

# Contents

## xv Preface

Ebisawa, M. (Sagamihara); Ballmer-Weber, B.K. (Zurich); Vieths, S. (Langen); Wood, R.A. (Baltimore, Md.)

### Background

## 1 Historical Background, Definitions and Differential Diagnosis

Sampson, H.A. (New York, N.Y.)

### 1 Abstract

### 1 Historical Background

### 3 Definitions and Differential Diagnosis

### 5 Recent History and the Future

### 7 References

## 8 Immunological Basis of Food Allergy (IgE-Mediated, Non-IgE-Mediated, and Tolerance)

Kim, E.H.; Burks, W. (Chapel Hill, N.C.)

### 8 Abstract

### 8 Introduction

### 9 IgE-Mediated Food Allergy

### 11 Non-IgE-Mediated Food Allergy

### 12 Mixed-Immune Food Reactions

### 13 Oral Tolerance

### 14 Conclusion

### 16 References

## 18 Food Allergens: Molecular and Immunological Aspects, Allergen Databases and Cross-Reactivity

Lorenz, A.-R.; Scheurer, S.; Vieths, S. (Langen)

### 18 Abstract

### 19 Molecular Features of Food Allergens

#### 19 Allergen Families

#### 20 Allergen Databases

### 22 Class I Food Allergens/Class II Food Allergens

#### 22 Class I Food Allergens

#### 23 Class II Food Allergens

### 23 Resistance to Food Processing and Digestion

#### 23 Thermal Stability of Allergens

#### 24 Influence of Digestion on Allergic Reaction to Food Allergens

#### 25 Influence of the Food Matrix on Digestion and Allergenicity of Food Allergens

|    |  |
|----|--|
| 25 | Immunological Features of Food Allergens     |
| 25 | T Cell and B Cell Epitopes of Food Allergens |
| 25 | T Cell Epitopes                              |
| 26 | B Cell Epitopes                              |
| 26 | Cross-Reactivity                             |
| 28 | References                                   |

## **30 Epidemiology: International Point of View, from Childhood to Adults, Food Allergens**

Wong, G.W.K. (Hong Kong)

|    |  |
|----|--|
| 30 | Abstract   |
| 30 | Epidemiology of Food Allergy                             |
| 31 | Reported Food Allergy and Epidemiology Study Methodology |
| 32 | Prevalence of Common Food Allergies                      |
| 36 | Changing Prevalence of Food Allergy                      |
| 36 | References   |

## Clinical Aspects

### **38 Food Allergy in Childhood (Infancy to School Age)**

Bergmann, M.M.; Eigenmann, P.A. (Geneva)

|    |   |
|----|---|
| 38 | Abstract  |
| 38 | Introduction  |
| 39 | IgE-Mediated (Immediate-Type) Food Allergy  |
| 39 | Food-Induced Urticaria and Anaphylaxis  |
| 41 | Food-Dependent Exercise-Induced Anaphylaxis   |
| 42 | Oral Allergy Syndrome   |
| 42 | Mixed IgE and Non-IgE-Mediated Food Allergy   |
| 42 | Atopic Dermatitis and Food Allergy  |
| 43 | Eosinophilic Gastroenteropathies (Esophagitis, Gastritis, Enteritis, and Gastroenteritis) |
| 44 | Non-IgE-Mediated Food Allergy   |
| 44 | Food Protein-Induced Enterocolitis Syndrome   |
| 46 | Food Protein-Induced Proctocolitis  |
| 47 | Food Protein-Induced Enteropathy  |
| 47 | Heiner Syndrome (Milk-Induced Pulmonary Disease)  |
| 48 | Conclusions   |
| 48 | References  |

### **51 Food Allergy in Adolescence and Adulthood**

Ballmer-Weber, B.K. (Zurich)

|    |  |
|----|--|
| 51 | Abstract   |
| 51 | Introduction   |
| 52 | Food Allergies Due to Cross-Reaction with Inhalant Allergens           |
| 52 | Birch Pollen-Mediated Food Allergy                                     |
| 53 | Mugwort Pollen-Mediated Food Allergy                                   |
| 54 | Grass, Ragweed, and Plane Pollen-Mediated Food Allergy                 |
| 54 | Other Cross-Reactive Food Allergies                                    |
| 54 | Allergic Reactions to Foods May Already Occur upon First Consumption   |
| 54 | Sensitization to Galactose-Alpha-1,3-Galactose and Allergy to Red Meat |
| 55 | Clinical Symptoms  |
| 55 | Local Oral Symptoms  |
| 55 | Warning Signs for Impending Systemic Reactions                         |
| 55 | Food Allergy-Induced Systemic Reactions                                |
| 56 | Differential Diagnosis of Food Allergy in Adults                       |
| 57 | Lactose Intolerance  |

|    |                        |
|----|------------------------|
| 57 | Fructose Malabsorption |
| 57 | Histamine Intolerance  |
| 57 | References             |

## Diagnosis and Management

### 59 **Hints for Diagnosis**

Poulsen, L.K. (Copenhagen)

|    |                                   |
|----|-----------------------------------|
| 59 | Abstract                          |
| 59 | The Purpose of the Diagnosis      |
| 59 | Is It Food Allergy?               |
| 61 | Which Is the Culprit Food?        |
| 62 | Which Allergens Are Involved?     |
| 62 | How Much Is Too Much?             |
| 63 | Prerequisites for Diagnosis       |
| 63 | The Diagnostic Process            |
| 66 | Who Should Perform the Diagnosis? |
| 66 | Conclusions                       |
| 66 | References                        |

### 68 **IgE-Related Examination in Food Allergy with Focus on Allergen Components**

Borres, M.P. (Uppsala); Sato, S.; Ebisawa, M. (Sagamihara)

|    |   |
|----|---|
| 68 | Abstract  |
| 68 | How IgE-Mediated Food Allergy Is Diagnosed  |
| 69 | Component-Resolved Diagnostics  |
| 69 | Development of a Test for Allergen Components   |
| 69 | Heat Stability in Proteins  |
| 71 | Species-Specific and Cross-Reactive Proteins  |
| 72 | New Allergen Component Test: An Emerging Field of Interest                                  |
| 73 | Temporal Development of Allergen Components   |
| 74 | Singleplex versus Multiplex Testing   |
| 75 | Future Perspectives   |
| 75 | Skin Prick Test   |
| 75 | Basophil Activation Test  |
| 75 | Mechanisms of Basophil Activation   |
| 76 | Histamine Release Test  |
| 76 | Expression of the Basophil Activation Markers CD63 and CD203c                               |
| 76 | Correlation of the Skin Prick Test and the Basophil Activation Test with Oral Immunotherapy |
| 77 | References  |

### 79 **Non-IgE-Related Diagnostic Methods (LST, Patch Test)**

Matsumoto, K. (Tokyo)

|    |                                    |
|----|------------------------------------|
| 79 | Abstract                           |
| 79 | Introduction                       |
| 80 | Lymphocyte Stimulation Test        |
| 80 | Peripheral Blood Mononuclear Cells |
| 81 | Antigens                           |
| 81 | Culture System                     |
| 81 | Measurements                       |
| 81 | Interpretation                     |
| 82 | Future Perspectives                |
| 82 | Patch Test/Atopy Patch Test        |
| 82 | Indication for Testing             |
| 83 | Atopy Patch Test Methods           |

|    |  |
|----|--|
| 83 | Food Antigens  |
| 83 | Reading of Atopy Patch Test Results                                |
| 83 | Atopy Patch Test for Non-IgE-Mediated Gastrointestinal Allergy     |
| 83 | Epicutaneous IgE Sensitization and Antigen Absorption via the Skin |
| 84 | Future Perspectives  |
| 84 | References   |

## **87 Diagnostic Elimination Diets and Oral Food Provocation**

Wood, R.A. (Baltimore, Md.)

|    |   |
|----|---|
| 87 | Abstract                                    |
| 87 | Introduction                                |
| 87 | Elimination Diets                           |
| 88 | Oral Challenge Testing                      |
| 89 | Methodology                                 |
| 89 | Open Challenges                             |
| 89 | Single-Blind Challenges                     |
| 90 | Double-Blind, Placebo-Controlled Challenges |
| 90 | Challenge Settings and Procedures           |
| 92 | Dosing Strategies                           |
| 93 | Risk and Treatment of Oral Food Challenges  |
| 94 | Summary                                     |
| 94 | References                                  |

## **96 Pharmacological Management of Acute Food-Allergic Reactions**

Richards, S.; Tang, M. (Melbourne, Vic.)

|     |   |
|-----|---|
| 96  | Abstract  |
| 96  | Introduction  |
| 98  | Pharmacological Management of IgE-Mediated, Food-Induced Acute Allergic Reactions |
| 98  | Mild to Moderate Reactions  |
| 99  | Anaphylaxis   |
| 99  | Adrenaline  |
| 101 | Adjunctive Therapies  |
| 102 | Subsequent Management of IgE-Mediated Food-Induced Allergic Reactions             |
| 102 | Observation   |
| 103 | Risk Minimisation   |
| 103 | Pharmacological Management of Non-IgE-Mediated Food-Induced Allergic Reactions    |
| 104 | Conclusions   |
| 104 | References  |

## **106 Oral Immunotherapy and Potential Treatment**

Sato, S.; Yanagida, N.; Ebisawa, M. (Sagamihara)

|     |   |
|-----|---|
| 106 | Abstract  |
| 106 | Introduction  |
| 106 | Oral Immunotherapy for Food Allergy                           |
| 106 | Efficacy and Safety of Oral Immunotherapy                     |
| 108 | Factors Affecting Safety of Oral Immunotherapy                |
| 108 | Mechanisms of and Immunologic Responses to Oral Immunotherapy |
| 109 | Clinical Use of Oral Immunotherapy                            |
| 109 | Desensitization and Permanent Tolerance                       |
| 110 | Optimal Dose and Duration of Oral Immunotherapy               |
| 110 | Novel Treatment for Food Allergy                              |
| 110 | Sublingual Immunotherapy                                      |
| 111 | Anti-IgE Monoclonal Antibodies (Omalizumab) for Food Allergy  |

111      **Epicutaneous Immunotherapy**

112      Conclusion

112      Acknowledgments

112      References

## Allergen-Based Food Allergies

### **114 Cow's Milk Allergy in Children and Adults**

Fiocchi, A.; Dahdah, L. (Rome); Albarini, M.; Martelli, A. (Milan)

114      Abstract

114      Introduction

114      Epidemiology

115      Pathogenesis

115      Allergens

115      Clinical Manifestations

116           Immediate Reactions

116           Delayed Reactions

117      Diagnosis

117           Clinical Evaluation

117           Diagnostic Tests

117                IgE-Mediated CMA

117                Non-IgE-Mediated CMA

118                Elimination-Challenge Testing

118      Natural History

118      Treatment of Cow's Milk Allergy

118           Avoidance of Cow's Milk Protein

119           Alternative Formulae (Milk Substitutes)

119           Oral Immunotherapy

120           Follow-Up

121           A Very Common Clinical Case

122      Conclusions

122      References

### **124 Hen's Egg Allergy**

Urisu, A.; Kondo, Y. (Nagoya); Tsuge, I. (Toyoake)

124      Abstract

124      Introduction

125      Symptoms

125      Allergenic Components of Egg White

126      Allergenic Components of Egg Yolk

126      Diagnosis

127      Natural History

128      Management and Therapy

128      Oral Immunotherapy to Egg Allergy

129      Clinical Case

129      Acknowledgments

129      References

### **131 Peanut and Tree Nut Allergy**

Cox, A.; Sicherer, S.H. (New York, N.Y.)

131      Abstract

131      Introduction

131      Epidemiology

- 132 Clinical Reactions
- 133 Age of Presentation or First Reaction to Peanut and Tree Nuts
- 133 Co-Allergy to Peanut and Tree Nuts and Allergy to Multiple Tree Nuts
- 133 Subsequent Reactions
- 134 Resolution of Peanut Allergy
- 134 Resolution of Tree Nut Allergy
- 134 Peanut and Tree Nut Allergens
  - 134 Peanut
- 136 Case Study
- 136 Tree Nut Allergens
  - 138 Hazelnut (*Corylus avellana*)
  - 138 Walnut (*Juglans regia*) and Pecan (*Carya illinoinensis*)
  - 139 Casewell (*Anacardium occidentale*) and Pistachio (*Pistacia vera*)
  - 139 Almond (*Prunus dulcis*)
  - 139 Other Tree Nuts
- 140 Pathogenesis
- 140 Conclusion
- 141 References

## **145 Grain and Legume Allergy**

Ito, K. (Aichi)

- 145 Abstract
- 145 Grain (Wheat) Allergies
  - 145 General Description of Wheat Allergens
  - 146 Baker's Asthma
  - 146 Immediate-Type Food Allergy to Wheat
  - 147 Wheat-Dependent Exercise-Induced Anaphylaxis
  - 147 Allergies to Hydrolyzed Wheat Proteins or Deamidated Gluten
  - 148 Allergies to Other Grains
  - 148 A Case of Successful Oral Immunotherapy for Wheat Allergy
- 148 Legume (Soybean) Allergies
  - 148 General Description of Legume Allergens
  - 149 Immediate-Type Food Allergy to Soybean
  - 149 Pollen-Related Soybean Allergies
  - 149 Other Legume Allergies
- 150 Conclusions
- 150 Acknowledgments
- 150 References

## **152 Fish and Shellfish Allergy**

Thalayasingam, M.; Lee, B.-W. (Singapore)

- 152 Abstract
- 152 Introduction
- 152 Prevalence
- 153 Classification of Seafood Species
- 154 Clinical Manifestations
- 155 Fish and Shellfish Allergens
- 157 Allergenic Cross-Reactivity
  - 157 Parvalbumin within the Fish Group and Frog
  - 157 Within the Shellfish Group
    - 157 Between Shellfish and Other Arthropods
- 158 Differential Diagnosis for Fish and Shellfish Allergy
- 159 Diagnosis
- 159 Natural History and Treatment

|     |             |
|-----|-------------|
| 160 | Conclusions |
| 160 | References  |

## **162 Fruit and Vegetable Allergy**

Fernández-Rivas, M. (Madrid)

|     |                                      |
|-----|--------------------------------------|
| 162 | Abstract                             |
| 162 | Introduction                         |
| 163 | Epidemiology                         |
| 163 | Pathogenesis: Allergen Sensitisation |
| 166 | Allergens                            |
| 166 | Clinical Symptoms                    |
| 167 | Diagnosis                            |
| 168 | Management                           |
| 169 | References                           |

## Disease-Based Food Allergies

### **171 Gastrointestinal Food Allergies**

Heine, R.G. (Melbourne, Vic.)

|     |  |
|-----|--|
| 171 | Abstract   |
| 171 | Introduction   |
| 172 | Clinical Presentation  |
| 172 | Food Protein-Induced Enteropathy   |
| 172 | Food Protein-Induced Enterocolitis Syndrome  |
| 173 | Food Protein-Induced Proctocolitis   |
| 173 | Multiple Food Protein Intolerance of Infancy   |
| 174 | Food Protein-Induced Gastrointestinal Motility Disorders in Infants and Young Children |
| 174 | Gastro-Oesophageal Reflux Disease in Infancy   |
| 174 | Constipation   |
| 175 | Infantile Colic  |
| 175 | Carbohydrate Malabsorption and Food Intolerance  |
| 176 | Lactose Intolerance/Malabsorption  |
| 176 | Coeliac Disease  |
| 176 | Diagnostic Evaluation and Differential Diagnosis                                       |
| 177 | Dietary Management   |
| 177 | Conclusion   |
| 178 | References   |

### **181 Atopic Eczema and Food Allergy**

Wassmann, A. (Hannover/Hamburg); Werfel, T. (Hannover)

|     |  |
|-----|--|
| 181 | Abstract   |
| 181 | Prevalence and Natural History of Food Allergies in Atopic Eczema  |
| 182 | Clinical Reaction Patterns to Foods in Patients with Atopic Eczema |
| 183 | Allergens  |
| 183 | Pathogenesis of Food Allergy in Atopic Eczema                      |
| 183 | Epidermal Barrier Dysfunction                                      |
| 184 | Gut Barrier Dysfunction  |
| 184 | Immune Response  |
| 185 | Diagnosis of Food Allergy in Atopic Eczema                         |
| 186 | In vitro Diagnostics   |
| 186 | In vivo Diagnostics  |
| 186 | Skin Tests   |
| 187 | Oral Food Challenge  |
| 188 | References   |

|            |  |
|------------|--|
| <b>191</b> | <b>Anaphylaxis in Food Allergy</b>           |
|            | Pesek, R.D.; Jones, S.M. (Little Rock, Ark.) |
| 191        | Abstract                                     |
| 191        | Introduction                                 |
| 192        | Diagnosis                                    |
| 193        | Laboratory Evaluation                        |
| 194        | Management of Anaphylaxis                    |
| 194        | Acute Management                             |
| 196        | Long-Term Management and Prevention          |
| 196        | Food-Dependent Exercise-Induced Anaphylaxis  |
| 197        | Summary                                      |
| 197        | References                                   |

|            |  |
|------------|--|
| <b>199</b> | <b>Eosinophilic Oesophagitis</b>           |
|            | Heine, R.G.; Allen, K.J. (Melbourne, Vic.) |

|     |   |
|-----|---|
| 199 | Abstract  |
| 199 | Introduction  |
| 200 | Epidemiology  |
| 200 | Clinical Presentation in Children and Adults                                    |
| 200 | Distinguishing Eosinophilic Oesophagitis from Gastro-Oesophageal Reflux Disease |
| 201 | Eosinophilic Oesophagitis in Patients with Coeliac Disease                      |
| 201 | Mechanisms of Disease   |
| 202 | Diagnostic Evaluation   |
| 202 | Natural History and Complications   |
| 203 | Treatment   |
| 203 | Proton Pump Inhibitors  |
| 203 | Elimination Diets   |
| 203 | Elemental Diet  |
| 203 | Targeted Elimination Diets  |
| 204 | Empiric Elimination Diet  |
| 204 | Corticosteroids   |
| 205 | Other Immune-Modulating Agents  |
| 205 | Endoscopic Oesophageal Food Disimpaction and Dilatation of Strictures           |
| 205 | Conclusion and Future Directions  |
| 205 | References  |

## Special Topics

|            |  |
|------------|--|
| <b>209</b> | <b>Nutritional Aspects and Diets in Food Allergy</b> |
|            | Nowak-Węgrzyn, A.; Groetch, M. (New York, N.Y.)      |

|     |   |
|-----|---|
| 209 | Abstract  |
| 209 | Elimination Diet in Food Allergy Diagnosis  |
| 210 | Elimination Diet in Food Allergy Management   |
| 210 | Loopholes in the Labeling Laws  |
| 211 | Changing Paradigms in the Management of Milk and Egg Allergy: Baked Milk and Egg Diet |
| 212 | The Effects of Allergen Avoidance on Nutrition in Children                            |
| 213 | Cow's Milk Allergy  |
| 215 | Grains  |
| 216 | Soy, Egg, Peanut, Tree Nut, Fish and Shellfish Allergies                              |
| 216 | Nutritional Impact of Specific Food-Allergic Disorders                                |
| 216 | Feeding and Developmental Needs   |
| 218 | Nutritional Issues in Adults with Food Allergy  |
| 219 | Summary   |
| 219 | References  |

**221 Food Allergy: Psychosocial Impact and Public Policy Implications**

Sharma, H.P.; Herbert, L.J. (Washington, D.C.)

221 Abstract

221 Introduction

222 Food Allergy Knowledge and Attitudes

222 Impact of Food Allergy on Daily Life

223 Current Food Allergy-Related Public Policy

224 Implications and Future Directions

225 References

**227 Worldwide Food Allergy Labeling and Detection of Allergens in Processed Foods**

Taylor, S.L.; Baumert, J.L. (Lincoln, Nebr.)

227 Abstract

227 Introduction

228 Labeling of Allergenic Foods

231 Ingredient Labeling and Exemptions

231 Advisory Labeling

233 Detection of Food Allergen Residues

233 Quantitative Immunoassay Methods

233 Qualitative Immunoassay Methods

233 Conclusion

234 References

**235 The Effects of Food Allergy on Quality of Life**

DunnGalvin, A. (Cork); Dubois, A.E.J.; Flokstra-de Blok, B.M.J. (Groningen); Hourihane, J.O'B. (Cork)

235 Abstract

236 Introduction

238 Main Body

238 The Parental Perspective: Quantitative

241 The Child, Adolescent and Adult Perspective: Quantitative

243 Qualitative Studies on the Impact of Food Allergy on Health-Related Quality of Life

244 The Parent Perspective

246 Children and Teens

248 Discussion

249 Improving HRQL

251 Conclusion

251 References

**253 Prevention of Food Allergy**

Tsakok, T.; Du Toit, G.; Lack, G. (London)

253 Abstract

253 Introduction

254 Methodological Challenges

254 Onset of Sensitisation and Food Allergy

254 Maternal Diet (During Pregnancy and/or Breastfeeding) and the Prevention of Food Allergy

254 Complementary Infant Feeding and the Prevention of Food Allergy

257 Combined Maternal and Infant Dietary Measures and the Prevention of Food Allergy

258 Routes of Sensitisation

258 Oral Tolerance Induction

259 Unpasteurised Milk, Probiotics and Prebiotics

259 Nutritional Supplements

259 Conclusions

260 References

**263 Educational Programmes in Food Allergy**

Kugler, C.; Brockow, K. (München); Ring, J. (Davos)

**263 Abstract****263 Introduction****263 Individual Dietetic Treatment of Food Allergy****264 Structured Educational Group Sessions for Patients and Families with Atopic Eczema or Anaphylaxis****264 Educational Programmes for Atopic Eczema**

264      Educational Programmes for the Control of Atopic Eczema in Children and Adolescents (According to 'Arbeitsgemeinschaft Neurodermitis-Schulung')

266      Educational Programmes for the Management of Atopic Eczema in Adults ('Arbeitsgemeinschaft Neurodermitis-Schulung für Erwachsene')

**267 Educational Program for Anaphylaxis Patients and Families****269 References****270 Acknowledgments****271 Author Index****272 Subject Index**