

Preface

100 million days per year. One can only imagine what could be achieved in that huge amount of time. This is the number of days people with allergies miss at work or in school in Europe within one year, because they do not feel well. Not counting the days when they are physically present, but not quite up to their tasks.

The burden of allergic diseases is high. Not only the symptoms of the diseases itself, such as running and blocked nose, sneezing, itchy skin and others, but also the accompanying impairment in terms of sleeplessness, abandonment of certain activities and food, anxiety of an allergic shock, as well as time-intensive and expensive treatments decrease the quality of life of the patients. Many patients develop mental health issues such as anxiety and depression. Often not only the patients themselves, but also their families suffer under these circumstances.

In 2025, according to estimations, every second inhabitant of the European Union will have to deal with some form of allergy: that makes more than 225 million people. Knowing about the increasing prevalence of allergic diseases, we work for understanding the mechanisms and developing effective prevention and management of allergies. This book aims at providing the current knowledge about allergic diseases to a large number of scientists, practitioners and also the people concerned.

In it, the knowledge and expertise of 65 leading scientists of the field from 8 different countries is brought together to take a close look at all aspects of allergies. What is known about their history, their different forms, the mechanisms of their development, about risk factors, diagnosis, disease management and – above all – about ways to prevent them are all collected in this single volume. It presents the ‘state of the art’ and also gives an overview of basic science beyond mere textbook knowledge. It maps what is established as well as what is still to be explored, hopefully in the near future, in order to lighten the burden for all the people suffering and prevent further increases in the prevalence of allergies.

This volume covers large ground.

Part I of this book explains the historical and epidemiological background of allergies. In the chapter on the *History of Allergy*, Ring starts with the first descriptions of allergy in antiquity, in the Middle Ages and in Renaissance. The chapter continues with the beginnings of allergology in the early 19th century and finally describes the developments in diagnosis, therapy and in understanding the pathophysiological mechanisms of allergic diseases in the 20th century. Genuneit

and Standl then summarize our knowledge on the *Natural course and risk factors of allergic diseases* in the 21st century from an epidemiological perspective.

Although the mechanisms at work when allergies develop or are triggered are not yet fully known – at least on the molecular level – the chapters of *Part II* describe some of the general mechanisms that have been identified as important. Knol and Gilles take a close look at the four types of hypersensitivity reactions that underlie the overreacting immune systems and bring this distinction that has been developed more than 60 years ago in line with actual findings. Biedermann et al. concentrate on the barrier function of the skin and stress the importance of its integrity which is protected by complex measures such as wound repair or anti-infective immune reactions. New methods, e.g. new sequencing technologies also offer fascinating new insights. Schwierzeck, Hülpiusch and Reiger use these for analyses of various microbiomes. In their article they explain research methods and report findings concerning alterations of the microbiome of the skin, the lung and nasopharynx that correlate with allergic diseases.

Part III then turns towards the various faces of allergic diseases and new forms of medical treatment. Papadopoulos et al. offer an up-to-date view on asthma, presenting up-to-date information on epidemiology, definitions, diagnosis and treatment options. Müller clarifies the peculiarities of allergic conjunctivitis. Traidl et al. give attention to the pathogenesis and pathophysiology of atopic eczema, focusing especially on new therapeutical possibilities offered by targeted treatments, e.g. the IL-4R alpha specific monoclonal antibody dupilumab. Maurer et al. outline the classification, diagnosis and management of urticaria. Pfützner et al. discuss the actual possibilities of Allergen Immunotherapy (AIT) and Wang fathoms the possibilities of precision medicine to treat chronic sinusitis.

Part IV of this book focuses on the treatment of various forms of allergic diseases with different environmental triggers. The first chapter of *Part IV* focuses on food allergies. Food as one relevant environmental trigger can cause allergic reactions, most commonly in the case of cow's milk, hen's eggs, fish, shellfish, peanuts, soybeans, tree nuts or wheat. Bohle and Werfel describe the different mechanisms and types of allergic reactions to food and the possibilities of treatment. The treatment options are exemplified by peanut and apple allergy. Another relevant trigger can be drugs. Mockenhaupt addresses adverse allergic reactions to drugs and focuses on manifestations on the skin. Also, the exposition to allergens at the workplace can lead to a higher risk for allergies in certain occupations. For example, bakers can become allergic against wheat flour proteins or other cereals, which can lead to baker's asthma. In the article by Raulf on *Occupational Respiratory Allergy* the important knowledge on the diagnosis and management of occupational allergies is summarized. In the following chapter, Giminez Arnau and João Luís present an overview on contact dermatitis and emphasize the relevance of patch testing in this context.

Part V now attends to the expressions of allergic diseases on the molecular level. Ferreira examines the role of B cells in the development of allergies as well as in the induction of tolerance with the help of AITs. Ohnmacht und Eyerich offer detailed insight into different kinds of Th- and Treg-cells and the roles they play in the

process of allergic inflammation. Martin and Esser in turn explain progress that has been made in understanding the cellular and pathomechanisms underlying the allergen-induced inflammation processes, findings clearing the way for new ways to treat allergies.

Some factors increase the risk for the development of allergic diseases. Those risk factors are described in *Part VI* of this handbook. There is a genetic component in allergies. Haider et al. summarize the current knowledge on *Genetics of Asthma and Allergic Diseases*. Identifying the specific asthma genes is connected with difficulties, but there are several approaches to disentangle the genetics of asthma and allergy, e.g. based on the definition of allergy subtypes. However, genetics only cannot explain the increase of allergies in the last decades. Environmental factors play an important role in this context. This is why understanding the epigenetic mechanisms, which are explained by Potaczek et al., have the potential to improve treatment and prevention of allergic diseases. Air pollution is one of the environmental factors that are linked to morbidity and mortality. Schikowski describes how air pollution affects our health and what we know about the effect of indoor and outdoor pollution on allergic diseases. The increasing prevalence and incidence of allergic diseases is often referred to lifestyle changes. But not only the behaviour and lifestyle, but also social and environmental structures are changing. Heuson describes how climate change and globalization both increase the exposure to allergens and therefore might increase the risk of allergies. As the exposure to allergens and the prevalence of allergic diseases follow a social gradient, also ethical questions are asked and implications for allergy policies are given.

Part VII now addresses diagnostic possibilities concerning different types of allergies. First, the diagnostic procedure in type-I allergy is depicted by Treudler and Simon. Mahler and Uter then precisely explain the processes and problems applying and analyzing epicutaneous patch tests, recurring to best practice recommendations developed within current guidelines.

The prevention of allergic diseases is a main public health goal. Therefore, *Part VIII* focuses on the primary (Landgraf-Raulf & von Mutius), secondary and tertiary prevention (Fieten et al.). As there are promising results on the effect of nutritional interventions for the prevention of atopic diseases, Szklany et al. provide an overview on this topic. Last but not least, it is important to educate patients. Patient education can improve the quality of life and decrease symptom severity. Traidl et al. reflect the positive effects of patient education programmes for atopic eczema. Not only patients with atopic eczema, but also patients with other chronic conditions, such as allergic asthma, could benefit from the implementation of education and training programmes.

Allergy research is characterized by enormous success in the recent years. Therapies have improved the lives of many patients. Still allergic diseases do not have the attention and the assessment they deserve. Many patients still trivialize their illness and patient centred care could be improved, also by creating regulations where helpful and necessary. In the course of climate change the numbers of allergic patients will increase. For example, the pollen season on the whole becomes longer, the number of pollen in the air increases, even pollen itself becomes more allergic.

We have to go on to search for solutions to achieve resilience in the face of the changes that will affect our lives. And to search for answers for the many questions that are still to be answered. What exactly turns a person into an allergic person, a certain substance into an allergen? A recent study discusses the possible evolutionary value of the allergic phenotype: being allergic might protect against parasitic infections, accelerate wound healing, protect against venoms or possibly even tumours. Many mechanisms still are not exactly known.

Further research is needed. We need studies that explain the mechanisms of the different types of allergic inflammation to different allergens, the underpinning mechanisms of chronification or the pathomechanisms that lead to the disease, especially ones that translate the results into the complex and sustainable disease management. We need studies that examine hypersensitivity reactions, personal thresholds to allergens and understanding in space and time why a sensitization moves into allergic disease. We need to know which environmental factors or psychosocial factors increase the risk to become allergic and the development of the disease, and we need to distribute this information as best we can. We need to know more about food allergies and intolerances, about allergic diseases of the intestinal tract, more about hypersensitivities against pharmaceuticals, more about allergic rhinoconjunctivitis, about its progression and possible therapies. Our list is not at its end here.

At the end of these introductory thoughts, it remains to say “Thank you” to all who contributed to this large compendium and helped this cornerstone of allergy research to materialize.

We progressed this far, part of the journey still lies ahead.

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