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Editorial

Regulation of upper airway inflammation facilitates comfortable breathing

In *Allergology International* (AI) Vol. 64 No. 2, we offer a set of review articles entitled "Regulation of upper airway inflammation facilitates comfortable breathing," as well as original articles and letters to the editor. We believe that this review series will provide you with the latest concepts in chronic rhinosinusitis (CRS) and allergic rhinitis (AR).

CRS and AR are the most widespread nasal diseases. CRS was dominant before 1980; thick, yellow, or greenish discharge drained from the noses of many children or was swallowed. For many adult CRS patients, Caldwell-Luc operations, which completely resect nasal mucosa in sinuses, were performed over a period of nearly 100 years, from 1893 through the mid-1980s. Then in 1986, Kennedy and Stammberger established a functional type of endoscopic sinus surgery to preserve sinus mucosa. Their approach has evolved into endoscopic sinus surgery (ESS), which has now become the standard treatment for CRS with nasal polyps (CRSwNP). The outcome of ESS is superior to that of the Caldwell-Luc operation. Furthermore, a long-term low-dose macrolide treatment has been developed for CRS patients. In East Asia, the combination of ESS and long-term, low-dose macrolide treatment is very effective for CRS patients because neutrophil infiltration is typically dominant in the nasal mucosa of East Asian CRS patients and neutrophil-dominant CRS responds well to macrolide treatment.

In Western countries, CRS is usually classified into CRS without nasal polyps (CRSsNP) and CRSwNP. It is generally accepted that CRSwNP is characterized by Th2-skewed eosinophilic inflammation, whereas CRSsNP is found in a Th1-predominant milieu. Eighty percent of the CRSwNP patients in Western countries showed eosinophilia in the lamina propria as well as in the epithelium of NP.[1] In this issue, Kato describes the different characteristics of CRSwNP in Western and in Asian countries.[2] He also focuses on immune cells and cytokines that control the initiation and amplification of CRS inflammation, demonstrating the involvement of B cell lineages, mast cells, dendritic cells, and ILC2 in the pathogenesis of CRSwNP.

Worldwide, the prevalence of AR has recently increased, whereas the prevalence of CRS has decreased. The "hygiene hypothesis" has been advocated to explain this phenomenon. Seasonal AR caused by Japanese cedar pollen (SAR-JCP), Japanese cedar pollinosis (JCP), is now the most common disease in Japan and has been called a "national affliction."[3] More than one-third of all Japanese people suffer from JCP. The "one airway, one disease" theory has been proposed based on the tight correlation between AR and atopic asthma. Furthermore, the association between CRS and asthma as well as AR has been recently pointed out, which is now called the second "one airway, one disease" theory, Okano et al. describe in their review article the association of eosinophilic inflammation between the upper and lower airways.[4] They focus on the epidemiology of AR and CRS, the effects of upper airway diseases on lower airway inflammation, and the intervention effects for upper airway diseases on the natural courses of bronchial asthma. Allergen immunotherapy, a curative treatment for AR, modifies the natural course of asthma. The pharmacotherapies for AR and CRS patients decrease the symptoms of asthma. Turbinate surgery for AR improves not only nasal symptoms, but also asthma control. Moreover, sinus surgeries for CRS patients with bronchial asthma improve their lower airway functions. They emphasize the importance of treatments for AR and CRS to improve the symptoms and the pulmonary functions of asthma patients, letting them breathe comfortably.

Among the contributors to this issue, Matsusaka et al. have analyzed serum periostin levels in 190 asthma patients and characterized "high-periostin" phenotypes.[5] Bronchial asthma is now considered a heterogeneous disease consisting of subgroups with different pathological backgrounds. To design optimal therapeutic approaches, it is of great importance to discriminate among asthma subgroups. Matsusaka and her colleagues identified as the "high-periostin" phenotype those patients manifesting eosinophilic-dominant, late-onset disease complicated by obstructive pulmonary dysfunction and nasal disorders. It has already been demonstrated that high serum periostin is associated with good responsiveness to type 2 antagonists such as anti-IL-13 antibodies and poor responsiveness to inhaled corticosteroids.[6,7] Their results may provide us with a therapeutic strategy for this specific phenotype of bronchial asthma.

Murakami et al. report the results of a prospective, randomized, short-term oral immunotherapy (OIT) for JCP.[8] Pharmacological treatments with antihistamines and corticosteroid nasal sprays offer temporary relief but are not curative. Thus far, subcutaneous and sublingual immunotherapies (SCIT and SLIT) are available as curative treatments for JCP. However, these treatments must be taken for long periods, usually a few years. OIT has an advantage in inducing immunotolerance in a short time because patients can take large amounts of antigen. They used galactomannan-conjugated Cry j 1 in this study to decrease the risk of adverse effects and to avoid digestion and accelerate the uptake of antigens

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in the gut. Their results indicate that administration starting one month before the peak pollen season is effective for improving symptoms and decreasing medication. Short-term OIT using the Cry j 1-galactomannan conjugate shows promise as a future replacement for SLIT or SCIT for JCP.

Takai et al. reported on the work of a Japanese Society of Allergology (JSA) task force regarding standardization of house dust mite (HDM) allergen vaccines.[9] Standardizing allergen vaccines/extracts is necessary for diagnosis and therapy. Whereas JCP allergen vaccines have been standardized in Japan since the 1990s, this had not yet been done for HDM allergen vaccines. This task force selected the JSA reference HDM extract and determined its *in vivo* allergic potency by intradermal testing. They showed that major allergen contents can be used as a surrogate *in vitro* assays because *in vitro* IgE binding potency is correlated with group 1 allergen (Der 1) content, group 2 allergen content, or their combined amounts. Based on this finding, they determined that 38.5 μg/ml Der 1 content corresponds to 100,000 JAU/ml of the *in vivo* allergenic potency and that 22.2–66.7 μg/ml of Der 1 can be labeled as 100,000 JAU/ml HDM allergen extract.

We offer our appreciation to all the authors for their contributions to the present issue of *Allergology International*.

Conflict of interest

The authors have no conflict of interest to declare.

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