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THE ALLERGENS OF ASTHMA

(An analysis of more than 5000 cases)

By

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Contrary to what appears to be a widespread belief, clinical sensitivities in asthma can be many and varied and the single factor is very much the exception. In this study of 5,187 patients, the fact that multiple sensitivities are the rule appears to be strongly confirmed.

The patients were referred by physicians throughout the United Kingdom for allergic investigation, between 1956 and 1961. They were of all ages and from all walks of life. The causative factors were determined from a careful study of the case history, environment, family background, etc., as outlined in a previous communication and confirmed by skin tests with a view to allergic management by avoidance or by specific hyposensitisation.

METHODS AND MATERIALS

While many physicians tend to group asthmatics into psychological, infective and allergic types, all the patients in this study were regarded as having a fundamental basis of allergic sensitisation with the super-imposition of emotional or infective disorders in some, this standpoint being supported by observational diagnosis before reference by the physician concerned. It cannot be over-stressed that the anamnesis is of paramount importance and the skin test, the significance of which is still a matter of controversy amongst allergists, was used in this series merely to confirm factors actually brought under sus-

picion as a result of anamneses. Skin testing should be confined solely to allergens indicated by the case history (3), a procedure strictly adhered to in the present study.

There is also and too frequently, the habit amongst workers in the field of allergy to use groups containing mixtures of allergens, when employing the skin test as a diagnostic tool. This should be avoided, except in such cases as sensitivity to grass pollens, closely related moulds, etc. since careful investigation should indicate the individual causative factors with a reasonable degree of precision.

The patients were divided into arbitrary age groups of:—

<i>Years</i>	16-25
0-3	26-40
4-10	41-60
11-15	61 +

The factors responsible for the conditions investigated were grouped as:—

- I - Common Inhalant Allergens
- II - Pollens
- III - Moulds
- IV - Bacteria
- V - Foods
- VI - *Candida albicans*

The percentage of positive skin reactions was plotted against the age groups for both number and sex and Figures 1-6 show the results obtained for the six groups of allergens enumerated above. It should be noted that the tests undertaken were for individual allergens and that the results were subsequently placed in groups to render their presentation less complex.

The materials employed were the standard Bencard extracts and the intradermal method of testing was used except where it was judged that the patient was too young, when prick or modified prick tests were applied. In all cases where food allergens were indicated, the modified prick test was the procedure of choice and, for pollens, the direct prick or pressure puncture

test was invariably employed. Reactions at the test sites were assessed in relation to the reaction, if any, at the control site by the degree of erythema and wheal formation evident after twenty minutes.

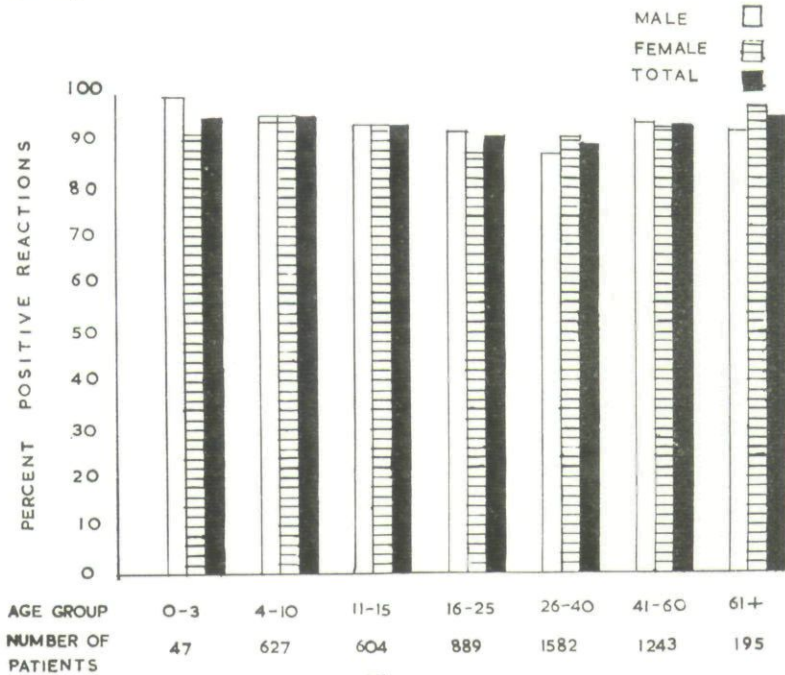


Fig. 1.

Group I Inhalants.

The factors commonly encountered in everyday life, that is, environmental allergens such as house dust, feathers, animal danders, wool, etc. were classified under the heading Common Inhalant Allergens (group I). It is interesting that one or more of these allergens was involved in 90 % or more of the total number of cases in each age group and that 100 % was reached in male infants of the 0-3 years group and almost 100 % of the females over 61 years of age. It will be noted, however, that the total numbers involved in both extremes is considerably less than in the intervening age groups. The overall percentage is consistently high in all age groups indicating the

extreme importance of common environmental inhalant allergens in the causation of allergic asthma.

There is a slight decrease in sensitivity evident which extends to the 26-40 years age group and thereafter climbs again to more than 90 % in patients over 61 years of age. This could reflect the more outdoor life indulged in by most people between adolescence and middle age, the peaks at each extreme representing the ages at which the individual is most house-bound. There is little, if any, difference in susceptibility between the sexes.

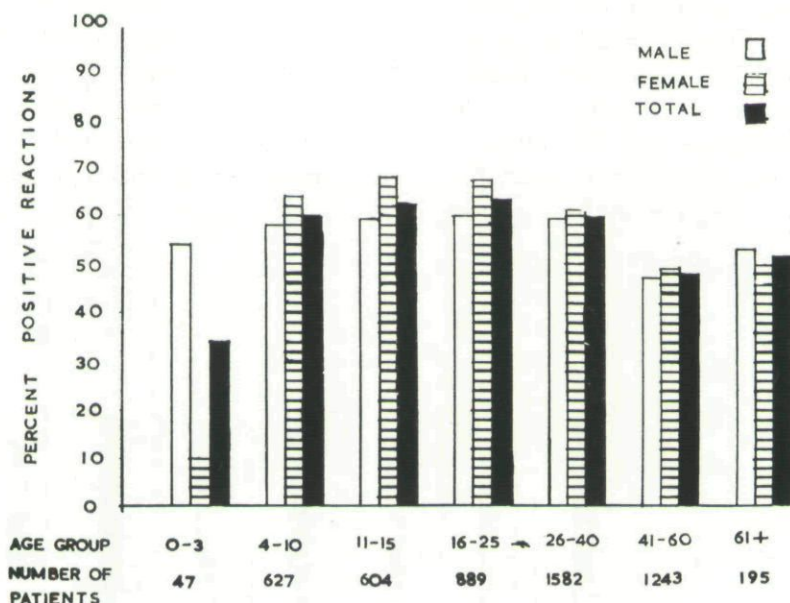


Fig. 2.
Group II Pollens.

Asthmatics affected by pollen can be placed in two categories:—

- 1) Those who experience difficulty only during the pollinating period.
- 2) Those whose perennial symptoms undergo seasonal exacerbation.

In Figure 2 it will be seen that all groups are affected, the highest peak being reached in the 16-25 year age group. Except in the extremes, females appear to be more susceptible than males but the discrepancy in the infant group is, in all probability, a sampling one.

The pollen cloud covers the country during six to eight weeks in the summer, the month of June being the peak period. Observation on the behaviour of perennial asthmatics during this season may well prove rewarding and proper allergic management for those who suffer an additional sensitivity to pollen should be instituted.

The average percentage of asthmatics with pollen involvement is somewhere in the region of 50% and many of these patients did in fact have hay fever and/or seasonal asthma as the basis for a condition which finally became perennial. In contrast to house dust, peak sensitivity is reached during the most active outdoor period of life.

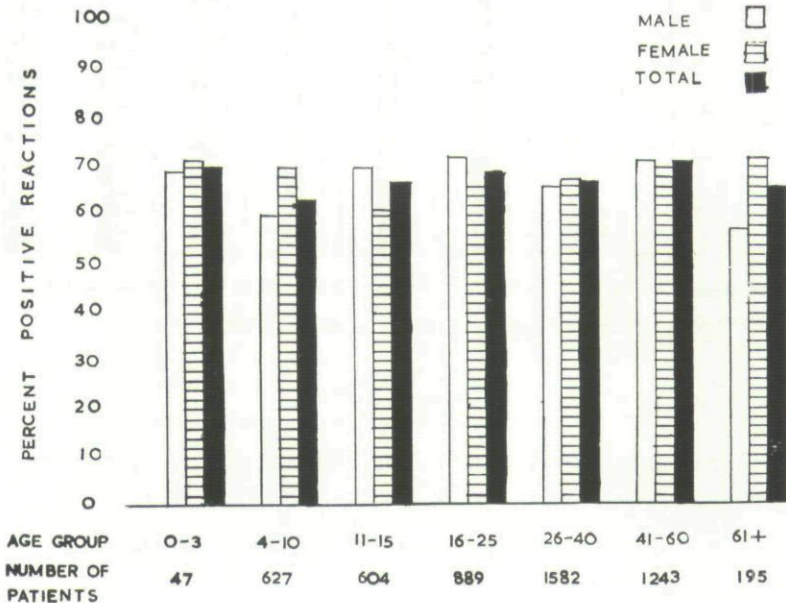


Fig. 3.
Group III Moulds.

The recognition that mould spores are important causative factors in allergic asthma is relatively recent and the incidence of sensitivity amongst those tested in this enquiry was high, reaching an average of about 65 %. (Fig. 3).

Moulds grow on any organic material and, since decay is universal, exposure of those with the allergic diathesis is inevitable. The degree of exposure is considerably modified by environment. While sporulation occurs throughout the year, the count is highest in a period roughly from July until September. Care must therefore be taken to ensure that mould and pollen sensitivities are not confused in the investigation of asthmatics whose symptoms undergo seasonal variation.

From this chart it will readily be appreciated that, in asthma of allergic origin, susceptibility to moulds is a factor to be borne in mind constantly.

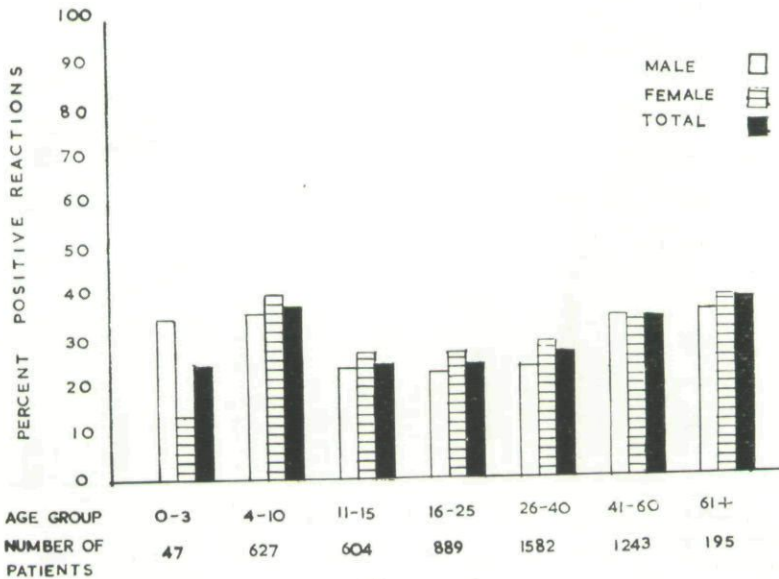


Fig. 4.
Group IV Bacteria.

The part that bacterial allergy plays in the production of atopic symptoms is a subject which has caused a great deal of

controversy amongst allergists. Discussion of this is not within the scope of the present study, the patients simply being tested with bacterial extracts where the case history indicated the necessity to do so. The pattern of the age incidence of bacterial sensitivity is found (Fig. 4) in the younger and older age groups, reaching a peak in the 4-10 year section, thereafter dropping steeply and rising slowly to attain a peak again in those over 60 years. The fact that infection, particularly respiratory infection, is common amongst the young and elderly makes the hypersensitivity pattern, as shown, extremely interesting. The remarkable incidence of immediate reaction in the 4-10 year age group suggests some connection between bacterial sensitisation and the ages between which nearly all the infectious diseases of childhood are experienced. This may well be worthy of more extensive investigation.

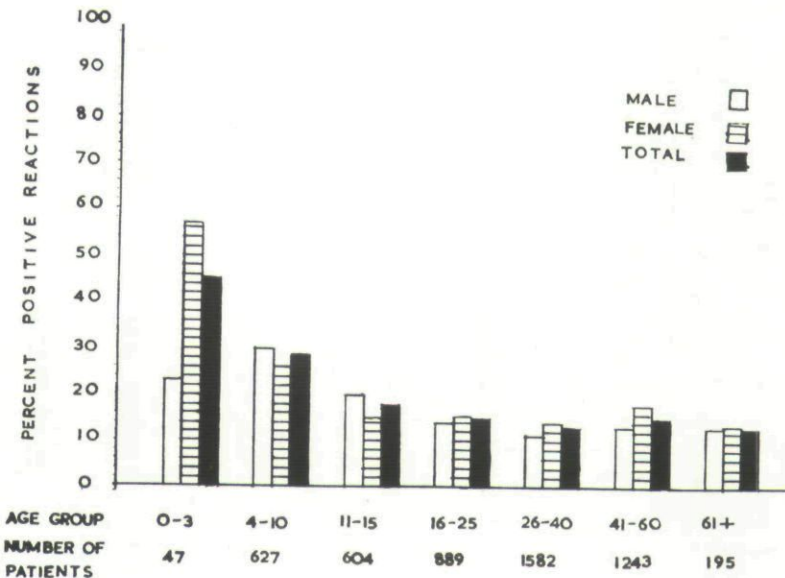


Fig. 5.
Group V Foods.

Foods may be responsible for practically any type of allergic manifestation, and age largely determines the incidence. In

the allergic infant, food allergens assume great importance but are later superseded by common inhalant allergens as the growing child follows the sequence of contact, exposure and sensitisation. Even if, in Figure 5, the high positive reaction rate for infants is accidental due to the small number of cases examined in this age group, there is still a steady downward trend from the 4–10 year group which culminates in a plateau from 16 years onwards.

When food allergy is a causative or contributory factor in asthma, the time between contact (ingestion) and symptoms is rather longer than is the case with inhalant allergy, reaction time being anything from half-an-hour to twenty-four hours, and it is considered that when the reaction time extends to several hours or more the sensitivity is to a product of partial digestion of the food concerned. *Rowe* (4) maintains that in 30–40 % of allergic patients the disease is caused exclusively by hypersensitivity to food. Food allergy may be “masked” in asthma, the history of frequent “colds” leading the investigator to concentrate on respiratory allergens. *Rowe* cites a study of 50 children whose asthma was due solely to food allergy and amongst whom 78 % had signs of “colds” at the onset of the attack.

From the present enquiry it would seem that from infancy through childhood, food allergy is likely to be an important factor in the causation of asthma, and beyond childhood the role played is a diminishing one which nevertheless must be borne in mind by the investigating physician.

The sixth group is very interesting as a study of the skin reaction pattern in asthmatics to the yeast-like fungus *Candida* (*Monilia*) *albicans*. Since the advent of the antibiotic era it has been recognised that such treatment tends to cause the replacement of the original infecting organism by another which is naturally resistant. *Candida albicans* is resistant to all antibiotics used in combatting bacterial infections and the widespread use of these, particularly the broad spectrum variety, favours proliferation of *Candida albicans* in the alimentary and

respiratory tracts, giving rise to thrush, intestinal disturbance, pruritus ani etc.

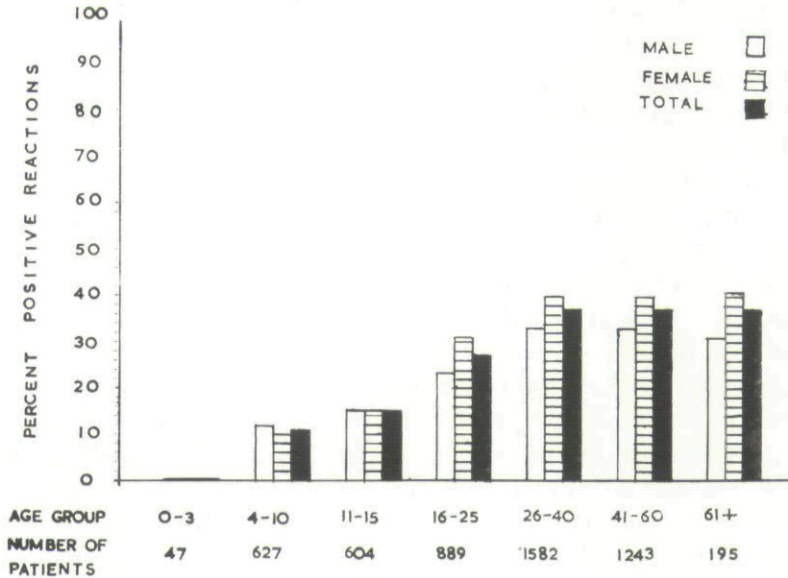


Fig. 6.

Group VI *Candida Albicans*.

Proliferation in its turn favours sensitisation in those with the allergic diathesis and skin testing was carried out in all patients whose history included prolonged antibiotic therapy. This test is particularly indicated in those cases in which the asthma becomes worse after antibiotic therapy.

The results show a jump from no incidence in infancy to about 10 % in childhood and thereafter a steady rise to about 38 % throughout adult life and old age. This accords well with the findings of *Charpin et al.* (1) who studied 1,131 subjects suffering from allergic conditions, mostly respiratory, for sensitivity to *Candida*. In their study, positive reactions were obtained in 431 subjects, a percentage of just over 38. *Lelong, Schlafer et al.* (2) however, found only 10.6 % of patients in their series sensitive to *Candida*. That this organism merits

more attention than it is usually given is evident from *Stenderup & Pederson's* statement (5) that they recovered *Candida albicans* from 68 % of pathological specimens submitted for mycological investigation.

It is not suggested that sensitivity to *Candida albicans* is a common single factor in respiratory allergy, although this is indeed sometimes the case, but in the middle-aged and elderly asthmatic who has a history of bouts of infection treated by antibiotics, and especially among those chronic infective cases on prophylactic antibiotic therapy, it would be wise to consider *Candida* as a super-added hazard.

DISCUSSION

There are many who believe that, while multiple sensitivities do exist in allergic individuals, a single major factor is usually responsible for the condition and that induced immunity is only possible with extracts of that particular allergen. Those who work in the field of allergy will acknowledge that house dust is probably the most significant single factor in chronic respiratory conditions of allergic origin, but from this study of a large group of asthmatics it is apparent that it is far from being the only one.

At our present stage of knowledge, hyposensitisation is the sole form of allergic management which attempts to deal fundamentally with the essential causes of allergic disease and, to be effective, it should be aimed at all the factors concerned and not at a single one, irrespective of its eminence. The identification of these factors depends upon a comprehensive, carefully taken case history and, in the event of the absence of positive, confirmatory skin tests, this should be accepted as a basis on which to apply a policy of elimination or avoidance, or to formulate a vaccine for specific treatment.

In view of the present findings and the large numbers of chronic asthmatics attending the out-patient departments of our hospitals, it would seem that a strong case exists for extending these observations. A large-scale investigation of such

patients by the methods outlined, together with treatment, where indicated, by immunisation with the relevant extracts and the whole combined with appropriate respiratory studies, should prove of great interest and reward to those who feel that more can be accomplished in this extensive section of respiratory disease.

SUMMARY

The causative factors in more than 5,000 cases of asthma are examined and the skin reaction patterns for six main types of allergens are presented.

We wish to thank Dr. *B. Dybas* and Sisters *J. Golson*, *D. Rimmel*, *M. Rogers*, *B. I. Uren* and *E. Wilson* for their help in the clinical work, and also Mr. *H. R. Quibell* for his work in checking the case records.

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