

KARTHIK R. KRISHNAN, MD*
EDWARD L. PETERSON, PhD†
GANESA WEGIENKA, PhD†
SUZANNE HAVSTAD, MS†
CHRISTINE COLE JOHNSON, PhD†
EDWARD M. ZORATTI, MD‡
DENNIS R. OWNBY, MD*

*Section of Allergy and Immunology
Medical College of Georgia
Augusta, Georgia

†Department of Biostatistics and Research Epidemiology
Henry Ford Hospital
Detroit, Michigan

‡Division of Allergy
Department of Internal Medicine
Henry Ford Hospital
Detroit, Michigan
krk742@gmail.com

1. Omenaas E, Bakke P, Elsayed S, Hanoa R, Gulsvik A. Total and specific serum IgE levels in adults: relationship to sex, age and environmental factors. *Clin Exp Allergy*. 1994;24:530–539.
2. Oryszczyn MP, Annesi I, Neukirch F, Dore MF, Kauffmann F. Longitudinal observations of serum IgE and skin prick test response. *Am J Respir Crit Care Med*. 1995;151:663–668.
3. Hollander A, Doeke G, Heederik D. Cat and dog allergy and total IgE as risk factors of laboratory animal allergy. *J Allergy Clin Immunol*. 1996;98:545–554.
4. Misiak RT, Wegienka G, Havstad S, Ownby DR, Johnson CC, Zoratti EM. Specific allergic sensitization in parents and their 18-year-old offspring in the Suburban Detroit Childhood Allergy Study. *J Allergy Clin Immunol*. 2009;123:1401–1406.
5. Ownby DR, Johnson CC, Peterson EL. Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *JAMA* 2002;288:963–972.

INCREASED AFFECTED SKIN GENE EXPRESSION AND SERUM LEVELS OF THYMIC STROMAL LYMPHOPOIETIN IN ATOPIC DERMATITIS

Atopic dermatitis (AD) is a chronic, highly pruritic inflammatory skin disease that has increased considerably in industrialized countries.¹ It is characterized by allergic inflammation in the skin,² and it has a strong association with other atopic disorders, such as asthma and allergic rhinitis (AR).¹

Thymic stromal lymphopoietin (TSLP), a cytokine that is closely related to interleukin 7 (IL-7),³ is mostly produced by epithelial cells and keratinocytes in response to infection, trauma, and inflammation. It mediates T_H2 responses through activation of dendritic cells, and it has emerged as an important regulator of allergic inflammation.⁴ Also, TSLP activates mast cells to release several cytokines, such as IL-5, IL-6, and IL-13, but only in the presence of IL-1 and tumor necrosis factor.⁴ One article³ reported increased TSLP protein expression in lesional skin of patients with AD.

We investigated gene expression of TSLP in lesional skin biopsy samples and serum TSLP levels in 9 patients with AD (3 males and

6 females; mean [SD] age, 41.33 [21.40] years) compared with 9 controls (3 males and 6 females; mean [SD] age, 42.8 [18.1] years).

All 10 mm punch skin biopsy samples were obtained from patients who had mild, localized, chronic AD (abdomen, arm, back, hand, and neck; there was no apparent correlation between any of these sites and TSLP levels) and from controls (back). No participant had received any anti-inflammatory medication for 15 days before the biopsy. Contact dermatitis, asteatotic eczema, and other types of dermatitis were excluded. The medical ethics committee of the University of Athens Medical School approved this protocol. All participants gave their written informed consent according to the Declaration of Helsinki principles. Patients were free of other major medical conditions except AR as noted.

All biopsy samples were placed in RNeasy lysis buffer (Qiagen, Crawfordsville, IN) and were stored at -20°C . Total RNA from skin biopsy samples was extracted using the TRIzol isolation method (Invitrogen, Carlsbad, CA). Complementary DNA (cDNA) was synthesized using the iScript cDNA Synthesis Kit (Bio-Rad, Hercules, CA). Quantitative polymerase chain reaction (PCR) was performed using Taqman probes (Applied Biosystems, Foster City, CA) on a 7300 Real-Time PCR System (Applied Biosystems). For quantitative PCR, the cDNA was reverse transcribed from 300 ng of RNA from each sample. Relative messenger RNA levels were normalized to the glyceraldehyde-3-phosphate dehydrogenase endogenous control.

Data were analyzed using the nonparametric Mann-Whitney *U* test because the values did not conform to a normal distribution. Relative TSLP gene expression was significantly increased in lesional AD skin samples (median, 4.93; range, 2.27–23.99) compared with controls (median, 0.84; range, 0.49–1.85; $P < .001$) (Fig. 1A).

Blood samples were obtained the day before the biopsy, and the serum sample was isolated, aliquoted, and stored at -20°C until use. Levels of TSLP were determined using enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN). There was a significant increase in TSLP levels in patients with AD (median, 130.5 pg/mL; range, 0–2,246 pg/mL) compared with controls (median, 0 pg/mL; range, 0–62.5 pg/mL; $P = .006$) (Fig. 1B). The 3 female patients with the highest serum levels (2,246.6, 859.4, and 768.2 pg/mL) also had AR confirmed by skin prick testing.

There was neither a positive nor a negative correlation between skin TSLP gene expression and serum levels in any participants. Local skin TSLP gene expression and production may be one of the earliest steps in the inflammatory process, preceding systemic increases in TSLP levels. These results contrast with those of another human study⁵ reporting that TSLP serum levels were not increased in AD ($n = 46$; average age = 26.5 years), but are in agreement with increased TSLP serum levels in children with atopic ($n = 75$) and nonatopic ($n = 70$) eczema compared with controls ($n = 87$).⁶ All of the present patients had mild, localized chronic AD and, therefore, do not permit an attempt to correlate with severity of disease. Besides, this study was not powered for such an analysis.

The highest serum values corresponded to patients with AD and concomitant AR confirmed using skin prick testing. This finding supports the hypothesis that increased serum TSLP levels may also precede other atopic diseases, such as AR and asthma. In fact, a study⁷ showed that skin-derived TSLP contributed to the aggravation of asthma in mice. The role of TSLP in human asthma is supported by another study⁸ that showed that bronchial TSLP expression was increased in asthmatic patients ($n = 20$) compared with in controls ($n = 15$) and correlated with disease severity. Based on the apparent association between increased serum TSLP levels and AR, investigation of atopic patients

Disclosures: Drs Alysandratos and Angelidou are recipients of postgraduate scholarships from the Hellenic State Scholarships Foundation. Dr Zhang is partially supported by a graduate student fellowship from Galenica SA.

Funding Sources: Aspects of this work were funded by grant AR47652 from the National Institutes of Health (Dr Theoharides).

© 2010 American College of Allergy, Asthma & Immunology.
Published by Elsevier Inc. All rights reserved.

doi:10.1016/j.anai.2010.09.017

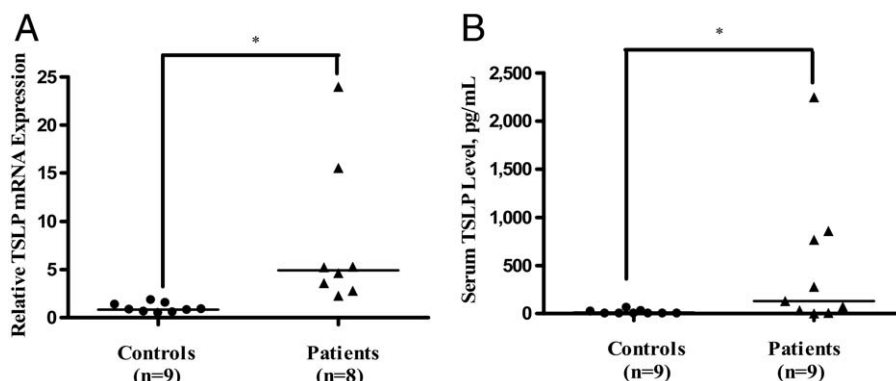


Figure 1. Scattergrams of thymic stromal lymphopoietin (TSLP) gene expression determined in skin using quantitative polymerase chain reaction (A) and TSLP levels in serum measured by means of enzyme-linked immunosorbent assay (B) in controls and patients with atopic dermatitis. The value for TSLP gene expression from 1 patient was not included because the quality of messenger RNA (mRNA) was poor, as also evidenced by low glyceraldehyde-3-phosphate dehydrogenase expression; inclusion of that value would have yielded even higher results for the patient group. The horizontal lines represent the medians. * $P < .01$.

without AD could provide further insight into the relationship between TSLP and allergic disease.

KONSTANTINOS-DIONYSIOS ALYSANDRATOS, MD*†
 ASIMENIA ANGELIDOU, MD*†
 MAGDALINI VASIADI, BS*†
 BODI ZHANG, MD, MPH*‡
 DIMITRIOS KALOGEROMITROS, MD, PhD†
 ALEXANDRA KATSAROU-KATSARI, MD§
 THEOHARIS C. THEOHARIDES, MS, PhD, MD*†‡¶||

*Molecular Immunopharmacology and Drug Discovery Laboratory
 Department of Pharmacology and Experimental Therapeutics
 Tufts University School of Medicine
 Boston, Massachusetts

†Allergy Research Center, Allergy Unit
 Attikon General Hospital
 University of Athens Medical School
 Athens, Greece

‡Department of Biochemistry
 Tufts University School of Medicine and Tufts Medical Center
 Boston, Massachusetts

§1st Department of Dermatology
 Andreas Syggros-Venereal and Skin Diseases Hospital of Athens
 University of Athens Medical School
 Athens, Greece

||Department of Internal Medicine
 Tufts University School of Medicine and Tufts Medical Center
 Boston, Massachusetts

¶Department of Psychiatry
 Tufts University School of Medicine and Tufts Medical Center
 Boston, Massachusetts
theocharis.theoharides@tufts.edu

1. Bieber T. Atopic dermatitis. *N Engl J Med*. 2008;358:1483–1494.
2. Metz M, Maurer M. Innate immunity and allergy in the skin. *Curr Opin Immunol*. 2009;21:687–693.
3. Soumelis V, Reche PA, Kanzler H, et al. Human epithelial cells trigger dendritic cell mediated allergic inflammation by producing TSLP. *Nat Immunol*. 2002;3:673–680.
4. Allakhverdi Z, Comeau M, Jessup HK, et al. Thymic stromal lymphopoietin is released by human epithelial cell in response to microbes, trauma, or inflammation and potently activates mast cells. *J Exp Med*. 2007;19:253–258.
5. Nakamura K, Tsuchida T, Tsunemi Y, Saeki H, Tamaki K. Serum thymic stromal lymphopoietin levels are not elevated in patients with atopic dermatitis. *J Dermatol*. 2008;35:546–547.

6. Lee EB, Kim KW, Hong JY, Jee HM, Sohn MH, Kim KE. Increased serum thymic stromal lymphopoietin in children with atopic dermatitis. *Pediatr Allergy Immunol*. 2010;21:e457–e460.
7. Zhang Z, Hener P, Frossard N, et al. Thymic stromal lymphopoietin overproduced by keratinocytes in mouse skin aggravates experimental asthma. *Proc Natl Acad Sci U S A*. 2009;106:1536–1541.
8. Ying S, O'Connor B, Ratoff J, et al. Thymic stromal lymphopoietin expression is increased in asthmatic airways and correlates with expression of Th2-attracting chemokines and disease severity. *J Immunol*. 2005;174:8183–8190.

URTICARIA DUE TO ALOE VERA: A NEW SENSITIZER?

Aloe vera (*Aloe barbadensis*) belongs to the Liliaceae family. Aloe vera originated in Northern Africa, and its name derives from the Arabic word *alloe*, which means bitter. It has been used as a cosmetic and medicinal plant since ancient times, although these properties have not been scientifically proved.¹ In recent years, the use of aloe vera products has substantially increased in the industry of cosmetology and alternative medicine, and recently it has been introduced in food products such as yogurts and beverages.

The aloe vera leaf can easily be separated into 3 parts. The rind (20%–30% of the whole leaf) is where the constituents are synthesized. Latex, a yellow, bitter liquid containing anthraquinones (aloin, emodin, barbaloin), in its dried form is approved by the US Food and Drug Administration as a laxative. The pulp contains aloe vera gel, rich in water, carbohydrates, and proteins, and is used in most commercial products (eg, creams, lotions, soaps, shampoos, and facial cleansers).² Scarce cases of allergy have been reported.

A 57-year-old woman reported an allergic reaction to aloe vera. After developing a wound in her left eyebrow, a peeled-off rind of an aloe leaf was applied to it. Four hours later, she woke up with intense generalized pruritus; hives in her arms, thorax, and abdomen; and erythema and edema in her hands, feet, and intensely on the eyebrow where she had placed the plant. She was treated in the emergency department, where she received methylprednisolone and dexchlorpheniramine. She experienced full recovery in 2 hours.

The woman experienced ischemic cardiopathy, osteoporosis, multinodular goiter, perennial rhinoconjunctivitis, and mild inter-

Disclosures: Authors have nothing to disclose.

© 2010 American College of Allergy, Asthma & Immunology.
 Published by Elsevier Inc. All rights reserved.
 doi:10.1016/j.anai.2010.09.016