

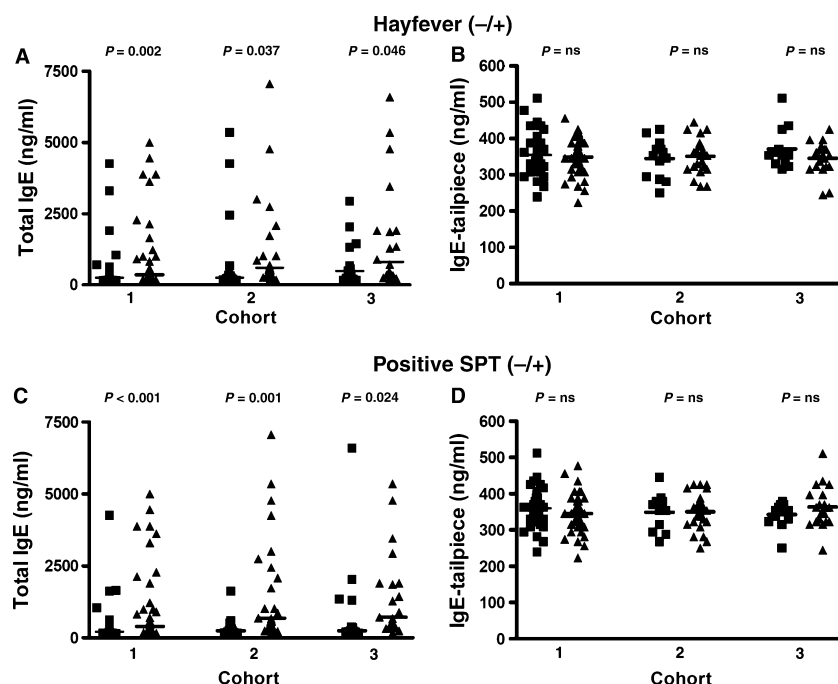


Figure 1. Plasma total IgE and IgE-tailpiece levels in the presence and absence of atopy. Total IgE (A, C) and IgE-tailpiece (B, D) levels were investigated in plasma taken from families with multiple-asthma children. These families were divided into non-related individuals, cohort 1 parents ($n = 80$), cohort 2 asthma sibling A ($n = 33$) and cohort 3 asthma sibling B ($n = 34$). Atopy was defined by the presence of hayfever (questionnaire) or positive skin prick test (SPT) to common allergens. Total IgE data were not normally distributed (histogram not shown); therefore, medians were compared using the Mann–Whitney U -test. IgE-tailpiece data were normally distributed (histogram not shown) and therefore means were compared using Student's t -test. Data represent all data points in the absence (squares) or presence (triangles) of atopy with median or mean values shown for total IgE and IgE tailpiece, respectively.

levels of IgE and lung function. The task ahead will be to investigate IgE-tp levels in other conditions, such as helminth infection, where total IgE levels are far higher than that for allergy and the Th2 immune response is more prominent (6).

We thank Professor Ian Hall for providing access to the Nottingham Family samples. We would also like to thank Professor Sherie Morrison (University of California, Los Angeles) and Dr Ke Zhang (University of California, Los Angeles) for their kind gifts of the recombinant human IgE-Tp and anti-IgE-Tp specific monoclonal Ab 367, respectively.

*School of Pharmacy
Centre for Biomolecular Sciences
University of Nottingham
Nottingham NG7 2RD
UK
Tel.: +44 (0) 115 8230327
Fax: +44 (0) 115 8468002
E-mail: akhmed.aslam@nottingham.ac.uk

Accepted for publication 13 February 2008
Allergy 2008; 63:942–943
© 2008 The Authors
Journal compilation © 2008 Blackwell
Munksgaard
DOI: 10.1111/j.1398-9995.2008.01708.x

References

1. Pekkarinen PT, von Hertzen L, Laatikainen T, Mäkelä MJ, Jousilahti P, Kosunen TU et al. A disparity in the association of asthma, rhinitis, and eczema with allergen-specific IgE between Finnish and Russian Karelia. *Allergy* 2007;**62**:281–287.
2. Ballardini N, Nilsson C, Nilsson M, Lilja G. ImmunoCAP Phadiatop infant – a new blood test for detecting IgE sensitisation in children at 2 years of age. *Allergy* 2006;**61**:337–343.
3. Chan LA, Lyczak JB, Zhang K, Morrison SL, Saxon A. The novel human IgE epsilon heavy chain, epsilon tailpiece, is present in plasma as part of a covalent complex. *Mol Immunol* 2000;**37**:241–252.

4. Aslam A, Quinn P, McIntosh RS, Shi J, Ghumra A, McKerrrow JH et al. Proteases from *Schistosoma mansoni* cercariae cleave IgE at solvent exposed interdomain regions. *Mol Immunol* 2008;**45**:567–574.
5. Wheatley AP, Bolland DJ, Hewitt JE, Dewar JC, Hall IP. Identification of the autoantigen SART-1 as a candidate gene for the development of atopy. *Hum Mol Genet* 2002;**11**:2143–2146.
6. Yazdanbakhsh M, Kremsner PG, van Ree R. Allergy, parasites, and the hygiene hypothesis. *Science* 2002;**296**:490–494.

Occupational asthma due to tampico fiber from agave leaves

S. Quirce*, M. Fernández-Nieto, C. Pastor, B. Sastre, J. Sastre

Key words: exhaled nitric oxide; induced sputum; occupational asthma; specific inhalation challenge; tampico fiber.

Tampico fiber is extracted from the leaves of *Agave lechugilla* which grows mainly in Mexico. The

material is used

extensively for making yard brooms, deck brushes and bath brushes. Agave-induced irritant contact dermatitis has been previously reported among workers

with *Agave tequilana* for tequila making (1, 2). Allergic reactions caused by tampico fibers have not been previously reported. We surveyed the five employees (two supervisors and three machine operators) at a brush making-plant. The two supervisors (patients 1 and 2), who were brothers and had been exposed to tampico for 13 and 10 years, respectively, reported work-related rhinitis and asthma symptoms. Patient 1 also experienced localized contact urticaria with tampico fiber. Patient 1 had experienced

Two brush-making workers who developed asthma and rhinitis symptoms following occupational exposure to tampico fiber are reported.

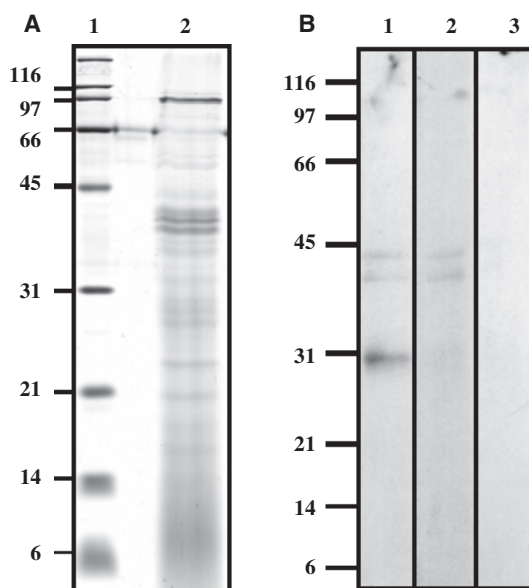


Figure 1. SDS-PAGE (A) and immunoblotting (B) of tampico fibers showing IgE-binding bands with serum from the two patients (lanes 1 and 2) and no reactivity with negative control serum (lane 3).

rhinitis and asthma symptoms for 10 and 2 years, and patient 2 for 8 and 5 years, respectively. The remaining workers did not report symptoms at work. Exhaled nitric oxide (eNO) measurements (Nioxmino; Aerocrine, Solna, Sweden) performed at the end of the work shift were elevated only in the two symptomatic employees (44 and 83 ppb), whereas they were normal in the remaining workers (<23 ppb). The mean concentration of total dust particles in the brush-making plant during an ordinary work shift using a laser-based aerosol monitor (DustTrack model 8520; TSI, St. Paul, MN, USA) was 0.42 mg/m³ (range: 0.28–0.68).

After obtaining written informed consent, single blind specific inhalation challenges (SIC) were carried out. On visit 1, methacholine inhalation test and sputum induction was performed. On visit 2, the patients underwent a SIC with nebulized aqueous tampico extract (3). Twenty-four hours later, on visit 3, sputum induction was performed again. On visit 4, a week apart from the tampico SIC, the patients underwent a SIC with horsehair extract.

Spirometry results were normal. Sputum was processed as previously described (4) and analyzed using FC scan cytometry (FACSCalibur flow cytometer; Becton Dickinson, San José, CA, USA). Monoclonal antibodies (Pharmingen, San Diego, CA, USA) used

to identify sputum cells are described elsewhere (4).

Skin prick testing with tampico extract 10% w/v was positive in patient 1 (5 mm) and patient 2 (3 mm), whereas it was negative with horsehair extract. Both patients also had positive skin prick tests to grass pollen, and patient 2 to house dust mites and cat and dog dander. The remaining workers had negative skin tests to tampico and horsehair extracts.

PC₂₀methacholine was 0.9 mg/ml (patient 1) and 8 mg/ml (patient 2). SIC with tampico at 10% w/v elicited an isolated early asthmatic response in both patients. An increase in sputum total cell count and neutrophils count (about threefold) as well as in eosinophil counts (fourfold) in induced sputum were observed 24 h after SIC. Two subjects with asthma underwent the same challenge protocol with tampico and no relevant changes in forced expiratory volume in 1 s or sputum were observed. The increase in eosinophil counts in sputum after tampico SIC in the patients, as well as the negative results obtained with exposure to horsehair support the specificity of the airway reaction to tampico. There is still conflicting evidence regarding the usefulness of eNO in the investigation of occupational asthma (5). A study reported an increase of eNO in individuals with symptoms of asthma when exposed to laboratory animals (6).

Sodium dodecylsulphate-polyacrylamide gel electrophoresis revealed several protein bands ranging from 14 to 97 kDa (Fig 1A). Immunoblotting was performed using the patient's serum diluted at 1/10, incubated overnight, and revealed with a second antibody (antihuman IgE) diluted at 1/5000. Three IgE-binding bands were recognized in the tampico extract of about 31, 39 and 43 kDa (Fig. 1B). These results point out that tampico fibers may give rise to upper and lower airway symptoms as well as to airway inflammation through an IgE-dependent mechanism.

*Hospital Universitario La Paz
Servicio de Alergia
P. Castellana, 261
28046 Madrid
Spain
Tel.: +34 91 727 7080
Fax: +34 91 549 94 98
E-mail: squirrel@gmail.com

Accepted for publication 19 February 2008
Allergy 2008; 63:943–945
© 2008 The Authors
Journal compilation © 2008 Blackwell Munksgaard
DOI: 10.1111/j.1398-9995.2008.01711.x

References

- Ogura T. Irritant contact dermatitis caused by needle-like calcium oxalate crystals, raphides, in *Agave tequilana* among workers in tequila distilleries and agave plantations. *Contact Dermatitis* 2001;**44**:94–96.
- High WA. Agave contact dermatitis. *Am J Contact Dermatitis* 2003;**14**:213–214.
- Quirce S, Fernández-Nieto M, Escudero C, Cuesta J, de Las Heras M, Sastre J. Bronchial responsiveness to bakery-derived allergens is strongly dependent on specific skin sensitivity. *Allergy* 2006;**61**:1202–1208.
- Fernández-Nieto M, Quirce S, Fraj J, del Pozo V, Seoane C, Sastre B et al. Airway inflammation in occupational asthma caused by styrene. *J Allergy Clin Immunol* 2006;**117**:948–950.
- Lemière C. Induced sputum and exhaled nitric oxide as noninvasive markers of airway inflammation from work exposures. *Curr Opin Allergy Clin Immunol* 2007;**7**:133–137.

6. Adisesh LA, Kharitonov SA, Yates DH, Snashell DC, Newman-Taylor AJ, Barnes PJ. Exhaled and nasal nitric oxide is increased in laboratory animal allergy. *Clin Exp Allergy* 1998;28:876–880.

Serum vascular endothelial growth factor and sublingual immunotherapy

G. Ciprandi*, B. M. Colombo, G. Murdaca, M. De Amici

Key words: allergic rhinitis; sublingual immunotherapy; vascular endothelial growth factor.

Allergic rhinitis (AR) is characterized by an inflammatory reaction, sustained by Th2 polarization (1). In this regard, angiogenesis is a complex and multifaceted process including endothelial cell proliferation and migration, recruitment of pericytes, and a maturation process (2). This sequence is tightly integrated and mediated by a balance between pro-angiogenic factors, including vascular endothelial growth factor (VEGF), angiopoietins, angiogenins, and a range of chemokines, and

anti-angiogenic factors, such as endostatin and constatin. Anyway, the most necessary and sufficient angiogenic protein is VEGF.

Vascular endothelial growth factor has been implicated as a driver not only of airway angiogenesis but also of enhanced allergic sensitization, upregulated Th2 inflammatory response, mucus gland hyperplasia, induction of metalloproteinase, chemotaxis for monocytes and eosinophils, airway edema, and airway hyperreactivity (3). Recently, it has been shown that VEGF is over-expressed in the nasal mucosa of patients with seasonal AR (4) and might be associated with the link between rhinitis and asthma (5). Sublingual immunotherapy (SLIT) is the unique causal treatment for AR affecting immune response (6).

Thus, the aim of this preliminary study was to evaluate serum VEGF levels in a cohort of AR patients, enrolled outside pollen season, and treated with a preseasonal course (3 months) of SLIT (Anallergo, Florence, Italy) and compared with healthy controls.

Forty patients (19 males and 21 females, mean age 38.86 years), with pollen allergy, and 15 normal subjects (eight males and seven females, mean age 43 years) were evaluated. Patients' blood samples for assessing VEGF serum levels were collected before initiating SLIT (baseline), after 3 month preseasonal SLIT course, and three months after.

The study was conducted with the approval of the local Ethics Committee and performed with the written informed consent of all participants.

The human VEGF Immunoassay (R&D Systems, Milan, Italy) was performed according to the Manufacturer's Instructions and expressed as $\mu\text{g/ml}$. The Wilcoxon test and Pearson's test were used for statistical analyses. The package 'S-PLUS' (MathSoft Corp, Rome, Italy) was used for all analyses.

Vascular endothelial growth factor serum levels were 532.09 pg/ml (± 262.6 SD) in normal subjects. In allergic patients, VEGF serum levels were 159.92 pg/ml (± 408.29 SD) at baseline and were significantly lower than in normal subjects ($P = 0$) as reported in Fig. 1. At the end of preseasonal SLIT course, i.e. after 3 months, VEGF serum levels significantly increased to 373.10 pg/ml (± 264.98 SD) in comparison with baseline levels. After 3 months, VEGF further increased to 404.65 pg/ml (± 206.99 SD), but without significant difference with the previous one. Finally, there was a significant correlation between times ($P = 0.0005$).

The findings of this preliminary study are surprising for two main reasons: firstly VEGF serum levels are significantly lower in AR patients than in normals. It is completely conflicting with previous studies (4, 5). However, these studies were conducted in symptomatic patients as exposed to pollens, whereas our patients were symptomless as they were initially studied outside the pollen season.

Secondly, SLIT induced an increase of VEGF serum levels. It may appear a paradox as VEGF may be considered a marker of allergic inflammation as it was reported to be over-expressed during acute phase of pollen AR. However, it is well known that SLIT is able to reduce the severity of allergic symptoms and the use of rescue medications down-regulating Th2-mediated inflammation (6).

A possible hypothesized explanation of this aberrant phenomenon might be that the VEGF over-expression mainly occurs at the level of the target organ, such as the nose, where it is effectively and significantly increased. Thus, this local 'capture' might justify the low 'peripheral' VEGF levels in basal conditions. Moreover, VEGF serum levels might reduce at nasal levels and consequently increase in the serum after SLIT.

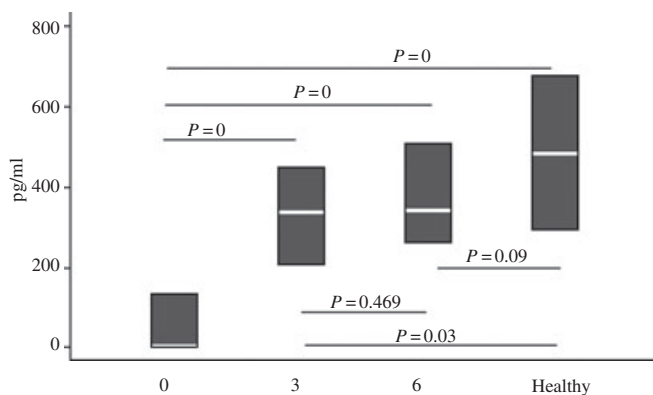


Figure 1. VEGF serum levels in patients with pollen AR evaluated before (0), after a 3-month preseasonal SLIT course (3), and after 3 months (6), and in healthy subjects.