

Toothpaste flavor-induced asthma

Javier Subiza, MD, Jose Luis Subiza, MD, Rommel Valdivieso, MD,
Pedro Martin Escribano, MD, Rosario Garcia, MD, Miguel Jerez, and
Eliseo Subiza, MD *Madrid, Spain*

We describe the case of a patient whose asthma was exacerbated by the mint flavor contained in her toothpaste.

CASE REPORT

A 21-year-old female nonsmoker had asthma and aspirin intolerance starting approximately 6 years ago. In spite of correctly following treatment with 1200 µg budesonide a day, inhaled beta-agonist, and adjusted doses of theophylline, in the past 11 months the patient required emergency care on 10 occasions because of acute asthma attacks. The patient was then referred to us for evaluation. The examination revealed polyps in both nostrils and wheezing in both lung fields. The radiograph showed a thickening of the mucosa in both maxillary sinuses and chest insufflation. White blood cell count was 6400 cells/mm³, of which 8% were eosinophils. Total IgE serum was 140 IU/ml. Initial spirometry revealed a forced expiratory volume in 1 second (FEV₁) of 2350 (77% predicted) that increased to 3800 (111% predicted) after a 7-day course of oral prednisone and nebulized albuterol. Once her asthma had been stabilized, a methacholine test showed a PC₂₀ of 0.6 mg/ml. Skin prick tests with inhalants were performed, with positive reactions for grass and olive pollens and cat dander. However, the patient did not report any clear seasonal worsening and denied any exposure to pets. In fact, the major cat allergen measured in patient's house dust revealed a very low level (<0.05 µg of *Fel d I* per gram of dust) (Abelló Lab, Madrid, Spain). In contrast, she did report a moderate increase in dyspnea after daily toothbrushing. Also, on one occasion she suffered an attack of bronchospasm after eating a menthol candy. A challenge was then performed with her toothpaste (Close-Up, Elida

Gibbs, Toledo, Spain); her lung function was monitored before and after each challenge with a technique that has been described.¹ On the control day, no significant changes in FEV₁ were observed in the 8 hours after she brushed her teeth with water alone. However, a strong immediate response (decrease in FEV₁ of 36%) without any late response was obtained after she used her toothpaste. The same test, performed with the same toothpaste but without any flavor, was completely negative. A challenge was then performed with each of the components of the patient's flavored toothpaste. Four cubic millimeters of anethole, 4 mm³ of eucalyptol, 4 mm³ of spearmint oil, 8 mm³ of peppermint oil, and 11 mg of menthol (which approximately represents the contents of each flavor in 2 gm of toothpaste) respectively, were diluted in 2 ml of 50% alcohol. The patient was instructed to rinse her mouth with each of the dilutions for 30 seconds and then spit them out. The challenge was begun with eucalyptol, which proved to be negative. The challenge was double-blind with the other components; the same dose of eucalyptol was used to hide the flavor. Thus no bronchial response was obtained with anethole, but an immediate and significant response was obtained with spearmint, peppermint, and menthol, although with a dose of 22 mg in the case of the latter (Fig. 1). On the other hand, results of the same test were negative in four patients with asthma and similar methacholine PC₂₀, three of whom also had aspirin intolerance.

The immediate bronchial reaction caused by menthol was completely inhibited by prior inhalation of cromolyn, even when the patient was challenged with the maximum dose of 100 mg. We were unable to detect specific IgE to those flavors in the patient's serum by ELISA; we performed a similar assay to that described to assess anticardiolipin antibodies.²

DISCUSSION

Our patient had an asthma attack a few minutes after using her toothpaste. This could be verified by means of a challenge test performed in our laboratory.

From the Centro de Alergia e Inmunología Clínica, General Pardiñas, Madrid; Servicio de Inmunología, Hospital Universitario San Carlos, Madrid, Spain.

Reprint requests: Javier Subiza, MD, Centro de Alergia e Inmunología Clínica, General Pardiñas, c/ General Pardiñas 116, Madrid 28006, Spain.

1/1/39904

Percent Decrease of FEV1

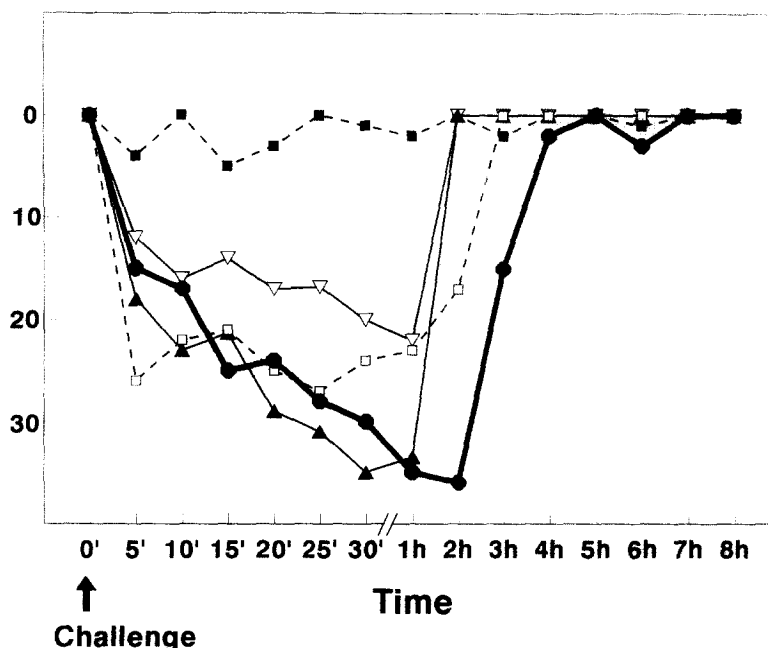


FIG. 1. Challenge with toothpaste (●), peppermint (▲), spearmint (▼), menthol 22 mg (◻), and menthol 100 mg (■), the last 30 minutes after cromolyn sodium inhalation.

However, the lack of bronchial response after challenge with an identical toothpaste without flavorings indicated that the flavorings were the cause of her asthma and ruled out any possibility of the asthma being caused by the preservatives and/or additives contained in the toothpaste. These conclusions are supported by the presence of a significant immediate bronchial response after double-blind challenge with three of the flavors: spearmint (*Mentha spicata*), peppermint (*Mentha piperita*), and menthol, a terpenic alcohol obtained from the volatile oils of various species of *Mentha* (labiateae).³ The negative results obtained in the subjects with asthma in the control group support the specificity of these findings. The patient's atopic status, the type of immediate bronchial response, and the good protection provided by inhaled cromolyn could lead one to think of a type I immunologic mechanism as underlying cause. However, the patient did not show any immediate skin response in the prick test performed with the three flavors obtained from *Mentha*, and no IgE activity against any of these flavors could be detected. Therefore a personal susceptibility or idiosyncratic pathway may be the underlying mechanism.

The patient was instructed to brush her teeth with water alone and to avoid contact or intake of mint or derivatives. Four months later the patient had not had an asthma attack. No decreases in her measurements

of greater than 20% in her peak expiratory flow compared with her personal best were observed, even though her chronic asthma therapy was similar to that which she was receiving before, except for the addition of inhaled cromolyn 20 mg four times a day. Because the patient was already receiving high doses of inhaled corticoids, it seems unlikely that the addition of cromolyn alone to her therapy was the sole cause of her remarkable improvement.⁴

Although mint and/or menthol are common ingredients in toothpaste, we have found only one case of asthma triggered by these agents in our review of the literature. Curiously enough, this was a woman of the same age whose wheezing dramatically disappeared when she stopped using her toothpaste.⁵ Challenge with that toothpaste caused an immediate bronchial response. The same test with the same toothpaste but without flavorings was negative. The patient also reported asthmatic symptoms when she chewed gum with spearmint or peppermint flavor. In conclusion, the results of the investigation performed show that the peppermint, spearmint, and menthol contained as flavorings in toothpastes may act as asthma-inducing agents.

We thank Mr. Cubero of the Research Department of Elida Gibbs and Mr. Cliff Perry of Quest International (Ashford, England) for the supply of and information on the flavors contained in Close-Up toothpaste.

REFERENCES

1. Subiza J, Subiza JL, Escribano PM, et al. Occupational asthma caused by Brazil ginseng dust. *J ALLERGY CLIN IMMUNOL* 1991;88:731-6.
2. Loizou S, McCrea JD, Rudge AC, et al. Measurement of anti-cardiolipin antibodies by an enzyme-linked immunosorbent assay: standardization and quantitation of results. *Clin Exp Immunol* 1985;62:738-44.
3. Martindale. The extra pharmacopoeia, 29th ed. London: The Pharmaceutical Press, 1989:1586.
4. Toogood JH, Jennings B, Lefcoe NM. A clinical trial of combined cromolyn/beclomethasone treatment for chronic asthma. *J ALLERGY CLIN IMMUNOL* 1981;67:317-24.
5. Spurlock BW, Dailey TM. Shortness of (fresh) breath-tooth-paste-induced bronchospasm [Letter]. *N Engl J Med* 1990;323:1845-6.

Localization of IgE to lung germinal lymphoid follicles in a patient with allergic bronchopulmonary aspergillosis

Raymond G. Slavin, MD, Gerald J. Gleich, MD, Patricia S. Hutcheson, BA,
Gail M. Kephart, BS, Alan P. Knutsen, MD, and Cheng C. Tsai, MD
St. Louis, Mo. and Rochester, Minn.

Allergic bronchopulmonary aspergillosis (ABPA) is a hypersensitivity disease of the lung caused by sensitivity to the ubiquitous organism *Aspergillus fumigatus* (Af).¹ The uniform presence in ABPA of positive immediate skin test reactions to *Aspergillus*, markedly elevated serum total IgE levels, and a marked increase in IgE anti-*Aspergillus* (IgE-Af) speak for the importance of IgE to *Aspergillus* in the diagnosis of ABPA.¹ Until now, only indirect evidence existed of IgE production in the lungs of patients with ABPA.² In this report we present evidence obtained from examination of a lung biopsy from a patient with ABPA of localization of IgE in the germinal lymphoid follicles of a lung with ABPA.

CASE REPORT

A 13-year-old boy was evaluated for persistent pulmonary infiltrates. Atopic dermatitis developed in him at age 18 months. At age 12 years a cough developed associated with left-sided pulmonary infiltrate and partial atelectasis found on chest radiography. Ten days of erythromycin resulted in symptomatic improvement but no change in chest radiog-

Abbreviations used

ABPA:	Allergic bronchopulmonary aspergillosis
IgE-Af:	IgE anti- <i>Aspergillus</i>
BAL:	Bronchoalveolar lavage
IgA-Af:	IgA anti- <i>Aspergillus</i>
H & E:	Hematoxylin and eosin
MBP:	Major basic protein

raphy findings. Bronchoscopy results were normal. One month later the pulmonary infiltrate increased. At this time the patient also had night sweats, headache, and a low-grade fever. Bronchoscopy on this occasion revealed purulent exudate from the lingula, with granular fragments. One month later thoracotomy with resection of the left lingular segment was performed. Our evaluation at this time revealed a strong positive *Aspergillus* skin test, positive serum precipitins to *Aspergillus*, peripheral blood eosinophilia of 13%, and a total serum IgE of 5500 IU/ml. The patient was started on oral prednisone, with resultant marked clinical improvement.

MATERIAL AND METHODS

Immunofluorescent staining

Indirect immunofluorescence was used to detect both the localization of IgE and the presence of eosinophil granule major basic protein (MBP) as previously described.³⁻⁶

RESULTS

By light microscopy, an intense inflammatory infiltrate was observed in the lung parenchyma. The

From the Departments of Internal Medicine and Pediatrics, St. Louis University School of Medicine, St. Louis, and the Department of Immunology, Mayo Clinic and Mayo Foundation Rochester.

Supported by National Institutes of Health grants HL30652 and AI15231.

Reprint requests: Raymond G. Slavin, MD, St. Louis University School of Medicine, 1402 S. Grand - Doisy R209, St. Louis, MO 63104-1028.

1/1/41436