

EDITORIAL

Is there a role for measurement of nasal IgE antibodies in

diagnosis of Alternaria-induced rhinitis in children?

Allergic rhinitis is defined as a type I hypersensitivity reaction in the nasal mucosa and its symptoms include sneezing, itching, rhinorrhoea and nasal obstruction. It occurs via an IgE-mediated Th2 cytokine pattern as a result of exposure to an inhalant allergen.¹

Allergic rhinitis can be subdivided into seasonal (intermittent) and perennial (persistent), the latter presenting with symptoms throughout the year. Common perennial allergens include Der p1, animal proteins and fungal spores. One of the commonest fungal allergens is Alternaria alternata. Diagnosing an allergy to fungal spores can be difficult, as exposure to it is not readily ascertained in the history.

Diagnosing allergic rhinitis involves taking a history; examination and investigations include skin prick testing (SPT), serum IgE titres, nasal provocation testing (NPT) and IgE in nasal secretions. The diagnosis is based on the presence of rhinitic symptoms in the light of objective tests as on their own these tests can give a false positive result. One example is that 15% of an asymptomatic population will have positive SPTs. Nevertheless, skin prick testing remains the most sensitive test.^{2,3}

In the current issue of Allergologia et Immunopathologia, Fuiano et al. found that in 56 children with suspected allergic rhinitis in a period when Alternaria was present in the air, 20 (37.5%) had a positive skin prick test to Alternaria whilst 45 (80.3%) had IgE to Alternaria in their nasal secretions.⁴

These findings further re-enforce the concept of local allergy⁵ which dates back to Huggins and Brostoff.⁶ Local mucosal allergy has been found in the absence of systemic atopy and has been termed "entopy".⁵ There have been several clinical and in vitro studies showing that IgE is produced locally in the rhinitic mucosa (and bronchial mucosa of asthmatic patients) and its presence is not simply the result of migration from elsewhere in the body.⁷⁻¹⁴ Fuiano et al. provide further evidence supporting the existence of local allergy and entopy. However, the practical role for the measurement of local IgE in the nasal secretions of children with rhinitis remains limited. This is because despite being able to find evidence of nasal IgE to Alternaria, this has little effect on clinical practice. There are various reasons why this is the case.

Perennial allergic rhinitis should be considered along with other common causes of nasal symptoms in children such as the frequency of upper respiratory tract infections in whom prolonged post-infective mucosal hypertrophy and secretions occur for many days in some children and adenoid hypertrophy. These factors often confound making a diagnosis for nasal symptoms in children less than seven years as well as reducing the efficacy of treatment (an age after which the adenoid has normally shrunk and immunity improved to reduce the number of upper respiratory tract infections). The management of allergic rhinitis centres on the use of non-sedative antihistamines for the symptoms of sneezing, itchy eyes and rhinorrhoea. Compliance in the use of topical nasal steroids primarily helps nasal obstruction but it may also reduce the other symptoms. Unfortunately compliance in children, particularly in those younger than six years, is very poor. There has been some concern that the regular use of topical steroids in children may inhibit growth by interfering with the hypothalamicpituitary-adrenal axis although proof to support this is weak, especially with the bioavailability of the recent generation of topical steroids. Over six years old a trial of medical treatment with a topical nasal steroid and non-sedative antihistamine for six weeks can be given and a response helps to confirm a probable diagnosis of allergic rhinitis. The evidence supporting the clinical efficacy and safety of immunotherapy for children singularly allergic to Alternaria is limited.¹⁵⁻¹⁷ Only one study from the 1980s treating rhinitis alone with immunotherapy showed any benefit.¹⁵ A double-blind randomised controlled trial concluded that immunotherapy led to a significant improvement in the peak expiratory flow rate of asthmatic children in all phases compared to placebo.¹⁷ One double-blind randomised controlled trial assessing the role of sublingual immunotherapy in the treatment of paediatric Alternaria-rhinitis showed a reduction in symptoms and drug intake scores compared to placebo but the subjects were mixed with only ten having rhinitis and two having a mono-sensitivity to Alternaria, thus limiting the conclusions that can be derived regarding the effectiveness of immunotherapy in the treatment of Alternaria-rhinitis.18

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Isolated allergy to *Alternaria* spores is uncommon therefore limiting the potential of avoidance measures or immunotherapy and the role of measuring nasal IgE. It has been shown that of patients sensitive to *Alternaria*, only 2% are monosensitised.¹⁹

In conclusion, this study provides further evidence for the concept of local allergy and ''entopy'' in the nasal mucosa. The ability to measure nasal IgE to *Alternaria* in the nasal mucosa and to identify patients who are sensitive to this allergen, even in those who are skin prick and serum IgE negative, adds to the diagnostic armamentarium. However, the clinical value of measuring nasal IgE remains limited as this does not result in a significant alteration in patient management.

References

- 1. Pawankar R. Inflammatory mechanisms in allergic rhinitis. Curr Opin Allergy Clin Immunol. 2007;7:1–4.
- Dreborg S. Allergy diagnosis. In: Mygind NN, editor. Allergic and non-allergic rhinitis. Clinical aspects. Copenhagen: Munksgaard; 1993. p. 82–94.
- Shyur SD, Jan RL, Webster JR, Chang P, Lu YJ, Wang JY. Determination of multiple allergen-specific IgE by microfluidic immunoassay cartridge in clinical settings. Pediatr Allergy Immunol. 2010;21:623–33.
- 4. Fuiano N, Fusilli S, Incorvaia C. A role for measurement of nasal IgE antibodies in diagnosis of Alternaria-induced rhinitis in children. Allergol Immunopathol. 2011 [Epub ahead of print].
- 5. Powe D, Mason M, Jagger C, Jenkins D, Jones N. "Entopy": localised mucosal allergic disease in the absence of systemic responses for atopy. Clin Exp Allergy. 2003;33:1374-9.
- Huggins KG, Brostoff J. Local production of specific IgE antibodies in allergic-rhinitis patients with negative skin tests. Lancet. 1975;2:148–50.
- Cameron L, Gounni AS, Frenkiel S, Lavigne F, Vercelli D, Hamid Q. S epsilon S mu and S epsilon S gamma switch circles in human nasal mucosa following ex vivo allergen challenge: evidence for direct as well as sequential class switch recombination. J Immunol. 2003;171:3816–22.
- 8. Fiset PO, Cameron L, Hamid Q. Local isotype switching to IgE in airway mucosa. J Allergy Clin Immunol. 2005;116:233-6.

- 9. Pawankar R, Okuda M, Yssel H, Okumura K, Ra C. Nasal mast cells in perennial allergic rhinitics exhibit increased expression of the Fc epsilonRI, CD40L, IL-4, and IL-13, and can induce IgE synthesis in B cells. J Clin Invest. 1997;99:1492–9.
- 10. Powe DG, Bonnin AJ, Jones NS. 'Entopy': local allergy paradigm. Clin Exp Allergy. 2010;40:987-97.
- 11. Smurthwaite L, Durham SR. Local IgE synthesis in allergic rhinitis and asthma. Curr Allergy Asthma Rep. 2002;2:231–8.
- Takhar P, Smurthwaite L, Coker HA, Fear DJ, Banfield GK, Carr VA, et al. Allergen drives class switching to IgE in the nasal mucosa in allergic rhinitis. J Immunol. 2005;174:5024–32.
- Toru H, Pawankar R, Ra C, Yata J, Nakahata T. Human mast cells produce IL-13 by high-affinity IgE receptor cross-linking: enhanced IL-13 production by IL-4-primed human mast cells. J Allergy Clin Immunol. 1998;102:491–502.
- Zurcher AW, Derer T, Lang AB, Stadler BM. Culture and IgE synthesis of nasal B cells. Int Arch Allergy Immunol. 1996;111:77–82.
- Cantani A, Businco E, Maglio A. Alternaria allergy: a three-year controlled study in children treated with immunotherapy. Allegol Immunopathol. 1988;16:1–4.
- Martinez-Canavate Burgos A, Valenzuela-Soria A, Rojo-Hernandez A. Immunotherapy with *Alternaria alternata*: present and future. Allegol Immunopathol. 2007;35:259–63.
- 17. Tabar AI, Lizaso MT, Garcia BE, Gomez B, Echechipia S, Aldunate MT, et al. Double-blind, placebo-controlled study of *Alternaria alternata* immunotherapy: clinical efficacy and safety. Pediatr Allergy Immunol. 2008;19:67–75.
- Cortellini G, Spandolini I, Patella V, Fabbri E, Santucci A, Severino M, et al. Sublingual immunotherapy for Alternaria-induced allergic rhinitis: a randomized placebocontrolled trial. Ann Allergy Asthma Immunol. 2010;105: 382–6.
- Corsico R, Cinti B, Feliziani V, Gallesio MT, Liccardi G, Loreti A, et al. Prevalence of sensitization to Alternaria in allergic patients in Italy. Ann Allergy Asthma Immunol. 1998;80:71–6.

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