Atopy, allergy and the alimentary canal

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Atopic disease is most easily defined clinically as hayfever, asthma and eczema running through families. The term atopy was first used by Coca in 1923 (Coca & Cooke, 1923), although Maimonides had recognized the familial nature of asthma as long ago as 1100 AD.

EPIDEMIOLOGY OF ATOPY

Cooke & Van der Veer (1916) proposed a simple Mendelian dominant inheritance in atopic disease but this seems to be an oversimplification. If both parents are atopic there is a 40–60% risk of a child developing atopic disease; if one parent is atopic, a 25–35% risk and if one sibling is atopic, a 5–15% risk of a child developing atopic disease. Children with both parents having atopic symptoms usually have the onset of allergy early in infancy or childhood. This is less likely to happen in those whose allergic symptoms exist on only one side of the family and the latter children are more likely to present with allergic symptoms later on in life.

The prevalence of atopic disease varies in different parts of the world. It is quoted as affecting 17% of the population of the USA and in a recent survey of the Wycombe Health Authority population, 28% of the population claimed to suffer from one of the atopic diseases. There does seem to be little doubt that allergic diseases are on the increase in the UK. Asthma has been stated to triple in prevalence from the years 1946–1986 and over the same period of time, atopic eczema appears to have increased fivefold in prevalence in children (Editorial, 1986). This increase in allergic diseases appears to be a problem particularly in developed countries and is a product of our civilization. There is still some debate as to whether the actual prevalence is increasing or whether improved diagnosis is affecting figures of prevalence. The difficulty in obtaining information from the developing countries has also complicated assessment of the problem.

Nevertheless, there does seem good evidence that there is no racial difference in the prevalence of allergic diseases if groups are matched for social status and environment (Turner, 1987). Factors complicating matters are the move of populations from a stable, relatively allergen-free environment to a different, allergen-rich environment and the introduction of new allergens into previously stable societies.

One classic example of this phenomenon is the increase in the prevalence of asthma in the adult population of Papua New Guinea over the last decade. This is almost certainly due to the introduction of cotton sleeping blankets which encase the adult completely, are seldom washed and which harbour enormous numbers of the house-dust mite, *Dermatophagoides Pteronyssinus*. The patients with asthma have positive prick-test reactions to house-dust mite and the evidence is very strong that this increase in asthma is due to a modification to a traditional life style. Likewise, a dramatic increase in asthma in Kuwait since the mid-1950s appears almost certainly to be due to the importation of Prosopis trees.

The introduction of new food allergens is, of course, another distinct possibility as a cause for the increase in allergic disease and the import of new foods into a population or the move of predisposed individuals to a new environment with different food allergens are all potential causes of increase in allergic diseases.

ATOPY AS A NUTRIENT–GENE INTERACTION

There are, therefore, two major factors in considering atopic disease. First, the genetics of the atopic disorder and second, the environment in which the predisposed individual is exposed to possible allergens.

Exciting new work from Oxford suggests that genetic control of atopic disease is probably located on chromosome 11 (Cookson *et al.* 1989). It is hoped that future research will lead to identification of the responsible gene with the possibility of treating atopic disease at the genetic level in the future. The hallmark of atopic disease is the production of specific IgE antibodies to low-molecular-weight allergens of the inhalent or ingested variety. IgE production is under genetic control (Katz, 1980) and since the discovery of IgE in 1966, much work has been done on the immunogenetics of atopic disease. Measurements of total IgE and specific IgE antibodies to individual allergens, as in the radioallegosorbent test (RAST) are, however, not specific for atopic or other disease.

Food allergens commonly implicated in atopic disease include: cow's milk, eggs, wheat, fish/shellfish, peanuts, nuts, soya bean and citrus fruit. The food most commonly implicated as causing problems is cow's-milk protein. This is generally a transient occurrence in early childhood and may affect up to 7% of the population (Jakobsson & Lindberg, 1979). Most foodstuffs cause immediate Type 1, IgE-mediated reactions occurring within minutes of ingestion in atopic subjects. Many of these implicated foods may also cause contact urticaria with the development of a wheal within a few minutes of the offending food touching the skin surface. The food intolerances that are most likely to be transient in childhood are those of cow's-milk protein and egg. These are most commonly implicated in the aggravation of pre-existing atopic dermatitis. It is interesting that the incidence of soya-bean allergy has increased in the USA over the past decade where it has been used increasingly as a substitute for cow's milk. The next decade may show a similar increase in soya-bean allergy in the UK as we increasingly use it.

Fish, shellfish, peanut and nut allergies are commonly severe in nature, frequently causing severe and life-threatening reactions of urticaria, angioedema, pharyngeal and laryngeal oedema. Patients suffering from reactions of this severity should wear a Medic Alert bracelet, carry adrenaline for self-administration and be counselled as regards the severity of their condition. Unfortunately, fish and nut allergies of this severity tend to be persistent, whereas the milder reactions to cow's milk and eggs are more likely to be transient illnesses of childhood.

Food allergy, in cases where there is an immediate reaction to an uncommonly ingested allergen such as shellfish or brazil nuts, is easily diagnosed, often accepted and not reported medically by the patient, and is simply avoided for ever more. Many food problems may exist, however, as hidden allergies maintaining a stimulus to disease through lack of recognition. Unfortunately, as yet, there is no specific diagnostic test for a food allergen. Skin-prick tests and RAST blood tests are in no way specific and the only definite way to identify a food allergy, as yet, is by means of exclusion and subsequent

Table 1. *Food perceived as causing problems*

Food	Percentage of population reporting problem
Chocolate	6·7
Additives	5·3
Citrus fruits	3·5
Fish/shellfish	2·9
Milk	2·7
Cheese	2·5
Eggs	2·3
Meat	1·9
Nuts	1·7
Alcohol	1·4
Caffeine	1·3
Tomatoes	1·2
Non-citrus fruit	1·0
Wheat	0·9

challenge and this should be done in a double-blind placebo controlled manner. From a clinical point of view, this process is difficult, time-consuming and expensive. Nevertheless, it has to be pursued where food intolerance is truly suspected.

The entire field of food intolerance has been well reviewed in the excellent and comprehesive report by the Royal College of Physicians and the British Nutrition Foundation (1984). This report prompted our previous work on food additive intolerance (Young, 1987) and our current study of epidemiology of food intolerance. Preliminary results indicate that 20% of the UK population perceive a problem with foods. Those most commonly implicated are shown in Table 1. Chocolate is by far the commonest offender and its most common association is with migraine headache; the mechanism is most probably pharmacological rather than immunological in nature. Food additives have had a bad press but the problem has been vastly overestimated. Our recent study showed that 7·4% of the population in 1985 perceived a problem with food additives but after double-blind placebo controlled challenge studies the prevalence rate of reactions was shown to be in the range of 0·01–0·23% of the population. Interest in additives has since declined but they still remain a perceived cause of concern.

It is interesting to note that fish, milk, egg, nuts and wheat, foods we know commonly cause true IgE-mediated food allergy, affect so many of the population. These perceptions are currently being evaluated by means of double-blind placebo controlled challenge studies. Although there is a discrepancy between perception and true food intolerance, preliminary results indicate that it is much less than in the case of food additives and the problem of 'natural' food intolerance is much greater than that of 'artificial' additive intolerance.

The gastrointestinal tract is continuously exposed to a wide variety of food antigens. The two main defences are that of the gut-associated lymphoid tissue (GALT) and the production of secretory IgA antibodies. It is known that large antigenic food molecules can penetrate the immature neonatal human intestine in quantities of immunological importance in the first 3 months of life before the gut epithelium matures (Eastham *et al.* 1978). Protective IgA concentrations are also low during the first few months of life and

this may be particularly important in the pathogenesis of atopic disease (Taylor *et al.* 1973). Infants of an atopic family are particularly at risk of developing food allergy in the neonatal period because of these deficiencies in the gut defences.

MANAGEMENT OF ALIMENTARY ATOPIC DISEASE

Drug therapy, particularly the use of sodium cromoglycate and ketoifen as mast-cell stabilizers have, as yet, failed to provide effective relief for sufferers from food allergy. The only effective treatment for food allergy is the removal of a known food allergen from the diet.

Much work has been done in an attempt to prevent atopic disease by manipulating diet. It does seem to be the case that, if an infant predisposed to atopic disease is exclusively breast-fed, there is less likelihood of development of disease (Host *et al.* 1988). There is also evidence that breast-feeding may protect from atopy to some degree because of the high concentration of IgA in breast milk. Undoubtedly, however, in some severely atopic infants, maternally ingested food allergens can be transmitted via breast milk and the suggestion has, therefore, been made that the maternal diet during breast-feeding where atopy is suspected should also be manipulated to exclude common food allergens (Machtinger & Moss, 1989).

It has been suggested more recently that babies of women who have received food elimination in early pregnancy are less likely to develop allergic or atopic disease than in those mothers who have not manipulated their diet (Zieger *et al.* 1989).

Much work, however, remains to be done along these lines before significant and accurate advice can be given. What does seem practical, at present, to suggest is that the mother of a baby who is likely to develop atopic disease would be well advised to breast-feed and to avoid all artificial milk feeds in the first year of life, and that when introducing foods to her baby for the first time, she should choose those of low allergenicity and avoid introduction of the major known food allergens in the first year of life. In practice, this means dietary exclusion of cow's milk, eggs and wheat for the first 12 months.

Atopy is the most common genetic disease of Western society and seems to be on the increase. There are probably many factors responsible for this and much work remains to be done on the genetic and immunological side of the disease where, hopefully, further knowledge may lead to hope of prevention in the future. Our environment and its increasing complexity must remain a matter of concern until potential allergens can be recognized and thereby avoided or, alternatively, until an effective drug therapy is developed.

To conclude on an optimistic note it appears as if the next 10 years are going to provide a wealth of information on atopic disease. This increased knowledge will hopefully lead us closer to an effective therapy or cure.

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