

The General Hospital, Nottingham, England.

TREATMENT OF SEASONAL
RESPIRATORY ALLERGY WITH
ALUM PRECIPITATED PYRIDINE EXTRACT
INCORPORATING POLLEN
AND SPORES¹

By

R. GWYN EVANS

INTRODUCTION

For successful hyposensitisation treatment of seasonal allergic rhinitis and asthma, it is imperative that the allergen or allergens responsible for provoking symptoms are individually identified. This can only be achieved if the physician takes a most detailed history of the months in which symptoms of respiratory allergy occur, and also ascertains any possible relationship between the attacks of rhinitis or asthma and variations in atmospheric temperature, humidity, or the time of day or night when symptoms tend to reach their peak. A carefully maintained diary-record of the patient's symptoms from day to day (including details of the number of anti-histamine or broncho-dilator tablets required to control symptoms) is invaluable in assisting the Allergist to obtain a clearer and more accurate clinical picture of each individual case. In the United Kingdom, as in other part of North West Europe the majority of patients suffering from seasonal allergic rhinitis and asthma are pollen-sensitive, many reacting only to grass

¹ Based on a paper read at the VIth International Congress of Allergology, Montreal—November, 1967.

pollen, but a number exhibiting additional sensitivities to tree pollen and nettle pollen.

There also exist a considerable number of patients whose symptoms extend well beyond the normal limits of the pollen season, often into the early autumn months, and it is this group which appear to be sensitised not only to pollen but also to certain airborne spores which attain heavy atmospheric concentrations in the late summer and early autumn. Most patients who exhibit clinical sensitivity to seasonal spores already suffer from symptoms of pollen sensitivity, and there seems little doubt that the first indication that a patient has become sensitised to seasonal spores is therefore a gradual spread of a "seasonal allergic spectrum". When this occurs, it is particularly important to test specifically, both by prick tests and by nasal provocation tests for allergy to the more common seasonal spores.

HISTORICAL BACKGROUND

Attention was first drawn to fungus spores as a cause of allergy by *Van Leeuwem* in 1924, and in the same year *Cadem* published his account of asthma due to grain rusts. *Hopkins* and his co-workers (*Hopkins et al.* 1930) reported asthma due to *Alternaria*, and there were later papers from *Bernton & Thom* (1933 and 1937) and by *Feinberg* (1936) describing the importance of *Alternaria*, *Aspergillus*, and *Cladosporium* in seasonal asthma due to moulds, showing that desensitisation could be successfully achieved to these antigens by using a suitable aqueous extract.

Rackemann et al. (1938) stressed the high degree of specificity amongst certain species of *Cladosporium*, indicating the problems which would be raised if this specificity existed, as well it might do in other mould groups. The consequent need for detailed study of particular species of mould to which any given patient may be exposed was duly emphasised. The advent of the Hirst Spore Trap (*Hirst* 1952) first enabled accurate air sampling to be undertaken, to assess concentrations of both pollen and moulds; this proved to be of the

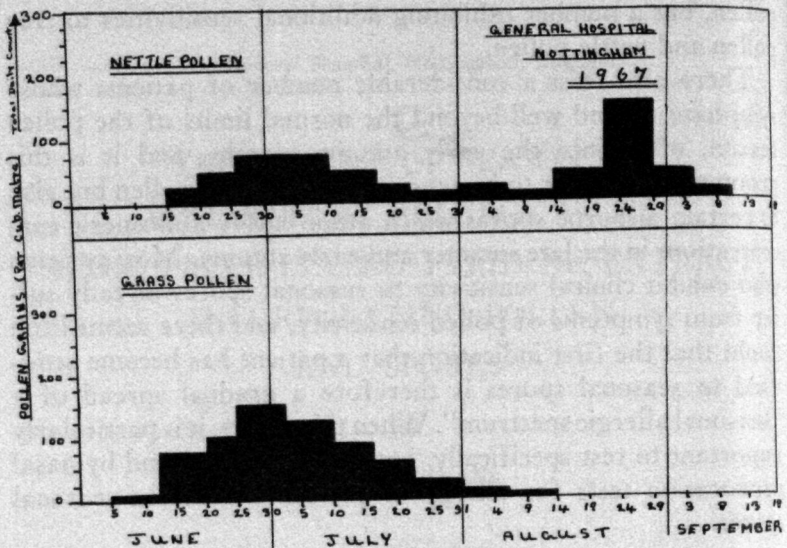


Fig. 1.

greatest help in contributing to our knowledge of seasonal allergy. In the United Kingdom weekly pollen and spore counts were made available, firstly from the Asthma Research Unit at Cardiff, and subsequently from the Wright Fleming Institute at St. Mary's Hospital, London. The information provided by these counts was of the greatest help in assessing individual patients' symptoms against the peak spore concentrations at the time their allergic symptoms were maximal. Hirst Spore Traps are now operating at several other centres in the United Kingdom in addition to those mentioned, and their operation should be extended (Fig. 1).

In a study conducted in the English Midlands 1961-65, it has been shown that the two most important seasonal spores are *Cladosporium Herbarum* and *Sporobolomyces Rosea*. In the North West Europe, very little trouble is encountered from *Alternaria*, contrary to experience in the North American continent. Although some 7 per cent of patients show positive reactions to *Alternaria* on skin testing, few of these show

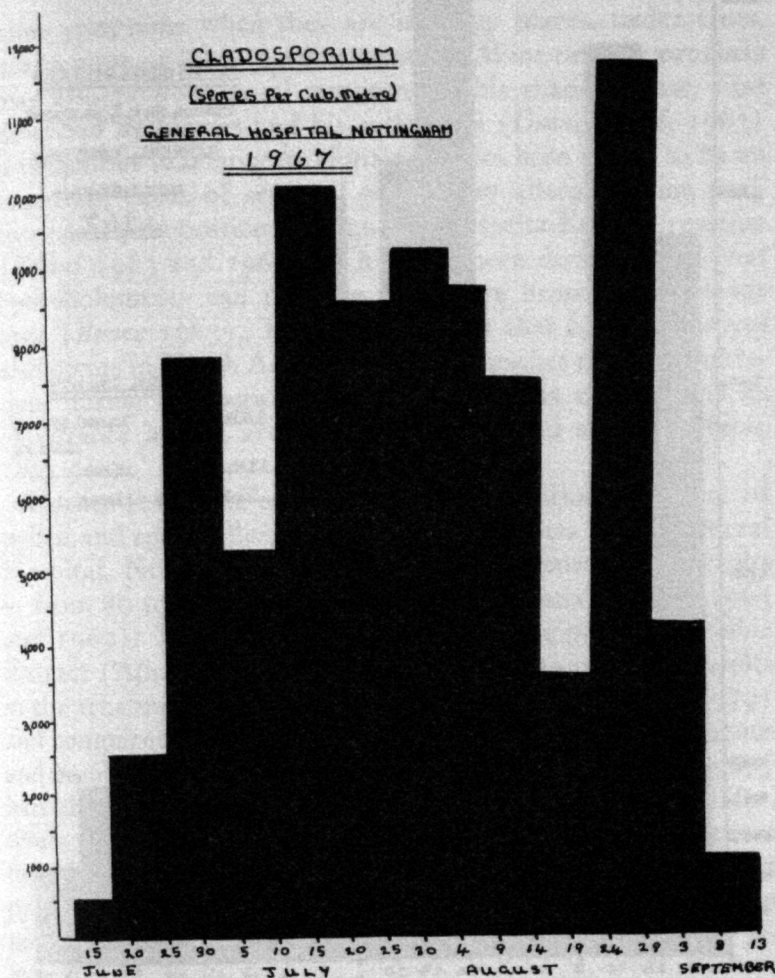


Fig. 2.

clinical sensitivity to *Alternaria* (Evans 1960). *Cladosporium* attains heavy peak concentrations during prolonged hot dry spells, and whilst it does cause allergic rhinitis, the majority of patients sensitised to this spore also experience troublesome asthma. (Fig. 2).

On the other hand, *Sporobolomyces* appears to be a very

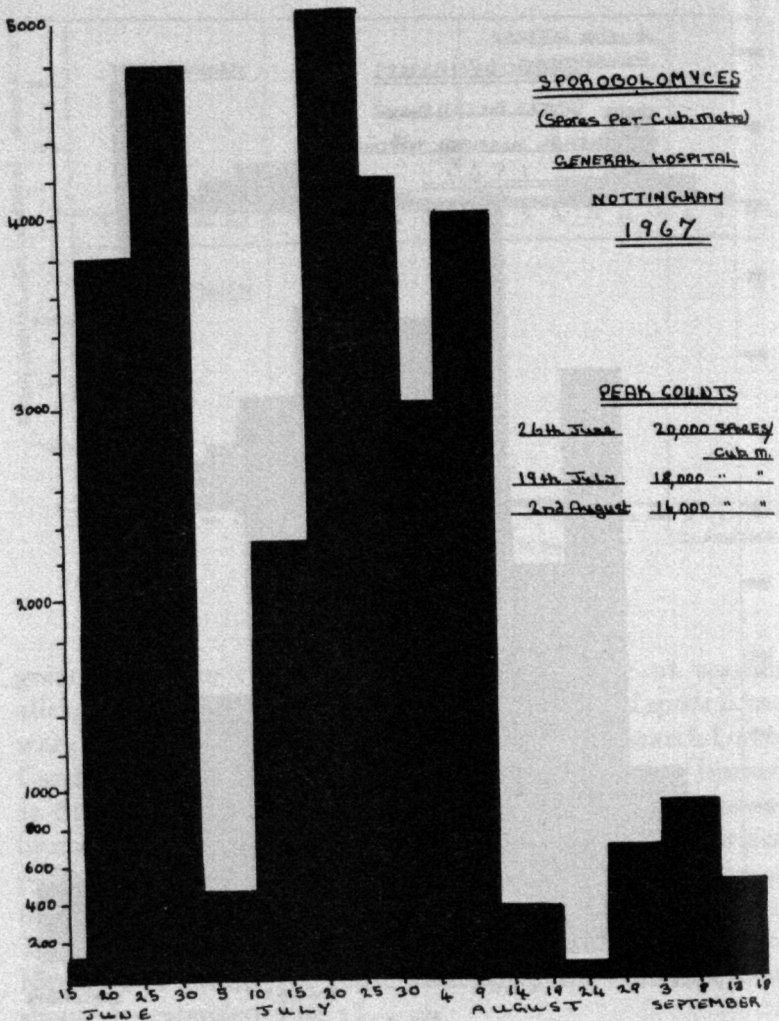


Fig. 3.

important allergen during warm damp conditions, and gives rise to symptoms particularly during dew fall, and immediately before and during light summer rain. It causes allergic rhinitis, but appears less liable than *Cladosporium* to cause asthma. Patients exhibiting allergy to *Sporobolomyces* experience trouble-

some symptoms when they are in damp places, under trees, near a river or lake, or when camping. Wine or wine products may also provoke nasal symptoms. This shadow yeast, first described by Davies and his colleagues (*Davies et al.* 1963) is ubiquitous in temperate climates. It has been shown to be an important cause of seasonal respiratory allergy, giving positive nasal provocation tests and a Prausnitz-Küstner reaction (*Evans* 1963 and 1965). It has also been demonstrated that *Sporobolomyces* can produce a positive bronchial challenge tests (*Bruce* 1963). There is no doubt that *Sporobolomyces* also occurs in North America, where it reaches peak concentrations during the ragweed season, which may explain why its importance in this area has so far received scant attention. (Fig. 3).

Earlier results of combined hyposensitisation treatment of pollen and spore allergy with aqueous extracts at the General Hospital, Nottingham 1962 to 1964 had shown good results in from 80 to 87.5 per cent of patients treated (*Evans* 1963 and 1965). The introduction of Alum Precipitated Pyridine Extract (Allpyral) had already given such encouraging results in the treatment of pollen sensitivity (*Fuchs & Strauss* 1959) and compared very favourably with those obtained by aqueous and emulsion pollen preparations (*Sobel* 1964). *Tuft* (1966) had shown that desensitisation to *Alternaria* could be effectively achieved with alum precipitated pyridine extract. It was therefore decided to assess the efficacy of alum precipitated pyridine extract ("Allpyral") in combined desensitisation to pollen and seasonal spores over the period 1966-67 in selected cases.

SELECTION OF CASES

Although ideally it might be desirable to desensitise separately, first to pollen and then to moulds, a combined programme offers the advantage of a reduced number of injections and consequently a considerable saving of both patients' and doctors' time. Cases selected were confined to those whose symptoms extended well outside the normal pollen season, and in whom

positive prick tests or positive nasal provocation tests had clearly indicated to which seasonal spores the patient was sensitive in addition to pollen.

TREATMENT

All patients were treated by the pre-seasonal method, commencing the injections during January or early February so as to allow a full three months of treatment before the commencement of the pollen season. For the majority of patients the initial dose was 20 P.N.U., the manufacturer's standard dosage scheme was followed working up to a final dose of 4,000 P.N.U. A small number of cases who either exhibited extreme clinical sensitivity to pollen or spores, or who gave very strongly positive reactions on prick testing, started on the smaller dose of 10 P.N.U. and the initial course terminated at 2,400 P.N.U. For patients who had previously been desensitised, unless otherwise indicated, the commencing dose was 50 P.N.U. working up to a final dose of 10,000 P.N.U.

REACTIONS

Reactions were minimal. Apart from local irritation at the site of the injection which caused very little trouble, the reaction most frequently encountered was one of nasal congestion occurring the day following the injection. In a few cases where this became really troublesome, the same dose was repeated after one to two weeks, and if a similar reaction resulted, this regarded as the "maximum tolerated dose" and the course concluded. In this series of over 200 cases, there were four instances of asthma developing during the twenty-four hours following a single injection, but of these only two appeared to be part of a true constitutional reaction, for the other two cases had developed a respiratory tract infection which appeared to be the cause of the asthma. The incidence of both general and local reactions was therefore much less than with aqueous pollen and depot pollen preparations (*Frankland et al.* 1963).

TABLE 1

Combined Desensitisation to Pollen with Cladosporium and Sporobolomyces using Alum Precipitated Pyridine Extract.

	Good results	Poor results	Total	% Good results
Pollen with Cladosporium	9	—	9	—
Pollen with Sporobolomyces	24	7	31	77.4
Pollen with both Cladosporium and Sporobolomyces	30	8	38	79
Total	63	15	78	
%	80.8 %	19.2 %		

TABLE 2

Combined Desensitisation to House Dust, Pollen and Seasonal Spores using Alum Precipitated Pyridine Extract.

	Good results	Poor results	Total	% Good results
Pollen and House Dust Only	32	4	36	87.5
House Dust with Cladosporium and/or Sporobolomyces	7	—	7	—
House Dust, Pollen and Cladosporium and/or Sporobolomyces	64	15	79	80
Total	103	19	122	—
%	83.8 %	16.2 %		

The results of combined desensitisation to pollen and seasonal spores are listed in Table 1, 80.8 per cent cases so treated giving a good result. Table 2 gives comparative figures for those patients whose symptoms were perennial due to house-dust but subject to seasonal exacerbations during the pollen or spore season; it is interesting to note that similarly encouraging results (83.8 per cent good responses) were obtained in this group (Table 2). Patients recording symptoms amounting to more than nuisance value or requiring anti-histamine/broncho-

dilator tablets on 12 or more days in the season were assessed as a "poor result". It will be noted that the best result were obtained from combined desensitisation with grass pollen and Cladosporium, whereas comparative figures for pollen and Sporobolomyces give a slightly lower proportion of good responses (probably because Sporobolomyces is less strongly antigenic than Cladosporium). The results are comparable with those obtained from desensitisation to pollen only (Table 3).

TABLE 3

Overall Results of Combined Desensitisation to Pollen/Dust and Seasonal Spores using Alum Precipitated Pyridine Extract.

Total Number Patients Treated and followed up	204
Good Results	166 (82.5 %)
Poor Results	34 (17.5 %)
Invalid Results	4
Comparable Group Desensitised to Pollen only (26 Patients)	
Good Results	23 (88 %)

TABLE 4

Combined Desensitisation to Pollen, Dust, Cladosporium and Sporobolomyces with Alum Precipitated Pyridine Extract.

Recommended Minimum Amounts of Antigenic Extract:

Grass Pollen	30-35 % W/V
Tree/Nettle Pollen	5-10 % W/V
Cladosporium	10-15 % W/V
Sporobolomyces	25-30 % W/V

Dosage Scheme: (Average Sensitivity)

From 10 PNU up to 4000 PNU (and up to 10,000 PNU in subsequent years).

When combining pollen with seasonal spores in the same alum precipitated extract, it would appear from experience gained over the past two years that for effective desensitisation with a mixture of this type, the Cladosporium content should be approximately 10 to 15 per cent weight/volume, so that the final dose of Cladosporium would be of the order 400 to 1,500 P.N.U. With Sporobolomyces the optimum content

should be 20 to 30 per cent weight/volume so as to give a final dose of 1,000 to 3,000 P.N.U., according to individual tolerance. When tree or nettle pollen appear to be contributory in pollen sensitivity (as often occurs in the United Kingdom), a relatively small dose of either tree mix or nettle pollen appears sufficient, so that a final dose of between 200 to 750 P.N.U. in addition to the grass pollen content suffices to produce the required degree of clinical tolerance during the appropriate pollen season (Table 4).

CONCLUSION

Patients with an "extended hay fever season" usually exhibit sensitivity to certain seasonal spores in addition to pollen sensitivity. In the United Kingdom, *Cladosporium Herbarum* and *Sporobolomyces Rosea* appear to be particularly important as a cause of symptoms of respiratory allergy occurring in the late summer and early autumn. Extracts of either or both of these spores can be incorporated in suitable proportions in Allpyral Alum Precipitated Pollen Mix, and the results obtained from this combined desensitisation are good. A satisfactory response should be regarded as an indication for further desensitisation over the succeeding two years.

Patients in this trial particularly appreciated the reduced number of injections compared with previous desensitisation with aqueous preparations. The overall reactions to injections (both local and generalised) was appreciably less than with aqueous pollen/spore mixtures, but the spore content of the mixture should be limited to the proportions suggested. This method of treatment could advantageously be extended to other seasonal spores shown to be clinically important as a cause of respiratory allergy.

SUMMARY

- 1) Many patients suffering from symptoms of respiratory allergy extending beyond the accepted limits of the pollen season are sensitive to certain seasonal spores.

- 2) In the United Kingdom, *Cladosporium Herbarum* and *Sporobolomyces* appear to be the most important of these. *Alternaria* and *Ustiligo* cause relatively little trouble clinically.
- 3) Alum precipitated pyridine extract ("Alpyral") offers a simple and effective means of desensitisation, combining pollen mix and spore extracts in suitable recommended proportions which can be adapted to the individual patient's "allergic spectrum".
- 4) In a series of over 200 patients, over 80 per cent of cases showed good results from this combined desensitisation.
- 5) Local and generalised reactions were minimal, and the preparation had a high "acceptance rate" from both patients and their medical practitioners.

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