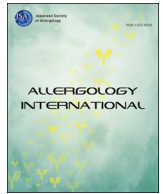




Contents lists available at ScienceDirect

Allergy International

journal homepage: <http://www.elsevier.com/locate/alit>

Editorial

Two facets of sweat: A defensive factor in skin tissues and an accelerating factor for allergic skin diseases

In Allergy International (AI) Vol. 67 Issue 4, we feature a set of review articles entitled “Two facets of sweat: a defensive factor in skin tissues and an accelerating factor for allergic skin diseases” as well as original articles and letters to the editor. We believe that this issue will greatly contribute to our readers’ understanding of the roles played by sweat in skin allergy.

Many investigators worldwide have performed studies on perspiration. Perspiration research developed dramatically in the 2000s.^{1,2} It has been shown that perspiration has not only a temperature-regulating function and a non-slip function for the hands and feet, but it also has a natural bactericidal function through the antimicrobial peptide contained in sweat called dermicidin.³ It has been proposed that obstruction of the sweat glands plays a major role in the onset of disorders such as parapsoriasis, lichen planus, and lichen amyloidosis,^{4,5} and that *Malassezia* is an allergen in sweat that exacerbates atopic dermatitis and cholinergic urticaria, suggesting that perspiration abnormalities may cause many allergic skin disorders.⁶

In this issue, Takahagi *et al.* review a major histamine-releasing antigen in sweat, MGL1304, which has been identified as a by-product of *Malassezia globosa* and is secreted into sweat, playing a major role in the pathogenesis of atopic dermatitis (AD) and cholinergic urticaria.⁷ On the other hand, Shiohara *et al.* discuss the physiological roles of sweat in maintaining both skin hydration and thermoregulation.⁸ They describe how sweating is linked to vital stratum corneum barrier function as well as the usefulness of applying moisturizers in the clinical care of allergic skin diseases. Katayama contributes to our understanding of the regulatory mechanism of impaired sweating function in allergic inflammatory skin diseases by introducing a clinical presentation of AD/Sjögren's syndrome overlap cases as a model of hypodrotic inflammatory diseases.⁹ In their article, Murota *et al.* discuss the roles of sweat in the pathogenesis of atopic dermatitis.¹⁰ They demonstrate that secretion of sweat and leakage into tissues is caused by dermatitis and is thought to promote itching. Moreover, it is known that the sweat glands play numerous roles, including the storage of stem cells for replenishing epidermal cells in the case of thermal burns and as water retention sites for replenishing moisture in the stratum corneum.¹¹ We hope that all of the roles of sweat for allergic skin diseases will be clarified by future research.

It is now widely appreciated that inhaled bronchodilator treatment with a long-acting muscarinic antagonist (LAMA) is

effective for treating COPD and asthma patients. These effects are thought to be mainly mediated by a bronchodilatory effect and an inhibitory effect on mucus secretion. However, evidence has recently accumulated showing the anti-inflammatory effects of anti-muscarinic drugs. In this issue, Koarai *et al.* have focused on recent findings concerning non-neuronal synthesis and anti-inflammatory/anti-remodeling functions of acetylcholine (ACh), a well-established neurotransmitter causing smooth muscle cell contraction.¹² Non-neuronal cells such as bronchial epithelial cells and leukocytes can synthesize and release ACh, which participates in various biological reactions such as airway inflammation and remodeling in the airways of asthma and COPD. Although there are some experimental data hinting at anti-inflammatory activities of long-acting muscarinic antagonists (LAMAs), evidence from the airways of asthma or COPD is limited. This comprehensive review will be informative to those wishing to understand the mechanisms of LAMAs in inhibiting disease progression and exacerbations.

In Japan, pollens from Japanese cedar and Japanese cypress are major causes of allergic rhinitis. Cross-reactivity between the pollen allergens of Japanese cedar and Japanese cypress is thought to be important in worsening allergic rhinitis in many patients. The major allergens of Japanese cedar, Cri j 1 and Cri j 2, are very homologous to the major allergens of Japanese cypress, Cha o 1 and Cha o 2, respectively.^{13,14} Recently, Osada *et al.* identified a novel allergen in Japanese cypress pollen named Cha o 3.¹⁵ In the present issue, they identify in Japanese cedar pollen a homologous allergen to Cha o 3 named Cry j 4.¹⁶ Since Japanese cedar pollen contains only a small amount of Cry j 4, allergen immunotherapy using Japanese cedar pollen extract may not be so effective in controlling naso-ocular symptoms induced by this pollen.

The association between eczema and mental health problems in school children is important. In surveys conducted in 2014 and 2015, Kuniyoshi *et al.* evaluated nearly 10,000 Japanese schoolchildren who lived in the area near the Great East Japan Earthquake.¹⁷ The subsequent huge tsunami caused massive damage on 11 March 2011. They found that mental health problems measured by the Strengths and Difficulties Questionnaire (SDQ) were associated with the severity of eczema, according to the ISAAC criteria. The association was still significant even after adjusting for covariates including tsunami experience and changing house experience. This study constitutes an example of a significant association between the severity of eczema and mental health problems such as a natural disaster in schoolchildren.

Peer review under responsibility of Japanese Society of Allergy.

<https://doi.org/10.1016/j.alit.2018.09.001>

1323-8930/Copyright © 2018, Japanese Society of Allergy. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Cochineal dye is an extract from *Dactylopius coccus*, which is widely used for red coloring foods and drinks. It contains carminic acid and unidentified 38 kDa protein as a contamination. Anaphylaxis due to cochineal dye ingestion is occasionally overlooked, as it is not well recognized by patients or even by physicians. Takeo *et al.* analyzed 28 Japanese cases of cochineal allergy in terms of clinical characteristics, skin prick tests (SPTs) with cochineal extract and carmine, and specific IgE against 38 kDa protein.¹⁸ A novel flow diagram combining SPT and specific IgE test is proposed, which should be useful for arriving at a clinical diagnosis of cochineal allergy.

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

Conflict of interest

The authors have no conflict of interest to declare.

Hiroo Yokozeki^a, Kenji Izuhara^{b,*}

^a Department of Dermatology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan

^b Division of Medical Biochemistry, Department of Biomolecular Sciences, Saga Medical School, Saga, Japan

* Corresponding author. Division of Medical Biochemistry, Department of Biomolecular Sciences, Saga Medical School, 5-1-1 Nabeshima, Saga 849-8501, Japan.

E-mail address: kizuhara@cc.saga-u.ac.jp (K. Izuhara).

References

1. Sato K, Sato F. Pharmacologic responsiveness of isolated single eccrine sweat glands. *Am J Physiol* 1981;**240**:R44–51.
2. Sato K, Sato F. Defective beta adrenergic response of cystic fibrosis sweat glands in vivo and in vitro. *J Clin Invest* 1984;**73**:1763–71.
3. Schitteck B, Hipfel R, Sauer B, Bauer J, Kalbacher H, Stevanovic S, et al. Dermcidin: a novel human antibiotic peptide secreted by sweat glands. *Nat Immunol* 2001;**2**:1133–7.
4. Hayakawa J, Mizukawa Y, Kurata M, Shiohara T. A syringotropic variant of cutaneous sarcoidosis: presentation of 3 cases exhibiting defective sweating responses. *J Am Acad Dermatol* 2013;**68**:1016–21.
5. Mizukawa Y, Ikehara Y, Nishihara S, Shiohara T, Narimatsu H. An immunohistochemical study of β 1,4-galactosyltransferase in human skin tissue. *J Dermatol Sci* 1999;**20**:183–90.
6. Hiragun T, Ishii K, Hiragun M, Suzuki H, Kan T, Mihara S, et al. Fungal protein MGL_1304 in sweat is an allergen for atopic dermatitis patients. *J Allergy Clin Immunol* 2013;**132**: 608–15.e4.
7. Takahagi S, Tanaka A, Hide M. Sweat allergy. *Allergol Int* 2018;**67**:435–41.
8. Shiohara T, Mizukawa Y, Shimoda-Komatsu Y, Aoyama Y. Sweat is a most efficient natural moisturizer providing protective immunity at points of allergen entry. *Allergol Int* 2018;**67**:442–7.
9. Katayama I. Dry skin manifestations in Sjögren syndrome and atopic dermatitis related to aberrant sudomotor function in inflammatory allergic skin diseases. *Allergol Int* 2018;**67**:448–54.
10. Murota H, Yamaga K, Ono E, Katayama I. Sweat in the pathogenesis of atopic dermatitis. *Allergol Int* 2018;**67**:455–9.
11. Lu C, Fuchs E. Sweat gland progenitors in development, homeostasis, and wound repair. *Cold Spring Harb Perspect Med* 2014;**4**.
12. Koarai A, Ichinose M. Possible involvement of acetylcholine-mediated inflammation in airway diseases. *Allergol Int* 2018;**67**:460–6.
13. Suzuki M, Komiyama N, Itoh M, Itoh H, Sone T, Kino K, et al. Purification, characterization and molecular cloning of Cha o 1, a major allergen of *Chamaecyparis obtusa* (Japanese cypress) pollen. *Mol Immunol* 1996;**33**: 451–60.
14. Mori T, Yokoyama M, Komiyama N, Okano M, Kino K. Purification, identification, and cDNA cloning of Cha o 2, the second major allergen of Japanese cypress pollen. *Biochem Biophys Res Commun* 1999;**263**:166–71.
15. Osada T, Harada T, Asaka N, Haruma T, Kino K, Sasaki E, et al. Identification and gene cloning of a new major allergen Cha o 3 from *Chamaecyparis obtusa* (Japanese cypress) pollen. *J Allergy Clin Immunol* 2016;**138**: 911–3.e7.
16. Osada T, Tanaka Y, Yamada A, Sasaki E, Utsugi T. Identification of Cha o 3 homolog Cry j 4 from *Cryptomeria japonica* (Japanese cedar) pollen: limitation of the present Japanese cedar-specific ASIT. *Allergol Int* 2018;**67**:467–74.
17. Kuniyoshi Y, Kikuya M, Miyashita M, Yamanaka C, Ishikuro M, Obara T, et al. Severity of eczema and mental health problems in Japanese schoolchildren: the ToMMo child health study. *Allergol Int* 2018;**67**:481–6.
18. Takeo N, Nakamura M, Nakayama S, Okamoto O, Sugimoto N, Sugiura S, et al. Cochineal dye-induced immediate allergy: review of Japanese cases and proposed new diagnostic chart. *Allergol Int* 2018;**67**:496–505.

Received 24 August 2018