New Trends in Allergy and Atopic Eczema
Chemical Immunology and Allergy
Vol. 96

Series Editors

Johannes Ring  Munich
Kurt Blaser  Davos
Monique Capron  Lille
Judah A. Denburg  Hamilton
Stephen T. Holgate  Southampton
Gianni Marone  Naples
Hirohisa Saito  Tokyo
New Trends in Allergy and Atopic Eczema

Volume Editors

Johannes Ring  Munich
Ulf Darsow  Munich
Heidrun Behrendt  Munich

24 figures, 8 in color, and 6 tables, 2012
## Contents

<table>
<thead>
<tr>
<th>XI</th>
<th>Preface</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ring, J.; Darsow, U.; Behrendt, H. (Munich)</td>
</tr>
</tbody>
</table>

### Allergy and Environment: Determinants of Allergy Development

<table>
<thead>
<tr>
<th>1</th>
<th>Allergy in Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Platts-Mills, T.A.E. (Charlottesville, Va.)</td>
</tr>
<tr>
<td></td>
<td>Abstract</td>
</tr>
<tr>
<td></td>
<td>Evolution of Protein Structures</td>
</tr>
<tr>
<td></td>
<td>‘Evolution’ of Allergic Diseases: 1870–2000</td>
</tr>
<tr>
<td></td>
<td>Conclusions</td>
</tr>
<tr>
<td></td>
<td>Acknowledgement</td>
</tr>
<tr>
<td></td>
<td>References</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7</th>
<th>Climate Change, Environment and Allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Behrendt, H.; Ring, J. (Munich)</td>
</tr>
<tr>
<td></td>
<td>Abstract</td>
</tr>
<tr>
<td></td>
<td>Environment and Allergy</td>
</tr>
<tr>
<td></td>
<td>Environmental Pollution</td>
</tr>
<tr>
<td></td>
<td>Western Lifestyle</td>
</tr>
<tr>
<td></td>
<td>Climate Change</td>
</tr>
<tr>
<td></td>
<td>Climate Change Effects upon Pollen</td>
</tr>
<tr>
<td></td>
<td>More Pollen</td>
</tr>
<tr>
<td></td>
<td>New Pollen</td>
</tr>
<tr>
<td></td>
<td>Altered Pollen</td>
</tr>
<tr>
<td></td>
<td>Other Allergens</td>
</tr>
<tr>
<td></td>
<td>Conclusion</td>
</tr>
<tr>
<td></td>
<td>Acknowledgement</td>
</tr>
<tr>
<td></td>
<td>References</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>15</th>
<th>The Hygiene Hypothesis Does Not Apply to Atopic Eczema in Childhood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cramer, C.; Link, E. (Düsseldorf); Koletzko, S. (Munich); Lehmann, I. (Leipzig); Heinrich, J.; Wichmann, H.-E. (Neuherberg); Bauer, C.-P. (Munich); v. Berg, A.; Berdel, D. (Wesel); Herbarth, O. (Leipzig); Schaaf, B. (Bad Honnef); Borte, M. (Leipzig); Behrendt, H. (Munich); Krämer, U. (Düsseldorf)</td>
</tr>
<tr>
<td></td>
<td>Abstract</td>
</tr>
<tr>
<td></td>
<td>Eczema in East and West Germany</td>
</tr>
<tr>
<td></td>
<td>Eczema and Day Care Center Attendance</td>
</tr>
<tr>
<td></td>
<td>Eczema, Older Siblings and FLG Mutations</td>
</tr>
<tr>
<td></td>
<td>Conclusion</td>
</tr>
</tbody>
</table>
22 Acknowledgement
22 References

24 Molecular Genetics of Atopic Eczema
Ring, J. (Munich); Möhrenschlager, M. (Davos); Weidinger, S. (Kiel)
24 Abstract
25 Classical Genetics
25 Linkage Studies
25 Genes of Skin Barrier Function
26 Genes Involved in IgE-Mediated Hypersensitivity
27 Genes with Unknown Function
27 Conclusions
27 Acknowledgement
28 References

Pathogenesis of the Deviated Immune Response

30 Mechanisms of Immune Tolerance to Allergens
Fujita, H. (Davos/Yokohama); Meyer, N.; Akdis, M.; Akdis, C.A. (Davos)
30 Abstract
31 Pathogenesis of Allergic Diseases
32 B Regulatory Cells
33 Mechanisms of Allergen-Specific Immunotherapy
33 Role of T Cells
34 Role of Allergen-Specific IgG4
35 Regulation of Basophils, Eosinophils and Mast Cells
35 Clinical Use
36 Conclusions
36 Acknowledgements
37 References

39 Th17 and Th22 in Skin Allergy
Cavani, A. (Rome); Pennino, D.; Eyerich, K. (Munich)
39 Abstract
40 Th17 in Atopic Dermatitis
41 Th22 in Atopic Dermatitis
42 Conclusions
43 References

45 IL-25 Induces Both Inflammation and Skin Barrier Dysfunction in Atopic Dermatitis
Deleuran, M.; Hvid, M. (Aarhus); Kemp, K.; Christensen, G.B. (Ballerup); Deleuran, B.; Vestergaard, C. (Aarhus)
45 Abstract
47 Conclusion and Perspectives
48 References

50 Angiogenesis, Lymphangiogenesis and Atopic Dermatitis
Genovese, A.; Detoraki, A.; Granata, F.; Galdiero, M.R.; Spadaro, G.; Marone, G. (Naples)
50 Abstract
51 Proangiogenic Factors
53 Angiogenic Factors in Atopic Dermatitis
54 Cellular Sources of Angiogenic and Lymphangiogenic Factors in Atopic Dermatitis
56 Angiogenesis and Lymphangiogenesis in Experimental Models of Atopic Dermatitis
What Can Dogs Bring to Atopic Dermatitis Research?
Olivry, T. (Raleigh, N.C.)

Abstract
Canine Atopic Dermatitis Is a Common Spontaneous Animal Heritable Skin Disease
Dogs and Humans with Atopic Dermatitis Exhibit the Same Hypersensitivity Patterns
Canine and Human Atopic Dermatitis Are Phenotypically Similar
Canine and Human Atopic Dermatitis Have Similar Treatment Outcome
Canine and Human Atopic Dermatitis Have Similar Pathogenesis
Skin Lesions of Canine (and Human) Atopic Dermatitis Can Be Modeled Experimentally
Intradermal Challenges with Allergens or Anti-IgE Antibodies
Epicutaneous Allergen Challenges of Sensitized Dogs
Environmental and Systemic Allergen Challenges of Sensitized Dogs
Conclusions
References

Can Microbial Superantigens Influence Atopic Dermatitis Flares?
Alomar, A. (Barcelona)

Abstract
Effects of Malassezia on Immune Response
Conclusion
References
Further Reading

Inflammation-Induced Alterations in the Skin Barrier Function: Implications in Atopic Dermatitis
Vestergaard, C.; Hvid, M.; Johansen, C. (Aarhus); Kemp, K. (Ballerup); Deleuran, B.; Deleuran, M. (Aarhus)

Abstract
References

Clinical Aspects

Itch and Eczema
Darsow, U.; Pfab, F.; Valet, M.; Tölle, T.R.; Ring, J. (Munich)

Abstract
Pathophysiology
Itch Questionnaires in Atopic Eczema
Processing of the Itch Sensation in the Human Brain
Volunteer Studies
Patient Studies
Therapy of Itch in Eczema
References

Eczema Herpeticum
Wollenberg, A. (Munich)

Abstract
History and Epidemiology
Diagnostic Procedures
Pathogenesis of Eczema Herpeticum
Therapy of Eczema Herpeticum
Antiviral Chemotherapy of Eczema Herpeticum
92 Topical Treatment of Eczema Herpeticum
93 Ophthalmic Therapy
93 IFN Therapy for Eczema Herpeticum
93 Outlook
94 References

96 Bone Mineral Density in Patients with Atopic Dermatitis
Haeck, I.; van Velsen, S.; de Bruin-Weller, M.; Bruijnzeel-Koomen, C. (Utrecht)
96 Abstract
98 Conclusions
99 References

100 Immunosuppressive Effect of Prolactin-Induced Protein
Sugiura, S. (Otsu); Fujimiya, M. (Sapporo); Ebise, H. (Osaka); Miyahira, Y. (Otsu); Kato, I. (Kanazawa); Sugiura, Y. (Tokyo); Kimura, T. (Osaka); Uehara, M. (Yasu); Sato, H. (Otsu); Sugiura, H. (Otsu/Kusatsu)
100 Abstract
101 Materials and Methods
101 Animals
101 Induction of Oxazolone-Induced Contact Sensitivity
101 Immunohistological Study of the Ear with Anti-Prolactin-Induced Protein Antibody in Oxazolone Challenged Mice
101 Construction of Mouse Prolactin-Induced Protein Peptide
101 Animals and Induction of Oxazolone-Induced Contact Sensitivity
102 Induction of an Immunomodulatory Effect by Prolactin-Induced Protein Peptide
102 Measurement of Ear Thickness and Tissue Sample Collections
102 Histology and Immunohistochemistry of Ears on Mice Treated with Oxazolone and Prolactin-Induced Protein Peptide
103 Statistical Analyses
103 Results
103 Expression of Prolactin-Induced Protein in Skin Lesions in a Mouse Chronic Allergic Contact Dermatitis Model
103 Immunosuppressive Effect of Prolactin-Induced Protein Peptide in a Mouse Chronic Allergic Contact Dermatitis Model
104 Local Inhibitory Effect of Prolactin-Induced Protein Peptide Observed by Histopathology
105 Discussion
107 References

Therapy and Management

108 Is Food Allergy Testing Reliable in Pediatric Atopic Dermatitis?
A Population-Based Study
108 Abstract
109 Methods
109 Results
110 Discussion
111 Acknowledgement
111 References

113 New Strategies for Dealing with Staphylococcus aureus Colonization and the Emerging Methicillin-Resistant Staphylococcus aureus Epidemic in Atopic Dermatitis
Boguniewicz, M. (Denver, Colo.)
113 Abstract
113 Community-Acquired Methicillin-Resistant Staphylococcus aureus

VIII Contents
Preface

Allergy and allergic diseases have increased in prevalence dramatically over the last decades. Relevant determinants influencing the development of allergic inflammation come from the environment and are either enhancing – promoting allergy – or protective in nature. The lack of protective factors such as early stimulation of the immune system through infection or parasite infestation by improved hygiene seems to go along with allergy promoting effects of environmental pollutants such as traffic exhaust – fine or ultrafine particles – or tobacco smoke in the indoor air. Climate change with higher CO₂ concentrations in the atmosphere and increases in the Earth’s surface temperature may contribute to an increase in allergic diseases by prolonging the flowering period of pollinating plants and immigration of allergenic neophytes.

Great progress has been made in elucidating the pathomechanisms of allergic reactions both at the level of molecular genetics and in the understanding of the complex orchestra of cells and mediators in the allergic inflammation.

It has become clear that not only the deviated immune response is a prerequisite for allergy with dominant Th2 reactions and consequent IgE production, but also the epithelial barrier is of crucial importance both in the mucosal surface of the airway and in the skin.

In spite of the great progress in the experimental allergology and immunology, there is still a tremendous gap between the theoretical knowledge and the practical performance in daily life treating allergic patients in the office or in the hospital. This becomes especially obvious when we think of subjective symptoms such as itch, which is the major symptom of allergic skin disease.

Only on the basis of a better understanding of the pathomechanisms and the molecular pathways involved can new therapeutic and preventive strategies for future management of allergic patients seem possible.

This volume brings together a carefully selected list of articles based upon lectures given at the International Symposium ‘New Trends in Allergy VII’ together with the ‘6th Georg Rajka Symposium on Atopic Dermatitis’ organized in Munich in July 2010. At this symposium, two remarkable traditions were joined: the symposia ‘New Trends in Allergy’, which began in 1980 in Munich and have since been held in 5-year intervals in Munich, Hamburg and Davos. The International Symposium on
Atopic Dermatitis was started by Professor Georg Rajka in Oslo and held five times in Norway. Since 1996, taking the name of the founder, they have been continued all over the world, taking place in Aarhus, Davos, Portland, Rome, Arcachon, Kyoto and Munich, and have brought together all the experts both from clinics and research interested in the field of atopic eczema. The next Georg Rajka Symposium will be held in 2012 in Moshi, Tanzania, in order to stress the fact that allergy and eczema is not a disease of the so-called Western world, but can be found also in rural regions in central sub-Saharan Africa.

We would like to thank Alberto Giannetti (Modena), Alain Taïeb (Bordeaux), Kristian Thstrup-Petersen (Aarhus) and Hirohisa Takigawa (Matsumoto) for help in the development of the Rajka symposia. Mr. Preussler and Mrs. Burk deserve thanks for the excellent organization of the symposium in Munich. A final highlight was the performance of an ‘allergy musical’ by the coworkers of the Department of Dermatology and Allergy as well as the ZAUM [Zentrum Allergie und Umwelt (Center for Allergy and Environment)] at the Biederstein Campus of the Technische Universität München in the Löwenbräukeller: ‘King Ludwig II – His Life, His Death, His Allergy!’ In this play, undiscussed aspects of the mysterious end of Bavaria’s dream king were put to stage in a humorous fashion, at the same time giving a new example of very well accepted allergy education.

Thanks also go to Mr. Nold and Mr. Brian from Karger Publishers for the excellent help in the production of this book.

We would also like to thank the Christine Kühne Center of Allergy Research and Education (CK-CARE) as well as the Munich Allergy Research Society (Verein zur Förderung der Forschung und Fortbildung auf dem Gebiet dermatologischer und allergologischer Erkrankungen e.V.) for their generous support.

Johannes Ring, Munich
Ulf Darsow, Munich
Heidrun Behrendt, Munich