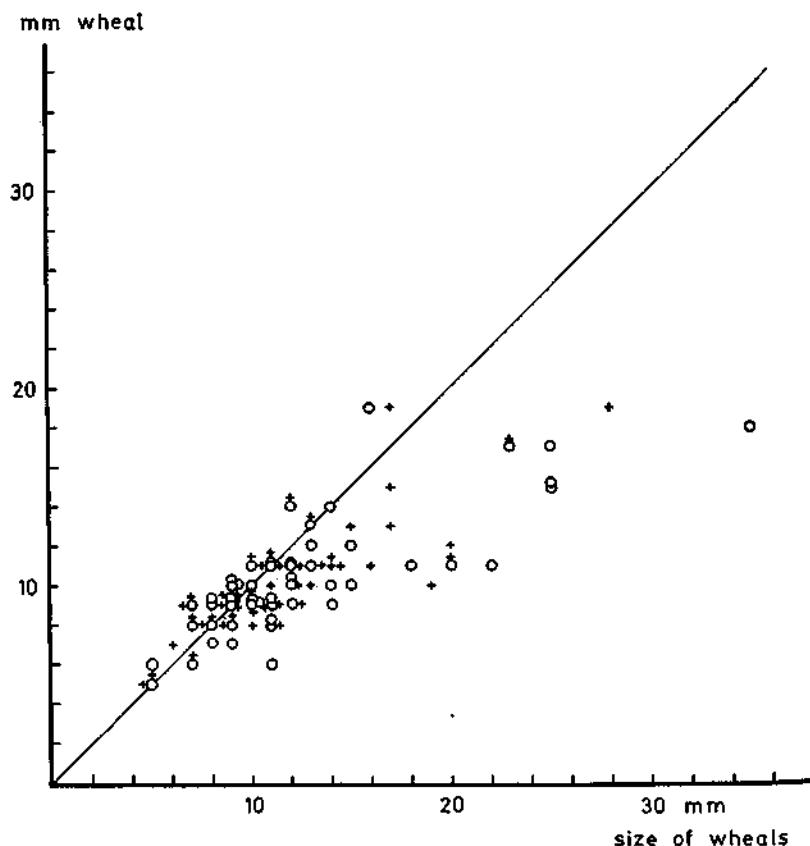
The main purpose of this trial was to investigate whether the immediate cutaneous reactions towards a specific allergen are reduced during treatment with cortico-steroids in therapeutic doses. No such reduction in the wheal size could be shown in our two studies and we were thus unable to confirm the findings of *Hauge & Vale* (3).

However, cortico-steroid treatment does have some inhibitory effect on the delayed-type allergy reaction. Dermatolo-

gists prefer to postpone patch testing for one week after discontinuation of steroid treatment. O'Quin (5) found an inhibition of patch test reactions after treatment with 40 mg. prednisone a day for 4 days. *Brodthagen* (6) found likewise an inhibition of the patch tests after application of hydrocortisone ointment 2 per cent on the test sites for 2-3 days. A clear and overall decrease in the delayed-type allergy reaction (tuberculin) was found during treatment with 70 mg. prednisone given orally over 4 days in 42 patients. 8 of the patients were Mantoux-negative. None of the patients had side-effects for the steroid treatment.



GRASS POLLEN before ○ and during + corticosteroid treatment



CONCLUSION

50 patients allergic to grass pollen were tested intradermally with 1:10,000 0.05 ml. grass pollen extract and had Mantoux injections with an initial diameter of 5 mm. before and during maximal oral treatment with prednisone. No statistically significant decrease of the immediate skin wheal reaction was found, whereas a clear and overall decrease in the delayed-type allergy reaction was revealed. The statistical analysis of

the control material shows the applicability of the method of measurement.

SUMMARY

In 50 grass pollen allergic patients the immediate skin wheal reaction was investigated measuring the size of the reaction towards 0.05 ml. aqueous grass pollen extract 1:10,000 before and *during maximal* oral treatment with a therapeutic dose of 20 mg. of prednisone a day for 4 days. Statistical analysis of the figures showed no significant decrease in the size of the immediate skin wheal reaction towards grass pollen.

Furthermore, the size of a tuberculin test (Mantoux) with an initial diameter of 5 mm was measured after 72 hours in 42 patients both before and during maximal, oral steroid treatment.

In this delayed-type allergy reaction we found a statistically clear and overall decrease.

In a control group consisting of 24 persons (18 allergic, 6 nonallergic), who had not received any treatment at all the size of histamine wheals measured with an interval of one week showed variations similar to those in prednisone treated patients.

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