

Seasonal allergic rhinitis and depot injection of a corticosteroid

Evaluation of the efficacy of medication early and late in the season based on detailed symptom recording

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It was the aim of this investigation to study the efficacy of a corticosteroid given as a depot injection in seasonal allergic rhinitis, the efficacy profile with regard to specific symptoms, and whether the injection is best given early in the season or later at the peak of the pollen count. An injection of 80 mg methylprednisolone showed a marked effect on nasal blockage lasting more than 4 weeks, and a moderate effect on eye symptoms, while the effect on nasal hypersecretion and sneezing could not be demonstrated. It is concluded that systemic corticosteroids may be indicated in severe hay fever, when symptoms, especially blockage, occur in spite of other types of therapy. If the physician prefers to give the corticosteroid as a depot injection, it is preferably given in the first half of the season when the pollen count is increasing.

Key words: allergic rhinitis; corticosteroid; hay fever; methylprednisolone.

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An injection of a corticosteroid preparation in depot form is often used in hay fever. Some general practitioners use it as a simple first-line treatment, while most specialists recommend systemic steroids only when other types of therapy have failed.

Although depot steroid injections have been widely used for more than two decades our knowledge of their overall efficacy, effect profile, and optimal timing is sparse. We have been able to find only one double-blind placebo-controlled study on the efficacy of depot steroid injections in hay fever, and that report describes a therapeutic schedule which is not widely used today, i.e. a total of 240 mg methylprednisolone given as 3 injections with weekly intervals (3). Not surprisingly, it was the authors' overall impression that the injections resulted in "a marked relief of symptoms". Other studies have claimed the treatment to be effective without offering details and without use of placebo (1, 4, 6, 7, 10, 11 14).

It has been the aim of this paper to study and evaluate: a) the degree of efficacy of a steroid depot injection in hay fever; b) the efficacy profile with regard to specific symptoms; and c) whether the injection is best given early in the season or later at the peak of the pollen count. Early medication is favoured by the possible inhibition of the allergen-induced increase in non-specific reactivity ("priming") (2, 5), while a late injection includes the possibility of avoiding the use of systemic steroid in all but the most recalcitrant cases.

MATERIAL AND METHODS

Design

The trial was undertaken with a double-blind, placebo-controlled, group comparative design. The investigation was performed as two separate

NASAL BLOCKAGE [DEGREE 0-10]

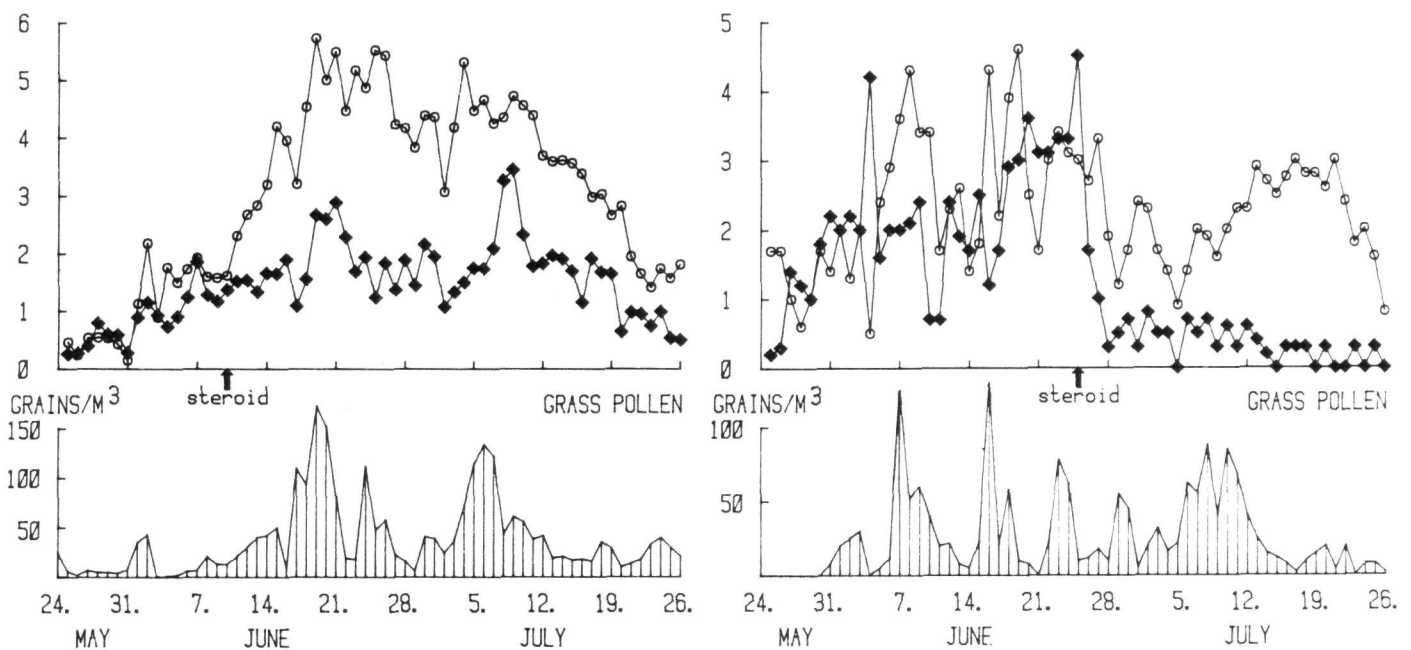


Fig. 1. Daily mean scores for nasal blockage in 24 allergic patients during two consecutive grass pollen seasons. In Trial 1 (left of figure), a depot injection of 80 mg methylprednisolone was given early in the season, and in Trial 2 (right of figure), the injection was given at the peak of the pollen season. Black diamonds: scores in steroid-treated group; open circles: scores in placebo-treated group. Lower part of the figure depicts the daily pollen count.

trials during two grass pollen seasons on the same patients. In the first trial the patients received a depot steroid injection or placebo at the start of the pollen season ("early medication") and in the second trial the medication was given at the pollen peak ("late medication").

Patients

Hay fever patients, allergic to grass pollen, were included in the two trials if they fulfilled the following criteria: a) aged 18 years and over; b) had rhino-conjunctivitis in June - July, which had required treatment for the last two seasons; c) had a positive skin prick test to timothy grass (at least of the same size as that of the histamine test (10 mg/ml)); d) stayed in Denmark during the entire period; and e) gave informed consent.

Applicants were excluded if: a) pregnancy could not be excluded; b) had a positive skin test to other pollens, house dust mite, or animal dander; c) had seasonal or perennial asthma; d) rhinoscopy revealed any gross anatomic abnormalities.

Treatment was initiated and completed in both trials by 24 patients: 12 were randomized into each

of the parallel groups; 16 were males and 8 females; the mean age was 24.0 years (range 18-36).

Medication

Coded ampoules containing 80 mg of methylprednisolone in a microcrystalline form, or identical placebo were supplied by Upjohn, Copenhagen. The drug was injected intramuscularly, in the first trial at the start of the pollen season (the 9th of June) and in the second trial at the peak of the pollen season (the 25th of June). The patients were permitted to use Antistina-Privin[®] eye drops (CIBA), maximum two drops four times a day, for eye symptoms, and chlorpheniramine maleate tablets of 2 mg (Schering), maximum one tablet three times a day, for the nasal symptoms. The use of these rescue medications was recorded on diary cards.

Symptom recording

Throughout the study, each volunteer carried a diary card on which he noted the number of

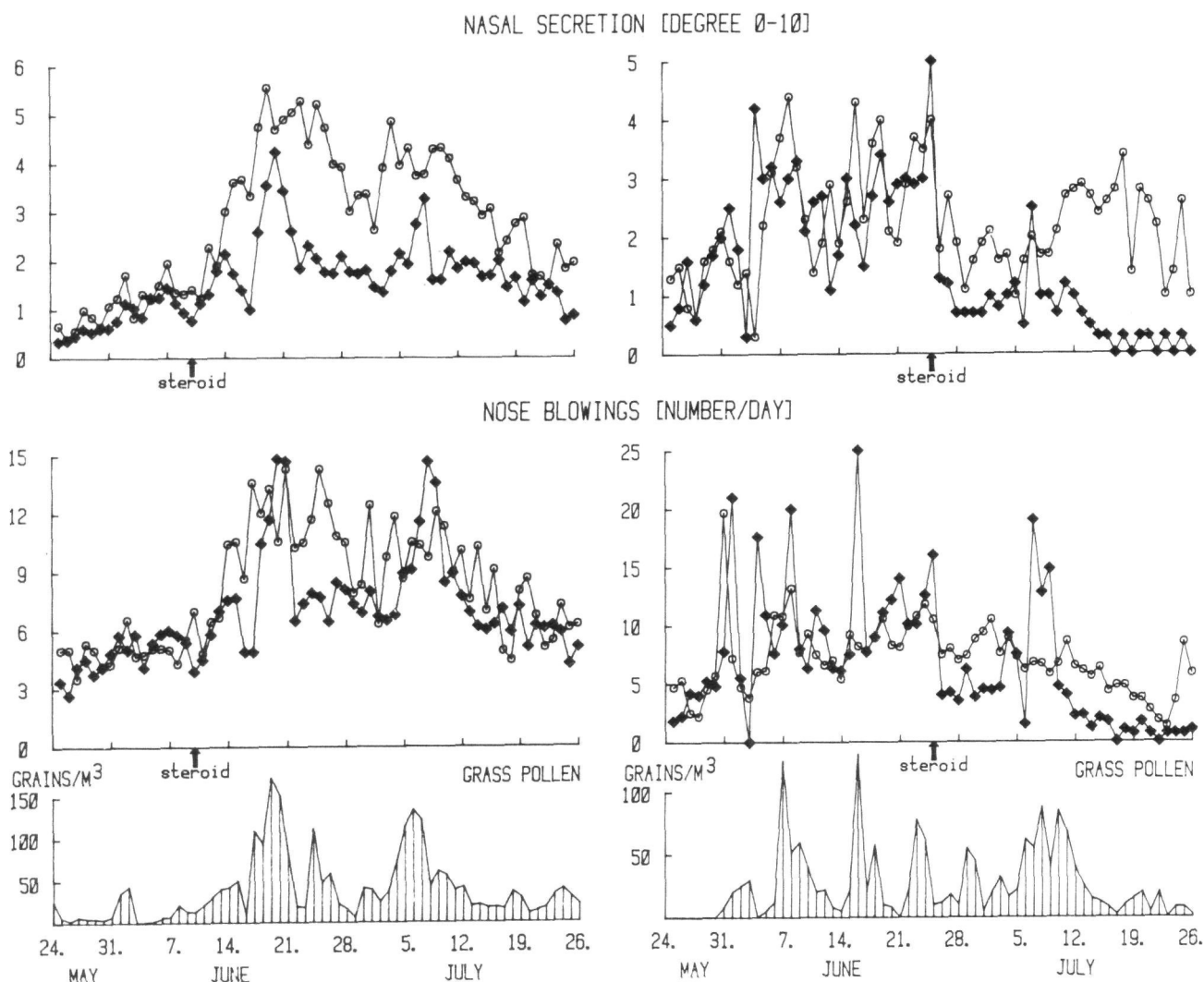


Fig. 2. Daily mean scores for nasal secretion, and number of nose blowings in hay fever treated with a depot steroid injection. See Fig. 1.

sneezes and nose blowings during the day. In addition, the patients in the evening estimated the degree of sneezing, rhinorrhoea and blockage on a 10-point rating scale, and eye itching on a 3-point scale.

Pollen counts

Pollen was collected in a Burkard trap, placed 15 m over ground level in the City of Copenhagen. The daily pollen count published in the Danish Pollen Bulletin, was used by permission of the Aero-biological Group, Danish Asthma-Allergy Association.

Statistical analysis

The differences between symptom scores in the

active- and placebo-treated groups in each season were calculated using a group comparative Student's t-test for two means, the means being calculated weekly.

RESULTS

Blockage

Trial 1 (early medication). Following placebo treatment the mean score for blockage rose in the week after the injection, remained stationary for 3 weeks, and decreased with the pollen count over the last 2 weeks of the trial period (Fig. 1, left). In the steroid-treated group, the mean score remained almost stationary throughout the entire pollen season, although the symptoms

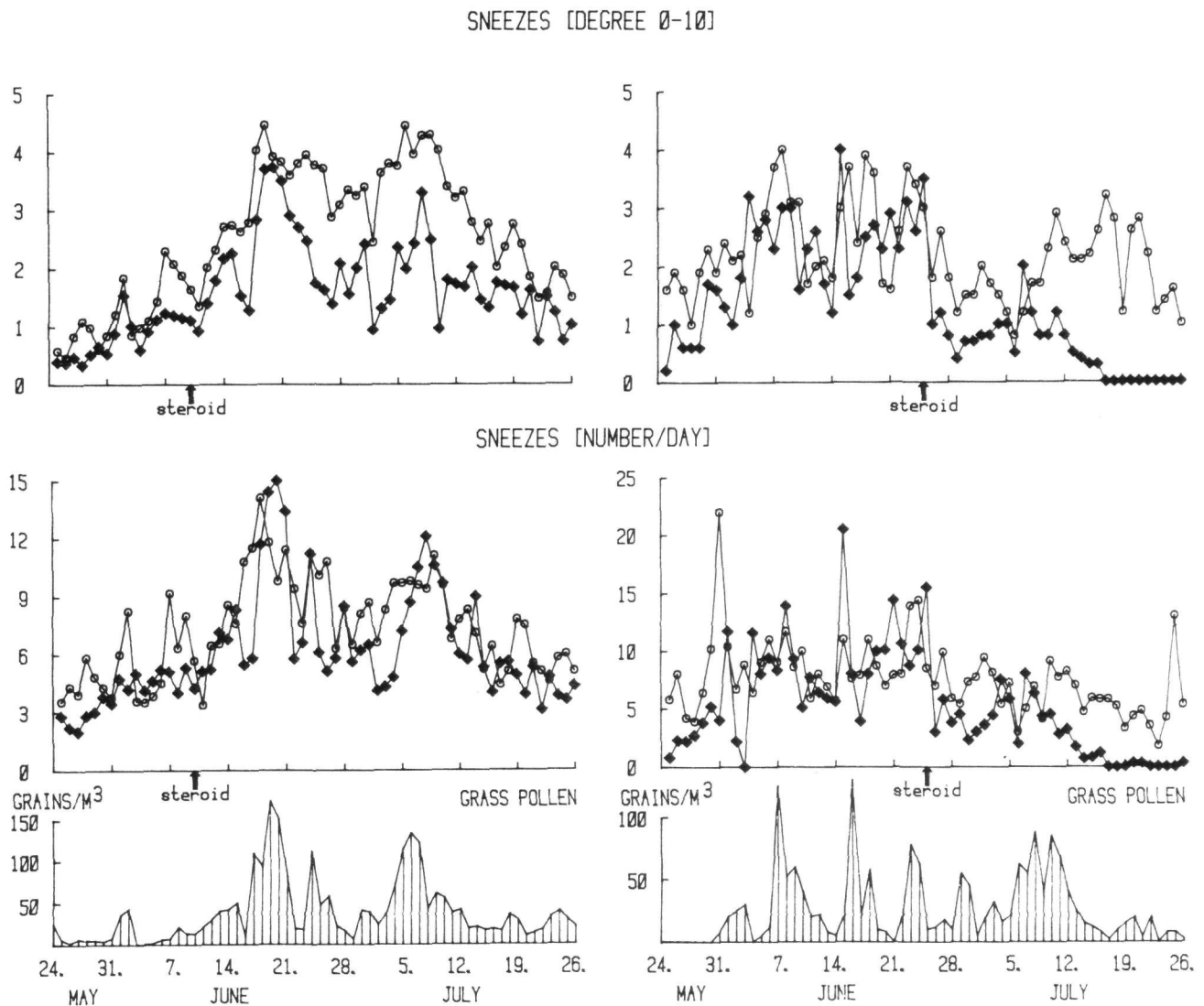


Fig. 3. Daily mean scores for sneezing, and number of sneezes in hay fever patients treated with a depot steroid injection. See Fig. 1.

increased somewhat during two pollen peaks. There was a significant difference between the two groups, lasting for 5 weeks after the injection ($P < 0.05$, in 4th week the difference was not significant)

Trial 2 (late medication). Associated with a fall in the pollen count, the mean score in the placebo-treated group decreased during the first 1-2 weeks after the injection; subsequently the symptom score increased (Fig. 1, right). The curve for the steroid-treated group showed a rapid and marked fall immediately after the injection; a few days later nasal blockage had almost disappeared and did not recur. The difference between the two groups did not reach a significant level until week 3-4 after medica-

tion ($P < 0.05$), probably due to the declining pollen count at the beginning of the period.

Rhinorrhoea

Trial 1 (early medication). Symptom scores for nasal secretion in the placebo-treated group (Fig. 2, upper left) were similar to those for blockage. In the treated group, however, the mean values for secretion tended to be higher than those for blockage. The difference between the two groups with regard to secretion reached only a statistically significant level in week 3 following the injection ($P < 0.05$).

Counting only the number of nose blowings showed a trend in favour of steroid treatment (Fig. 2, lower left). As some of the patients on

EYE ITCHING (DEGREE 0-3)

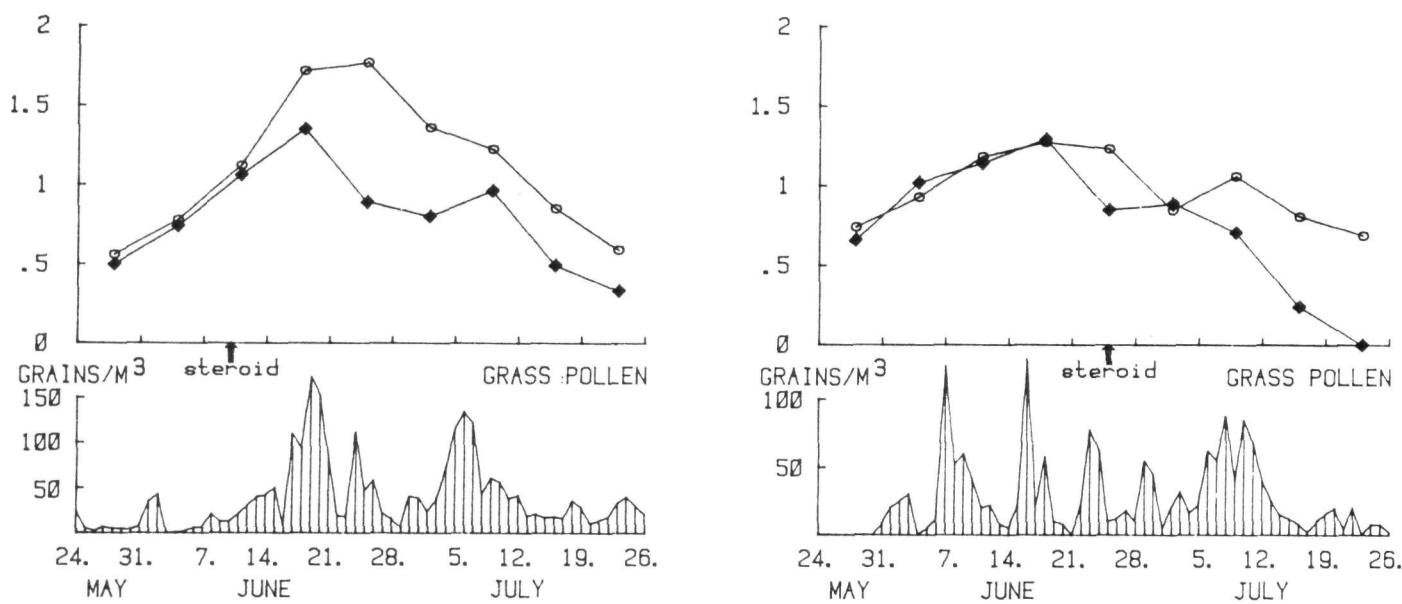


Fig. 4. Weekly mean scores for eye itching in hay fever patients treated with a depot steroid.

days with high pollen counts noted more than 100 nose blowings, while others had only a few, the mean curve for nose blowings varies considerably.

Trial 2 (late medication). Symptom scores fell in both groups following the injection, but in week 3-4 the curves separated with the highest values in the placebo-treated group ($P < 0.05$) (Fig. 2, upper right). The exact counting of nose blowings showed no significant differences and only

a weak trend in favour of the steroid group (Fig. 2, lower right).

Sneezing

Trial 1 (early medication). There was a trend in favour of the steroid treatment when symptom scores were used, but statistically significant levels were not reached (Fig. 3, upper left). The two treatment groups were similar with regard to the exact number of sneezes (Fig. 3, lower left).

Trial 2 (late medication). After an initial fall in both treatment groups, the score values in week 3-4 were lowest in the steroid group ($P < 0.05$) (Fig. 3, upper left). The difference was less clear with regard to the exact number of sneezes ($0.1 > P > 0.05$) (Fig. 3, lower right).

Table 1

Daily mean of rescue medication used in entire period following the injection of 80 mg methylprednisolone or placebo in 24 patients with grass pollen hay fever

	Methyl prednisolone	Placebo	P-value
Trial 1 (early medication)			
Antihistamine tablets	0.45	1.04	< 0.001
Eye drops	0.62	1.27	< 0.001
Trial 2 (late medication)			
Antihistamine tablets	0.17	0.21	NS
Eye drops	0.33	0.30	NS

Eye itching

Not all patients had daily eye symptoms, and weekly means are used for the figure drawings. There was a clear tendency in favour of the steroid group in both trials, only reaching a statistically significant level in Trial 1, week

2-3 ($P < 0.05$), and in Trial 2 week 4-5 ($P < 0.05$).

Rescue medication

The use of rescue tablets for nasal symptoms and eye drops for eye symptoms is shown in Table 1 as total usage for the entire period following the injection. The steroid patients generally used less medication than those injected with placebo; levels of significance were reached for both types of medication in Trial 1 (early medication) but not in Trial 2 (late medication).

DISCUSSION

The present study appears to be the first placebo-controlled investigation of the effect of a single depot injection of corticosteroid in hay fever. It showed that the effect of 80 mg methylprednisolone on nasal blockage was marked and lasted for more than 4 weeks. That this beneficial effect outlasted the pharmacological action of the drug, estimated by the effect on the hypothalamic-pituitary-adrenal axis to be about 2 weeks (8, 9), suggests that an impact steroid therapy in rhinitis can break some vicious circles, probably caused by chronic inflammation and the development of mucosal hyperreactivity ("priming effect") (5).

It is difficult to separate drug action on different symptoms when a 0-10 score system is used, as the filling-in of the score card in the evening will result in influence of one symptom on the others. Using a more exact scoring system with current recording of all symptoms we have earlier found that the H_1 antihistamine, astemizole, has a marked effect on sneezing and hypersecretion, but a poor or no effect on blockage (15). In the present investigation the placebo-treated patients used more antihistamines than the steroid-treated patients, and can maybe explain the relatively small difference in the effect on sneezing and hypersecretion by steroid versus placebo. Our experience with intranasally applied steroids is that these medications have a good effect on all three parameters in patients with allergic rhinitis (12), so

we had expected an effect on all symptoms, also by systemic steroid.

In this study we gave the depot steroid injection at the beginning of the pollen season in the first trial. In our opinion this can not be recommended in clinical practice (13) as it will result in a too widespread use of systemic steroids for hay fever; it is a general opinion among specialists that other types of therapy should be tried first. In the second part of the study we gave the injection at the peak of the pollen season. The effect appeared to be marked, but it was partly accounted for by the falling pollen count; treatment with systemic steroids for a few days had been sufficient. It is most correct in all cases to start with either antihistamines and/or topical therapy with sodium cromoglycate or steroid. If the physician prefers to give a depot injection of a steroid as second choice, it would be best administered after 2-3 weeks of significant pollen counts/symptoms, when the first-line therapy has proven insufficient. In this way, only a minority of patients will need systematic steroid, and a given injection will provide maximum benefit. In conclusion, we find the best time to administer a depot steroid injection is neither at the beginning nor peak of the season, but in the first half of the season when the pollen count is increasing and symptoms follow in spite of medication with antihistamines and topical therapy.

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