Future Horizons in Allergy

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KEYWORDS

• Allergic rhinitis • Aspirin-exacerbated respiratory disease • Allergen immunotherapy • Immunoglobulin E

KEY POINTS

- Testing of local immunoglobulin E (IgE) in the nasal mucosa using mucosal brush biopsy may improve diagnostic accuracy.
- Urinary leukotriene E4 may be useful in identifying patients with aspirin sensitivity.
- Recombinant allergens and alternative approaches to allergen immunotherapy may offer disease-modifying treatment with improved safety and dosing compared with subcutaneous immunotherapy.

INTRODUCTION

There have been numerous advances in the diagnosis and management of atopy relevant to the allergy-treating otolaryngologist. These include emerging technologies, new devices, and refinement of existing methods, and in many ways reflect an overall trend in health care toward personalized medicine.[1] At the diagnostic level, these advances will help to identify specific allergic conditions in a clinically useful way, and even differentiate these from nonallergic diseases with shared symptomatology. Improved diagnostic precision is in turn fundamental to delivering targeted therapies.

Several developments in the diagnosis of allergy and related nonallergic conditions may aid the otolaryngologist in identifying and differentiating specific entities. Local immunoglobulin E (IgE) in the nasal mucosa can be useful in the diagnosis of allergic rhinitis, and mucosal brush biopsy may make this a practical test.[2–4] Urinary leukotriene E4 (LTE4) can identify aspirin sensitivity among patients with different respiratory diagnoses.[5–9] Lipidomics[10–12] and microRNA expression in extraceullar microvesicles[13,14] allow for the identification of extracellular allergic biomarkers, and may complement the traditional identification of intracellular proteins. Furthermore,

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nasal provocation testing with optical rhinometry may help to differentiate allergic and nonallergic rhinitis.[15–17]

The management of allergy may be improved through the introduction of targeted therapeutics as well as the refinement of existing treatments. Intranasal steroids and antihistamines are part of the traditional management of allergic rhinitis, and the use of these drugs is supported by clinical guidelines.[18] New delivery systems and formulations may improve the efficacy of intranasal steroids and antihistamines by enhancing bioavailability.[19,20] Recombinant allergens offer the potential to be a targeted therapy with modifications for increased immunologic properties and decreased allergenic activity.[21–23] Meanwhile, alternative administration routes for allergen immunotherapy, such as epicutaneous,[24] intralymphatic,[25] and sublingual,[26] may allow for enhanced patient convenience, dose reduction, and improved safety. Monoclonal antibodies, such as omalizumab and dupilumab, may be useful in managing allergic rhinitis, and might be particularly useful in patients with comorbid conditions.[27,28] Finally, intranasal capsaicin may represent a treatment option for a subgroup of patients with nonallergic irritant rhinitis.[29–31] The various advances in allergy diagnosis and management are summarized in **Table 1**.

DIAGNOSIS

Local Immunoglobulin E and Mucosal Brush Biopsy

Allergen-specific IgE is defining of the pathophysiology of allergic disease, and is, therefore, used as a marker for these conditions. Typically, serum IgE levels have been used in clinical practice. Testing for IgE in the nasal mucosa may improve diagnostic accuracy when assessing for conditions such as allergic rhinitis.[4] Furthermore, there is a subgroup of patients with detectable allergen-specific IgE localized in the nasal mucosa, but who have negative skin prick testing and serum allergen-specific IgE.[32] Obtaining nasal mucosal tissue biopsy from patients for the diagnosis of allergic rhinitis is a significant barrier to the routine use of local IgE levels.[4]

Mucosal brush biopsy has been described as a technique for the collection of epithelial cells, monocytes, neutrophils, and eosinophils in the nasal mucosa as early as 1988.[33] In that study, Pipkorn and colleagues[33] indicated that mucosal brush biopsy might also be useful for biochemical analysis. More recently, Reisacher[3] demonstrated that antigen-specific IgE could be detected via nasal mucosal brush biopsy, including patients for whom skin prick testing was negative. Cells are collected from the mucosal surface of the inferior turbinates with a cytology brush and IgE is harvested from the lysed cells. Microarray analysis of nasal mucosal brush biopsy are more sensitive at detecting IgE levels than standard in vitro IgE assays, and may improve diagnostic accuracy.[2] A limitation of this technique, however, is the rate at which IgE is detectable in nonallergic patients has not been well-defined. Overall, testing the nasal mucosal for local IgE using a minimally invasive technique such as mucosal brush biopsy may improve the clinical diagnosis of allergic rhinitis, particularly among patients with negative skin prick testing and normal serum IgE levels.

Urinary Leukotriene E4

Several recent studies have described urinary LTE4 as potentially useful in the diagnosis of allergic disease,[5–8] particularly for identifying aspirin sensitivity.[5–7] In 2006, Micheletto and colleagues[9] demonstrated that urinary LTE4 excretion increased in aspirin intolerant-asthmatics who underwent nasal provocation testing with lysine aspirin. A systematic review and metaanalysis by Hagan and colleagues[5] examined publications pertaining to the use of urinary LTE4 as a diagnostic testing for aspirin