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SYMPOSIUM ON 'FOOD ALLERGIES IN MAN'

Food allergy—fact or fiction?

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It is long established that one man's food is another man's poison, although it is only in very recent times that a serious attempt has been made to describe and quantify this phenomenon. Bender & Mathews (1981) found that in a sample of 580 adults, approximately two-thirds avoided one or more specific foods for a variety of reasons. Taste, texture, weight control and adverse physiological reactions were the major reasons for avoiding a wide range of food categories. One-third of respondents avoided foods because of an adverse physiological reaction, recording symptoms such as headache, nausea, vomiting, skin reaction, diarrhoea, indigestion and tremor. However, an adverse physiological reaction to a food does not necessarily imply allergy.

Forms of adverse reaction to food

There are four classes of adverse reaction to food; pharmacological, psychological, idiosyncratic and allergic. Finn & Cohen (1978) investigated six patients with long-standing physical and mental symptoms who were found by single-blind, intragastric challenge to show very strong reactions to either tea or coffee. The possibility of a metabolic defect leading to the accumulation of pharmacologically active compounds was discussed by the authors. That many of the symptoms encountered by a substantial number of food allergy sufferers are due to psychological factors is evident from the double-blind challenges of Atherton *et al.* (1978), Bock *et al.* (1979) and Brown *et al.* (1981). This subject has been recently reviewed (Bell & King, 1982). A small minority of individuals are required to avoid certain foods for idiosyncratic reasons, the two most celebrated being alactasia, a deficiency of intestinal lactase, and phenylketonuria, an inability

to metabolize phenylalanine. Finally, an unknown number, perhaps as much as 5% of the population, encounter adverse reactions to foods through immunological dysfunction. Such individuals are food allergic.

Immunological response to ingested antigens

An immunological response to ingested antigens should not be regarded as peculiar to food-allergic subjects. It is now well-established in many species that dietary macromolecules can traverse the gut intact, evoking an immediate, systemic, immune response and a localized (intestinal) secretory immune response. Thus, subsequent passage of the antigen is reduced by the presence of antigen-specific secretory IgA in the gut which, although effective, still permits some dietary macromolecules to enter circulation. There the antigen encounters its specific, systemic antibody (mostly IgG) with which it complexes for eventual removal from circulation by the reticulo-endothelial system. This subject has been extensively reviewed by Walker (1981).

That such an immune response is physiological is evident from the results of Gallagher *et al.* (1983). These authors found equal levels of circulating antibodies of the IgG, IgA and IgM classes to soya bean and cows' milk protein in healthy volunteers. This indicates that the frequency and amount of a protein consumed does not dictate the level of antibody to that protein in blood. These authors also recorded a post-prandial transient rise in total circulating immune complexes following meals containing egg and soya-bean protein. Food allergy represents a malfunction of one or more aspects of the immunological handling of ingested antigens and will be discussed elsewhere in this symposium.

Symptoms and their provocation in double-blind challenges

The adverse physiological reactions to foods can be placed in either of two categories. The first category includes those symptoms which would by most normal criteria require immediate medical attention, e.g. anaphylaxis, recurrent vomiting or diarrhoea, urticaria, eczema, asthma, etc. Adverse reactions of the second category are more prevalent and would not normally require urgent medical attention, i.e. indigestion, cramp, aches, pains, insomnia, mood change, itch, etc. For neither category of adverse reaction is there a single laboratory test or group of tests which would objectively establish food allergy. Thus Denman (1979) describes two cases, one demonstrating an adverse reaction to food on repeated challenge in spite of negative laboratory tests for allergy, the other demonstrating symptoms with placebo challenge. This highlights the essential role which double-blind food challenges must play in the diagnosis of food allergy.

Atherton *et al.* (1978) used a double-blind food challenge to investigate the hypothesis that infantile eczema could be due to an allergy to the proteins of egg or milk. Their results are summarized in Table 1. Although the allergen-free diet showed a significant increase in the relief from symptoms ($P<0.01$), seven out of the twenty children fell into the category of no change, or even deterioration. Similar results (Table 2) were obtained by Bock *et al.* (1979) with 171 children

who demonstrated 'an impressive history of an adverse reaction associated with the ingestion of one or more foods'. Symptoms could not be confirmed in almost 60% of this allegedly, albeit undiagnosed, food-allergic group. The foods reported to have caused adverse reactions were well-tolerated in a majority of the children when subsequently re-introduced into the normal diet. These results, together with those of Atherton *et al.* (1978), can be interpreted in several ways. It may be argued that the symptoms in those children who failed to respond to the antigen-avoidance diet were psychosomatic in origin. Secondly, it could be argued that different individuals will require different approaches to food challenge in order to verify symptoms. Perhaps, therefore, Bock *et al.* (1979) would have recorded a higher incidence of positive reactions had the allergen presentation been prepared differently, e.g. solution *v.* capsule, or had the frequency and duration of exposure been increased. Finally, it is possible that individuals will encounter a deterioration of symptoms on first undertaking an antigen-exclusion diet (Radcliffe, 1982).

Double-blind challenges have also been used to investigate adverse reactions to food in the polysymptomatic patient suffering one or more symptoms such as nausea, indigestion, muscle ache, insomnia, mood change, headache, etc. (Brown *et al.* 1979). The results of a recent, double-blind food challenge of polysymptomatic patients being treated for food allergy are given in Table 3 (E. Dauncey, M. J. Gibney, R. Husbands and M. Radcliffe, unpublished results). The severity of

Table 1. *The benefit of an egg- and milk-exclusion diet in atopic eczema under double-blind conditions* (n 20)†

	Control diet	Egg- and milk-free diet
Improvement	3	13
No change	11	6
Deterioration	6	1

Diet effect: $P<0.01$.
†From Atherton *et al.* (1978).

Table 2. *The effect of double-blind food challenge on the development of symptoms in children pursuing an antigen-exclusion diet*•

	Under 3 years	Over 3 years
Number	52	119
Confirmation of symptoms		
number	22	49
%	42	41
Total number of challenges	95	264
% Positive challenges	36	22

•From Bock *et al.* (1979).

Table 3. *The effect of double-blind food challenge on the onset and severity of symptoms in polysymptomatic patients*† (n 8)

	Allergen soup		Placebo soup
Total severity score‡	136		86
Rank sums	50	*$P<0.05$	30

*Friedman non-parametric analysis of variance.

†From E. Dauncey, M. J. Gibney, R. Husbands and M. Radcliffe, unpublished results.

‡Patients record the onset and duration of symptoms rated 0 (absent) to 5 (severe). This is followed by an independent panel evaluation of the patients' return using the following criteria:

	Score
No symptoms	1
Weak transient reaction	2
Weak persistent reaction	3
Strong transient reaction	4
Strong persistent reaction	5

reactions was found by non-parametric analysis of variance to be significantly reduced with placebo challenge as opposed to allergen challenge ($P<0.05$). Immunological investigations of these patients are currently in progress.

Nutritional implications of food avoidance diets

Brown *et al.* (1979), using the 7 d weighed inventory method, failed to find any evidence of a nutritional deficiency in food-allergic subjects pursuing an antigen exclusion diet. The patients on exclusion diets had a significantly lower intake of energy, fat, carbohydrate, calcium, magnesium and riboflavin ($P<0.05$) than age- and sex-matched controls. However, in neither group did the intakes of these nutrients fall below the recommended levels (Department of Health and Social Security, 1979). The same may not be true of infants where the nutrient requirements for a rapid growth phase are provided by a limited number of foods. Thus milk (cows' milk and infant milk formulae based on cows' milk) provides on average 31% total protein intake, 64% Ca intake, 48% riboflavin intake and 24% energy intake in infants aged 6–30 months (Department of Health and Social Security, 1975). Clearly, a milk-free diet which is not properly formulated could lead to serious nutritional deficiencies in infants.

Although the immunological advantages of breast-feeding are frequently stated, these advantages are limited, by and large, to secretory antibodies acting within the lumen of the gut (Bullen, 1981). Since a high proportion of samples of breast milk contain immunologically significant levels of common antigens (Table 4), it cannot be assumed that breast-feeding will protect an 'at-risk' child from exposure to an antigen and hence from developing symptoms.

Reducing the risk of infantile allergy is also a possibility. The probability of developing infantile eczema is twice as great in the offspring of atopic parents as opposed to non-atopic parents and to introduce solid feed before 4 months is to increase the probability of eczema by 50% (Ferguson *et al.* 1981). However, the

Table 4. *The incidence and maximum concentration of egg protein and soya-bean protein in human colostrum and mature breast milk**

	Colostrum		Mature milk	
	Negative	Positive	Negative	Positive
Egg protein				
Incidence	3	22	8	15
Maximum conc. (ng/100 ml)	—	100	—	100
Soya-bean protein				
Incidence	11	12	15	8
Maximum conc. (ng/100 ml)	—	570	—	50

*From J. Pitts, P. J. Gallagher, J. Morgan and M. J. Gibney, unpublished results.

same study showed that the incidence of eczema was similar in two groups of infants, one fed only on breast milk, the other on alternative milks. Clearly, the correct counselling of atopic mothers during pregnancy and lactation could lead to a reduced incidence of infantile allergens.

Conclusions

Conjecture and refutation represent the opposing forces responsible for the successful development of scientific theories (Popper, 1959). The problem with the theories of food allergy is that there has been excessive conjecture by, for example, the media or the authors of best-selling allergy-related paperback books, with inadequate refutation. In contrast, there has been some unwillingness by conventional medicine to entertain any worthwhile conjecture in this field of food allergy. Only in recent years has the study of food allergy enjoyed a limited scientific and clinical investigation which employs the proper process of conjecture and refutation from which, one hopes, the facts and fiction will eventually become unravelled.

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