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Abbreviations

AAA Action Against Allergy

ACE angiotensin converting enzyme

ADSA Association for Dietitians in South Africa

ALBA Dutch Food Intolerance Databank

BAF British Allergy Foundation

BCA bicinhoninic acid

BDA British Dietetic Association
BHA butylated hydroxyanisole
BHT butylated hydroxytoluene
BRC British Retail Consortium

CCP critical control point CMA cow's milk allergy

DBPCFC double-blind placebo-controlled food challenge

DNA deoxyribonucleic acid

EAACI European Academy of Allergology and Clinical Immunology

EC European Commission

EFID European Food Intolerance Databanks

EFLA European Food Law Association eHF extensively hydrolysed formula ELISA enzyme-linked immunosorbent assay

EU European Union

FARRP Food Allergy Research and Resource Program

(University of Nebraska)

FCAA Food and Chemical Allergy Association

FCPMC Food and Consumer Products Manufacturers of Canada

FDA (US) Food and Drug Administration

xii Abbreviations

FDF Food and Drink Federation

FEIA fluorescent enzymatic immunoassay
FEV1 forced expiratory volume in 1 second
FIDB Food Intolerance Databank (South Africa)

FLAG Food Labelling Agenda

FLEP Food Law Enforcement Practitioners

FSA Food Safety Act

GMP Good Manufacturing Practice

GP general practitioner

GPSR General Product Safety Regulations

HACCP hazard analysis and critical control points

HF hydrolysed formula

HLA human leucocyte antigen

Ig immunoglobulin

JECFA Joint Expert Committee on Food Additives

LIVO National Information Centre for Food Hypersensitivity

(Netherlands)

MAFF Ministry of Agriculture, Fisheries and Food

ME myalgic encephalomyelitis
NHS National Health Service
OAS oral allergy syndrome

PARNUT food for particular nutritional use

PEFR peak expiratory flow rate pHF partially hydrolysed formula

RA Research Association
RAST radioallergosorbent test
RCP Royal College of Physicians

RIA radioimmunoassay RNA ribonucleic acid SPT skin prick test

TEI Technological Educational Institution Thessaloniki

TGF transforming growth factor

Th T-helper

TNO Netherlands Organisation for Applied Scientific Research

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Introduction

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1.1 Background

The documentation of food intolerance goes back to 55 BC when Lucretius, a distinguished Latin poet and philosopher, wrote his poem *De Rerum Natura* (On the Nature of Things) and said 'What is food for some, may be fierce poison for others'.

Hippocrates recognised the adverse effects of milk on some individuals when he noted:

Cheese does not harm all men alike; some can eat their fill of it without the slightest hurt. ... Others come off badly. So the constitutions of these men differ, and the difference lies in the constituent of the body which is hostile to cheese, and is roused and stirred to action under its influence. ... But if cheese were bad for the human constitution without exception, it would have hurt all.

In 1808 Robert Willan described a case where a severe allergic reaction was provoked by eating a small amount of almonds:

These symptoms were soon followed by an oedematous swelling of the face, especially of the lips and nose, which were very hot and itchy. There was at the same time an uneasy tickling sensation in the throat, which excited a troublesome cough and a constriction of the fauces, which seemed to threaten suffocation. The tongue, likewise, became enlarged and stiff, causing slowness and faltering in the speech. Soon after going to bed an eruption took place over the whole body of spots nearly as large as a sixpence, of a dead white colour, a little elevated above the skin, like weals produced by the sting of a nettle, and intolerably itching.

There are many such anecdotes in medical history literature. What is noteworthy is that, unlike most other disciplines where scientific research starts soon after such anecdotes, in the food intolerance area there has been a large gap between the case reports and scientific investigation of the field. This has created opportunities for many people to blame food intolerance for a wide range of unexplained disorders, and for many years food intolerance was regarded to be on the fringe of scientific enquiries. The fact that for decades the diagnosis of food intolerance relied mainly on clinical history created many opportunities for individuals and groups offering all sorts of unscientific and bizarre tests for diagnosis of food intolerance. It is only fairly recently, with the introduction of double-blind placebo-controlled food challenges, that opportunities for more scientific approaches have been created and research into this area has provided us with good quality evidence.

Just as high quality research evolved in the midst of anecdotes, the terminology in this field also evolved, and terms such as food hypersensitivity, food intolerance, food allergy and adverse reactions to food are used at times interchangeably. In the next section, some of these terms are described in more detail.

1.2 Terminology

When reading different texts in this area, it becomes evident that in the medical and scientific community, there is no single global consensus on what is food allergy and what is food intolerance. For example, there are authorities who consider coeliac disease as a type of food allergy and others who regard it as a form of food intolerance. Some may not consider it as either. Indeed, it appears that it all depends on what definition one has used. The terminology which appears to have gained credibility amongst many peers is that adopted by the European Academy of Allergology and Clinical Immunology (EAACI). The distinguishing feature of this terminology is that it is based on mechanisms rather than clinical symptoms. The structure of this terminology is outlined in Fig. 1.1. Broadly, adverse reactions are divided into toxic and non-toxic reactions.

1.2.1 Toxic food reactions

In principle, these are reactions which could occur in any individuals if the dose is high enough to trigger a reaction. They are usually caused by direct action of food components without involvement of immune mechanisms. Toxic compounds which trigger such reactions can occur naturally, such as from eating a puffer fish complete with its poison sac! Or they can be contaminants of food. Although such reactions are fairly distinguishable from non-toxic food reactions in terms of mechanism, one has to be careful when diagnoses are made, since some of the symptoms may be similar.

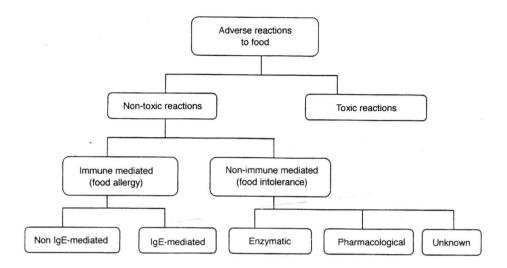


Fig. 1.1 Classification of adverse reactions to food.

1.2.2 Non-toxic food reactions

These reactions are either immune-mediated or non-immune-mediated. When the reaction is immune-mediated the term 'food allergy' is applied, and when non-immune-mediated the term 'food intolerance' is recommended. Both types of reactions are reproducible and depend on an individual's susceptibility.

Food allergy

Food allergy itself can be subdivided into two categories, IgE-mediated food allergy and non-IgE-mediated food allergy (Fig. 1.1). Immunoglobulin (Ig) E, or IgE, is the main antibody involved in induction of immediate allergic reactions. Most of the research evidence available on food allergy has been focused on IgE-mediated food allergy. Indeed, most common food allergies are mediated by IgE antibodies. The mechanism underlying IgE-mediated food allergy is fairly well established. Symptoms of this form of food allergy appear rapidly, are varied and range from anaphylaxis to skin reactions.²

Non-IgE-mediated food allergy is less well understood. Such allergies include reactions involving other immunoglobulin isotypes such as IgG and its subclasses, food immune complexes and cell-mediated immunity. Diagnosing this form of food allergy has been difficult and none of the above-mentioned mechanisms have been proven to be causative by double-blind, placebo-controlled food challenges (DBPCFC).