
Case report

Eucalyptus as a specific irritant causing vocal cord dysfunction

John T. Huggins, MD*; Allen Kaplan, MD*; Bonnie Martin-Harris, PhD†; and Steven A. Sahn, MD*

Background: Vocal cord dysfunction (VCD) is a well-recognized clinical entity that frequently mimics asthma and is characterized by inappropriate adduction of the vocal cords during inspiration. The pathogenesis of VCD has not yet been defined. The only previous report suggested that respiratory irritants may trigger paradoxical motion of the vocal cords.

Objective: To report the case of a 46-year-old woman with VCD precipitated by eucalyptus exposure.

Methods: A masked flexible fiberoptic nasolaryngoscopy was performed to confirm whether VCD occurred with eucalyptus and not with other known respiratory irritants. The patient underwent inhalation challenges consisting of water, ammonia, pine oil, and a combination of eucalyptus (dried leaves) and ammonia. Two independent observers before patient challenge could not identify eucalyptus.

Results: Vocal cord dysfunction occurred within minutes of exposure to eucalyptus. This is the first report to prospectively document that a specific irritant, eucalyptus, can precipitate VCD. Negative skin prick test results, total IgE level, and negative IgE eucalyptus-specific antibodies support a nonimmunologic mechanism.

Conclusions: A new pathogenic mechanism for this clinical entity is supported by our observations. Furthermore, a nonimmunologic mechanism in which respiratory irritants may induce VCD is suspected. Future studies to elucidate this mechanism need to be performed in individuals with irritant-specific VCD.

Ann Allergy Asthma Immunol. 2004;93:299–303.

INTRODUCTION

Vocal cord dysfunction (VCD) is a clinical entity with a diagnosis that can be problematic to establish. It often presents with symptoms suggestive of asthma, ie, dyspnea, cough, and wheezing. Such patients frequently seem to be refractory to agents typically used to treat asthma; thus, these individuals are frequently treated with long-term systemic corticosteroids.^{1,2} The diagnosis can be established when a flow-volume loop indicates a flattened inspiratory phase indicative of airway inflow obstruction or by endoscopic observation of adduction of the vocal cords with inspiration.³

The pathogenesis of VCD has not yet been clearly defined but seems to be associated with stress and panic attacks. We describe a unique patient with VCD precipitated by inhalation of eucalyptus who was otherwise asymptomatic. This case was documented by using a “masked” inhalation challenge under direct flexible fiberoptic nasolaryngoscopy.

CASE REPORT

A 46-year-old woman with a past medical history of hypothyroidism, migraine headaches, peptic ulcer disease, depres-

sion, and allergic rhinitis became ill in October 2001 when she developed a sore throat and complained of episodic dyspnea that appeared primarily at work. She reported that chest tightness and wheezing seemed to be associated with exposure to a eucalyptus plant. In 1 instance, her severe respiratory symptoms required hospitalization. Spiral chest computed tomography excluded pulmonary emboli, and high-resolution chest computed tomography showed a few areas of ground-glass densities. She had a normal IgE level (63 IU/mL). She was treated with corticosteroids and bronchodilators but had no improvement in her symptoms. Reexposure to eucalyptus caused recurrent bouts of chest tightness, dyspnea, cough, hoarseness, and wheezing. She received multiple corticosteroid tapers with these exposures during the next year and was referred to us with a diagnosis of eucalyptus-induced hypersensitivity pneumonitis and asthma.

This patient had a history of perennial rhinitis that began in her 20s and that is particularly prominent in the spring. There was no history of asthma before October 2001, and there was no history of urticaria, angioedema, sinus infections, or atopic dermatitis. She had negative skin test results for immediate hypersensitivity to a variety of inhalant allergens, including tree pollens, grasses, weeds, dust mites, cockroaches, cats, dogs, and multiple fungi, suggesting that she was nonatopic.

The patient was a never-smoker and was employed as a nurse. She has 3 children with asthma. Her current medications included formoterol, budesonide, levalbuterol, albuterol-ipratropium, mometasone nasal spray, montelukast, esomeprazole, loestrin, levothyroxine, and diphenhydramine.

* Division of Pulmonary and Critical Care Medicine, Allergy and Clinical Immunology, Medical University of South Carolina, Charleston, South Carolina.

† Evelyn Trammell Institute for Voice and Swallowing Disorders, Otolaryngology, Head and Neck Surgery, Medical University of South Carolina, Charleston, South Carolina.

Received for publication February 2, 2004.

Accepted for publication in revised form May 2, 2004.

On physical examination, her temperature was 100° F; pulse rate, 100 bpm; respiratory rate, 20/min; blood pressure, 150/80 mm Hg; and oxygen saturation, 98% by pulse oximetry on room air. Her pupils were equal and reacted normally to light and accommodation. Nasal mucosa was normal in color, and there was no nasal discharge, submucosal edema, turbinate hypertrophy, or nasal polyps. Ear and pharynx examination results were unremarkable. Lung examination findings were normal. Heart examination revealed a minimal, regular tachycardia. Abdominal, integumentary, and neurologic examination results were also unremarkable.

Laboratory examination showed a white blood cell count of 4,720 cells/ μ L, with 59% neutrophils, 27% lymphocytes, 10% monocytes, and 2% eosinophils. The hemoglobin concentration was 14 g/dL, and the platelet count was 320,000 cells/ μ L. The Westergren sedimentation rate was 20 mm/h. A repeated IgE level was negative at 29.6 IU/mL. IgE-specific antibodies to eucalyptus were also negative. Results of a hypersensitivity pneumonitis panel for IgG antibody to eucalyptus were negative.

Pulmonary function studies were performed when the patient was asymptomatic. Spirometry revealed a forced vital capacity (FVC) of 3.41 L/s (116% of predicted), a forced expiratory volume in 1 second (FEV₁) of 2.56 L/s (114% of predicted), and an FEV₁-FVC ratio of 75. The forced expiratory flow between 25% and 75% was 1.89 L/s (62% of predicted). There was a 33% increase in the forced expiratory flow between 25% and 75% after albuterol-ipratropium use. There was no significant bronchodilator response noted in either FEV₁ or FVC. The flow-volume loop was normal. Results of methacholine bronchoprovocation were normal.

Lung volumes showed a total lung capacity of 102% of predicted, a functional residual capacity of 76% of predicted, a residual volume of 77% of predicted, and an expiratory reserve volume of 75% of predicted. The diffusing capacity for carbon monoxide adjusted for hemoglobin level was 116% of predicted, and when adjusted for alveolar volume, it was 146% of predicted.

METHODS

The patient underwent 2 challenges to eucalyptus performed 1 month apart. The initial challenge was with eucalyptus and was not masked. There was obvious adduction of the vocal cords within 30 seconds of the inhalation. We then decided that another challenge test with the eucalyptus odor and several control irritant substances was needed to provide evidence of specificity. The patient underwent a masked flexible fiberoptic nasolaryngoscopy to confirm whether VCD occurred with eucalyptus and not with other known respiratory irritants. Videostroboscopy using a rigid intraoral fiberoptic laryngoscope was performed before the inhalation challenges to determine baseline laryngeal function (Fig 1). There was normal abductor/adductor vocal cord movement during phonation, and closure of the vocal cords was complete, without evidence of paradoxical motion. The glottis was patent during quiet inspiration and expiration. Laryngeal function then was observed during flexible fiberoptic naso-

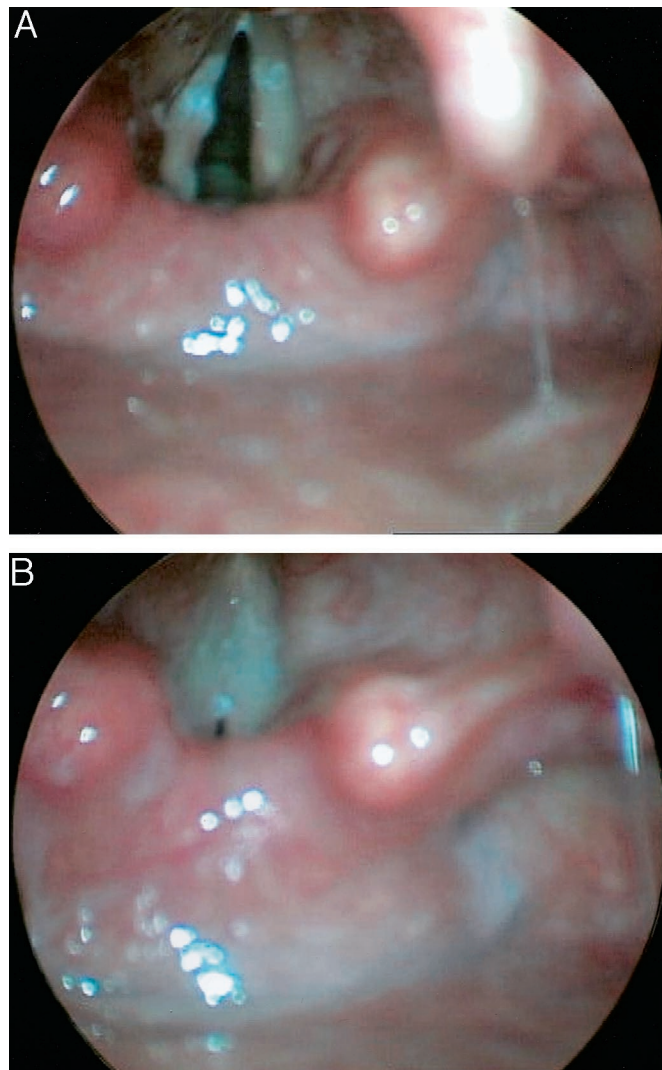


Figure 1. Pretest videostroboscopy shows normal abduction (A) and adduction (B) of the vocal cords.

laryngoscopy. The patient demonstrated normal abduction of the vocal cords during rest inspiration and full inspiration.

Inhalational challenges then were performed with the patient and the observer masked to the types of chemicals used. Both were informed that 1 of the test challenges might contain eucalyptus. The patient was tested with water, ammonia, pine oil, and a mixture of ammonia and eucalyptus. All stimuli were applied to 4 × 4 gauze held approximately 5 inches from the nares.

RESULTS

During the initial inhalation challenges, the patient was exposed first to water, followed by ammonia, and then pine oil. Both the observer and the patient were informed that 1 of the challenges might contain eucalyptus; however, eucalyptus was not present. A normal pendulous movement of the vocal cords was noted.

During the second inhalation series, the patient was ex-

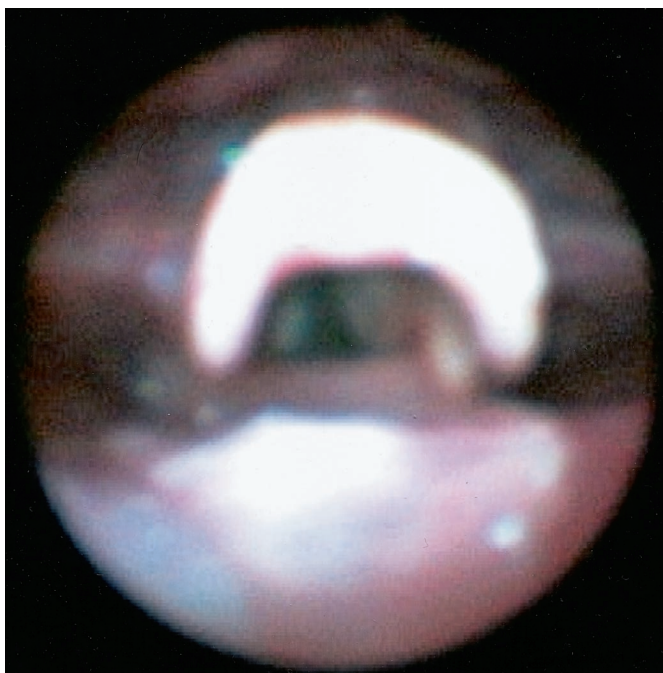


Figure 2. Flexible nasolaryngoscopy during water challenge shows full abduction of the vocal cords during inhalation.

posed to water first, followed by ammonia, pine oil, and the ammonia-eucalyptus mixture. Again, the patient and the observer were told that 1 of the test challenges might have eucalyptus. A normal pendulous movement of the vocal cords

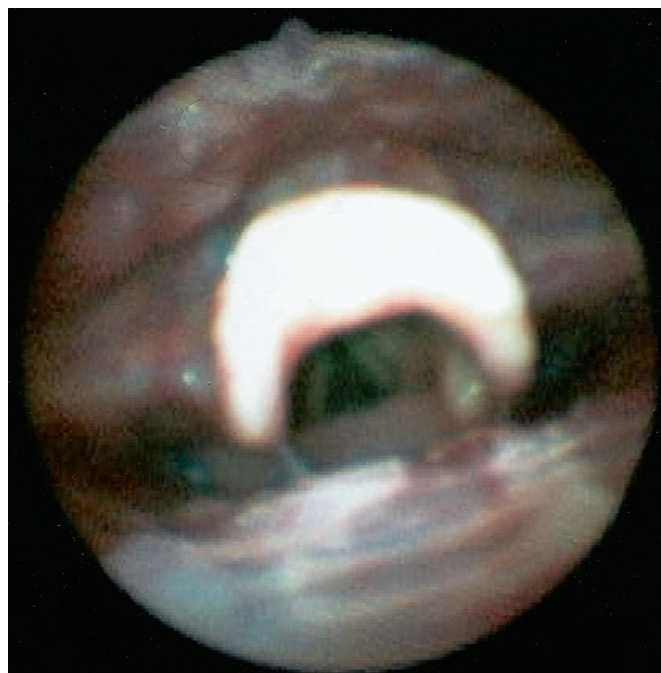


Figure 4. Flexible nasolaryngoscopy during pine oil challenge shows full abduction of the vocal cords during inhalation.

was again noted with exposure to water, ammonia, and pine oil. Figures 2–4 show the laryngoscopic findings of these inhalation challenges.

Dry eucalyptus leaves were used to impregnate the euca-

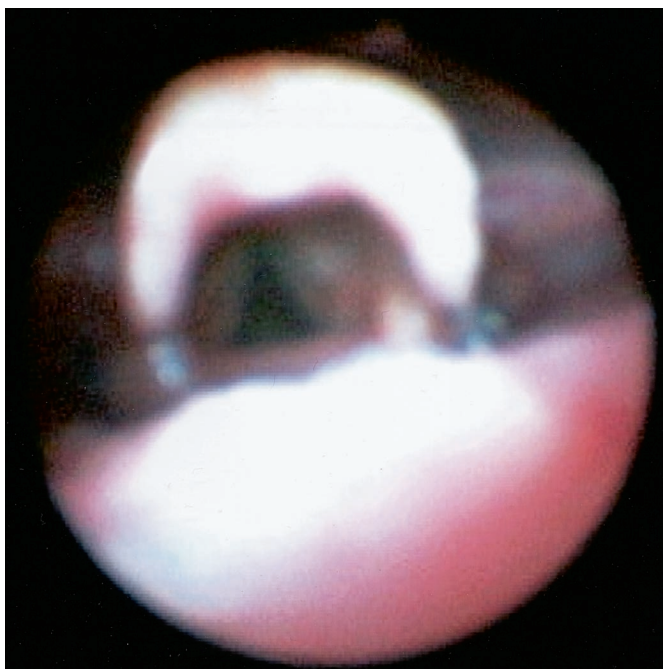


Figure 3. Flexible nasolaryngoscopy during ammonia challenge shows full abduction of the vocal cords during inhalation.

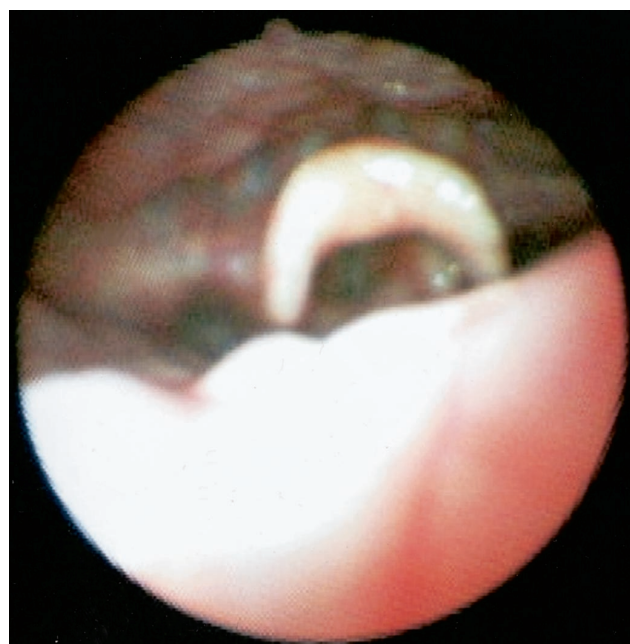


Figure 5. Flexible nasolaryngoscopy during eucalyptus and ammonia challenge shows adduction of the vocal cords during inhalation. This finding is consistent with the diagnosis of vocal cord dysfunction.

Table 1. Summary of the Inhalation Challenges and Corresponding Laryngoscopic Findings

Inhalation agent*	Laryngoscopic findings
Water	Normal
Ammonia	Normal
Pine oil	Normal
Water	Normal
Ammonia	Normal
Pine oil	Normal
Ammonia-eucalyptus	Vocal cord dysfunction

* The inhalation challenges are listed in the order of exposure to the patient.

lyptus odor on the gauze. Ammonia was then applied to the gauze in an attempt to mask the eucalyptus smell. The ammonia-eucalyptus mixture was tested by 2 volunteers before patient exposure to determine whether the ammonia completely masked the eucalyptus odor. Neither of the 2 volunteers identified the presence of eucalyptus before patient exposure.

When the patient was exposed to the ammonia-eucalyptus mixture, she began to experience the paradoxical vocal cord motion after a few minutes of exposure (Fig 5). The VCD persisted for several minutes after the testing and was exacerbated with talking. The patient was instructed in facilitative breathing techniques by the speech-language pathologist and was able to cease the paradoxical movement. Table 1 summarizes the laryngoscopic findings, with the inhalation agent in the order in which the patient was exposed.

DISCUSSION

Vocal cord dysfunction is a well-recognized clinical entity in the medical literature. This clinical syndrome frequently mimics asthma, anaphylaxis, angioedema, or other causes of upper airway obstruction, and it is characterized by inappropriate adduction of the vocal cords during inspiration, with resultant airflow limitation.⁴ The airflow obstruction can be severe enough to cause wheezing, chest tightness, dyspnea, cough, and dysphonia. The clinical presentation of VCD can be dramatic and often paroxysmal. Misdiagnosis is common and often leads to inappropriate treatments, such as intubation, high-dose corticosteroids, and even tracheotomy.^{2,5}

The prevalence of VCD is unknown; however, it may be common in patients referred to tertiary care centers for refractory asthma.² Newman and Dubester² published a retrospective study of all patients hospitalized at National Jewish Hospital between 1984 and 1991 in whom VCD was diagnosed. Ninety-five patients met the diagnostic criteria for VCD; 42 (44%) had isolated VCD and 53 (56%) had VCD and coexisting asthma. The patients with VCD without asthma were predominantly young women who were misdiagnosed for an average of 4.8 years. Thirty-four (81%) of the 42 patients with VCD only were receiving daily systemic corticosteroids (average daily dose of 29 mg of prednisone). During the course of their disease, 27 patients with VCD (28%) had been intubated. Patients with uncomplicated VCD averaged 9.7 emergency department visits and 5.9 hospital admissions in the year before hospitalization at

National Jewish Hospital. These data support an enormous medical utilization and cost in these patients.

Common symptoms of patients with VCD are wheezing, stridor, dyspnea, hoarseness, and chest tightness. Attacks of VCD occur predominantly during the day and are paroxysmal, with abrupt onset and quick resolution, often mimicking asthma. The wheezing is typically monophasic and is best auscultated over the larynx, in contrast to the wheezing of asthma, which is polyphasic. Symptoms of VCD may be temporally relieved when attention is diverted. Cyanosis, respiratory arrest, or hypoxia is inconsistent with the diagnosis of uncomplicated VCD.^{6,7} Therapy with β -agonists not only fails to alleviate but may worsen VCD symptoms.

The cause of VCD remains controversial. The typical patient with VCD is a single woman aged 20 to 40 years. Psychiatric conditions are common and include depression, anxiety, obsessive-compulsive behavior, and other personality disorders.⁸ Christopher and coworkers¹ suggest that VCD represents a conversion disorder; however, it is known that patients cannot volitionally reproduce the paradoxical vocal cord motion. Vocal cord dysfunction is not a factitious disorder. An increased proportion of individuals employed as health care providers have VCD.

Perkner and colleagues⁹ described 11 patients with a temporal relationship between environmental exposure and VCD. These researchers described a new clinical entity called "irritant-associated VCD." The respiratory irritants identified included ammonia, smoke, flux fumes, organic solvents, ceiling tile fibers, and cleaning chemicals; however, no challenge studies were performed to document these observations. Our patient may fit into this subgroup, with the unusual presentation of irritant-associated VCD specific to a particular odor/irritant, eucalyptus, which is reproducible. We excluded an IgE-dependent mechanism that could confer sensitivity; nevertheless, our patient's symptoms seemed to be reproducible even when the eucalyptus odor was masked so that apprehension associated with odor identification was eliminated. Perkner and colleagues⁹ speculated that the pathogenic mechanism was a direct inflammatory reaction at the level of the vocal cords. However, laryngeal biopsies that could have supported this mechanism were not performed.

Diagnostic studies performed on patients with asthma may suggest the presence of VCD. Chest radiographs in acute asthmatic patients with exacerbation often reveal hyperinflation and peribronchial thickening,¹⁰ whereas in uncomplicated VCD, findings from chest radiographs are usually normal. Other features that may help differentiate VCD from asthma include that (1) patients with symptomatic VCD have truncation of the inspiratory limb of the flow-volume loop, (2) VCD patients are unable to perform reproducible forced expiratory maneuvers, (3) normal airway resistance is seen in uncomplicated VCD, and (4) the concentration of methacholine that causes a 20% decline in FEV₁ is usually similar to that of healthy subjects.^{3,8}

The definitive diagnosis of VCD is best established by using flexible fiberoptic nasolaryngoscopy. In VCD, the true vocal cords medialize and/or fully adduct during inspiration. In contrast to impaired subjects, the vocal cords in healthy

subjects are fully abducted during inspiration, with only minimal medialization during expiration. The glottis remains open throughout the entire respiratory cycle during quiet breathing. Adduction that occurs in the last half of expiration is not pathologic. In VCD, the vocal cords are adducted anteriorly, and an open posterior glottis chink is maintained. This finding unequivocally establishes the diagnosis of VCD.^{11,12}

An important aspect in the treatment of patients with VCD is to reassure them that there is no physical impairment. Martin et al⁸ and Blager et al¹³ are among the foremost clinicians to have published treatment techniques for VCD. Patients are taught breathing exercises by trained speech-language pathologists for hyperfunctional voice disorders to decrease laryngeal muscle tone. These breathing techniques include deep breathing with relaxed abdominal muscles, followed by a deep inspiration quickly through the nose (sniffing) while the jaw is in a relaxed position; this is followed by slow exhalation (relaxed throat breathing technique). Ninety percent of patients with VCD indicated marked improvement in symptom control when using these breathing techniques.^{8,13} During acute attacks, the administration of helium and oxygen (heliox) has been shown to be effective in resolving symptoms in some patients.¹⁴ In recalcitrant cases, biofeedback, hypnosis, and psychotherapy have been used successfully.

CONCLUSION

VCD is a poorly identified clinical entity. Asthmatic regimens for patients with uncomplicated VCD are ineffective and can lead to iatrogenic complications. Conversely, it is important not to dismiss the diagnosis of asthma in patients who are diagnosed as having VCD because coexisting disease is common, and the removal of necessary medications may exacerbate symptoms.

This is the first report to prospectively document that a specific irritant, eucalyptus, can precipitate VCD. The mechanism of eucalyptus-induced VCD in this patient remains unknown. However, an allergic mechanism does not seem to be operative. A nonimmunologic mechanism is supported by negative skin prick test reactions to common inhalant allergens, normal IgE levels, and negative IgE eucalyptus-specific antibodies. We suspect that the eucalyptus acts as an irritant and possibly involves a neuronal reflex mechanism, leading to paradoxical vocal cord motion. An identifiable trigger of VCD masquerading as asthma may be more common than previously appreciated and should be considered when atypical asthma is encountered.

Within 2 to 3 minutes of exposure to eucalyptus during the inhalation test, the patient demonstrated paradoxical vocal cord motion. She was restructured in facilitative breathing behavior and was able to control the severity of the paradoxical motion. The presence of coexisting asthma was not

evident in this case and is supported by a negative methacholine challenge test result. All of her asthma medications have been successfully discontinued. She is gaining confidence in her ability to control her laryngeal muscles and is still maintaining follow-up with a speech-language pathologist, who is providing ongoing instruction in the breathing techniques necessary to abort eucalyptus-induced VCD.

REFERENCES

1. Christopher KL, Wood RP Jr, Eckert RC, Blager FB, Raney RA, Souhrada JF. Vocal cord dysfunction presenting as asthma. *N Engl J Med*. 1983;308:1566–1570.
2. Newman KB, Dubester SN. Vocal cord dysfunction: masquerade of asthma. *Semin Respir Crit Care Med*. 1994;15:161–167.
3. Bahrainwala AH, Simon MR, Harrison DD, Toder D, Secord EA. Atypical expiratory flow volume curve in an asthmatic patient with vocal cord dysfunction. *Ann Allergy Asthma Immunol*. 2001;86:439–443.
4. Patterson R, Schatz M, Horton M. Munchausen's stridor: non-organic laryngeal obstruction. *Clin Allergy*. 1974;4:307–310.
5. O'Connell MA, Sklarew PR, Goodman DL. Spectrum of presentation of paradoxical vocal cord motion in ambulatory patients. *Ann Allergy Asthma Immunol*. 1995;74:341–344.
6. McFadden ER Jr. Glottic function and dysfunction. *J Allergy Clin Immunol*. 1987;79:707–710.
7. Newman KB, Mason UG, Schmalzing KB. Clinical features of vocal cord dysfunction. *Am J Respir Crit Care Med*. 1995;152:1382–1386.
8. Martin RJ, Blager FB, Gay ML, et al. Paradoxical vocal cord motion in presumed asthmatics. *Semin Respir Med*. 1987;8:332–337.
9. Perkner JJ, Fennelly KP, Balkissoon R, et al. Irritant-associated vocal cord dysfunction. *J Occup Environ Med*. 1998;40:136–143.
10. Wood RP, Milgrom H. Vocal cord dysfunction. *J Allergy Clin Immunol*. 1996;98:481–485.
11. Selner JC, Koepke JW. Rhinolaryngoscopy in the allergy office. *Ann Allergy*. 1985;54:479–482.
12. Selner JC. Concepts and clinical application of fiberoptic examination of the upper airway. *Clin Rev Allergy*. 1988;6:303–320.
13. Blager FB, Gay ML, Wood RP. Voice therapy techniques adapted to treatment of habit cough: a pilot study. *J Commun Disord*. 1988;21:393–400.
14. Weir M. Vocal cord dysfunction mimics asthma and may respond to heliox. *Clin Pediatr*. 2002;41:37–41.

Requests for reprints should be addressed to:

John T. Huggins, MD

Division of Pulmonary and Critical Care Medicine

Allergy and Clinical Immunology

Medical University of South Carolina

PO Box 250625

Charleston, SC 29425

E-mail: hugginjt@usc.edu