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PREDNISONE IN THE TREATMENT OF BRONCHIAL ASTHMA

*Comparative Study on the Effect of Cortisone and
Prednisone*

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Prednisone is a synthetic adrenal corticosteroid recently synthesized by SCHERING Corporation and released under the name of Meticorten. Prednisone differs from cortisone in having a double bond between the first and second carbon atoms. Clinical testing of prednisone was commenced in November 1954. *Bunim et al.* (1) studied the metabolic and clinical effect of the new steroid in 7 patients suffering from rheumatoid arthritis. They found prednisone to possess the biological effect of glucocorticoids, but to be 5 times more potent than cortisone. Unlike cortisone, prednisone does not cause sodium retention and potassium excretion. Otherwise, the metabolic effects are the same. Continued investigations have confirmed *Bunim et al.*'s preliminary report (2).

On the whole, the side effects are stated to be the same as those of cortisone. Only, prednisone seems to be more apt to give rise to ulcers of the gastro-intestinal tract (3). The latter phenomenon may be due to the effect of prednisone upon the gastric hydrochloric acid being considerably more marked than that of cortisone in equivalent doses (4). During long term prednisone therapy *Bollet et al.* recommend the

use of an aluminium hydroxide gel as well as routine X-ray control of the gastro-intestinal tract. *E. Schwartz* (5) has treated 2 patients with severe bronchial asthma who had previously received cortisone with little effect. They were given prednisone in doses of from 15 to 25 mg daily with an excellent clinical result. One of the patients had large nasal polyps which disappeared during the treatment. No side effects were observed during prednisone therapy. *Skaggs et al.* (6) treated 8 patients suffering from bronchial asthma with prednisone in doses of 20 to 50 mg daily. They report a good clinical result in all 8 cases, but the results did not differ from those previously obtained by cortisone. In their opinion the advantage of prednisone was that oedemas were avoided. Therefore, they recommend prednisone in treating patients who develop oedema during administration of cortisone. According to *Sheldon* (7) prednisone is at present the best of the adrenal corticosteroids for the treatment of severe bronchial asthma. He treated 15 patients with severe asthma for periods ranging from 42 to 131 days. The initial dose was 25 to 35 mg, reduced at the end of 3-4 days to about 15 mg daily. One patient was maintained on $2\frac{1}{2}$ mg every 12 hours. A good effect was obtained in 14 out of the 15 cases. Subjective improvement was obtained within 18 to 48 hours. One patient developed mild gastrointestinal symptoms which did not recur when therapy was interrupted and then re-instituted. Two patients showed an elevation of blood pressure during treatment. All patients gained, from 5 to 22 lbs. The weight gain was attributed to improved general health and increased appetite. Oedema was not observed in any case. *Rose* (8) treated 35 patients with severe bronchial asthma, with a good effect in 34. One asthmatic who had failed to respond to other steroids, also had no effect from meticorten. The daily dose ranged from 20 to 40 mg. *Rose* did not observe any particular side effects, gain of weight, or change in blood pressure.

Thus, the literature seems to permit the conclusion that in prednisone we have a new synthetic glucocorticoid with a marked therapeutic effect in bronchial asthma. Moreover, it

does not cause sodium retention or potassium excretion. The doses reported, however, do not confirm *Bunim et al.*'s (1) contention that prednisone is about 5 times more potent than cortisone, at any rate not in asthma.

AUTHORS' INVESTIGATIONS

The effect of prednisone was studied in a group of patients with severe bronchial asthma who had been treated with cortisone for months without essential improvement. The dosage was kept at a level corresponding to about one-third to one-quarter of the cortisone or hydrocortisone dosage previously used.

Out of a large series treated for some months with cortisone and hydrocortisone with the usual good response in most cases, the author selected 15 patients with severe bronchial asthma who had failed to exhibit essential improvement. These 15 patients were treated with meticorten in doses of from 7.5 to 20 mg daily. Table I gives the results. It will be seen that improvement was obtained in 14 out of the 15 patients. Nine became entirely symptom-free. In the only unresponsive case the explanation is probably that further improvement was not obtainable without increasing the daily dose of cortisone or meticorten. Table II sets out the fluctuations in body weight during cortisone and prednisone therapy. With cortisone there was a steady gain in weight. During prednisone treatment, started after the course of cortisone, the patients first lost weight and then—after varying intervals—began to gain, but not as much as during administration of cortisone. Table III shows the fluctuations in body weight in 5 asthmatics given placebo tablets after having been treated with cortisone for some length of time. All 5 deteriorated after 1 or 2 weeks on placebos. The loss of weight during placebo treatment corresponds approximately to that seen when cortisone is replaced by prednisone. At the time of writing, prednisone has been continued for a little more than 3 months, and no complications have been observed. In particular, there have

TABLE I

Comparative studies on the effect of cortisone (hydrocortisone) and prednisone in 16 patients with severe bronchial asthma. The condition of the patients is stated on the basis of an average evaluation.

Case no.	Signs and symptoms during cortisone or hydrocortisone	Daily dose	Signs and symptoms during prednisone	Daily dose	Improvement during prednisone
3634/44	++++	20 mg×2	o	5 mg×2	Yes
4464/44	++	20 mg×2	o	5 mg×2	Yes
4830/44	+	20 mg×2	o	7.5 mg	Yes
1879/48	++	20 mg×2	+	5 mg×4	Yes
2960/49	+	20 mg×2	o	5 mg×2	Yes
251/52	++++	20 mg×2	+	5 mg×2	Yes
400/52	+	20 mg×2	o	5 mg×2	Yes
1885/52	++	20 mg×3	o	5 mg×3	Yes
2476/52	+++	20 mg×2	o	5 mg×4	Yes
2692/52	++	20 mg×2	+	5 mg×3	Yes
3072/52	+	20 mg×3	+	5 mg×2	Unchanged
3704/52	+++	20 mg×2	++	5 mg×4	Yes
2836/53	+++	20 mg×2	+	5 mg×2	Yes
559/54	++	20 mg×2	+	5 mg×2	Yes
2616/54	+++	20 mg×2	o	5 mg×2	Yes

o: none; +: slight wheezing; ++: slight to moderate asthma; +++: moderate to severe asthma; ++++: severe asthma.

not been any dyspeptic complaints. Weekly counts of white cells and eosinophils revealed moderate leucocytosis and eosinopenia. The latter was more marked during prednisone than cortisone therapy. Routine urin-analyses showed no pathological components. There was no alteration in blood pressure. Thorough metabolic studies were not carried out in this group of ambulatory patients, as the results are not believed to be dependable in patients who are not under constant observation day and night.

DISCUSSION AND RESULTS

The present study shows that asthmatics who respond poorly to cortisone may be improved by prednisone. The dosage

TABLE II
Fluctuations in body weight during cortisone (hydrocortisone) and prednisone therapy.

Case no.	Weight (kg) during cortisone of hydrocortisone therapy				Weight (kg) during prednisone therapy			
	Before treatm.	At end of 1 months	At end of 2 months	At end of 3 months	Before treatm.	At end of 1 months	At end of 2 months	At end of 2 months
3634/44	66.1	67.4	68.1	70.1	70.0	68.8	69.5	71.5
4464/44	64.2	65.5	65.2	66.0	66.1	65.5	65.1	66.0
4830/44	59.2	60.1	61.2	61.5	61.5	60.0	60.2	60.1
1879/48	51.8	53.0	54.1	54.4	54.4	51.1	52.5	53.0
2960/49	58.2	59.1	60.5	61.8	61.8	61.2	62.4	62.8
251/52	66.0	67.0	67.9	69.0	69.1	68.5	66.5	66.9
400/52	69.1	70.5	71.9	72.2	72.5	72.0	70.0	69.5
1885/52	68.0	68.2	68.5	69.0	69.0	67.9	68.2	69.3
2476/52	80.5	81.2	82.0	84.0	84.1	81.8	82.3	83.4
2692/52	81.1	82.0	82.2	83.6	83.8	82.0	82.6	84.2
3072/52	60.0	61.5	62.1	62.4	62.4	61.0	61.5	61.2
3704/52	55.0	57.3	58.4	58.5	58.5	57.6	58.9	60.3
2836/53	67.3	68.0	69.1	70.0	69.9	68.0	69.1	69.0
559/54	66.0	67.1	67.9	67.7	67.9	67.0	70.0	72.1
2616/54	83.1	83.9	84.2	85.8	85.9	85.2	86.2	86.7

Dosage of cortisone (hydrocortisone) and prednisone as shown in Table I.

was kept on a level which, according to experience in rheumatoid arthritis, corresponds approximately to the previous dose of cortisone, so the improvement is not due to an increase in the dosage. Furthermore, the patients lost weight during the initial prednisone therapy, as the hormone does not affect the sodium and potassium metabolism. The placebo experiments show that the loss of weight corresponds approximately to that occurring upon withdrawal of cortisone. The gain of weight observed at a later stage of prednisone therapy is probably due to increased appetite combined with alterations in the metabolism (2).

As mentioned above, 3 months' treatment of the 15 ambulatory patients did not give rise to complications, particularly no dyspeptic symptoms. This series, therefore, does not

TABLE III
Fluctuations in body weight during cortisone (hydrocortisone) and placebo therapy.

Case no.	Weight (kg) during cortisone or hydrocortisone therapy				Weight (kg) during placebo therapy	
	Before treatment	At end of 1 month	At end of 2 months	At end of 3 months	Before treatment	At end of 1 month
3634/44	66.1	67.4	68.1	70.1	70.1	68.8
4464/44	64.2	65.5	65.2	66.0	66.0	64.5
4830/44	59.1	60.1	61.2	61.5	61.5	59.0
1879/48	51.8	53.0	54.1	54.4	54.4	52.2
2476/52	80.5	81.2	82.0	84.0	84.0	80.0

Dosage of cortisone (hydrocortisone) as shown in Table I.

indicate that prednisone should involve more risk than cortisone.

The findings appear to show that prednisone represents a hormone which is effective in cases which fail to respond sufficiently to cortisone. At the same time, prednisone does not affect the water-salt metabolism and consequently does not involve the marked gain of weight and tendency to oedemas associated with cortisone.

SUMMARY

After having failed to respond to cortisone, 15 patients with severe bronchial asthma were treated with prednisone. A good effect was obtained in 14 out of the 15 cases. The prednisone therapy, which has been continued for more than 3 months, did not give rise to complications. A decrease in body weight was observed when cortisone was replaced by prednisone. The author concludes that in prednisone we have a new steroid which is effective perhaps in most of those cases which fail to respond to cortisone.

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