

Contents

- XII **Contributors**
- XVIII **Preface**
Bergmann, K.-C. (Berlin); Ring, J. (Munich)
- 1 Allergy through 20 Centuries**
- 2 **History of Allergy in Antiquity**
Ring, J. (Munich)
- 2 Abstract
- 2 Mesopotamia
- 3 Egypt
- 4 Indigenous Populations in America
- 5 China
- 6 Ancient India
- 6 Allergy in the Bible
- 6 Greek-Roman Tradition
- 7 Hay Fever/Rhinitis
- 8 Herodotus
- 8 Marcus Terentius Varro
- 8 Asthma
- 9 Aretaeus from Cappadocia
- 9 Urticaria
- 10 Food Allergy
- 10 Eczema
- 11 Famous Allergic Individuals in Antiquity
- 11 Pharaoh Menes from Egypt
- 12 Emperor Augustus, Emperor Claudius and
Britannicus: The First Family History of Atopy in
the Julio-Claudian Emperor Family
- 12 Octavianus Augustus
- 12 Emperor Claudius
- 12 Britannicus
- 13 Seneca
- 14 Conclusion
- 14 Acknowledgements
- 14 References
- 15 **History of Allergy in the Middle Ages
and Renaissance**
Ring, J. (Munich)
- 15 Abstract
- 15 History of Medicine in the Middle Ages
in the Middle East
- 15 Al Rhazes
- 15 Ibn Sina (Avicenna)
- 16 Moses Maimonides
- 17 The Period from 1300 to 1700 BC
- 17 The 15th and 16th Centuries
- 18 Rose Fever
- 20 Conclusion
- 20 References
- 21 **Landmarks in Allergy during the 19th Century**
Kay, A.B. (London)
- 21 Abstract
- 22 Hay Fever and Ragweed Pollinosis
- 23 Anaphylaxis
- 23 Asthma
- 24 Eosinophils and Mast Cells
- 26 References
- 27 **Milestones in the 20th Century**
Bergmann, K.-C. (Berlin)
- 27 Abstract
- 28 Patients First – The First Patient’s Organization for
Allergy Sufferers
- 30 Immunotherapy against Pollen and
Other Allergens – The ‘Backbone of Allergology’
- 31 Anaphylaxis – The Discovery of a New Field in 1902
- 32 The Determining Word Is Born in 1906
- 33 Serum Sickness and the ‘Case Langerhans’
- 34 The Idea of Anaphylaxis Received
Growing Interest ...
- 35 Local Anaphylaxis
- 35 Anaphylactic Shock and ‘Local Immunity’
- 36 Alimentary Anaphylaxis

36	Anaphylaxis in the Clinical Routine
36	The Word 'Atopy' Has Remained to This Day
37	The Transferability of an Allergy by Blood, or the Search for the 'Malefactor'
38	The Transferability of an Allergy through Serum Is Proved
39	Passive Cutaneous Anaphylaxis Test
39	Scientific Allergy Diagnostics
39	Scratch Test
40	Precursor of the Prick Test
41	Intracutaneous Test
41	Rub Test
41	Conjunctival Provocation
42	Nasal Provocation Test
42	Inhalation Tests
43	Discovery of IgE and Slow Reacting Substances
44	Discovery of Leukotrienes
44	References
46	Terminology of Allergic Phenomena Ring, J. (Munich)
46	Abstract
47	Idiosyncrasy
48	Antipathy
48	Hypersensitivity
49	Anaphylaxis
49	Allergy
50	Atopy
51	Conclusion
51	References

2 Most Common Allergic Diseases: Historical Reflections in Understanding

54	Anaphylaxis Ring, J.; Grosber, M.; Brockow, K. (Munich); Bergmann, K.-C. (Berlin)
54	Abstract
55	The Voyage on the Yacht Princesse Alice II
59	Pathophysiology
61	References
62	Allergic Rhinitis Mygind, N. (Copenhagen)
62	Abstract
62	An Allergy Giant in 1873
63	Terminology and Definition
63	Epidemiology and Natural History
64	Allergens
64	Histopathology and Pathogenesis
64	The Epithelial Lining
64	The Mast Cell

64	Histamine
65	The Eosinophil
65	Nasal Polyps
65	Symptoms
65	Treatment
65	Antihistamines
66	Cromoglycate
66	Topical Steroids
66	Systemic Steroids
66	Allergic Rhinitis
67	Nasal Polyposis
67	Oral Treatment or a Depot Injection
67	Vasoconstrictors
67	Ipratropium Bromide
67	Immunotherapy
67	References
69	Asthma Bergmann, K.-C. (Berlin)
69	Abstract
69	The Beginning in the East
70	The Beginning in the West
72	The Middle Ages
72	Modern Times
79	Acknowledgements
79	References
81	Atopic Dermatitis/Atopic Eczema Wallach, D. (Paris); Taïeb, A. (Bordeaux)
81	Abstract
82	Chronological Agenda
82	Atopic Dermatitis before 1800
84	Atopic Dermatitis in Willanist Dermatology
85	Atopic Dermatitis as a Diathetic Prurigo
87	Birth of Atopic Dermatitis
89	Criteria and Scores in the Contemporary Era
90	Will Semantic Discussions End?
90	Pathogenic Theories and Their Therapeutic Consequences
91	Humoralistic Theories and Reluctance to Treat
91	Digestive Theories and Diet
92	Parasitic/Bacteriological Dimension of Eczema
92	Allergological Theories, Hyposensitization and Allergen Eviction
93	Fear of Treatment Side Effects
93	Neuropsychological Considerations
94	Other Hypotheses
94	Dermatological Approach and Topical Therapy
94	Conclusion
95	References

97	Allergic Contact Dermatitis Alikhan, A. (Rochester, Minn.); Maibach H.I. (San Francisco, Calif.)	113	Double-Blind Placebo-Controlled Food Challenge – The Gold Standard and the Diagnosis of Food Allergy
97	Abstract	113	Fatal Food Allergies
97	Patch Testing – Jadassohn and Bloch	113	Pollen-Associated Food Allergies and the ‘Oral Allergy Syndrome’
98	Important Early Basic Science Discoveries	114	‘Derivative Allergy’ – A Rare Pathway of Elicitation of Food Allergy
98	Standard Series – Bonnevie	115	Food-Induced/Food-Dependent Exercise-Induced Anaphylaxis
98	Contact Dermatitis and Public Health – Ramazzini and Prosser White	116	Oral Desensitization – Long Controversial, but Now Established
98	Contact Dermatitis Societies	117	Acknowledgement
99	Improving Convenience – The TRUE Test	117	References
99	Moving into the Computer Age – The CARD Database		
99	The Future of Allergic Contact Dermatitis	120	Drug Hypersensitivity Bircher, A.J. (Basel)
100	Conclusion	120	Abstract
100	References	120	Drug Hypersensitivity – The Emergence of New Disorders
101	Urticaria and Angioedema Maurer, M. (Berlin)	121	Terminology – An Ongoing Controversy
101	Abstract	121	Early History – Poisons and Placebos
101	Urticaria	122	19th Century – The Dawn of Drug Hypersensitivity
103	Angioedema	124	Drug-Induced Syndromes – The Bad and the Ugly
104	References	124	Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis
105	Allergy and the Eye Bonini, S. (Rome)	125	Ampicillin Rash
105	Abstract	125	Drug Hypersensitivity Syndrome
106	The Contribution of Ocular Allergy to a Better Understanding of Mechanisms of the Immune Reaction	126	Acute Generalized Exanthematous Pustulosis
107	The Contribution of Ocular Allergy to Clinical Practice in Allergy and Clinical Immunology	126	Hoigné Syndrome
107	How Ocular Allergy Can Contribute to a Continuing Progress of Allergy and Clinical Immunology	127	Selected Drugs
108	Conclusion	127	Halogenated Drugs – Iodine and Bromides
108	References	127	Analgesics
109	History of Food Allergy Wüthrich, B. (Zurich)	128	Salvarsan
109	Abstract	128	Anticonvulsants
110	Food Allergy in Antiquity and the Middle Ages: Myth or Reality?	129	Sulfonamides
111	First Documentation of Food Allergy – Skin Test as Diagnostic Routine Method	129	Penicillin
111	Other Test Methods for Food Allergy Prior to the Discovery of Immunoglobulin E	129	<i>p</i> -Amino Benzoic Acid
112	Radioallergosorbent Test – Significant Progress in the Diagnosis of Immunoglobulin E-Mediated Food Allergies	130	Outlook
112	Component-Resolved Diagnostic Techniques	130	References
		132	Aspirin Hypersensitivity Sánchez-Borges, M. (Caracas)
		132	Abstract
		132	The Discovery of Aspirin
		132	Ancient Times
		133	From Willow Bark to Salicin to Salicylic Acid
		133	From Natural to Synthetic Acetylsalicylic Acid
		134	Mechanisms of Action
		134	Cyclooxygenase Isoenzymes
		135	Antithrombotic Effects of Aspirin

135	Hypersensitivity Reactions to ASA and NSAIDs	159	Regulation of the Th2 Response in Allergy
135	Early Observations	159	Immune Deviation or Redirection
136	Samter's Disease	160	Immune Suppression or Regulation
136	Classification of Hypersensitivity Reactions to ASA and NSAIDs	161	Impaired Immune Deviation and Reduced Immune Suppression Account for Reduced Prevalence of Allergy, but the Role of Impaired Immune Deviation Is Prevalent
136	Pathogenesis	161	Possible Pathogenic Role in Allergy of CD4+ Effectors other than Th2 Cells
137	Genetics	161	Possible Pathogenic Role of Natural Killer T Cells
137	Developments in Diagnostic Methods	162	Role of Innate Immunity in Allergic Disorders
138	Advances in Patient Management	163	Concluding Remarks
138	Conclusions	163	References
138	References		
140	Bradykinin-Mediated Disease	165	Mast Cell Research
	Kaplan, A.P. (Charleston, S.C.)		Saito, H. (Tokyo)
140	Abstract	165	Abstract
141	Inhibition of Bradykinin Degradation by Angiotensin-Converting Enzyme Inhibitors	166	Discovery of Histamine in Mast Cells/Basophils
142	Hereditary Angioedema	167	Discovery of IgE Receptors on Mast Cells/Basophils
143	C1 Inhibitor as Inhibitor of the Bradykinin-Forming Cascade	167	Discovery of Mast Cell Origin and the Culture Methods
143	The Myth of C2-Kinin	169	Mast Cell Phenotypes
143	Bradykinin Is the Mediator of Hereditary Angioedema	170	Discovery of Cytokine Production by Mast Cells
145	Treatment of Hereditary Angioedema	170	Future Perspective
146	Future Considerations	170	References
146	References		
		172	Basophils: Historical Reflections and Perspectives
			Marone, G.; Borriello, F.; Varricchi, G.; Genovese, A.; Granata, F. (Naples)
		172	Abstract
		173	The Different Eras of Basophil Biology
		174	Activating Receptors on Human Basophils
		177	Inhibitory Receptors on Human Basophils
		177	Mediators
		178	Histamine-Releasing Factor
		179	Basophils as Potential Inducers of Type 2 Immunity
		179	Basophils as Antigen-Presenting Cells: An Unsettled Controversy
		181	Human Basophils and Angiogenesis
		181	Basophils in Immunity against Parasites
		182	Bidirectional Interactions between Bacteria and Basophils
		184	Basophils and Viral Infections
		184	Basophils and Autoimmune Disorders
		185	Basophils in Allergic Disorders
		185	Conclusions and Perspectives
		186	Acknowledgements
		186	References
3	Mechanisms of Allergy: Important Discoveries		
150	The Discovery of Immunoglobulin E and Its Role in Allergy		
	Johansson, S.G.O. (Stockholm)		
150	Abstract		
150	The Search for the Elusive Factor		
151	IgE and the Allergic Inflammation		
151	Allergy Diagnosis		
152	Treatment		
153	The Beneficial Function of IgE		
153	References		
155	T Cell Subpopulations		
	Romagnani, S. (Florence)		
155	Abstract		
156	Effector CD4+ T Cells		
156	The Th1/Th2 Paradigm		
157	Beyond the Th1/Th2 Paradigm		
157	Regulatory CD4+ T Cells		
158	<i>Foxp3</i> + Regulatory T Cells		
159	Type 1 Regulatory T Cells		
159	Role of T Cell Subsets in Allergic Disorders		
159	Th2 Cells in Allergic Disorders		

193	Eosinophils Radonjic-Hösli, S.; Simon, H.-U. (Bern)
193	Abstract
193	The Discovery
194	The Origin of the Eosinophil and Its Granules: Different Views over Time
194	The Eosinophil Granule: Extrinsic Origin
195	The Eosinophil Granule: Metamorphosis – Transformation from the Neutrophil Granule
196	The Eosinophil Granule: Intrinsic Origin
196	Eosinopoiesis: Precursors and Transcription Factors
197	Eosinopoiesis: Cytokines and Their Receptors
198	Eosinophil-Mediated Diseases
198	Mechanisms of Eosinophilia
198	Development of Therapeutic Strategies
199	The Functions of the Eosinophil: Different Views over Time
199	The Anti-Inflammatory Role of Eosinophils
200	The Effector Role of Eosinophils
201	The Immunoregulatory Role of Eosinophils
202	The Role of Eosinophils in Tissue Remodeling
202	Conclusions
202	References
205	The Bradykinin-Forming Cascade: A Historical Perspective Kaplan, A.P. (Charleston, S.C.)
205	Abstract
206	Factor XII
208	Prekallikrein
208	Kininogen
209	Binding to Endothelial Cells
212	A Surprise: Prekallikrein Is an Enzyme
212	Concluding Remarks
213	References
214	Histamine Receptors and Antihistamines: From Discovery to Clinical Applications Cataldi, M.; Borriello, F.; Granata, F.; Annunziato, L.; Marone, G. (Naples)
214	Abstract
215	The Discovery of Histamine
215	The Synthesis of the First Antihistamines and the Identification of H ₁ R
216	The Identification of H ₂ R and the Synthesis of the First H ₂ Blockers
216	Histamine in the Brain
217	Cloning of H ₁ R, H ₂ R and H ₃ R, and Generation of Histamine Receptor Knockout Mice
219	Identification and Cloning of H ₄ R
222	Closing Thoughts
222	Acknowledgements
222	References

4 Detection of Environmental Influences and Allergens

228	Pollen and Pollinosis Smith, M.; Berger, U. (Vienna); Behrendt, H. (Munich); Bergmann, K.-C. (Berlin)
228	Abstract
229	Analysis of Airborne Pollen and Pollen Allergens
231	First Descriptions of the Disease
232	Monitoring and Monitoring Networks
232	Acknowledgements
233	References
234	Mites and Allergy Fernández-Caldas, E. (Madrid/Tampa, Fla.); Puerta, L.; Caraballo, L. (Cartagna)
234	Abstract
237	Allergens from House Dust Mites
238	Allergens from Storage Mites
239	Cross-Reactivity of Mite Allergens
240	Effect of Parasitic Infections on Mite Allergy
240	Environmental Control
241	Mite Immunotherapy
241	References
243	Mammalian Airborne Allergens Aalberse, R.C. (Amsterdam)
243	Abstract
244	Mammalian Allergens and the Identification of 'the House Dust Allergen'
244	The Postulated Role of Maillard Reaction Products
244	Developments in Technologies for the Characterization of Allergens
245	Persistent Contaminants and Mind-Boggling Complexities
245	The Lipocalin Family
246	The Secretoglobulin Family
246	Perspective: From Dust Back to Dust
246	References
248	The Latex Story Raulf, M. (Bochum)
248	Abstract
248	Latex as a Rubber and Protein Source
249	History of Latex Allergy – When Did the Problems Start?
251	Who Were at Risk? Risk Factors and Epidemiology Aspects
251	Characterization of Relevant Allergens
252	Latex-Fruit/Plant Syndrome – Problems with Cross-Reactivity

252	Latex as a Model for Molecular Allergology – How to Improve the Diagnosis?
253	Preventive Measures – Successful Avoidance Strategy
254	References
256	Peanut Allergens Becker, W.-M. (Borstel); Jappe, U. (Borstel/Lübeck)
256	Abstract
257	Prevalence of Peanut Allergy
257	Geographical Origin of Peanuts
258	Class I Food Allergy
259	Class II Food Allergy
260	Allergens of Peanut
260	Ara h 1 and Ara h 3
262	Ara h 2, Ara h 6 and Ara h 7
263	Ara h 9
264	Ara h 5 and Ara h 8
264	Peanut oleosin, Ara h 10 and Ara h 11
264	Ara h 12 and Ara h 13
264	Peanut Agglutinin and Cross-Reactive Carbohydrate Determinants
265	Conclusion
265	Acknowledgements
265	References
268	Environmental Pollution and Allergy: Historical Aspects Behrendt, H.; Alessandrini, F.; Buters, J. (Munich); Krämer, U. (Düsseldorf); Koren, H. (Durham, N.C.); Ring, J. (Munich)
268	Abstract
270	Epidemiology Studies
270	Early Studies in Japan
270	Early Studies in Germany
272	East/West Comparison Studies in Germany and Europe
274	Aerobiological Studies
275	In vitro Studies
275	Animal Experiments
275	Clinical Studies
275	The Concept of 'Allergotoxicology'
276	References
278	Farmers and Their Environment: Protective Influences of the Farming Environment against the Development of Allergies Gassner, M. (Zurich)
278	Abstract
278	Farmers and Their Environment
278	Agriculture, the Art of Adaptation
280	Drying
280	Wrapping

281	Mechanical Technology
281	Allergology
281	The Paradox of Dose Effect
282	The Paradox of Toxic Interactions
282	The Paradox of Tolerance or Adaption
283	The Paradox of Chronic Obstructive Lung Disease
283	The Paradox of Endotoxins
284	The Paradox of Organ Distribution
284	The Paradox of Gnotobiotics
285	The Paradox of Genetics
285	The Paradox of Migration
286	The Paradox of Slums
286	References

5 Progress in Allergy Management

288	History of Catecholamine Research Starke, K. (Freiburg im Breisgau)
288	Abstract
288	Adrenaline in the Adrenal Medulla: Preludes
289	Adrenaline in the Adrenal Medulla: Oliver and Schäfer, 1893/1894
290	Adrenaline in the Adrenal Medulla: Independent Discoverers
291	Chemistry
291	Catecholamine Neurotransmitters: Adrenaline
292	Formation and Destruction
293	Catecholamine Neurotransmitters: Noradrenaline
294	Catecholamine Neurotransmitters: Dopamine
295	Membrane Passage
296	Receptors
299	References
302	Antihistamines Church, M.K.; Maurer, M. (Berlin)
302	Abstract
303	The Discovery of Antihistamines
304	The Discovery of H ₂ , H ₃ , and H ₄ Antihistamines
305	First- and Second-Generation H ₁ Antihistamines
305	H ₁ Antihistamines and the Central Nervous System
306	H ₁ Antihistamines and Cardiotoxicity
307	The Anti-Inflammatory Properties of H ₁ Antihistamines
307	Receptor-Independent Mechanisms
307	Receptor-Dependent Mechanisms
308	H ₁ Antihistamines Are Not Receptor Antagonist but Are Inverse Agonists
308	Conclusions
308	References

311	Glucocorticoids Barnes, P.J. (London)
311	Abstract
311	Early Studies with Glucocorticoids
312	First Controlled Trial of Glucocorticoid in Asthma
313	Inhaled Glucocorticoids
314	Combination Inhalers
315	Mechanisms of Action
315	Future Directions
316	References
317	Chromones Edwards, A.M. (Newport)
317	Abstract
317	Background
318	The Chromones
321	References
323	Characterization and Standardization of Allergen Extracts Løwenstein, H. (Nødebo)
323	Abstract
323	The Beginning
324	The First Purified Allergen Molecules
327	Standardization Becomes International
329	The Nomenclature of Allergens
329	New Attempts for Allergens Standardization
330	Concluding Remarks
331	References
333	Allergen-Specific Immunotherapy Nelson, H.S. (Denver, Colo.); Norman, P.S. (Baltimore, Md.)
333	Abstract
333	Spread of Immunotherapy
334	Proof of Efficacy
335	Improvement in Allergen Extracts
335	Disease Modification by Immunotherapy
336	Immunologic Mechanisms
337	Alternative Approaches to Immunotherapy
337	Additional Allergic Conditions Treated with Immunotherapy
337	References

6 Pioneers of Allergy: Personal Reflections

340	K. Frank Austen
342	John Bienenstock
344	Kurt Blaser

346	Alain de Weck (1928–2013)
350	Alfred William Frankland
353	Oscar L. Frick
356	Kimishige Ishizaka
361	Lothar Jäger
363	Terumasa Miyamoto
365	Harry Morrow Brown (1917–2013)
368	Albert K. Oehling
371	Heimo Reulecke
373	Václav Špičák

7 Allergy Societies and Collections

378	AAAAI
380	APAAACI
383	CIA
388	EAACI
392	JSA
394	SLAAI
397	WAO
402	AAAAI Archives
405	The Ilya Mechnikov Collection in Riga

8 Online Supplementary Material

410	Movie 1: Anaphylaxie et Allergie www.karger.com/chial100_movie1
411	Movie 2: Worl Allergy: The Disease of Civilization www.karger.com/chial100_movie2
413	List of Illustrations/Figure Credits
417	Subject Index