# ADVANCES IN NUTRITIONAL RESEARCH

## VOLUME 7

Edited by Harold H. Draper

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# Preface

Volume 7 of *Advances in Nutritional Research* continues the theme of this series in providing authoritative accounts of the current state of knowledge regarding major topics of research in the nutritional sciences. The topics have been selected for their interest to researchers, students, and teachers in medicine, agriculture, and the various branches of the biological sciences which relate to nutritional health. The authenticity of the accounts is assured by the widely recognized contributions of the authors to research on their respective topics.

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Chapter 1

# Food Allergy

David J. Pearson and Alison McKee

## 1. Introduction

### 1.1. General Introduction

Food allergy can be responsible for a wide variety of diseases involving different, and sometimes multiple, organ systems. It is a relatively common cause of gastrointestinal symptoms in infants and children. In both adults and children, it can produce acute urticaria and chronic eczema in the skin, and asthmatic reactions in the lung. It has been incriminated in the generation of headache in some cases of migraine. Severe acute reactions may produce potentially fatal angioedema or anaphylactic shock, while the disability associated with its more chronic manifestations can lead indirectly to considerable disruption of personal or social functioning.

The literature concerning food allergy can be very confusing. This is due, in part, to different usages of terminology and, in part, to the history of the subject. Although it is plain that many valid observations were included within early reports, it is equally clear that the subject was bedevilled by bias, overconfidence in clinical impressions, misinterpretation of diagnostic tests, and a failure to appreciate the power of the placebo effect (May, 1982). In recent years, the use of double-blind feeding tests has stimulated a more objective approach. Such experiments, with modern information concerning immunologic mechanisms, enable us to reassess several attitudes concerning food allergy and the place of tests in its diagnosis.

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Recently, it has also become increasingly clear that immunologic mechanisms are only one means by which reactions can occur. Some of these non-allergic processes can produce results which mimic the effects of recognized immunologic disease and have, therefore, been described as pseudo-allergic, or anaphylactoid. Both types of mechanisms can be responsible for symptom exacerbations in the same individual, a situation which is quite common in conditions such as asthma. There seems little doubt that the relative frequency of anaphylactoid reactions has been an important cause of confusion in the investigation of allergic disease.

The term "allergy" was introduced to describe altered reactivity, whether protective or detrimental, secondary to a previous exposure to the same substance (Von Pirquet, 1906). Some immunologists therefore apply the term to any immunologic response, in contrast to many lay people who use it to describe any undesirable reaction. Some recent clinical reviews have suggested restricting allergy to describe IgE-mediated reactions alone (McCarty and Frick, 1983). However, as a result of its long-term clinical usage, many clinical immunologists prefer to apply "allergy" to adverse reactions in which there is clear evidence for any form of immunologic etiology. Other terms are also used with different shades of meaning. Differences in usage are notable between clinical and non-clinical, and pediatric and adult literature, and between the two sides of the Atlantic. For example, "sensitivity" and "hypersensitivity" have been used both to describe adverse reactions of immunologic and indeterminate etiology (in the former usage often being qualified as in immediate-hypersensitivity, reaginic sensitivity, etc.). In the pediatric literature in particular, "intolerance" is used to describe either non-immunologically mediated reactions or organic reactions of uncertain cause. The problem with this last term is that, at least in adults, the most common cause of failure to tolerate a specific food is almost certainly psychological rather than organic disease (Lessof, 1983).

## 1.2. Classification of Adverse Reactions to Foods

In the absence of generally accepted, precise terminology, we must stress that the classification of adverse reactions shown in Fig. 1 depends upon our personal definitions of each of the terms. We define as *usual (or toxic) reactions* those reactions which occur in virtually all individuals ingesting a sufficient quantity of a particular substance. These include responses to toxins and the effects of pharmacological agents (caffeine in coffee, etc.).

*Unusual reactions* are those which occur in only some individuals who react adversely to substances which are eaten without ill-effect by most of the population. We prefer to use *intolerance* to describe this situ-

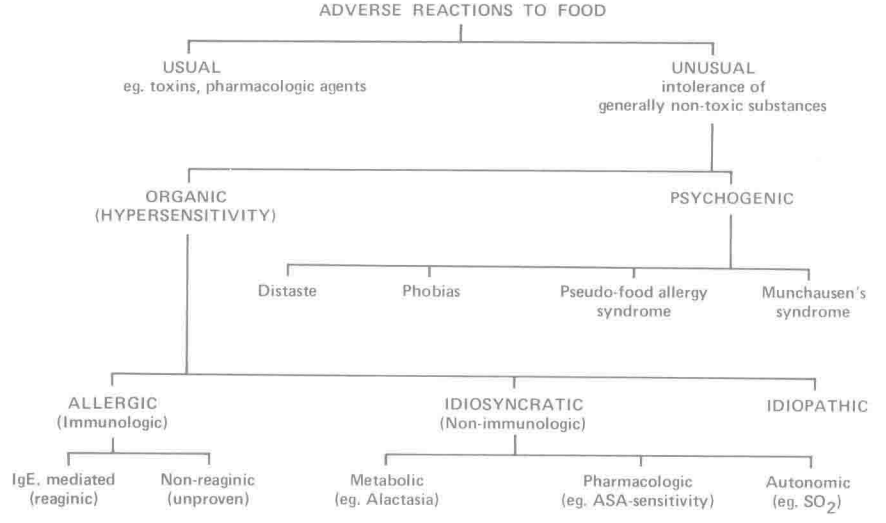


Fig. 1. Classification of adverse reactions to food.

ation and subdivide it into psychogenic and organic. However, we recognize that many authors imply an organic etiology by the non-qualified use of the word intolerance, and prefer to continue to use the descriptive term, e.g., "cow's milk protein intolerance" and "lactose intolerance" for these well-defined organic entities.

We use *hypersensitivity* synonymously with organic intolerance and define it as an organic host-damaging reaction which is qualitatively different from, or quantitatively greater than, the effects that the same dose of that substance would have on the generality of the population. This definition has no implications as to the mechanism of the reaction and it can, therefore, be qualified as allergic (immunologic) or non-allergic (non-immunologic). Because of its wide usage, we continue to use the term *food allergy* for adverse reactions to food in which there is evidence of an immunologic etiology, i.e., allergic food hypersensitivity. This can be further subdivided according to the immunologic process. IgE-mediated hypersensitivity is the only immunologic mechanism whose etiologic role has been demonstrated convincingly in adverse reactions to food to date, but the occurrence of other types of allergic reaction seems probable.

We retain *idiosyncrasy* for non-immunologic reactions to food which are peculiar to only certain individuals and which can be attributed to the metabolic or pharmacological properties of the inciting substances, e.g., the response to lactose in alactasia. A group of reactions in which the mechanism is unknown must be classified as *idiopathic*. We describe as

*anaphylactoid*, non-allergic organic reactions whose clinical features resemble those of classical IgE-mediated allergy.

Psychogenic food intolerance can be due to simple distaste or to overt phobia. We have applied the term *pseudo-food allergy* to a clinical syndrome in which patients with common psychiatric disorders come to attribute their problems to food allergy in the absence of any objective evidence of organic intolerance. Patients have also been described who have deliberately simulated allergic manifestations in themselves or their children: Munchausen's syndrome and Munchausen's syndrome by proxy (Hendrix *et al.*, 1981).

## 1.3. Classification and Time Course of Allergic Reactions

Further confusion in the field of allergy is also generated by the use of the same words to define specific types of allergic reaction and as general clinical descriptive terms, and by the use of different words to describe identical clinical observations.

Coombs and Gell (1963) have classified all immunologic (allergic) reactions into four types (I to IV). The classification of Types I to III depends on whether antigen or antibody is cell-fixed or in solution. Type IV is cell-mediated and is typified in the skin by responses such as the tuberculin reaction which develops macroscopically over 36–48 hr and lasts for 72–96 hours. This is the classical delayed hypersensitivity reaction.

Type I reactions are those in which antibody is attached to the surface of a mast cell. Contact with antigen in solution results in release of the soluble mediators of anaphylaxis, producing in the skin the typical immediate weal and flare reaction. This commences within minutes of antigen administration, is maximal after 15–20 min, and is usually no longer detectable macroscopically after 1 hour. In humans, most immediate hypersensitivity is produced by antibodies of the IgE-class. However, in many animal species, similar reactions are commonly produced by IgG subclass antibodies. There is also some evidence that immediate-type reactions also can be produced occasionally in humans by non-reaginic IgG subclass antibodies (Parish, 1970).

Type II reactions are due to antibody in solution reacting to cell surface or membrane-associated antigens which may be an integral part of the structure or absorbed onto it. Membrane damage usually follows subsequent activation of the complement cascade. Immune damage to jejunal cells following non-specific binding of gliadin is one of several mechanisms postulated as occurring in coeliac disease.

Type III reactions occur when antigen and antibody in solution combine to form immune complexes. Inflammation, often with damage to