

Allergy in childhood asthma

J. O. WARNER, M.D.

Brompton Hospital, London, U.K.

INTRODUCTION

Bronchial hyperresponsiveness and allergy are seen as the two prerequisites for most asthma in childhood. However, the definition of asthma only incorporates the concept of bronchial hyperresponsiveness in stating that rapid variations in airflow limitation is the characteristic feature of the disease. However, bronchial hyperresponsiveness cannot explain the chronicity of the condition or the intense inflammatory response in the airways which is characteristic of more severe disease and is a typical finding of post mortem following asthma deaths. The hypothesis that allergy is fundamental to the disease will be discussed in this chapter.

Bronchial hyperreactivity

The degree of bronchial hyperreactivity correlates well with the severity of disease and is predictive of the therapeutic requirements for control of the disease (10). When asthma remits during adolescence the degree of bronchial hyperreactivity also changes (1). This suggests that the asthmatic state and bronchial hyperreactivity are closely related though not necessarily causally. Bronchial hyperreactivity can occur in non asthmatic conditions where inflammation of the airway is prominent, such as cystic fibrosis (12) and following viral respiratory tract infections (8).

Bronchial responses to agents such as methacholine or histamine have frequently been employed to study bronchial hyperreactivity and to investigate the value of various therapeutic

agents. However there are inconsistencies in the way such induced responses can be prevented or aborted by drugs in relation to the response by the same drugs clinically. Thus calcium antagonists block metacholine responses significantly, but sodium cromoglycate produces inconsistent responses. This is in contrast to the beneficial effects of sodium cromoglycate in clinical practice which has not been the case for inhaled calcium antagonists and a number of other sodium cromoglycate like compounds (3). Furthermore population studies in children utilising tests of hyperresponsiveness neither identify all asthmatics nor if abnormal reliably predict the presence of asthma (14).

Allergy

Asthma is one of the classical atopic diseases with a high frequency of first degree relatives with allergic problems. Positive allergy prick skin tests occur in 93% of asthmatic children beyond the age of 5 (13) and both raised total IgE levels and detectable IgE antibodies to allergens commonly occur (9). The presence of a raised total IgE at birth predicts a considerably increased risk of the development of asthma (5). The presence of allergy and atopic eczema in early childhood is associated with subsequently more severe asthma (11).

Direct bronchial challenge with allergen produces not only an immediate response but in up to 75% of asthmatics also a late reaction (15). The late reaction develops between 3 and 4 hours after allergen challenge and lasts for more than 12 hours. This late reaction is usually more severe than the immediate response and

its lung function characteristics are more similar to severe asthma than the immediate response. The presence of an immediate and late reaction is associated with more severe clinical disease (15). The late reaction responds to standard anti asthma therapies in a way that would be predicted from clinical responses. Thus bronchodilators are relatively less effective in relieving the air flow limitation whilst steroids and cromoglycates can be demonstrated to prevent the response. Thus the late reaction is probably associated with more than just bronchospasm and presumably is due to mucosal oedema and increased secretions involving small airways. In other words it mimicks severe disease. In addition late allergen induced bronchial reactions are associated with an enhancement of bronchial hyperreactivity (7). This is comparable to the clinical situation in pollen sensitive asthmatics who develop increased bronchial hyperreactivity during the course of the pollen season (4).

Primary allergen avoidance

Allergen avoidance as a preventive approach to asthma has not been properly investigated. There is some evidence that dietary manipulations may reduce the incidence of eczema (6). This is based on the premise that there are transient periods of susceptibility to sensitisation particularly in early infancy in association with immaturity of immune mechanisms. Indirect evidence suggests that aeroallergen avoidance in infancy might alter the incidence of asthma. Thus individuals born during the house dust mite season in the late Autumn and early Winter have greater likelihood of developing house mite sensitivity than individuals born at other times of the year (17). The same is true of pollen allergy and birth just before or during the pollen season (2). This suggests that aeroallergen avoidance in early infancy might reduce allergy and therefore asthma, but long term studies are required to establish this.

Secondary allergen avoidance

House dust mite sensitivity is the commonest allergy in asthmatics in most parts of the world

(16). Unfortunately attempts to reduce exposure to this agent have predominantly been a failure. Nevertheless admission of house mite sensitive childhood asthmatics to a high altitude school for 9 months where house dust mite exposure is minimal is associated with a progressive improvement in asthma and decrease in bronchial hyperreactivity (19). Thus avoidance of essential allergens can have a dramatic and fundamental effect on the condition.

Immunotherapy

Apart from allergen avoidance the only other specific therapy available is immunotherapy, sometimes known as hyposensitisation. There is good evidence of efficacy of hyposensitisation from double blind controlled trials for house dust mite sensitive asthma in childhood. One trial in moderately severe asthmatic children demonstrated considerable clinical benefit and a highly significant and large reduction in requirements for other standard anti asthma therapies comparing active with placebo groups. Whilst there was no effect on immediate skin or bronchial responses to house dust mite a significant number of the actively treated patients lost their late bronchial reactions after treatment and this did not appear in the placebo group.

The greatest clinical improvements occurred in those patients who had lost their late bronchial reaction (18). This observation establishes the importance of allergy in relation to asthma and indicates that the late rather than the immediate bronchial reactions is the principle factor in this relationship.

CONCLUSION

Thus it is clear from many studies that allergy is important both in the genesis and potentiation of asthma. However, it is equally clear that other factors and in childhood particularly viral infection are also involved.

Currently the most effective therapies for asthma will be administered irrespective of allergy status but this should not deter a search for underlying causes and this may indicate new approaches both to prevention and effective specific therapy.

REFERENCES

1. Balfour-Lynn, L., Tooley, M., Godfrey, S.: Relationship of exercise-induced asthma to clinical asthma in childhood. *Arch. Dis. Childhood* 56, 450-454, 1981.
2. Björkstén, F., Suoniemi, I., Koski, V.: Neonatal birch pollen contact and subsequent allergy to birch pollen. *Clin. Allergy* 10, 585-591, 1980.
3. Bonner, A. L., Vallone, G., Andreoli, A., Biancotto, R., Warner, J. O.: Nebulised sodium cromoglycate and verapamil in methacholine induced asthma. *Arch Dis Child* 62, 264-268, 1987.
4. Boulet, L. P., Cartier, A., Thomson, N. C., Roberts, R. S., Dolovich, J., Hargreave, F. E.: Asthma and increases in non-allergic bronchial responsiveness from seasonal pollen exposure. *J Allergy Clin. Immunol.* 71, 399-406, 1983.
5. Chandra, R. K., Puri, S., Cheema, P. J.: Predictive value of cord blood IgE in the development of atopic disease and role of breast feeding in its prevention. *Clin. Allergy* 15, 517-522, 1985.
6. Chandra, R. K., Puri, S., Suraiya, C., Cheema, P. S.: Influence of maternal food antigen avoidance during pregnancy and lactation on incidence of atopic eczema in infants. *Clin. Allergy* 16, 563-569, 1986.
7. Cockcroft, D. W., Ruffin, R. E., Dolovich, J., Hargreave, F. E.: Allergen-induced increase in non-allergic bronchial reactivity. *Clin. Allergy* 7, 503-513, 1977.
8. Empey, D. W., Laitinen, L. A., Jacobs, L., Gold, W. M., Nadel, J. A.: Mechanisms of bronchial hyperreactivity in normal subjects after upper respiratory tract infection. *Amer. Rev. Respir. Dis.* 113, 131-139, 1976.
9. Foucard, T.: A follow-up study of children with astmatoid bronchitis. 1 Skin test reactions and IgE antibodies to common allergens. *Acta Paediatr Scand* 62, 633-644, 1973.
10. Hargreave, F. E., Ryan, G., Thomson, N. C., O'Byrne, P. M., Latimer, K., Juniper, E. T., Dolovich, J.: Bronchial responsiveness to histamine or methacholine in asthma: measurement and clinical significance. *J. Allergy Clin. Immunol.* 68, 347-355, 1981.
11. McNichol, K. N., Williams, H. E.: Spectrum of asthma in children. 2. Allergic components. *Br. Med. J.* 4, 12-16, 1973.
12. Mellis, C. M., Levison, H.: Bronchial reactivity in cystic fibrosis. *Pediatrics* 61, 446-450, 1978.
13. Russell, G., Jones, S. P.: Selection of skin tests in childhood asthma. *Br. J. Dis. Chest.* 70, 104-106, 1976.
14. Sears, M. R., Jones, D. T., Holdaway, M. D., Hewitt, C. J., Flannery, E. M., Herbison, G. P., Silva, P. A.: Prevalence of bronchial reactivity to inhaled methacholine in New Zealand children. *Thorax* 41, 283-289, 1986.
15. Warner, J. O.: The significance of late reactions following bronchial challenge with house dust mite. *Arch. Dis. Child.* 51, 905-911, 1976.
16. Warner, J. O.: Mites and asthma in children (review article). *Br. J. Dis. Chest* 72, 79-87, 1978.
17. Warner, J. O., Price, J. F.: House mite sensitivity in childhood asthma. *Arch. Dis. Child* 53, 710-713, 1978.
18. Warner, J. O., Price, J. F., Soothill, J. F., Hey, E. N.: Controlled trial of hyposensitisation to *Dermatophagoides pteronyssinus* in children with asthma. *Lancet* 2, 912-915, 1978.
19. Warner, J. O., Boner, A. L.: Allergy and childhood asthma. *Clin. Immunol. and Allergy* 2, 217-229, 1988.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.