PROLONGED CORTICOSTEROID THERAPY IN CHRONIC ASTHMA

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Though the value of corticosteroids in controlling acute episodes of bronchial asthma has been proved beyond reasonable doubt (Medical Research Council, 1956a; Walton, 1956; Thursby-Pelham and Kennedy, 1958), the place of these agents in the treatment of chronic asthma still remains an unsolved problem and, at times, a matter of fierce controversy (Herxheimer, 1955; Medical Research Council, 1956b; Brockbank *et al.*, 1957).

A corticosteroid preparation administered for 7 to 10 days to a patient with chronic asthma will often provide considerable or even complete relief of wheeze and dyspnoea, but the effect is temporary and symptoms recur with monotonous regularity at varying intervals after each course of treatment. Often in these cases a clinician, in desperation, resorts to continuous corticosteroid therapy on a long-term basis; in many instances he is persuaded to adopt this policy by patients who have already experienced the dramatic but tantalizingly short-lived relief afforded by brief courses of treatment. Such patients are exposed to the very real danger of the side-effects so commonly encountered with prolonged corticosteroid therapy. The clinician's dilemma is to decide whether the benefits of treatment outweigh the risks.

It is generally accepted that the danger of corticosteroid therapy is related both to the size of the daily dose and to the duration of treatment. In our experience it is seldom possible to suppress chronic asthma completely with a daily dose of less than 10–15 mg. of prednisolone. Within a few months, however, this level of dosage will produce minor, yet unpleasant side-effects, and in the course of a year or so render the patient liable to the major complications of corticosteroid therapy. In this paper we describe our efforts to provide a useful measure of symptomatic improvement with a minimum of side-effects by giving treatment intermittently instead of continuously, and so reducing the total intake of corticosteroid.

The investigation was planned so as to compare the results of intermittent treatment with prednisolone in a dosage equivalent to an average daily intake of less than 10 mg. with those of *continuous* treatment in a daily dose of 10–15 mg. Two groups of patients with chronic asthma were given intermittent treatment and a third group received continuous treatment. In the two groups having intermittent treatment the total dose of prednisolone was the same, but the rhythm of administration differed (see below). Treatment was

given in two phases, during the second of which the dose of prednisolone was increased by 50% in both groups. In order to determine whether intermittent therapy was of genuine value in patients claiming a subjective improvement, inert tablets were at some stage substituted for prednisolone tablets.

The patients on continuous treatment received prednisolone twice or thrice daily for periods of up to three years. In some cases triamcinolone was administered for part of the time.

Selection of Cases and Allocation to Treatment Groups

All the 33 cases studied had chronic asthma. Their symptoms had been severe and virtually constant for at least two years, having failed to respond to treatment along generally accepted lines with bronchodilator drugs. Many patients had chronic bronchitis in addition to asthma. Those with a past history or present evidence of congestive cardiac failure were excluded.

At the time the investigation began we were not certain that intermittent treatment in severe cases was completely safe. We therefore did not feel justified in allocating patients at random to the three groups.

Twenty adult patients (7 male and 13 female) with chronic asthma of moderate severity were therefore given intermittent treatment, 10 in group A and 10 in group B. The patients in these two groups were matched as closely as possible with regard to age, sex, and severity of asthma. Group C consisted of 14 patients (8 male and 6 female), aged between 11 and 60 years, with more severe chronic asthma, who received continuous treatment with prednisolone or triamcinolone for periods of between one and three years. Seven of these patients had been treated in this way for several months before the investigation began; six had previously received intermittent treatment with cortisone or prednisolone outside the present investigation; the other patient was transferred from group B to group C because of his failure to respond to intermittent treatment. This transfer accounts for the total number of cases in the treatment groups (34) exceeding by one the total number of cases studied (33).

Procedure

All patients were given a preliminary course of either cortisone, 100 to 200 mg., or prednisolone, 20 to 40 mg., daily for at least seven days before long-term therapy was instituted. In general, cortisone was used for this purpose until 1957, but when prednisolone became available it was used almost exclusively. The object of the preliminary course of treatment was twofold: (a) to ensure that so far as possible all patients entered the long-term trial with approximately the same advantage so far as corticosteroid therapy was concerned; and (b) to determine whether the results of long-term treatment were related to the initial response to corticosteroids. No case was excluded from the long-term trial solely because of failure to respond to the initial course of corticosteroid therapy. The detailed procedure in the individual groups was thereafter as follows:

Intermittent Treatment (Groups A and B)

For the first six months of treatment (phase 1) the patients in both groups were given a total of 160 mg. of prednisolone during each four-week observation period in two different rhythms of dosage. Those in group A received 5 mg. four times daily on two

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consecutive days only per week, while those in group B were given the same daily dose for only the first eight consecutive days of each four-week period. These regimes were maintained for 20 weeks in 19 cases and for 16 weeks in one.

A clinical assessment, along with an estimate of forced expiratory volume (F.E.V.), was made at four-weekly intervals in every case. The assessments were invariably carried out on the day before the resumption of treatment—that is, when patients in group A had received no treatment for five days, and those in group B none for 20 days.

During the second phase of treatment the total dosage of prednisolone given during each four-week period was increased by 50%, from 160 to 240 mg., the principle of intermittent administration being maintained. This was done by changing the number of days on treatment from two to three consecutive days each week in group A and from eight consecutive days every four weeks to six consecutive days a fortnight in group B, the dose of prednisolone being maintained at 5 mg. four times daily. Twelve of the 20 patients in phase 1 entered phase 2 of treatment, five from group A and seven from group B. Of the eight patients who did not proceed to phase 2, four were withdrawn from the trial because they lived many miles from the hospital and were unable to attend regularly, and two because they had become so introspective that it was thought desirable to curtail the frequency of their visits. In the seventh patient corticosteroid treatment was withdrawn because of excessive gain of weight, and the eighth had to be transferred to group C for treatment with daily prednisolone.

Phase 2 continued for at least 12 weeks, the clinical assessments and estimates of F.E.V. being carried out at four-weekly intervals as in phase 1.

Continuous Treatment (Group C)

Patients in this group were treated continuously with prednisolone for periods of 15 months to over three years. The dose prescribed was 5 mg. thrice daily for adults and 5 mg. twice daily for children under the age of 14 years. In 9 of the 14 cases triamcinolone, in a dose of 6 to 12 mg. daily, was later substituted for prednisolone because of claims made that it caused fewer side-effects. No attempt was made at a comparative assessment of the two corticosteroids.

Clinical assessments and estimations of F.E.V. were carried out at four-weekly intervals as in groups A and B.

Other Treatment

Treatment other than with corticosteroids was at the discretion of the clinician in charge of the patient. Bronchodilator agents were seldom used, apart from inhalations of adrenaline and isoprenaline aerosols to control excessive bronchospasm, but antibiotics were often required for respiratory infection, the form of treatment usually favoured being tetracycline, 0.25 g. four times daily for five to seven days.

In an attempt to prevent permanent depression of adrenal function, all patients on continuous corticosteroid therapy received corticotrophin, 30 units on two consecutive days fortnightly or monthly. After we had encountered osteoporosis and spontaneous fracture in one patient in 1957, all adult males receiving corticosteroids daily were given sublingual testosterone, 25 mg. on alternate days. Adult females received a non-

virilizing androgen, methylandrostanolone. None of the patients on intermittent corticosteroid therapy received corticotrophin or androgens.

Assessment of Progress

Clinical Observations.—The response to treatment was defined as follows: (1) Satisfactory: the patient was relieved of serious asthmatic symptoms for 75% of each four-week period and was able to resume a mode of life previously made impossible by chronic asthma. (2) Fair: definite though less impressive relief was obtained for approximately 30 to 70% of each four-week period. (3) Unsatisfactory: the relief obtained was no better than could be expected from ordinary measures.

Serial Estimations of F.E.V.—The method employed was that described by Needham *et al.* (1954) with a time interval of two seconds. A shorter time interval could not be used as the apparatus required for this was not available until the trial had been in progress for some months. At the beginning of the investigation the maximum voluntary ventilation (M.V.V.) was also measured, but this was later abandoned, as the rapid breathing required to make the test accurate tended to produce wheezing or to increase its degree, thus making the test unreliable from the observer's point of view and unpopular with the patients. To a less extent the performance of three or four estimations of F.E.V. in rapid succession also caused a slight increase in wheezing, and it was frequently observed that the first recording obtained was the highest. The highest value was always accepted. The values of F.E.V. obtained have been expressed as a percentage of the predicted normal value for each patient (Needham *et al.*, 1954).

Results of Intermittent Treatment (Groups A and B)

The results of the four-weekly clinical assessments were similar in the two groups. In phase 1 a satisfactory clinical response was recorded in 23 (46%) and a fair response in 20 (40%) of the 50 clinical assessments made in the patients in group A. In group B a satisfactory clinical response was recorded in 22 (45%) and a fair response in 18 (37%) of 49 similar clinical assessments. At the time of each assessment the patients were asked whether the asthma was any better on the days on which prednisolone was taken. Five of the 10 patients in group A and 8 of the 10 in group B said that such an association existed. This difference between the results in the two groups is not unexpected, in view of the longer consecutive period of treatment in group B. In general, the patients who did not experience an improvement on the days they were taking prednisolone tablets were those who showed the poorest results at four-weekly assessments.

The results of serial estimations of F.E.V. obtained before treatment, after the preliminary intensive course of prednisolone, and for the following 16 to 20 weeks, are shown in the form of a scattergram in the first sections of Figs. 1 and 2. The results were similar in the two groups, and in both the mean value of F.E.V. was always above the pre-treatment level. In the last four to eight weeks, however, the mean F.E.V. was well below the optimum level recorded after seven days' intensive treatment, and in some cases the improvement in function in the later stages was negligible. It must be remembered, however, that all the estimations of F.E.V. were made at a time when the patient was least

likely to be obtaining benefit from prednisolone. No attempt was made to obtain recordings of F.E.V.₂ during the periods when the patients were taking prednisolone tablets.

During phase 2 the patients in group A recorded a satisfactory response on 50% of the clinical assessments as compared with 46% in phase 1, while those in group B recorded a satisfactory response on 73% as compared with 45% in phase 1. These results seemed to suggest that there was slightly greater improvement with the change to treatment on six consecutive days per fortnight (group B) than with that to three consecutive days per week (group A), but estimations of F.E.V.₂ (Figs. 1 and 2) did not provide objective confirmation of the superiority of this treatment regime.

Prednisolone therapy was interrupted in 18 of the 20 cases in groups A and B, by substituting inert tablets without the patient's knowledge, the clinician observing progress or the respiratory physiologist estimating F.E.V.₂. Psychological or geographical reasons rendered such a change inadvisable in the remaining two cases. The substitution was never made before the 16th week of phase 1 of treatment, and in some cases it was deferred until phase 2 was in progress. Within four weeks of the interruption of treatment the clinician reported marked deterioration in nine patients, moderate deterioration in three, and slight deterioration in four. In two patients the change was not detected by the clinician. In several cases the deterioration was so striking that the patient was referred to the hospital as an emergency case by the general practitioner. When a deterioration was recorded by

FIG. 1.—Group A. Four-weekly recordings of F.E.V.₂ (2 seconds) expressed as a percentage of the predicted normal value in 10 patients treated with prednisolone, 20 mg, a day. Phase I—on two consecutive days a week. Phase II—on three consecutive days a week. (Mean level represented by unbroken line.)

In Figs. 1, 2, and 3 the number of recorded points at each four-weekly assessment does not always add up to the total number of patients under observation. Such omissions usually occurred because the patient did not feel well enough to perform the tests or because he or she could not attend at the proper time. The absence of these recordings may cause the average figures to appear more favourable than would have been the case had all the patients been tested on all occasions.

FIG. 2.—Group B. Four-weekly recordings of F.E.V.₂ (2 seconds) expressed as a percentage of the predicted normal value in 10 patients treated with prednisolone, 20 mg, a day. Phase I—on eight consecutive days every four weeks. Phase II—on six consecutive days every two weeks. (Mean level represented by unbroken line.)

the clinician he was informed of the change of treatment and prednisolone therapy was resumed. In all such cases the asthmatic symptoms returned to their former level within four to eight weeks.

The effect on F.E.V. of interrupting intermittent prednisolone therapy is shown in Table I. The figures in the first column indicate the level of the F.E.V. for

TABLE I.—Effect on F.E.V. (Expressed as Percentage of Predicted Normal) of Substituting Inert Tablets for Prednisolone in Patients Treated in Groups A and B

F.E.V. before Substitution of Inert Tablets (% of Predicted Normal)	F.E.V. after Substitution of Inert Tablets (% of Predicted Normal)	Interval between F.E.V. Estimations (Days)
	<i>Group A</i>	
52	42	28
53	22	28
36	31	28
*26	18	28
29	25	28
63	57	28
69	48	28
40	Too ill to attend	8
41	18	7
	<i>Group B</i>	
49	44	28
26	34	28
*43	36	28
33	36	28
53	Unfit for tests	28
52	31	28
69	43	20
42	35	17
66	15	14
	40	7

* In these two patients a clinical deterioration was not recognized by the observer.

each patient on the day before the change to inert tablets was made, and the subsequent changes in F.E.V. are shown in the second column. The fact that an unbiased observer was able to recognize a deterioration in no fewer than 16 of the 18 patients in whom treatment was interrupted, and that this deterioration was reflected in a marked reduction in F.E.V., leaves little doubt about the existence of a causal relationship between the interruption of treatment and the increase in asthmatic symptoms.

Results of Continuous Treatment (Group C)

In 8 of the 14 cases there was a dramatic clinical improvement, which was maintained throughout the whole period of treatment. These patients all eventually became asymptomatic and their way of life changed from one of chronic invalidism to almost complete normality. In three, the improvement was considerable but not constant. In the other three there was apparently no response to treatment, and corticosteroid therapy was discontinued a few months later. Over a period of two years 206 four-weekly clinical assessments were made of the 11 patients responding to treatment.

TABLE II.—Analysis of the Recordings of F.E.V. (2 seconds), Expressed as a Percentage of the Predicted Normal Value in the 11 Patients Successfully Treated with Continuous Prednisolone (P.) or Triamcinolone (T.)

Case No.	Age	Duration Continuous Treatment (Months)	Values of F.E.V.				Type of Treatment		
			Pre-treatment	At 1 Month	At 1 Year	At 2 Years	At 1 Month	At 1 Year	At 2 Years
1	13	15 (4P. 11T.)	34	73	46	100 (15th month)	P.10	T.6	T. 6
2	14	21 (14P. 7T.)	43	81	84	81 (21st ")	P.10	P.10	T. 6
3	47	21 (17P. 4T.)	23	57	97	74 (" ")	P.15	P.10	T. 8
4	56	36 (All P.)	29	49	63	63	P.15	P.15	P.10
5	15	27 (23P. 4T.)	16	49	27	60	P.15	P.10	T. 8
6	14	29 (24P. 5T.)	44	58	56	63	P.15	P.15	T. 8
7	17	24 (All P.)	21	60	44	49	P.15	P.15	P. 7-5
8	10	42 (37P. 5T.)	26	84	83	54	P.15	P.15	P.10
9	21	40 (35P. 5T.)	47	81	85	68	P.15	P.15	P.10
10	58	26 (22P. 4T.)	23	93	81	78	P.15	P.15	T. 8
11	63	24 (19P. 5T.)	32	65	58	66 (22nd month)	P.15	P.15	T. 8

The numerals in the treatment column indicate amount of drug in milligrams administered daily. Only 7 patients are shown as having changed from prednisolone to triamcinolone. Cases 8 and 9 did so after the second year of treatment.

A satisfactory response was recorded 172 times (83%), a fair response 24 times (12%), and an unsatisfactory response 10 times (5%). Two patients have been on continuous treatment for over three years and four for over two years; in all six the good initial response to corticosteroids has been consistently maintained.

The results of serial estimations of F.E.V. over the first two years are shown in Table II and Fig. 3. The three patients who showed no improvement are omitted from Table II and are specifically identified in Fig. 3, in which it is evident that their F.E.V. showed no increase above the pre-treatment level throughout. All the others showed a striking improvement, the average F.E.V. for every four-week period being twice that of the pre-treatment figure. Triamcinolone appeared as satisfactory as prednisolone in the treatment of these cases.

Relationship of Initial Response to Corticosteroids and the Results of Long-term Treatment

The results are summarized in Table III. In the patients receiving continuous treatment there was a close relationship between the response of F.E.V. to the initial

TABLE III.—Results of Long-term Treatment Analysed According to Initial Response to Steroid Therapy

*Increase in F.E.V. following Initial Course of Steroid Therapy	No. of Patients	Response to Long-term Steroid Treatment. Increase in F.E.V. at Four-weekly Intervals			Total No. of F.E.V. Recordings
		<10%	10-25%	>25%	
<i>Groups A and B:</i>					
Less than 10%	8	17 (48%)	13 (37%)	5 (15%)	35
10-25%	4	5 (30%)	12 (70%)	0	17
Over 25%	8	16 (48%)	7 (22%)	10 (30%)	33
<i>Group C:</i>					
Less than 10%	0	0	0	0	0
10-25%	3	21 (95%)	1 (5%)	0	22
Over 25%	11	15 (8%)	43 (21%)	148 (71%)	206

* The increase in F.E.V. is expressed as a percentage of the predicted normal value for each patient. Patients in groups A and B received prednisolone intermittently and those in group C received prednisolone or triamcinolone continuously.

high-dosage treatment with corticosteroids and the subsequent response to long-term treatment with prednisolone or triamcinolone. For example, in the 11 patients in group C whose F.E.V. increased by more than 25% initially, this level of improvement was maintained in 71% of the subsequent F.E.V. recordings.

On the other hand, there was no such relationship in the patients in group A and B receiving prednisolone intermittently. In the eight patients whose F.E.V. increased by more than 25% initially, this increase was maintained in only 30% of subsequent recordings. Neither with continuous nor with intermittent treatment was a satisfactory long-term result obtained when the initial response was poor.

Side-effects from the Administration of Corticosteroids

Minor Side-effects.—The two side-effects most commonly encountered with prednisolone were "moon-face" and excessive weight gain. These occurred in almost all the patients who received prednisolone daily but not in any of those given intermittent therapy. The gain in weight was readily controlled by attention to diet, provided the patient co-operated. It appears that moon-face cannot be avoided if a relatively high dosage of prednisolone is given. With the change to triamcinolone, moon-face was commonly unaltered, but five out of nine patients showed slight loss of the weight gained during the period of treatment with prednisolone.

Serious Side-effects

Four patients, all of whom were receiving prednisolone daily (group C), developed one of the serious side-effects of corticosteroid therapy, and in one of these patients two such complications were encountered.

Osteoporosis and Fracture.—A spontaneous fracture of the shaft of the left femur occurred in Case 4 (Table II) after daily treatment with corticosteroids for two and a half years and is reported in detail elsewhere (Lamb and Somner, 1958). In Case 10 a compression fracture of a lumbar vertebra developed after prednisolone daily for 10 months. This fracture was associated with a fall, but prednisolone probably contributed to the ease with which it occurred.

Tuberculosis.—A girl of 10 years (Case 8) developed an active tuberculous lesion in the lung after daily treatment with prednisolone for 14 months, but this

responded completely to antituberculous drugs while prednisolone therapy was maintained.

Peptic Ulcer.—A woman aged 54, who had received prednisolone daily for five months without a satisfactory response, developed abdominal pain and was shown on radiological examination to have an ulcer crater in the duodenum. Patient No. 4, who had previously sustained a spontaneous fracture while on corticosteroid therapy, developed dyspeptic symptoms 11 months later and was found on radiological examination to have two ulcer craters in the duodenum. In the interval between healing of the fracture and the development of dyspepsia 10 mg. of prednisolone was given daily.

Evidence of severe adrenal depression with failure to respond to corticotrophin stimulation has been found in all but 2 of the 11 patients who received prednisolone or triamcinolone continuously for more than one year. The results of these investigations will be reported later.

No serious side-effects were encountered in any of the 20 patients receiving intermittent corticosteroid therapy in groups A and B.

Factors Concerned in the Response to Long-term Corticosteroid Therapy

Those patients with chronic asthma who did not respond to corticosteroid therapy all had a greater degree of associated chronic bronchitis than those who did; in addition, many of them were subject to frequent episodes of respiratory infection. In those cases the appearance of pus in the sputum often heralded a return of asthma, which previously had been well controlled by either continuous or intermittent corticosteroid

FIG. 3.—Group C. Four-weekly recordings of F.E.V. (2 seconds) expressed as a percentage of the predicted normal volume in 14 patients receiving continuous treatment with prednisolone or triamcinolone. (Mean level represented by unbroken line.) $\diamond$, $\circ$, $\times$ = Identity recordings of the three patients who showed no response to initial course of prednisolone and whose subsequent response remained unsatisfactory. All have been excluded from calculation of means.

therapy. The frequency of respiratory infection and its liability to precipitate asthma was much greater in those receiving intermittent therapy than in those being treated continuously. There are two possible reasons for this. The first is that in the allocation of cases to intermittent or continuous corticosteroid therapy a higher proportion of patients who were particularly subject to respiratory infection were included in the group receiving intermittent therapy. The second and more likely explanation is that the relative freedom from asthma experienced by patients given continuous therapy ensured more efficient bronchial drainage and rendered them less liable to develop respiratory infection.

The reason why the patients on intermittent treatment (groups A and B) who had exhibited a good response to the preliminary intensive course of corticosteroid therapy obtained less benefit from long-term treatment than those treated continuously (group C) probably was that the patients in groups A and B were denied the opportunity of maintaining their good initial response because of the restricted dosage of prednisolone.

Conclusions

It can be stated with confidence on the basis of this investigation that continuous treatment with prednisolone, 10–15 mg. daily, or triamcinolone, 6–12 mg. daily, as given to the 14 patients in group C of this series, will, in a majority of cases, suppress the symptoms of chronic asthma for long periods. Such a result can be expected when chronic bronchitis and recurrent respiratory infection are not conspicuous features and when an obvious clinical improvement accompanied by an abrupt increase in F.E.V. rapidly follows the start of treatment. Eight patients satisfying these criteria have achieved a remarkable measure of sustained symptomatic improvement. There has been nothing to suggest that the treatment becomes any less effective with the passage of time, even in patients who have received prednisolone continuously for two or three years. Chronic bronchitis and recurrent respiratory infection were the factors probably responsible for the failure of the other six patients to obtain a sustained response.

Unfortunately these results are offset by the frequency of serious side-effects which occurred in 4 of the 14 patients treated continuously. Progress is, however, being made in the management of two of the more important side-effects—tuberculosis and osteoporosis. Periodical chest radiographs will detect the development of pulmonary tuberculosis, which, if active, can be effectively controlled by antituberculous drugs without interrupting the corticosteroid therapy. Osteoporosis due to the catabolic effect of corticosteroids on the protein matrix of bone may be inhibited and osteoblastic bone formation encouraged by the administration of testosterone and other anabolic steroids. Unfortunately, it is usually impossible to discover the presence of a peptic ulcer until the appearance of dyspepsia. Furthermore, it is unwise to continue oral corticosteroid treatment in such cases because of the danger of haematemesis or perforation.

There are undoubtedly some patients with chronic asthma in whom respiratory distress is so crippling that even if serious side-effects were inevitable it might still be preferable to accept the consequences rather than to deny such patients the prospect of relief which corticosteroid therapy alone can offer.

It was this therapeutic impasse which prompted the present investigation into the value of regimes of corticosteroid therapy employing dosages apparently below the danger level. The small numbers in the various treatment groups have made assessment difficult and possibly unreliable, but we feel justified in drawing the following tentative conclusions:

1. Prednisolone in a dose of 10–15 mg. a day, or triamcinolone 6–12 mg. daily, is capable of suppressing chronic asthma indefinitely in a high proportion of cases, but at this level of dosage minor side-effects are common and serious side-effects by no means rare.

2. Prednisolone given intermittently in a dose of 20 mg. a day on either two or three consecutive days of every week, on eight consecutive days of every month, or on six consecutive days of every fortnight provides a useful though fluctuating degree of symptomatic improvement for an indefinite period apparently without any serious danger from side-effects.

3. The response to long-term prednisolone therapy, whether given continuously or intermittently, is adversely influenced by chronic bronchitis and by frequent episodes of respiratory infection. Patients in whom a marked improvement is not rapidly obtained after they have been given prednisolone in a dose of 20 mg. a day seldom benefit from long-term treatment, whether continuous or intermittent.

Summary

An attempt has been made to assess the value of long-term corticosteroid therapy in relieving symptoms of chronic asthma in 33 patients. The assessments, at four-weekly intervals, were made clinically and by estimation of forced expiratory volume.

Ten patients were given prednisolone on either two or three consecutive days of each week and another 10 either on eight consecutive days per month or on six consecutive days each fortnight. These various regimes provided a useful but fluctuating degree of symptomatic improvement.

A group of 14 patients received prednisolone or triamcinolone daily for periods varying from 15 months to over 3 years. A remarkable measure of sustained improvement was obtained in eight. The presence of chronic bronchitis in addition to chronic asthma was believed to be the main reason why the other six patients failed to show an equally satisfactory response.

Serious side-effects from corticosteroid drugs were encountered in four patients given continuous treatment. Such treatment can be recommended only in exceptional cases where there is no effective alternative.

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