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Study of mold allergy in asthmatic children in Hungary

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SUMMARY

We studied the change in sensitivity to propagating aerogenic fungi (spores, conidia) in extrinsic asthmatic children living in an urban environment from 1977 to 1988. According to the skin test, 10.6% of those examined in 1977 were sensitive to the fungi, the proportion being 30.4% in 1985 and 38.5% in 1987/88. The increase may be explained by the increasing frequency of sensitivity to Alternaria alternata and Phoma betae. In skin tests with Bencard allergens, reaction to both types was frequently observed. Of those sensitive to P. betae, 83% were also sensitive to A. alternata, and 87.5% of those sensitive to A. alternata were also sensitive to P. betae. The frequency of cross-reactions observed both with skin tests and specific IgE determinations suggests the presence of a common allergen, or epitope. The effect of environmental factors was analyzed with computer techniques. P. betae allergy was not related to detectable mold, humidity or number of pot plants in the home. The living conditions changed during the study period as follows: 1) housing conditions improved; 2) energy-saving building technologies were generally accepted; and 3) air pollution increased, also affecting the vegetation. The sensitizing masses of spores and conidia originated most likely from molds living on plants weakened and diseased by environmental pollution.

Key words: Mold allergy - *Phoma betae* - *Alternaria alternata* - Asthma symptom score - Computer analysis

INTRODUCTION

As a result of urbanization, the rising number of industrial units and technological changes in the building and furniture industries, our biological environment has undergone a considerable transformation during the past decade. An indicator of these changes are allergic patients. This process may be followed parallel with their changing sensitivity. The increase in ragweed allergy may be related to the expansion of uncultivated areas. Also, housing conditions are different: homes are more hygienic and easy to keep clean. The only factor counteracting the above is the use of floor carpets. Richly upholstered furniture is out of date, the timber used is of poorer quality and, at present, furnishings no longer serve several generations. It is likely that all these factors have decreased the incidence of mite allergy (Fig. 1, unpublished data). With respect to hyphomycetes, a comparable change could have been expected, but this has not occurred. Their frequency has steadily increased in the past 15 years. In the present study, we attempted to investigate the importance and cause of this increase.

MATERIALS AND METHODS

This study was based on the data from children with extrinsic asthma examined between the ages of 3 and 14 years. Skin tests were performed with the prick method and Bencard allergens. In addition to the negative reaction to physiological salt solution, edema with a diameter of $\geq$ 3 mm and erythema with a diameter of $\geq$ 10 mm were considered positive. We used only the data from children with skin tests performed with *P. betae* and fungus group A-13. If the latter was positive, all species representing the group were individually examined, including *A. alternata*. If A-13 also containing *A. alternata* was negative, the child was included in the group not allergic to *A. alternata*. We reviewed and used the data from skin prick test reactions of 200 children from the period 1977/78 and of 500 children from the period 1987/88. With respect to *A. alternata* and *P. betae*, specific IgE determination in the serum of 40 children was carried out (Phadebas RAST, Pharmacia). We also performed clinical analyses. The data from the group showing a

positive reaction to *P. betae* were compared with those from extrinsic asthmatics not allergic to *P. betae*. We studied the degree of symptoms using two scoring systems. One was the internationally accepted 12-point scale of Kraepelien, taking into consideration the number of attacks per year (Table 1, A). The maximum of 12 points represents more than 25 wheezing attacks per year. The second was an extended variation of the first and has been used in our service for several years with good results (Table 1). In addition to the incidence, it considers the degree of wheezing, the number of sick days per year and the duration of attack (maximum value = 21 points). We attempted to determine the significance of environmental factors from the history recorded according to strictly identical aspects. For this and for the statistical estimation we used a Commodore-64. Programs drawn up by us in BASIC language served for obtaining the data base, for the selection of data and for calculations.

RESULTS

Comparing the results of cutaneous reactions in the years studied, it was found that in our patients suffering from extrinsic asthma, the rate of mold allergy increased steadily. This may be seen in Figure 2. The composition according to species is illustrated in Figure 3. The data were obtained from the results in 1988; the positive cutaneous reactions were counted, not the children examined. It should be pointed out that after *A. alternata*, *P. betae* takes second place.

Table 1
Scoring system* for the estimation of the degree of asthma in children.

A	Number of insults per year:	
	> 25	12 points
	11-24	9 points
	5-10	6 points
	1-4	3 points
B	Degree of choking (max. dyspnea considered):	
	Requiring intensive care (intubation, artificial respiration)	4 points
	Prompt medical care	3 points
	Dyspnea weakening the patient	2 points
	Wheeze not disturbing condition	1 point
C	Duration of choking:	
	> 3 days	3 points
	1 - 3 days	2 points
	4 - 24 h	1 point
D	Days of respiratory symptoms per year:	
	> 60 days	2 points
	20 - 60 days	1 point

* Maximum value: A+B+C+D=21 points.

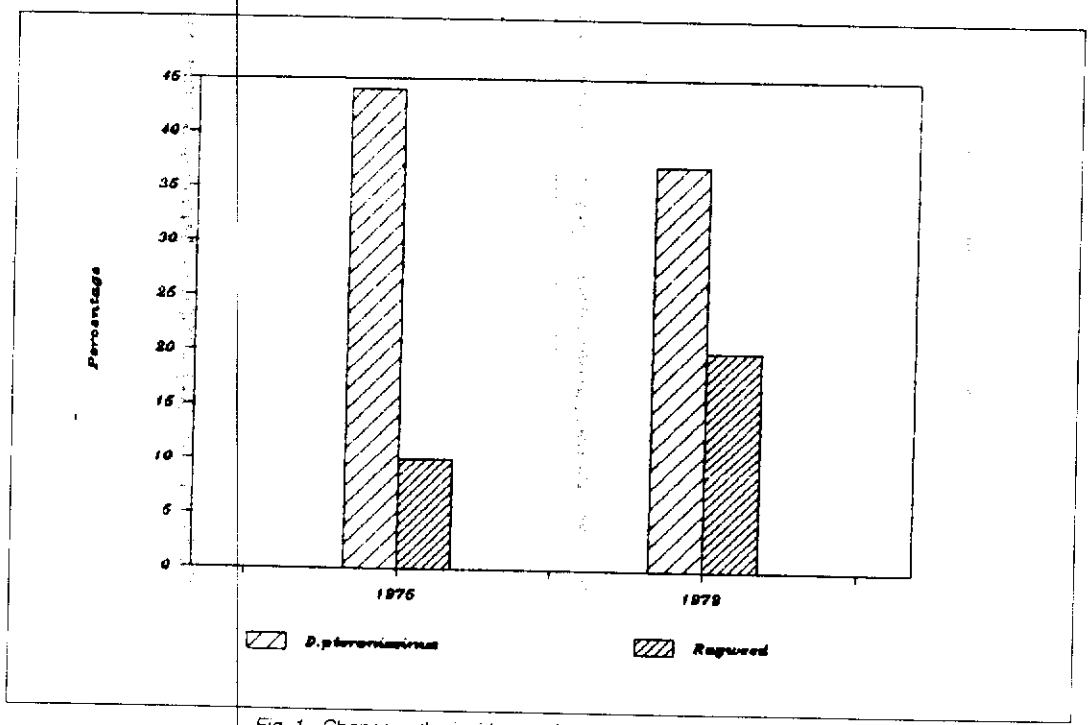

Fig. 1. Change in the incidence of two main allergens in Hungary.

Of our patients sensitive to mold, 35% showed a positive reaction to *P. betae* extract in 1985, and 58% in 1988. Studying the patients allergic to *P. betae* separately, it is striking how many are polyallergic (Fig. 4). The relationship is significant ($p < 0.05$). Because of the large number of polyallergics, there were many patients in this group with high IgE levels. *P. betae* hypersensitivity is frequently associated with other mold allergies, *i.e.* 83% of cases were also sensitive to *A. alternata*. Similarly, 87.5% of patients allergic to *A. alternata* were sensitive to *P. betae*.

The results from skin tests were controlled with *in vitro* studies, *i.e.* specific IgE determinations. Comparing the two methods, a close correlation was ob-

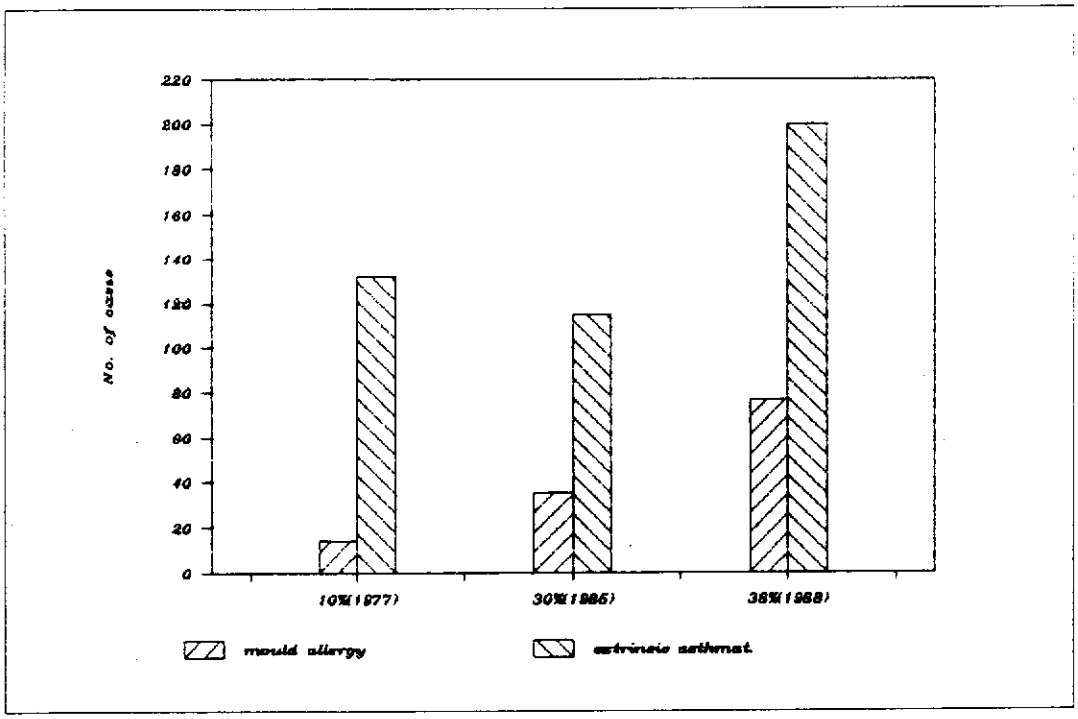

Fig. 2. Incidence of mold allergy among extrinsic asthmatic children in Hungary.

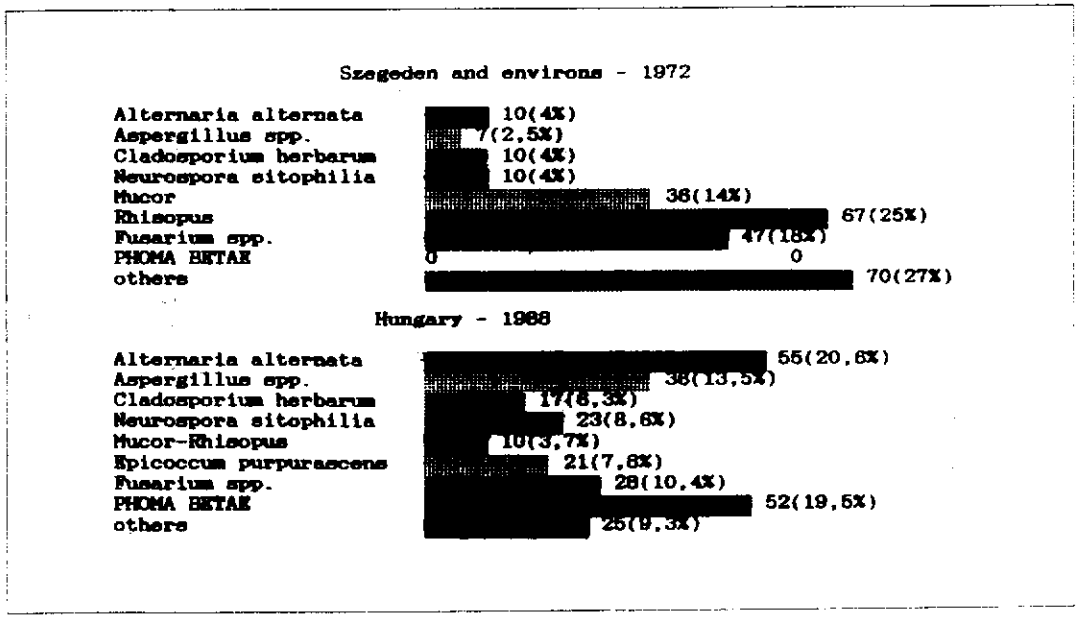

Fig. 3. Incidence of allergizing fungi in Hungary from 1972 to 1988.

served (Figs. 5, 6 and 7). However, in the case of *P. betae*, there were more positive skin tests, which could not be proved with RAST examination.

Comparison was made between the group allergic to *P. betae* and extrinsic asthmatics not sensitive to *P. betae* with respect to anamnestic data, environmental factors and scoring systems estimating the degree of symptoms. A difference was not noted between the two groups. The results are presented in Table 2. We should point out that, in the case of patients allergic to *P. betae*, a greater frequency of moldy homes or house plants was not found.

DISCUSSION

The skin tests carried out over several years under identical conditions enabled us to acquire knowledge not only of one given case, but also of our biological environment, with this simple method of allergological examination of children of the same age and living in an urban environment. Our data may be accepted as a general model, because the condition of admission was only suspected allergy; selection was not based on moldy housing conditions or an undefinable seasonality in the manifestation of symptoms determined by the living conditions of fungi. Thus, we may state that in Hungary mold allergy became more frequent in children during these years.

Substantial changes may be observed in the composition of allergenic fungi. On the basis of our skin tests and RAST examinations, the two most frequent allergenic species are *A. alternata* and *P. betae*. The better known *A. alternata* is the most frequent in the US, and is also a dominant species in the western

Table 2
Environmental and clinical data.

	Asthmatics allergic to *Phoma* (n=22)	Other extrinsic asthmatics (n=36)
Onset in infancy	3	6
First choking with fever	8	14
In general choking and fever	3	2
Moldy home	3	6
Plants in home		
< 10 pots	16	31
10 - 20 pots	4	3
> 20 pots	2	2
Time of first choking (years)	4.6	4.2
Number of choking/year (points)	5.0	5.2
Score of degree (points)	10.8	10.9

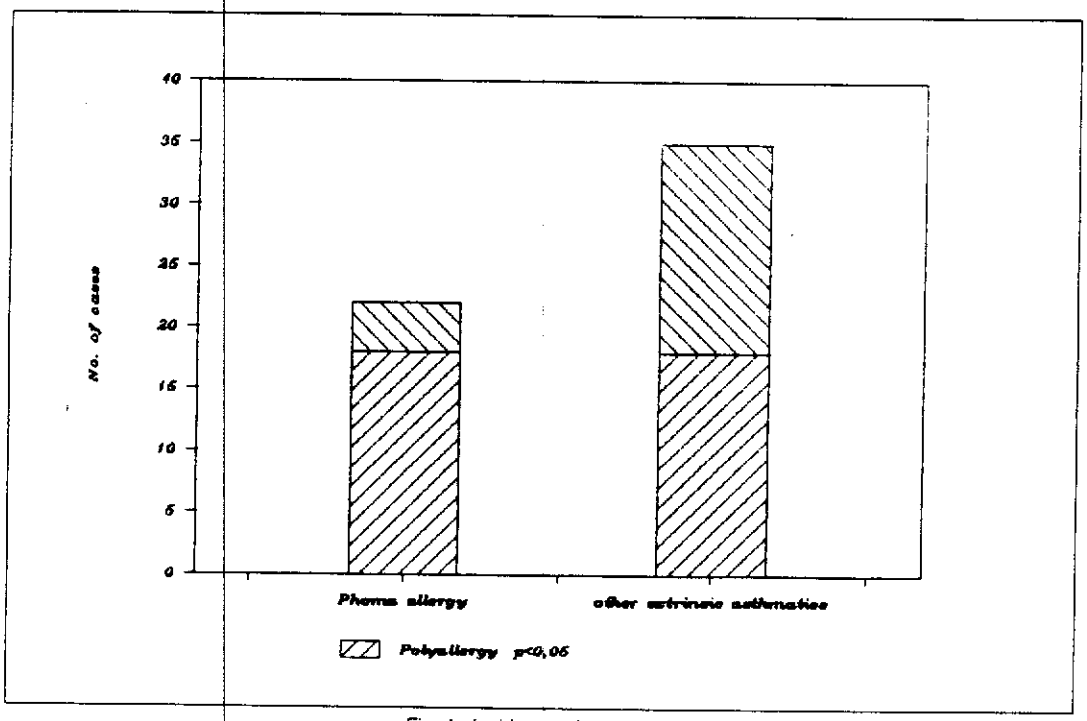

Fig. 4. Incidence of polyallergy.

part of Europe. It is found in soil and compost (1,2). *P. betae* is a common soil fungus and plant pathogenic. It affects weak, decaying plants. It has been found on damp wall surfaces within living quarters (2,3), although it was also observed in Hungary in a damp cellar with an aquarium (4). Both species belong to the imperfect fungi forming pigment-producing dark-colored beds. In relation to *P. betae*, found on a shower curtain, allergic pneumonitis has been described (2,5). According to data published in 1972 (6,7), *Mucor* and *Rhizopus* were the most frequently observed mold allergens in Hungary. These two groups are allergens found within homes, so-called poverty fungi, because they multiply and allergize mainly within agricultural environments in neglected, damp houses with mud walls and tamped floors. Parallel with the improvement of housing conditions, they have lost their importance as allergens.

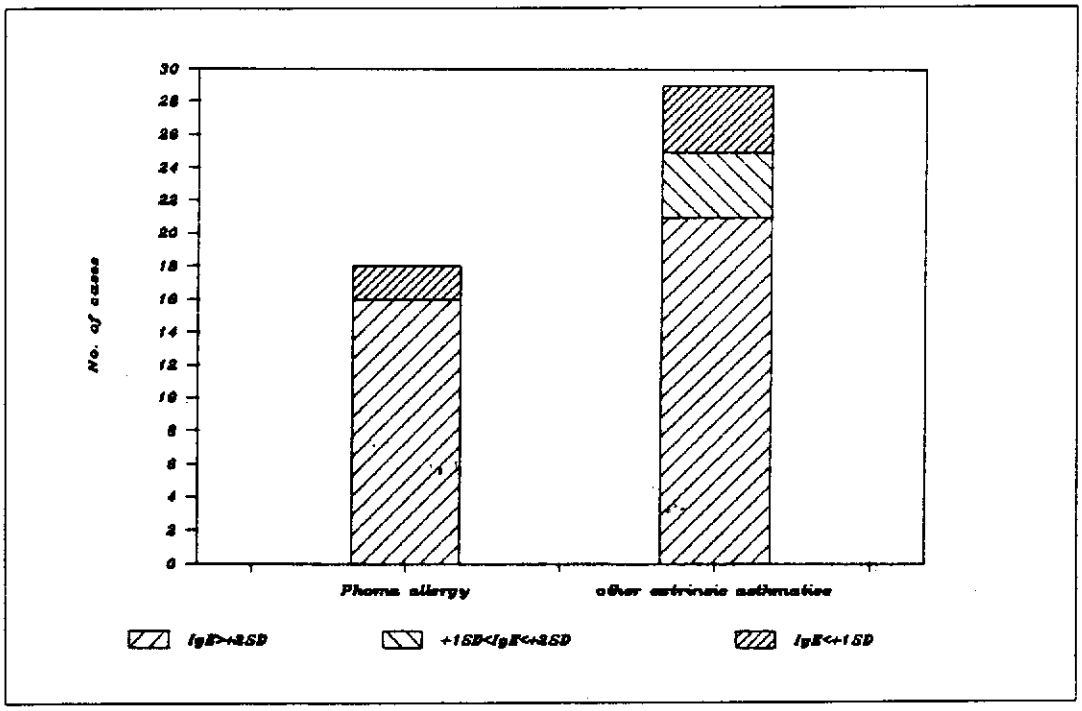

Fig. 5. IgE level of Phoma allergics.

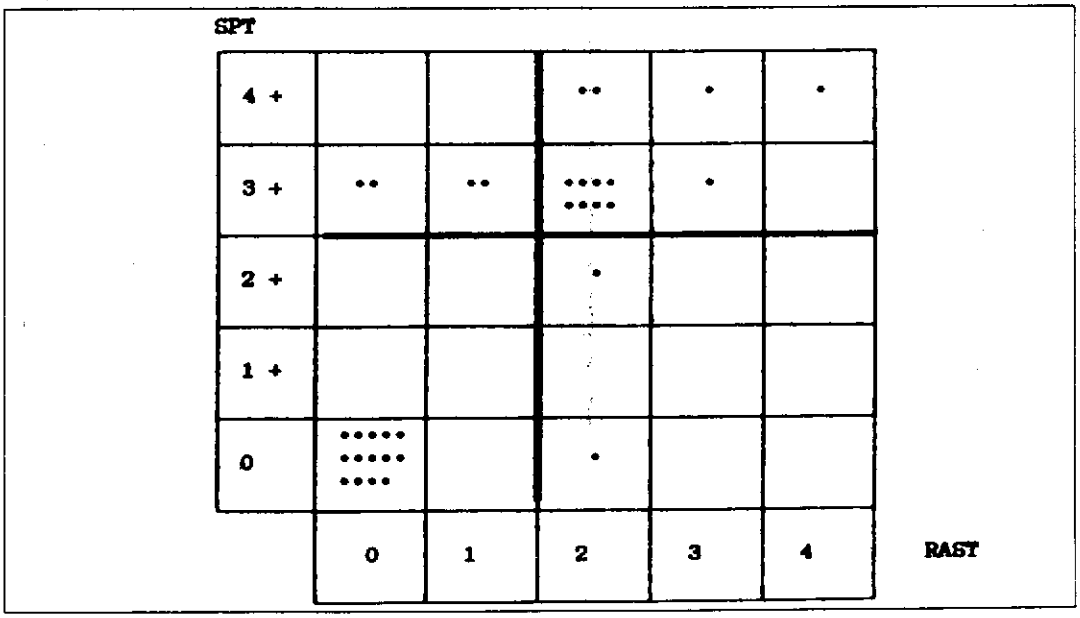

Fig. 6. Relationship between skin test and specific IgE level in Alternaria allergy. n = 33; chi-square = 13.6; p < 0.01.

It is interesting that from the early 70s on, *Cladosporium herbarum* is far less frequently detected in Hungary as an allergizing fungus as compared to the western part of Europe, although in 1989 it was the fungi with the highest concentration in the air of Budapest (1,3,8-10). Our studies demonstrated that *P. betae* is one of the two most generally sensitizing fungal allergens, the frequency of which is increasing rapidly. It may be that their reproductive form is present in the air in a larger quantity than 10 years ago. In the literature, differentiation is made between indoor - within the home - and outdoor - outside the home - allergenic sources. The possibility of the development of wall molding has not disappeared with the increase in building panel houses. Precipitation of moisture due to incorrect heat insulation, frequent roof leaks and energy-saving building technologies preventing natural ventilation have created essential conditions for fungi in homes poor in vapor content. However, this does not explain the rapid spread of mold allergy, as the average housing hygiene has definitely improved during the past decades. A confirmation of this is the answer of parents given on inquiry about environmental anamnesis: among those living in damp, moldy homes, the number of fungal allergics is not higher. Therefore, it is not within the home that we have to look for allergenic sources.

Vegetation weakened and killed by air pollution may provide an ideal culture medium for plant pathogenic fungi. For the identification of reproductive forms in the air, samples obtained from pollen traps are especially suitable for identifying certain fungal varieties

Table 3
Relationship between *P.betae* and *A.alternata* RAST and skin prick test reactions.

PRICK	RAST: Positive — *P.betae*	RAST: Positive — *A.alternata*	RAST: Positive — *P.betae* + *A.alternata*	RAST: Negative
Positive — *P.betae*				
Positive — *A.alternata*				
Positive — *P.betae* + *A.alternata*				
Negative				

such as *Cladosporium*. However, *P. betae* has no characteristic conidium discernible on the slide. Mycological and phytopathological investigations are needed for the confirmation of the above hypothesis.

A second assumption is that the positive skin reaction to *P. betae* extract is the result of cross-reaction between related fungal varieties. Cross-reactions are shown in Table 3.

Different opinions may be found in the literature concerning this type of relationship between fungi (2,6,11-13). The most plausible position at present is

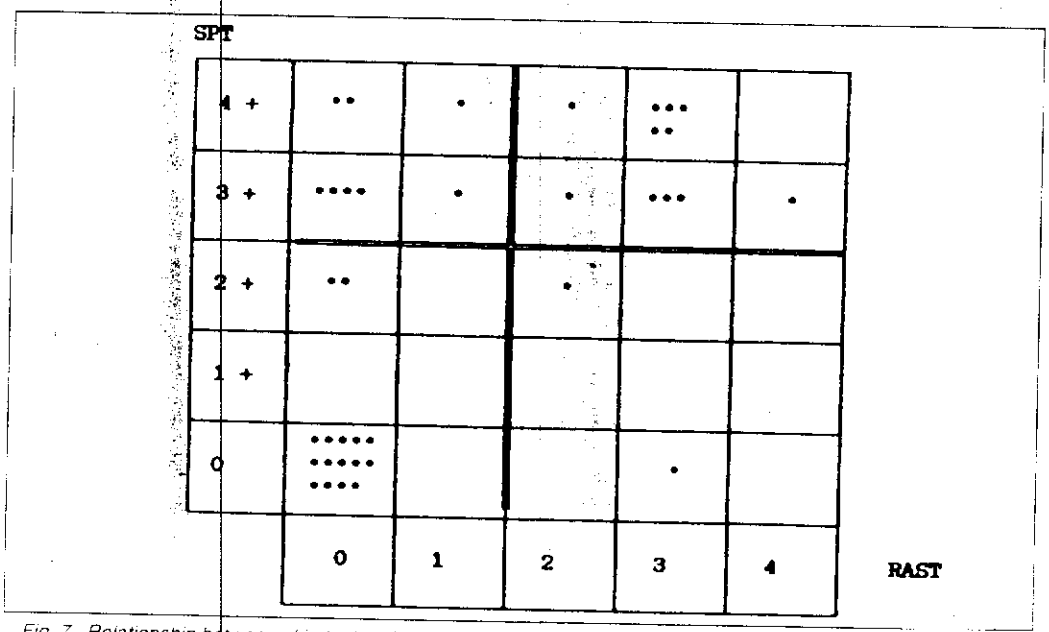

Fig. 7. Relationship between skin test and specific IgE level in Phoma allergy. n = 37; chi-square = 8.67; p < 0.01.

that polyallergic conditions are induced by fungi collaterally, but independently from each other. Indeed, our data show that *P. betae*-sensitive patients are polyallergized and generally present positive skin reactions to various fungi. Inconsistent with an incidental common allergen for *P. betae* and *A. alternata* is the fact that sensitivity has not increased in parallel, and that *P. betae* has shown a rapid expansion. However, this does not exclude the presence of a common allergen. For proving this hypothesis, detailed biochemical analysis of allergens is needed.

RESUMEN

Se trata de un estudio de la sensibilidad hacia hongos aerogénicos en estado de reproducción (espora, conidio) en niños asmáticos extrínsecos que viven en ambientes urbanos. Observamos que, según los test cutáneos, el 10,6% de los pacientes presentaban sensibilización hacia el hongo en 1977, mientras que en 1985 fueron el 30,4% y en 1987-88 fueron el 38,5%. Este aumento puede ser debido a una mayor frecuencia de sensibilización hacia Alternaria alternata y Phoma betae. En test cutáneos con alergenos de Bencard se observaron frecuentemente reacciones cruzadas. De los pacientes alérgicos a P. betae, el 83% presentaron también sensibilización hacia A. alternata, y el 87,5% de los alérgicos a A. alternata fueron también positivos a P. betae. La frecuencia de las reacciones cruzadas observada en test cutáneos y en determinaciones de IgE sugieren la presencia de un alergeno común o epítope. El efecto de los factores ambientales fue analizado con técnicas computarizadas. La sensibilización hacia P. betae no está relacionada con la aparición de moho, humedad o un número determinado de plantas de interior. Las condiciones de vida cambiaron en el periodo de estudio de la siguiente manera: mejoraron las condiciones en las viviendas, se utilizaron medidas tecnológicas de ahorro de energía y aumentó la polución, afectando también a la vegetación. Las esporas y los conidios se originan fundamentalmente a causa de mohos de plantas debilitadas por la contaminación ambiental.

Palabras clave: Alergia a hongos - *Phoma betae* - *Alternaria alternata* - Puntuación de síntomas asmáticos - Análisis computarizado

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