

IMMUNOLOGICAL ASPECTS OF LOMUDAL TREATMENT IN POLLEN ALLERGIES

Torsten Berg: It is recognised that patients with pollen allergy have pronounced seasonal variations in serum levels of specific antibodies. This was first shown in studies of histamine release from leucocytes. Some years ago Johansson and I showed that this was also true for total serum IgE levels, which are, of course, a relatively unspecific parameter (1). We studied seasonal IgE variations in a group of children who were sensitive to birch or to timothy grass pollen. Serum IgE levels increased quite rapidly at the beginning of the pollen season and declined more slowly at the end of the season (Fig. 1). This typical cyclical effect can be regarded as a booster effect. On exposure to the relevant allergen, these patients are "boosted" and serum reagin levels are increased during the season.

In patients with a pure pollen allergy, the variations in IgE levels may in large part be due to an increase in a specific IgE antibody (2). Thus in children sensitive to timothy grass, there were marked changes in levels of IgE antibody specific for this antigen. These variations in specific antibodies are more pronounced than that in total IgE. In some patients we could find no specific IgE against timothy grass pollen before the start of the season, but a marked IgE during the season. One patient gave anomalous results, with a decline during the season (Fig. 2).

We studied the effect of Lomudal treatment in a group of 16 children with birch pollen allergy (2). The majority had a single hypersensitivity to birch pollen but some were, in addition, also sensitive to timothy grass. In most cases, the presenting symptoms were those of asthma rather than rhinitis.

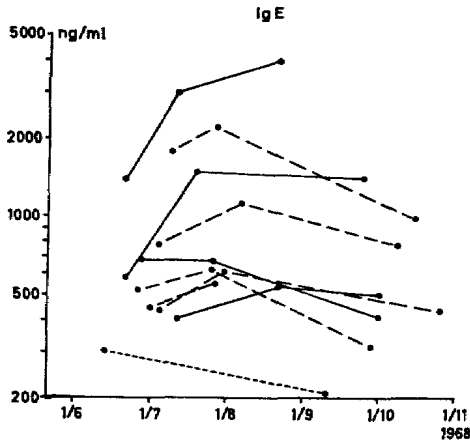


Fig. 1.

IgE concentrations during and after the pollen season in 10 children with pollen allergy. Children with symptoms only during spring and early summer ●-----●; only during summer ○-----○; during spring and summer ●——●.

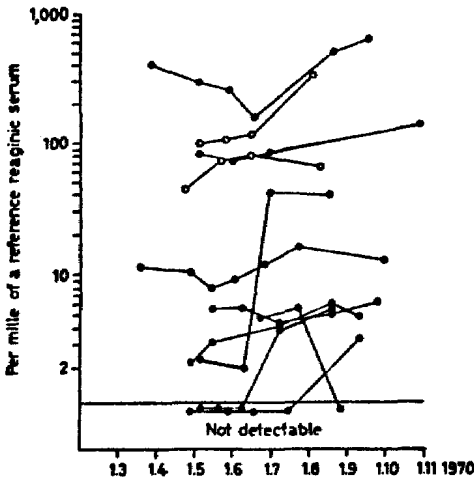


Fig. 2.

Changes in serum concentrations of IgE antibody against timothy pollen in timothy-allergic children: ○—○ untreated patients; ●—● patients treated with Lomudal.

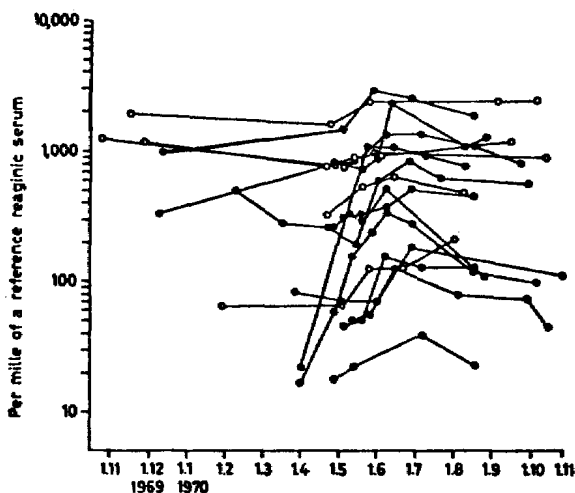


Fig. 3.

Changes in serum concentrations of IgE antibody to birch pollen in birch-allergic children: ○—○ untreated patients; ●—● patients treated with Lomudal.

Eleven children were treated with Lomudal and 5 children were untreated. Levels of both specific birch reagins and total IgE were recorded. Clinically, treatment with Lomudal was very effective. As judged by daily record cards, only one of the treated group suffered any notable symptoms. The others were virtually symptom-free. They were able to play out-of-doors and were thus exposed to birch pollen. Both treated and untreated groups shared marked increases in IgE levels during the season. In the untreated group, the average increase in levels of specific birch reagin was 90 per cent, compared to an increase of 170 per cent in the group treated with Lomudal. The numbers of patients are too small to permit statistical comparisons. The corresponding increases in total IgE levels were 101 per cent and 22 per cent, respectively (Fig. 3, Table 1).

It is apparent that in these patients there were some im-

TABLE 1

Changes in IgE Antibody to Birch (Birch Reagin) and Total IgE in Serum from 16 Children Allergic to Birch Pollen.

	Untreated	Treated with Lomudal	Total
Total number	5	11	16
Number of patients with demonstrable increase of reagins	5	11	16
Number of patients with increase of total IgE	5	9	14
Average increase of reagins as per cent of the initial value	90	173	146
Average increase of IgE as per cent of the initial value	101	22	47

munological consequences of the freedom from symptoms resulting from Lomudal treatment. They were exposed to the antigen to which they were sensitive and reacted by synthesizing specific IgE antibody. It is therefore a point for discussion whether this increase in reagin levels is in any way undesirable. Is it possible that treatment with Lomudal increases the patient's hypersensitivity? This is a very difficult question to answer satisfactorily. Clinically we have seen no signs of an increased sensitivity after a season's treatment with Lomudal. It is possible that sensitivity is not increased after Lomudal treatment because changes in the mucous membrane are reduced. It is known that sensitization occurs via the mucous membrane and that Lomudal, by inhibiting the release of histamine and other mediators, may prevent membrane changes.

REFERENCES

1. Berg, T. & Johansson, S. G. O. (1969): IgE concentrations in children with atopic diseases. A clinical study. *Int. Arch. Allergy* 36, 219.
2. Berg, T. & Johansson, S. G. O. (1971): *In vitro* diagnosis of atopic allergy. IV. Seasonal variations of IgE antibodies in children allergic to pollens. *Int. Arch. Allergy* 41, 452.

Inga Engström: During a double-blind trial of Lomudal in birch pollen rhinitis in 1971 (1), we examined total IgE and specific birch pollen reagin levels in serum (2). There were 17 children in the treated group and 18 in the placebo group, aged between 8 and 18 years. All had had symptoms for at least two seasons previously. Sensitivity to birch pollen was confirmed by intradermal testing and nasal challenge. None had previously been treated with hyposensitization (Table 1).

Serum for IgE determinations was taken on four occasions: before the season, as near the peak pollen period as possible, 2 to 3 weeks later (in fact, immediately after the season ends) and finally 3 to 4 months later. The determinations were carried out at the Blood Centre of Akademiska Sjukhuset in Uppsala, using the RAST method. An increase in birch pollen reagins during the season was found with a maximum shortly after the end of the season. Thereafter, the values decreased but remained above the pre-season level for several months. There was wide individual variation, but no apparent difference between the Lomudal group and the control group (Figs. 1 and 2). The mean percentage increase in the control group was 393 per cent and in the Lomudal treated group 259 per cent. The difference was not statistically significant.

Further, no relationship could be found between specific

TABLE 1
Patient Material: Children with Birch Pollen Rhinitis.

	DSCG	Placebo
Number of children	17	18
Sex distribution		
boys	15	15
girls	2	3
Age in years		
mean (range)	12 (8-17)	12 (8-16)
Duration of diseases in years		
mean (range)	6 (2-10)	6 (3-12)

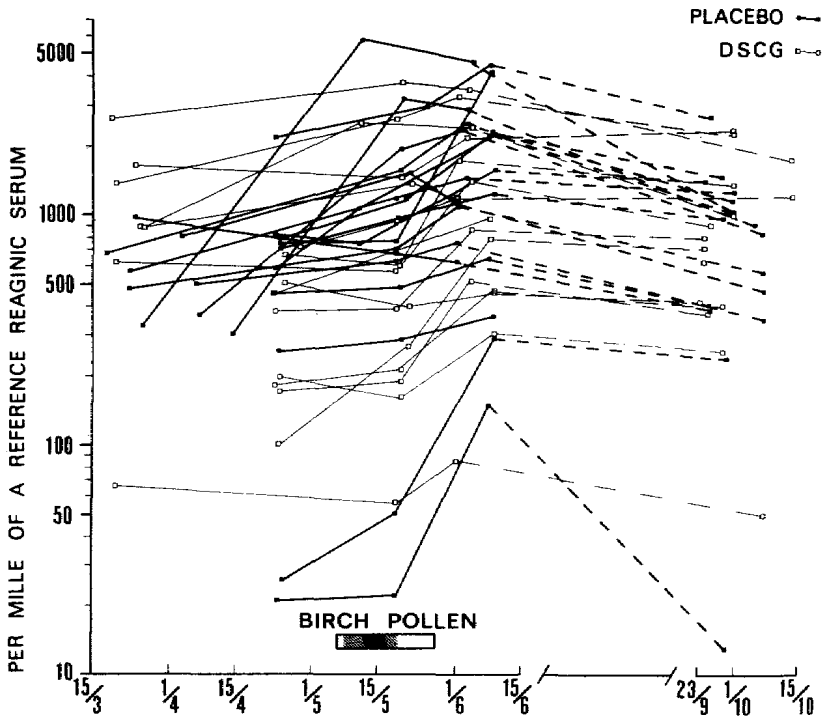


Fig. 1.

Birch pollen reagin levels before, during and after the pollen season.

reagin levels and the total symptom score during the peak pollen period (Fig. 3).

The increase in birch pollen reagins during the pollen season thus seems to be unaffected by Lomudal treatment and independent of the degree of symptoms. If serum levels of specific reagins reflect hypersensitivity, then Lomudal treatment would seem to carry no risk of increased sensitivity.

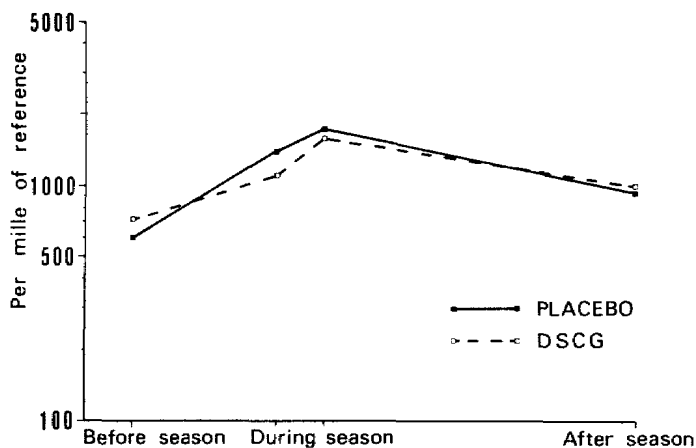


Fig. 2.
Mean levels of birch pollen reagins.

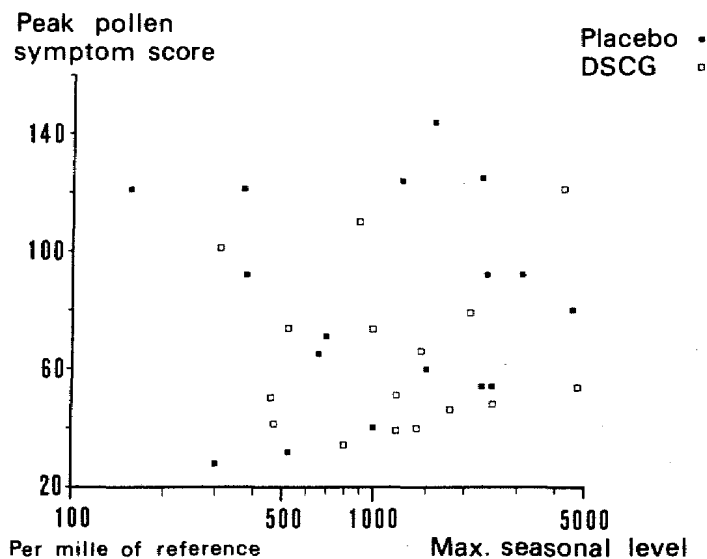


Fig. 3.
Symptom score in relation to levels of birch pollen reagins.

REFERENCES

1. Engström, I., Oberger, E., Blychert, A. & Kraepelien, S. (1971): Disodium cromoglycate in the treatment of seasonal allergic rhinoconjunctivitis in children. *Ann. Allergy* 29, 505.
2. Engström, I., Oberger, E., Blychert, A., Kraepelien, S. & Johansson, S. G. O.: To be published.

Discussion

B. Arner: How closely do you think plasma levels of specific reagins reflect the sensitivity of the individual?

T. Berg: I do not think the relationship is a simple one. Many studies have shown a poor correlation between reagin levels and degree of hypersensitivity. I think that the work we have reported here shows only that the exposure of Lomudal-treated patients to allergen has an immunologic sequel. It is impossible to say whether or not they become more hypersensitive to the relevant allergen.

B. Arner: In contrast, there is a positive correlation between the so-called skin titre and bronchial sensitivity. This is related to the clinical condition, as Colldahl and many others have shown.

T. Berg: Experience in hyposensitization is also of interest. Initially, hyposensitization leads to increased reagin levels, but eventually to a gradual reduction. This reduction is paralleled by a decrease in skin sensitivity, as shown by skin titration. One can speculate as to the reasons for this gradual reduction in levels of reagin—possibly an interference between blocking antibodies and reagins, with reagin synthesis decreasing as blocking antibodies increase.

I. Engström: Do you see this post-hyposensitization decrease in reagin levels during exposure in the pollen season?

T. Berg: That is an interesting question. With birch pollen allergy, I have found a very marked increase in reagin levels during the first phase of hyposensitization, without necessarily increased hypersensitivity.

I. Engström: In 1970 we studied reagin levels and the de-

gree of sensitivity in the nose. We could find no correlation.

B. Simonsson: Have there been any studies of both blocking antibodies and reagin? If both rise together, then one could understand the absence of symptoms even with high IgE levels.

T. Berg: As far as I know, nobody has studied this aspect. There is no doubt that IgG antibodies are formed during hyposensitization, but methods used to date have been rather unreliable. Slight modifications in technique and varying the allergen used have affected the results. It has been demonstrated, however, that there is little correlation between serum levels of blocking antibodies and symptom score.

J. Pepys: We carried out a controlled trial of hyposensitization with extracts of *Dermatophagoides pteronyssinus* and placebo extracts, using a course of about 12 injections. We found that about a third of patients had IgG antibody to *Dermatophagoides* before we started injections. Of the remainder of the patients treated with active material, approximately half developed IgG antibody, but showed no increase in specific IgE. In these patients we saw definite clinical improvement. The remaining patients in the treated group showed quite a large increase in specific IgE levels, but did not develop IgG antibodies. These patients showed the same level of symptoms as the control group. In studying these problems, I think one must sub-divide the treatment groups, look for a specific immunological change and then attempt to relate this to clinical assessment. In this way we have been able to link one parameter with clinical improvement. I think that you might be able to do this with your pollen studies.

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