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EDITORIAL

The past, present, and future of allergic diseases in China

Allergic diseases have become a global health problem and pose a significant burden on healthcare resources due to their increasing prevalence, severity, chronic nature, and associated management cost. If the current increasing trend continues, it is expected that allergic diseases will reach 4 billion cases worldwide by the 2050s.[1,2] Currently, approximately 30%–40% of the global population suffers from some form of allergies, and an increasing trend in the prevalence of various allergic diseases has been reported in China in recent years.[3] A national cross-sectional China Pulmonary Health study reported that the overall prevalence of asthma was 4.2%, and a 6-year period survey based on 18 major cities found that the prevalence of self-reported allergic rhinitis (AR) was 17.6%.[4] Furthermore, another multi-center study demonstrated that the overall prevalence of self-reported AR and physician-diagnosed AR was 32.4% and 18.5%, respectively, in the northern grassland region of China.[5] Zheng et al. analyzed the clinical characteristics of AR patients in 13 metropolitan cities of China and reported variances in AR pathogenesis due to regional differences, presence of dust mites, and autumn pollens that contribute to peak periods of AR during summer and early autumn in China. Furthermore, the prevalence of self-reported food allergy in northern China is about 18.0%,[6] and a multi-center cross-sectional study from 39 tertiary hospitals in 15 provinces demonstrated that the incidence of atopic dermatitis (AD) in outpatients was 7.8% (95% CI: 7.3–8.4).[7] In addition, chronic rhinosinusitis (CRS), as a heterogeneous inflammatory disease occurs in mucosa of the nasal and paranasal sinus, affects approximately 8% of Chinese adults.[8] Based on the presence or absence of nasal polyps, CRS can be divided into 2 major clinical phenotypes. In recent years, the inflammatory endotypes of CRS with nasal polyps (CRSwNP) have received increasing attention. Our previous study found that CRSwNP patients from Beijing demonstrated that Th2 and non-Th2 mixed patterns and those from Chengdu existed a non-Th2 pattern.[9] We also found that the comorbidity of eosinophilic CRSwNP increased over the past 2–3 decades with the urbanization in China.[10] Thus, the increasing prevalence of allergic diseases in China poses significant challenges for their prevention, diagnosis, and treatment.

Increasing contributions by Chinese scholars in the field of allergic diseases are reflected in the number of articles published by Chinese scholars in *Allergy*, with China ranking among the top five contributing countries. The discovery of hay fever in 1819 by John Bostock, as he described a periodic affliction of the eyes and chest, is considered the first case report of AR. Nevertheless, the symptoms of allergic diseases have been described since ancient times. In fact, more than 3000 years ago, the book of "Rites," which describes the social norms, governmental organization, and the guidelines to conduct rituals during the Western Zhou Dynasty, recorded that there were AR patients as early as that time and there existed a correlation between the occurrence of AR and changes in the natural environment.[3]

Rapid industrialization in China continues to accelerate environmental degradation, resulting in significant environmental challenges. Moreover, changes in the living environment and lifestyles are responsible for the increased prevalence of allergic diseases. The epithelial barrier hypothesis proposes that the epithelial barrier damage caused by the toxic agents present in the modern environment may induce an increase in allergic diseases.[11] This hypothesis brings together the hygiene and biodiversity hypotheses. Studies have demonstrated that the microbiome goes deeper in the epithelial barrier disrupted areas and initiates a microbial translocation to deeper tissues through the epithelial barrier. Microbial dysbiosis occurs with the colonization of opportunistic pathogens followed by the development of an immune response to the microbiome and chronic mucosal inflammation takes place. Accordingly, the microbiota plays a crucial role in regulating epithelial inflammation via modulating the immune response. Although our understanding of the mechanisms by which the microbiota influences AR has improved, the driving forces behind the global increase in AR remain to be elucidated.

In the current issue, Zhao et al. reported differential nasal microbiota composition in recurrent and non-recurrent chronic rhinosinusitis with nasal polyps (CRSwNP) samples.[12] Abundances of *Shewanella* and *Peptostreptococcus* were markedly decreased in recurrent samples compared with non-recurrent counterparts, whereas *Friedmanniella*, *Curvibacter*, and *Pseudoxanthomonas* were far more abundant in recurrent samples than in non-recurrent counterparts. A LASSO regression-based model was established to predict CRSwNP recurrence with high accuracy (91.4%). This was the first study to report a nasal microbiota-based prediction model of CRSwNP recurrence and to propose nasal microbiota as a predictive marker of CRSwNP recurrence. Zhong et al. investigated the mechanisms underlying non-eosinophilic CRSwNP inflammation by measuring the expression levels of INOS, CD86, p-mTOR, HIF-1α, and VEGF in non-eosinophilic CRSwNP samples and controls. Their findings suggest M1 macrophage polarization through mTOR/HIF-1α/VEGF signaling.[13]

To elucidate the mechanisms by which gut microbiota inhibits food allergic reactions, Wu et al. demonstrated that the

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antibiotic-mediated depletion of commensal gut bacteria in mice leads to the bile acid (BA) activation, which could enhance retinoic acid (RA) signaling in mucosal dendritic cells. Furthermore, the BA-RA pathway could enhance food allergen-specific immunoglobulin E (IgE) and G1 (IgG1) production.[14] This study highlighted BA-RA signaling as a potential therapeutic target for food allergies.

Using endobronchial optical coherence tomography (EB-OCT), Su et al. assessed the changes in airway structures and bronchodilator responses in patients with various degrees of asthma. Airway remodeling was positively correlated with asthma severity and medium-sized airways had a quicker response to bronchodilation than small airways.[15] Zhan et al. investigated the immune mechanisms driving nonasthmatic eosinophilic bronchitis (NAEB) and found increased numbers of ILC2s and $CD4^+CRth2^+$T cells in NAEB and eosinophilic asthmatics (EA) patients compared with healthy controls.[16]

House dust mites have been reportedly the most prevalent allergens in south China. Zhou et al. were the first ones to demonstrate that the expression of genes encoding allergens could be regulated via miRNAs in a *Tyrophagus putrescentiae* mite. They performed deep miRNA and whole-transcriptome sequencing during the different stages of a mite life cycle and analyzed the expression of allergen-encoding mRNA and miRNAs. They found that miRNAs could bind to target allergen-encoding mRNAs, thereby highlighting the role of miRNAs in regulating the expression of allergen-encoding mRNAs in mites. These findings will help us develop novel treatment strategies for allergic diseases caused by dust mites.[17] The miRNAs, a class of short non-coding RNAs, can regulate gene expression post-transcriptionally, and miRNA-mediated regulation of gene expression has been widely investigated in allergic diseases. Zhang et al. demonstrated that miR-146a enhances regulatory T cell differentiation and their function in AR by targeting STAT5b.[18] Overactive immune responses are a hallmark of allergic diseases, wherein IgE responses are induced in response to allergen recognition. To explore the origin of IgE in atopic dermatitis and psoriasis, Luo et al. analyzed the B cell receptor repertoire and reported a heterogeneous origin of IgE generated in atopic dermatitis and psoriasis, and proposed that skin inflammation may contribute to increased production of natural IgE.[19] Furthermore, Wu et al. elucidated the basis for insufficient protection provided by the *Mycobacterium bovis* bacillus Calmette-Guérin (BCG) vaccine against tuberculosis (TB).[20] They demonstrated that deletion of *BCG_2432c*, an autophagy inhibitory factor, could promote antigen presentation and improve the vaccine effectiveness against TB.

Collectively, the articles published in the present issue of *Allergy*, which is dedicated to Chinese allergy science, not only elucidate the microbiota changes related to the recurrence of nasal polyps and food allergies based on precision medicine but also highlight the regulatory roles of non-coding RNAs and the immune system in the pathogeny of allergic diseases. With the rapid development of China's economy and changes in the environment, the heavy burden of allergic disease in China is increasing. This highlights that further studies are needed for advancing in basic research and clinical investigations to develop more effective strategies on prevention, control, and therapy of the allergic diseases. We acknowledge the continuous efforts of Chinese scholars in the field of allergy and the progress made by them. As editors of *Allergy*, we look forward to more international cooperation and contributions from Chinese scholars to the field of allergy.

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CONFLICT OF INTEREST

CA and LZ are editors of Allergy.

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