# FOOD ALLERGY

## Adverse Reactions to Foods and Food Additives

Edited by Dean D. Metcalfe,
Hugh A. Sampson and Ronald A. Simon

FOURTH EDITION

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# Food Allergy

## Adverse Reactions to Foods and Food Additives

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Food Allergy

We dedicate this edition to our wives and children who have supported and encouraged (and tolerated) our career interests; and to the many dedicated investigators who are helping those with adverse reactions to foods and additives.

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# Preface

It is the privilege of the editors to present the fourth edition of Food Allergy: Adverse Reactions to Foods and Food Additives. As in the first three editions, we have attempted to create a book that in one volume would cover pediatric and adult adverse reactions to foods and food additives, stress efforts to place adverse reactions to foods and food additives on a sound scientific basis, select authors to present subjects on the basis of their acknowledged expertise and reputation, and reference each contribution thoroughly. The growth in knowledge in this area continues to be gratifying, and is reflected in the increased length of this edition. Again this book is directed toward clinicians, nutritionists, and scientists interested in food reactions, but we also hope that others interested in such reactions will find the book to be a valuable resource.

The chapters cover basic and clinical perspectives of adverse reactions to food antigens; adverse reactions to food additives; and contemporary topics. The number of chapters addressing these areas has been increased from 29 chapters in the first edition, 38 chapters in the second edition, and 42 chapters in the third edition, to 47 chapters in the fourth edition. Basic science begins with overview chapters on immunology of particular relevance to the gastrointestinal tract as a target organ in allergic reactions and the properties that govern reactions initiated at this site. Included are chapters relating to biotechnology and to thresholds or reactivity. This is followed by chapters reviewing the clinical science of adverse reactions to food antigens from the oral allergy syndrome to anaphylaxis. The section on diagnosis of adverse reactions to foods constitutes a review of the approaches available for diagnosis; and their strengths and weaknesses. Adverse reactions to food additives include chapters addressing specific clinical reactions and reactions to specific agents. The final section on contemporary topics includes discussions of the pharmacologic properties of food, the history and prevention of food allergy, diets and nutrition, neurologic reactions to foods and food additives, psychological considerations and adverse reactions to seafood toxins.

Each of the chapters in this book is capable of standing alone, but when placed together they present a mosaic of the current ideas and research on adverse reactions to foods and food additives. Overlap is unavoidable but, we hope, is held to a minimum. Ideas of one author may sometimes differ from those of another, but in general there is remarkable agreement from chapter to chapter. We, the editors, thus present the fourth edition of a book that we believe represents a fair, balanced, and defensible review of adverse reactions of foods and food additives.

*Dean D. Metcalfe*
*Hugh A. Sampson*
*Ronald A. Simon*

# Abbreviations

| | |
|---|---|
| AA | Arachidonic acid |
| AAF | Amino acid-based formula |
| AAP | American Association of Pediatrics |
| ACCD | 1-Aminocyclopropane-1-carboxylic acid deaminase |
| ACD | Allergic contact dermatitis |
| AD | Atopic dermatitis |
| ADA | Americans with Disabilities Act |
| AE | Atopic eczema |
| AEC | Absolute eosinophil count |
| AERD | Aspirin exacerbated respiratory disease |
| AFP | Antifreeze protein |
| AGA | Anti-gliadin antibodies |
| AI | Adequate intake |
| ALA | Alimentary toxic aleukia |
| ALDH | Aldehyde dehydrogenase |
| ALS | Advanced Life Support |
| ALSPAC | Avon Longitudinal Study of Parents and Children |
| AMDR | Acceptable Macronutrient Distribution Ranges |
| AMP | Almond major protein |
| APC | Antigen-presenting cell |
| APT | Atopy patch test |
| ASCA | Anti-Saccharomyces cerevisiae |
| ASHMI | Anti-asthma Herbal Medicine Intervention |
| ASP | Amnesic shellfish poisoning |
| AZA | Azaspiracid |
| AZP | Azaspiracid shellfish poisoning |
| BAL | Bronchoalveolar lavage |
| BAT | Basophil activation test |
| BCR | B-cell receptor |
| BER | Bioenergy regulatory |
| BFD | Bioelectric functions diagnosis |
| BHA | Butylated hydroxyanisole |
| BHR | Basophil histamine release |
| BHT | Butylated hydroxytoluene |
| BLG | β-lactoglobulin |
| BMI | Body mass index |
| BN | Brown–Norway |
| BP | Blood pressure |
| BPRS | Brief Psychiatric Rating Scale |
| BTX | Brevetoxins |
| CAS | Chemical Abstract Society |
| CCD | Cross-reactive carbohydrate determinants |
| CCP | Cyclic citrullinated peptide |
| CDC | Centers for Disease Control and Prevention |
| CFA | Chemotactic factor of anaphylaxis |
| CFR | Code of Federal Regulations |
| CGRP | Calcitonin gene-related peptide |
| CIU | Chronic idiopathic urticaria |
| CIUA | Chronic idiopathic urticaria/angioedema |
| CLA | Cutaneous lymphocyte-associated antigen |
| CLSI | Clinical and Laboratory Standards Institute |
| CM | Cow's milk |
| CMA | Cow's milk allergy |
| CMF | Cow's milk formula |
| CMP | Cow's milk protein |
| CMV | Cucumber mosaic virus |
| CNS | Central nervous system |
| COX | Cyclo-oxygense |
| CRH | Corticotropin-releasing hormone |
| CRP | C-reactive protein |
| CRS | Chinese restaurant syndrome |
| CSPI | Center for Science in the Public Interest |
| CSR | Class-switch recombination |
| CTL | Cytotoxic T-lymphocyte |
| CTX | Ciguatoxins |
| CU | Cholinergic urticaria |
| DAO | Diamine oxidase |
| DBPC | Double-blind, placebo-controlled |
| DBPCFC | Double-blind, placebo-controlled food challenge |
| DC | Dendritic cell |
| DHA | Docosahexaenoic acid |
| DMARD | Disease modifying anti-rheumatic agent |
| DoH | Department of Health |
| DRI | Dietary reference intakes |
| DSP | Diarrhetic shellfish poisoning |
| DTH | Delayed-type hypersensitivity |
| DTT | Dithiothreitol |
| DTX | Dinophysistoxins |
| EAR | Estimate average requirement |
| EAV | Electroacupuncture according to Voll |
| ECP | Eosinophil cationic protein |
| EDN | Eosinophil-derived neurotoxin |
| EDS | Electrodermal screening |

| | |
|---|---|
| EE | Eosinophilic esophagitis |
| EEG | Electroencephalogram |
| EER | Estimated energy requirement |
| EFA | Essential fatty acid |
| EFSA | European Food Safety Authority |
| EGID | Eosinophil-associated gastrointestinal disorders |
| EIA | Enzyme immunoassay |
| ELISA | Enzyme-linked immunosorbent assays |
| EMA | Anti-endomysial |
| EMT | Emergency Medical Technical |
| EoE | Eosinophilic esophagitis |
| EoG | Eosinophilic gastroenteritis |
| EoP | Eosinophilic proctocolitis |
| EPA | Eicosapentaneoic acid |
| EPO | Eosinophilic peroxidase |
| EPSPS | Enzyme 5-enolpyruvylshikimate-3-phosphate synthase |
| EPX | Eosinophil protein X |
| ESR | Erythrocyte sedimentation rate |
| FAAN | Food Allergy & Anaphylaxis Network |
| FAE | Follicle-associated epithelium |
| FAFD | Food-additive-free diet |
| FALCPA | Food Allergen Labeling and Consumer Protection Act |
| FAO | Food and Agricultural Organization |
| FASEB | Federation of American Societies for Experimental Biology |
| FDA | Food and Drug Administration |
| FDDPU | Food-dependent delayed pressure urticaria |
| FDEIA | Food-dependent exercise-induced anaphylaxis |
| FEC | Food-and-exercise challenge |
| FEIA | Fluorescent-enzyme immunoassay |
| FFQs | Food Frequency Questionnaires |
| FFSPTs | Fresh food skin prick tests |
| FPIES | Food protein-induced enterocolitis syndrome |
| FSIS | Food Safety Inspection Service |
| GALT | Gut-associated lymphoid tissue |
| GBM | Glomerular basement membrane |
| GER | Gastroesophageal reflux |
| GERD | Gastroesophageal reflux disease |
| GFD | Gluten-free diet |
| GH | Growth hormone |
| GHRH | Growth hormone releasing hormone |
| GI | Gastrointestinal |
| GINI | German Infant Nutritional Interventional |
| GOX | Glyphosate oxidoreductase |
| GrA | Granzymes A |
| GRAS | Generally recognized as safe |
| GrB | Granzymes B |
| GRS | Generally regarded as safe |
| GSH | Glutathione |
| GVHD | Graft-versus-host disease |
| HACCP | Hazard analysis and critical control point |
| HAQ | Health Assessment Questionnaire |
| HBGF | Heparin-binding growth factors |
| HCN | Hydrogen cyanide |
| HE | Hen's egg |
| HEL | Hen's egg lysozyme |
| HEV | High endothelial venules |
| HKE | Heat-killed *Esherichia coli* |
| HKL | Heat-killed *Listeria monocytogene* |
| HKLM | Heat-killed *Listeria monocytogenes* |
| HLA | Human leukocyte antigen |
| HMW | High molecular weight |
| HNL | Human neutrophil lipocalin |
| HPF | High-powered field |
| HPLC | High-performance liquid chromatography |
| HPP | Hydrolyzed plant protein |
| HRFs | Histamine releasing factors |
| HRP | Horseradish peroxidase |
| HSP | Hydrolyzed soy protein |
| HVP | Hydrolyzed vegetable protein |
| IAAs | Indispensable amino acids |
| ICD | Irritant contact dermatitis |
| IDECs | Inflammatory dendritic epidermal cells |
| IEC | Intestinal epithelial cells |
| IEI | Idiopathic environmental intolerances |
| IgA | Immunoglobulin A |
| IgE | Immunoglobulin E |
| IgG | Immunoglobulin G |
| IgM | Immunoglobulin M |
| ISB | Isosulfan blue |
| ISS | Immunostimulatory sequences |
| IST | Intradermal skin test |
| ITAM | Immunoreceptor tyrosine-based activation motif |
| ITIM | Immunoreceptor tyrosine-based inhibitory motif |
| IUIS | International Union of Immunological Societies |
| JECFA | Expert Committee on Food Additives |
| KA | Kainic acid |
| KGF | Keratinocyte growth factor |
| KLH | Key-hole limpet hemocyanin |
| LA | Linoleic acid |
| LCPUFA | Long-chain polyunsaturated fatty acids |
| LCs | Langerhans cells |
| LFI | Lateral flow immunochromatographic |
| LGG | Lactobacillus rhamnosus GG |
| LLDC | Langerhans-like dendritic cell |
| LMW | Low molecular weight |
| LOAELs | Lowest observed adverse effect level |
| LOX | Lipoxygenase |
| LP | Lamina propria |
| LPL | LP lymphocytes |
| LPS | Lipopolysaccharide |
| LRTIs | Lower respiratory tract infections |
| LSD | Lysergic acid diethylamide |
| LT | Leukotrienes |
| LTP | Lipid-transfer protein |
| MALDI | Matrix-assisted laser desorption/ionization |

| | |
|---|---|
| MALT | Mucosa-associated lymphoid tissue |
| MAO | Monoamine oxidase |
| MAPK | Mitogen-activated protein kinase |
| MAS | Multicenter Allergy Study |
| MBP | Major basic protein |
| MC | Mast cell |
| MCS | Multiple chemical sensitivity |
| MED | Minimal eliciting dose |
| MFA | Multiple food allergies |
| MHC | Major histocompatibility complex |
| MIP | Macrophage inflammatory protein-1 |
| MMP | Matrix metalloproteinase |
| MMPI | Minnesota Multiphasic Personality Inventory |
| MMR | Measles–mumps–rubella |
| MPO | Myeloperoxidase |
| MSG | Monosodium glutamate |
| MTX | Maitotoxins |
| MUFA | Monounsaturated fatty acids |
| MWL | Mushroom worker's lung |
| NADPH | Nicotinamide dinucleotide phosphate |
| NASN | National Association of School Nurses |
| NCHS | National Center for Health Statistics |
| NDGA | Nordihydroguaiaretic acid |
| NIAID | National Institute of Allergy and Infectious Diseases |
| NIOSHA | National Institute for Occupational Safety and Health |
| NK | Natural killer |
| NLEA | National Labeling and Education Act |
| NOEL | No observable effect level |
| NPA | Negative predictive accuracy |
| NPIFR | Nasal peak inspiratory flow |
| NPV | Negative predictive values |
| NSAID | Non-steroidal anti-inflammatory drugs |
| NSBR | Non-specific bronchial responsiveness |
| NSP | Neurotoxic shellfish poisoning |
| OAS | Oral allergy syndrome |
| ODN | Oligodeoxynucleotides |
| OFC | Oral food challenge |
| OPRA | Occupational Physicians Reporting Activity |
| OT | Oral tolerance |
| OVA | Ovalbumin |
| PAF | Platelet-activating factor |
| PAMP | Pathogen-associated molecular pattern |
| PBB | Polybrominated biphenyls |
| PBMC | Peripheral blood mononuclear cell |
| PBT | Peripheral blood T-cells |
| PCB | Polychlorinated biphenyls |
| PEF | Peak expiratory flow |
| PEFR | Peak expiratory flow rate |
| PFS | Pollen–food syndrome |
| PFT | Pulmonary function testing |
| PHA | Phytohemagglutinin |
| PK | Prausnitz-Küstner |
| PKC | Protein kinase C |
| PMN | Polymorphonuclear leukocytes |
| PPA | Positive predictive accuracy |
| PPI | Protein phosphatase inhibition |
| PPs | Peyer's patches |
| PPT | PP-derived T-cells |
| PPV | Positive predictive value |
| PR | Pathogenesis-related |
| PSP | Paralytic shellfish poisoning |
| PST | Prick skin test |
| PTX | Pectenotoxins |
| PUFA | Polyunsaturated fatty acids |
| PUVA | Psoralen + ultraviolet A radiation |
| RADS | Reactive airways dysfunction syndrome |
| RAST | Radioallergosorbent test |
| RBA | Receptor-binding assay |
| RBL | Basophilic leukemia |
| RDA | Recommended dietary allowances |
| RDBPC | Randomized double–blind, placebo-controlled |
| RF | Rheumatoid factor |
| RIA | Radioimmunoassay |
| ROS | Reactive oxygen species |
| SBPC | Single-blinded placebo-controlled |
| SC | Secretory component |
| SCF | Stem cell factor |
| SCIT | Subcutaneous immunotherapy |
| SCN | Soybean cyst nematode |
| SFAP | School Food Allergy Program |
| SGF | Simulated gastric fluid |
| SHM | Somatic hyper mutation |
| SIF | Simulated intestinal fluid |
| SIgA | Secretory IgA |
| SIgM | Secretory IgM |
| SIT | Specific immunotherapy |
| SLIT | Sublingual immunotherapy |
| SPECT | Single photon emission computed tomography |
| SPT | Skin prick test |
| STX | Saxitoxins |
| SVR | Sequential vascular response |
| TCM | Traditional Chinese medicine |
| TCR | T-cell receptor |
| TLP | Thaumatin-like protein |
| TLR | Toll-like receptor |
| TNF | Tumor necrosis factor |
| TPA | Tetradecanoylphorbol-13-acetate |
| TSA | Transportation Security Administration |
| TTG | Tissue transglutaminase |
| TTX | Tetrodotoxin |
| UGI | Upper GI |
| UL | Upper intake level |
| USDA | United States Department of Agriculture |
| VAR | Voice-activated audiotape recording |
| VIP | Vasoactive intestinal peptide |
| WHO | World Health Organization |
| YTX | Yessotoxin |

# Contents

PART 1

# Adverse Reactions to Food Antigens: Basic Science