Pollen on their way astray – First contact via cross-kingdom signaling leading to far-reaching consequences for the atopic march

Exposure to anemophilous pollen has both acute and chronic effects on mucous membranes and skin surfaces. Allergic rhinitis, asthma, contact urticaria, conjunctivitis, eczema, and eosinophilic esophagitis belong to the wide array of diseases and symptom-complexes induced, caused and triggered by wind-dispersed pollen.[1] Textbook knowledge describes pollen as a trigger of IgE-mediated, Th2-dominated immune responses at mucosa and skin.[2] However, since the beginning of this century, the concept has been extended to pollen as non-specific pro-inflammatory and immunomodulatory actors beyond their function as allergen carriers.[3–5] Yet, why particular pollen-derived proteins tend to act as allergens in susceptible hosts is a fundamental mechanistic question that remains still today largely unanswered. We know that the allergen can often, although not always, cause direct activation of the innate immune system through intrinsic activity (proteases/RNAse) or through a receptor-mediated responses.[3] This not only describes an intriguing mechanism for enhancing allergenicity but also exemplifies an important principle for driving allergic sensitization. Beyond intrinsic activity of the allergen, we and others described that pollen release low molecular weight substances such as phytoprostanes, adenosine, and as yet unidentified mediators that bind to specific immune system receptors such as LTB4 receptors, PPAR-gamma, and activating NF-kappaB-dependent mechanisms.[6–8] In the "normal life" of a pollen, proteins, lipids, and sugars released on contact with wet surfaces are in part responsible for the pollen stigma recognition process. Thus, they are mediators indispensable for the pollen fertilization process. The binding of plant mediators to human receptors suggests a cross kingdom signal transduction originating from a molecular mimicry that has also been described for other aeroallergens, such as house dust mites.[9] Interestingly, pollen per default induces tolerogenic immune responses via adenosine—a pathway that is hampered in allergics, for yet unknow reason.[10] The vast immunogenic effect of pollen is even more expand by the new finding that pollen is not only harmful for allergic patients but also induce symptoms in non-allergics.[11] This observation culminates in the realization that pollen impair the mucosal innate immune response leading to a higher susceptibility to viral infection.[12,13] Taking this comprehensive knowledge into account, it is all the more threatening that pollen is increasing in quantity, occurrence and aggressiveness due to climate change and environmental polluters. Long-term data from all continents show that pollen season is becoming longer, more pollen are flying and new, invasive species such as ambrosia are on the rise.[14,15] Especially the interaction between genetics and (a-)biotic factors regulating pollen production and release were recently elucidated.[16]

The other side of the coin shows that environmental and pollen-triggered respiratory diseases such as asthma, allergic rhinitis (AR), and chronic obstructive pulmonary disease (COPD) affect millions worldwide and pose a significant global public health burden.[17] Increasing concentration of pollen implicates increasing symptoms of allergenic patients.

This complex interaction of environmental factors with human health and disease makes comprehensive epidemiological studies urgently needed. The challenge for these studies is to link health, disease, and environment in space and time. First, the available medical data sets are mostly from different sources, and some are poorly structured. In order to use them for interdisciplinary analysis, they need to be processed in advance using novel medical informatics techniques. The integration of these disparate data streams adds a new level of complexity and thus poses a challenge for scientific studies. However, the ability to integrate more aspects of the complexity in which we live into scientific analyses holds great potential to better understand the precise relationships between the human health, behavior, and the environmental exposome.

In this view, the study presented by Gisler et al is right on target. Their research focused on the environmental impact in the first year of life on the development of asthma. The authors aimed at a comprehensive exposome approach including biogenic (pollen) and also pollutants such as PM2,5 and NO_2. The impressive part of the study is the high granularity of the data with symptom data of 401 term-born infants of 14,874 measurement time points.

The key finding of Gisler et al pollen exposure as early as during the first year of life is associated with an increased risk of respiratory symptoms. This becomes even more interesting when considering that this effect is independent of maternal atopy and the sex of the child. This study validates and expands the finding of a prospective study up to adolescence in the GINIplus and LISA cohort[18] that also provides suggestive evidence that early pollen exposure has a negative effect on later lung function, which is in turn influenced by

acute pollen exposures. Since the first year of life is a particularly sensitive period for lung development, the observed deleterious effect of pollen exposure could be important for the development of chronic asthma in childhood. In light of the epithelial barrier hypothesis,[19,20] this observation takes on even greater significance, as cumulative environmental exposures during the first year of life could be detrimental and crucial for the development of the atopic match. A positive aspect of this observation is that the first years of life also seem to be the window of opportunity for the prevention of chronic inflammatory mucocutaneous diseases by protecting the barriers. Shaping the environment to be protective has far-reaching effects, ranging from saving the climate to saving the environment of sustainable health.[14,15]

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CONFLICT OF INTEREST

The author declares that there are no conflicts of interest in relation to this work.

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