Allergy and Immunology

AIMS Allergy and Immunology, 1(1): 15-20.
DOI: 10.3934/Allergy.2017.1.15
Received: 22 April 2017
Accepted: 24 April 2017
Published: 24 April 2017

http://www.aimspress.com/journal/Allergy

Editorial

On the way to allergy prevention—future perspective or illusory aim?

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Prevention and treatment of allergies must be of global interest [1]. The reasons for this statement are manifold. First of all, allergies are the earliest in life occurring non-communicable diseases (NCDs). Chronic non-communicable diseases have at least two features in common–the impact of the environment and their chronicity. This fact points to a specific vulnerability of the developing immune system to modern environmental changes. Reasons for the increase in the prevalence of allergic diseases have not become entirely clear yet but are thought to be closely linked to environmental factors that affect the regulation of tolerance in the immune system [1,2]. Different epidemiological studies have underlined the importance of environmental exposures for health as exemplified by the allergy-protective effect of a farming environment [3,4].

The loss of peripheral tolerance to environmental agents and the development of allergic disease are influenced by several factors including host-specific such as genetics and environmental factors. Gene-environment interactions lead to epigenetic changes which proves finally that the indeed “the environment matters”.

Innate and adaptive immune mechanisms play a crucial role in the decision making that occurs in allergy in two steps: Initial sensitization in type I allergy is associated with type-2 immunity and secondarily development of symptomatic disease with a spectrum from seasonal disease down to chronic manifestation in various organs. Sensitization affects 40%, symptomatic disease 20%, and chronic to severe about 5% of the population at all ages. There are currently no biomarkers available that can reliably predict which patients are at risk progress to step into the next level of disease escalation and my research efforts will face those biomarkers, too.

We know today that exposure to allergens is necessary but not sufficient alone for the development of allergy [5]. Pollen allergenicity it no more only a function of the allergen itself. The analysis of allergenic and non-allergenic substances of pollen has brought profound insights about the impact of pollen as allergen carrier on the human immune system [6,7]. Pollen contain non-allergenic mediators such as proteases and oxidases which may trigger or enhance the immunological reaction. Among these non-allergenic factors are PALMs (pollen-associated lipid mediators) and adenosine, which have an immune-modulating and immune stimulating effects [8].

Studies on the environmental exposure to multiple agents have not so far clarified the interplay between multiple factors of internal and external environment at the molecular level. Many different factors-the role of individual microbiome and environmental microbes, the potential impact of the wide-spread use of drugs and chemicals, body weight, physical inactivity, and food ingredients-with regard to allergy development are mostly unknown [2,9]. The impact of climate change on allergy incidence is likely but unclear in detail. But this urgently needs further investigation [10]. Importantly, tools for predicting the impact of future changes in environmental exposure have to be developed.

This is why, nowadays research on allergies encompasses translational immunology and the study of our environment. In order to understand the impact of the environment on the human immune system it has to be defined holistically as the sum of exposure to biological, chemical, microbial, physical, and psychosocial factors. The biological aspect begins with phenological observation and continues with the measurement of pollen in different altitudes [11] and should be expanded to allergen concentration in different fractions of the air [12].

One major goal must be to identify environmental factors responsible for allergy initiation and perpetuation. This in turn represents a prerequisite for the development of prevention strategies to stop allergy-development. Environmental factors impact on allergy development at least in two different ways. On the one hand, they influence the susceptibility of individuals towards the development of allergies i.e. barrier disruption. Furthermore, the role of environment has gained significant importance since the effects on the individual are today “measurable” on an epigenetic basis. On the other hand, they act on the allergen carrier itself enhancing its allergenic potency. We and others have proven that anthropogenic factors such as traffic-related air pollutants and climate change-especially ozone-affect the plant phenology [13], pollen’s allergenicity [14], and microbial load of pollen [15].

A new player in the environment is the so called “microenvironment”–the microbiome. Microbial diversity seems to be like central theme in the context of both–the environmental microbiome [16] and the individuals’ one [17]. Of special interest for allergy research is the microbiome on skin and mucosa of the upper airways [18]. It is also called “The Molecular Revolution in Cutaneous Biology” [19]. We know that microbial factors influence the physical barrier function of the skin and the surface structure of the respiratory tract. The latter two are the first contact zone for allergens and environmental pollutants. A well-functioning skin barrier protects from allergens whereas a defect barrier allows for the intrusion of allergens and thus elicits an immunological response other than tolerance. The patho-bacteria *Staphylococcus aureus* has been identified years ago as a major cause for the strong inflammation in atopic eczema patients [20]. But the mechanism underlying the increase in abundance of this microbe are supposed to be related to the loss of abundance of commensal microbes. The epithelial-microbiome interaction must therefore

stand in the center of our research efforts. We have to develop methods to nurture the "good" microbes in order to rebalance the microbiological skin population.

But also the environmental microbiome should be further investigated since recent data clearly shows that the environmental microbiome impacts on the human microbiome [21]. In this respect, it is of special interest in allergen research to study the microbiome on pollen which contains bacterial and fungal species for which the respective function has not been explored in full terms yet. Most interestingly, the microbial diversity on pollen is species specific and can be influenced by environmental factors [15].

Further reasons for bringing allergies and NCDs into the centre of medical translational research are the negative consequences on the quality of life of patients and their families. Environmental trigger factors delimit outdoor and indoor activities similarly. Another factor which enhances the course of allergic and non-communicable disease is stress [22]. However, the neurogenic component in atopy and allergy has been insufficiently investigated to date even though it is potentially of great pathogenic relevance. Stress was recently shown to activate elements of this component and is vividly discussed as a cause of exacerbation [23]. Scientific proof of stress-induced neuronal plasticity and neuro-immune interaction in atopy or allergy remains lacking. This is for sure one ideal field of future research because psychosocial factors such as stress can influence the hormone expression in patients with significant changes to the immunological warning system.

The impact of allergies and NCDs can also be attested in economic terms. Yearly damage numbers of three-digit trillion euros due to lowered performance ability at school, training, study, and work-place (let alone the treatment costs for the relevant follow-up diseases) stand in marked contrast to about 150 euros per year and patient for the treatment of an allergy. The awareness in politics and among physicians about the promising treatment possibilities must therefore be steadily increased.

A special focus of current medical research in Allergy is on the refinement of the specific immune therapy (SIT). Allergen-specific immunotherapy (ASIT) affects the immune response towards allergens at different levels and is currently the only causal treatment of allergic diseases and thus considered a cornerstone in the management of allergic diseases. The understanding of the immunological mechanisms occurring during ASIT encompasses the building of specific blocking antibodies, tolerance-inducing cells and mediators. Despite this knowledge, several factors limit the broad application of ASIT. Today, allergy vaccines are based on natural allergen extracts which are often of poor quality which is perhaps the cause for the comparable low efficacy in the clinical practise. This is why much more research is need to better understand the mechanisms and to make ASIT more effective than it is today.

Therapy is important, however the final aim of all our efforts is to come up with a full-explanatory prevention plan. This will only be possible by means of interdisciplinary work of allergologists, biologists, immunologists, medical staff, and many more. The chances are realistic to find new ways of preventing an epidemiological disease spreading. This can be effected with the help of education programs on the one hand and the control of environmental factors (or at least their full understanding) on the other. The result must be an increase of awareness in politics and society for allergic diseases in general and improved medical training on how to treat that kind of diseases effectively in particular.

The Global Allergy Forum [1,2,24] stands exemplary for an interdisciplinary approach in order to face challenges and opportunities toward a precision medicine with special attention to atopic

dermatitis, eczema, and above all allergies. The declaration addresses key questions with regard to epidemiological studies and standardized approaches of future research. Under consideration of prenatal factors and validated methodologies as well as proper definitions of regional and global factors, therapeutic and preventive measurements may ensure better conditions for patients and healthy people equally. With regard to research on skin barrier, the declaration puts a focus on epigenetic variations of gene functioning. To get a full understanding of the acquired and epigenetic regulation, to research the impact by individual microbiota, and finally to improve systemic and targeted therapies on the barrier function are among the main issues in the declaration. Not to forget the education programs for patients and training possibilities for medical staff. All this includes the formulation of guidelines, an improved collaboration between different disciplines, and the implementation of interprofessional learning.

My current position as ordinaria and director at the Chair and Institute of Environmental Medicine, UNIKA-T, can be seen as a further example of such interdisciplinary research efforts. Together with the Chairs of Health Care Operations/Health Information Management and Epidemiology, an important step has been taken toward a unique research approach in fighting allergies and related skin diseases. This also encompasses informing patients about environmental trigger factors especially about pollen air measurements. Therefore, a collaboration of several institutions with a wide range in research fields enables a pollen information service which delivers data in 2-hour-intervals on pollen flight. By the help of this kind of data, allergic patients become empowered to better regulate their medication and to plan their activities according to actual pollen flight information.

For conclusion, I will pave the way to elaborate on what is the common ground in all the above mentioned topics, questions, opportunities, and challenges. Clearly, this is the environment and its manifold interactions with the immune system. One major issue therefore is to me the exploration of environment-host interaction.

AIMS Allergy and Immunology is a journal which provides the perfect platform for researchers and physicians likewise to bring the most recent findings in therapeutic, preventive, and educational matters to the fore. Thus AIMS contributes to an increase in awareness for allergic diseases on a world-wide basis. Let us address this together and find new avenues of understanding and interacting with the environment for a better health in the near future.

Conflict of Interest

The author declares no conflicts of interest in this paper.

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