Allergy and Asthma in Modern Society:
A Scientific Approach

Dedicated to Kurt Blaser

Volume Editor

Reto Crameri  Davos

29 figures, 3 in color, and 12 tables, 2006
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Abstract

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Costimulatory Molecules Displayed on DC Surfaces Modulate Th-Cell Differentiation

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M. Akdis, K. Blaser, C.A. Akdis, Davos

Abstract

Anergy, Tolerance and Active Suppression Are Not Fully Distinct Events

Essential Features of Allergic Inflammation

T_{Reg} Cells

Tr1 Cells

Th3 Cells

CD4+ CD25+ T_{Reg} Cells

Other Regulatory Cells

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Dendritic Cells That May Play a Regulatory Function

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Suppression Mechanisms of T_{Reg} Cells

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M. Jutel, Davos/Wroclaw; K. Blaser, C.A. Akdis, Davos

Abstract

Cellular Sources of Histamine

Synthesis and Metabolism of Histamine

Histamine Receptors
Allergic diseases and asthma constitute a growing health care problem, especially in industrialized countries. In spite of marked worldwide variation, the prevalence of symptoms of asthma, eczema and allergic rhinoconjunctivitis is increasing. Although genetic factors defining the atopic background of a population are undoubtedly important, they cannot explain this phenomenon. As the genetic background of a population must be regarded as quite stable over short periods of time, environmental factors must be included to explain the remarkable changes in the prevalence and severity of asthmatic and allergic diseases during the last 40 years. As brilliantly summarized by Platts-Mills et al., environmental factors can influence the spread of these diseases; however, single changes in environmental parameters alone cannot explain the consistency or the scale of the rise in allergy and asthma observed between 1960 and 2000. Our environment is extremely complex, poorly defined and difficult to monitor. However, a direct demonstration of the pivotal influence of environmental factors on the severity of asthma comes from a recent reinvestigation by Schultze-Werninghaus of a very old observation describing the beneficial role of sojourns at high altitude. The therapeutic value of such sojourns for severe bronchial asthma patients is well documented, and there is no scientific reason to doubt it. Obviously, our limited knowledge about host-environment interactions and atopic diseases favored the development of various, more or less attractive hypotheses and theories aiming to explain this phenomenon. Among these, the hygiene hypothesis, discussed by Renz et al., is perhaps the most attractive. According to current scientific views, it tries to integrate the interaction between environmental factors, innate and adaptive immunity into a sophisticated
model. We must realize that the human body is not an isolated system. To survive, we need a continuous selective exchange with our environment, allowing the uptake of essential biovital elements and excretion of unwanted metabolites, but aiming to avoid offending agents. Physical barriers and an orchestrated primary and secondary line of defense are required to allow survival. Skin and mucosal surfaces represent by far the largest interface between a human being and the environment and from this point of view it is not astonishing that the respiratory tract (Simon, Kay), skin (Breuer et al., Santamaría-Babi, Bonini) and digestive tract determine an individual’s quality of life. However, other diseases, notably conjunctivitis, an often forgotten disease (Bonini), significantly contributes to the health burden of modern society as well.

Inappropriate immune responses to normally harmless environmental antigens, following, for example, exposure to fungi (Crameri et al.) still represent an unsolved health care problem although our understanding of the structural basis of allergens (Aalberse) and their role in the pathogenesis of chronic allergic diseases (Schmid-Grendelmeier et al.) is rapidly increasing. Complex mechanisms regulate the healthy immune responses to allergen exposure (Carballido et al., Akdis et al.) and it is the long-neglected study of these responses that recently contributed to a better understanding of the orchestrated cascades resulting either in normal, protective, or abnormal, disease-related immune responses. Antigen-antibody interactions at the end of the cascade are relatively easy to access experimentally and, as a consequence, our knowledge about these phenomena is quite advanced. Early, tightly regulated cellular interactions resulting from the complex interplay between cytokines, receptors and small molecules, such as histamine (Jutel et al.), strongly depending on genetic background and environmental influences, determine the immune response initiated and the fate of each single individual. It becomes increasingly evident that such immune responses in allergy and asthma are extremely complex. New global technologies based on gene expression profiling (Schmidt-Weber) and proteomic approaches will be required to integrate our knowledge about molecular and cellular interactions into more complete networks aimed at understanding the pathophysiology of allergy and asthma.

However, there is light at the end of the tunnel. The considerable progress in our understanding of molecular and cellular interactions starts to translate into new strategies to combat allergic diseases (Akdis et al., Achatz et al.). Although many drugs are available to control the symptoms of allergy and asthma, immunotherapy is the only treatment currently able to cure these diseases. Several new treatments have been or will be introduced soon for clinical use and will hopefully strongly improve immunotherapy and benefit the patients.
Allergy and asthma are very important diseases, and as a consequence, an overwhelming number of original contributions, reviews and books covering the different aspects of these diseases are published every year. Why a book more about this topic? The answer to this justified question can be found in the introduction by Johannes Ring: Kurt Blaser, the director of the Swiss Institute of Allergy and Asthma Research, celebrated his 65th birthday on June 25, 2005. He dedicated all his life to allergy and asthma research and has become one of the most prominent and appreciated global players in this field. I am convinced that, together with me, all authors of this book and many other scientists worldwide are grateful to him for many exceptional scientific contributions and political fights to speed up progress in a field which, in spite of its recognized socio-economic impact, still lacks the political support to mobilize the financial resources required to satisfy its needs. Thank you Kurt!

I am especially grateful to Thomas Nold and his team for their excellent cooperation in editing this book, to the industrial sponsors and to Johannes Ring who supported the idea from the beginning. Of course, I am very grateful to the authors, who have spent much time for the preparation, revision and final checking of the manuscripts. Finally, a big thanks goes to Rosalina and Danja, the unlucky members of the family, waiting at home until I am back from work every day. I am not so sure that I would have that much patience.

Reto Crameri