

for treatment of asthma symptoms, and these were documented in our article.

Dr. Niemann suggests that improvement in rhinitis alone might have been the basis for the improvement we observed in asthma. Certainly, this is a possibility, and additional trials will be necessary to provide the final answer. However, it is relevant to point out that several investigators have used terfenadine, 60 mg twice daily, rather than placebo as a control when evaluating new antihistamines, including cetirizine, in asthma.¹⁻³ It is accepted that terfenadine at this dose is ineffective in treating asthma. We believe that the changes we recorded for asthmatic symptoms are greater than those seen in previous investigations in which antihistamines were used at conventional doses for managing rhinitis. We are at a loss to comment on the analogy to concomitant rhinitis and depression.

The writer addresses our conclusion that "Cetirizine may be considered an additional agent for treating patients with asthma." When our manuscript was originally submitted for publication, one of our reviewers asked us whether we would "recommend cetirizine as first line therapy for mild-moderate asthma over the standard inhaled antiinflammatories (cromolyn, nedocromil, inhaled steroids)?" We presume the reviewer believed that a strong statement was indicated regarding the future role of cetirizine for patients with asthma. We added the above comment because we believed it was the most conservative conclusion possible from our data. We agree that other investigations are now indicated to explore the role of cetirizine in asthma.

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REFERENCES

1. Bousquet J, Emonot A, Germouty J, et al. Double-blind multicenter study of cetirizine in grass-pollen-induced asthma. *Ann Allergy* 1990;65:504-8.
2. Kurzeja A, Riedelsheimer B, Hulhoven R, Bernheim J. Cetirizine in pollen-associated asthma [Letter]. *Lancet* 1989; 1:556.
3. Dijkman JH, Hekking PRM, Molkenboer JF, et al. Prophylactic treatment of grass pollen-induced asthma with cetirizine. *Clin Exp Allergy* 1990;20:483-90.

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Hypodermic epinephrine spray and uvular angioedema revisited

To the Editor:

We would like to share with your readers our experience with a venerable epinephrine delivery system, which we have successfully used in treating angioedema of the uvula.

A 40-year-old woman with a 3-year history of chronic idiopathic urticaria and angioedema came to our clinic with dysphagia of 3 hours' duration. She was receiving no medications, and no clear incitant could be identified. Her uvula and adjacent soft palate were markedly swollen and prolapsed posteriorly. Vital signs were normal, and she manifested no stridor, wheezing, urticaria, or gastrointestinal symptoms. She was treated with 0.3 mg (0.3 ml of 1:1000 solution) epinephrine administered subcutaneously, 50 mg of diphenhydramine administered intramuscularly, and 150 mg of ranitidine and 40 mg of prednisone both administered orally. There was no change in her angioedema after 1 hour of close observation.

Our first choice for further therapy was epinephrine administered by metered-dose inhaler (MDI), but this was unavailable. We carefully explained our intention of using a needle and syringe to direct epinephrine topically to the patient's uvula. After illuminating her mouth, we used a 1 ml syringe with a 27-gauge needle (Becton Dickinson and Company, Rutherford, N.J.), the tip of which was just inside her open mouth, to direct an atomized jet of 0.3 mg of epinephrine (0.3 ml of 1:1000 solution) at her uvula.

Ten minutes later, the uvular swelling had decreased by 50%, and she no longer experienced dysphagia. A repeat dose of 0.3 mg of epinephrine, delivered in a similar manner, had no further effect. There was no change in her vital signs during administration of topical epinephrine, and she was subsequently discharged after 8 hours of observation. She was given an EPI-PEN autoinjector (Center Laboratories, Port Washington, N.Y.), a 24-hour tapering course of prednisone, a prescription for doxepin (10 mg by mouth three times daily) and an epinephrine MDI (Primatene Mist; 2 sprays directed at her uvula, without inhaling, every 3 hours as needed for 24 hours). There was no evidence of uvular angioedema 24 hours later.

The first use of topical epinephrine was in 1907 by the otolaryngologist, H. S. Birkett, who observed angioedema of the uvula and soft palate after administration of antitoxin.¹ In a discussion of treatment he stated that "a spray of Adrenalin chloride (1:5,000) will often lessen the edema."¹ It is most likely that Birkett's epinephrine was delivered by hypodermic spray or possibly by atomizer mist. Epinephrine delivered by MDI did not become commercially available until the late 1950s. The current recommendations for the treatment of acute anaphylaxis in adults are: parenteral administration of epinephrine 0.1 to 0.5 mg subcutaneously or intramuscularly with simultaneous administration of epinephrine by MDI when there is airway obstruction.² The latter offers the advantage of fewer systemic effects over parenteral administration. Warren et al.³ found that the mean peak plasma level of epinephrine, after oral inhalation of 15 puffs from a MDI (2.4 mg of epinephrine), was only 61% of the mean peak level after subcutaneous administration of 0.3 mg of epinephrine. Advantages of hypoder-

mic epinephrine spray over MDI delivery include its concentrated stream delivering more drug to the target (uvula) than an equal amount of drug delivered by a diffusing aerosol (MDI). Most epinephrine MDIs (epinephrine bitartrate) deliver 0.16 mg of epinephrine per actuation, with a recommended dose for treatment of asthma of 1 to 2 sprays every 3 hours as needed. A hypodermic spray of 0.3 mg of epinephrine would not be expected to cause systemic effects because the uvula provides substantially less surface area for absorption than the lungs. Most of the epinephrine will drip off the uvula and subsequently be swallowed or spat out. The latter is preferable because it can prevent epigastric pain, which may be associated with swallowing epinephrine.⁴ Ingested epinephrine is rapidly inactivated as a result of metabolism in the gut and liver, and systemic levels are not reached.⁴

This case report illustrates that although epinephrine delivered by hypodermic spray has only a transitory action (effect is within 5 minutes and lasts approximately 1 hour⁴), it can bring about a rapid detumescence of the swollen uvula and provide palliation with few side effects. Additionally, syringes and standard 1 mg epinephrine ampules are more readily available in physicians' offices and emergency departments than epinephrine MDIs. Allergists today should be aware of this

time-honored epinephrine delivery system, which can be a useful adjunct in treatment of uvular angioedema.

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REFERENCES

1. Birkett HS. Diseases of the larynx. In: Osler W, McCrae T, eds. *Modern medicine: its theory and practice*. Philadelphia: Lea Brothers & Company, 1907;3:633-4.
2. Fink JN, Lockey R, Ballow M, et al. Medical knowledge self-assessment program in the subspecialty of allergy & immunology. Philadelphia: American College of Physicians, 1993:55-64.
3. Warren JB, Doble N, Dalton N, et al. Systemic absorption of inhaled epinephrine. *Clin Pharmacol Ther* 1986;40:673-8.
4. McEvoy GK, Litvak K, Welsh OH. *American Hospital Formulary Service*. Bethesda, Maryland: American Society of Health—System Pharmacists, 1995:818-24, 1945-6.

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