Background: Vocal cord dysfunction (VCD) is an involuntary functional disorder commonly misdiagnosed as asthma. Previous reports describe the disorder and treatment but not the long-term outcome.

Objective: To determine the long-term outcome of VCD.

Methods: A retrospective medical record review identified 49 patients, ages 8 to 25 years, diagnosed as having VCD from 1989 to 2002. Telephone contact was attempted in all.

Results: Of the 49 patients, 41 had previously been treated for asthma; that diagnosis was confirmed by us as a comorbidity in only 12 patients. Two distinct phenotypes of VCD were observed. Symptoms were limited to exercise-induced VCD (EIVCD) in 29 and spontaneously occurring VCD (SVCD) in 20, only 4 of whom additionally had EIVCD. Twenty-eight of the 49 were successfully contacted by telephone. Eight of the 11 contacted patients with SVCD followed the recommendation to see our speech therapist, all of whom learned to control symptoms. However, 2 who also had EIVCD continued with that problem. Pretreatment with an anticholinergic inhaler prevented EIVCD in 6 patients in whom this was tried. Complete absence of symptoms, at times ranging from 1 week to 5 years (median, 5 months), was reported in 26 of the 28 contacted patients.

Conclusions: VCD continues to be frequently misdiagnosed as asthma. Two phenotypes of VCD are apparent: EIVCD and SVCD. Speech therapy provides relief of symptoms for SVCD. Prevention of EIVCD with an anticholinergic inhaler in 6 patients suggests that a controlled clinical trial is warranted. Regardless of treatment, eventual spontaneous resolution was common.

INTRODUCTION
A medical textbook published in 1842 by Robley Dunglison described a disorder of the laryngeal muscles brought on by “hysteria.” Patterson termed this disorder Munchausen’s stridor.1 The physiology of this disorder was subsequently characterized as paradoxical vocal cord movement.2 Vocal cord dysfunction (VCD) is now recognized as a cause of respiratory distress that is frequently misdiagnosed as asthma.3–6

VCD is characterized by the inappropriate adduction of the vocal cords during inspiration.3,4 The typical presentation of VCD is the sudden onset of labored breathing with inspiratory stridor that has often been mistakenly described as “wheezing.”3 In at least some cases, this is precipitated by physical activity.5 This paradoxical adduction during inspiration produces airflow obstruction severe enough to cause the inspiratory wheezing-like sound (actually a high-pitched stridor), chest tightness, and shortness of breath.7 The acute onset and severity of symptoms in some patients with VCD have resulted in intervention with endotracheal intubation or tracheotomy for severe upper airway obstruction.8,9

Management described for VCD subsequent to confirmation of the diagnosis has included patient education and speech therapy.3,4,7,10–12 Techniques used have focused on training exercises to decrease the tension of extrinsic laryngeal muscles.13 Although high rates of success for this treatment have been reported, the long-term outcome is not well characterized. In this retrospective review of our experience during a 13-year period, we identified 2 distinct patterns of VCD and report the long-term outcome of patients diagnosed as having VCD in our Pediatric Allergy and Pulmonary Clinic.

METHODS
Patient Selection
Patients seen in the Pediatric Allergy and Pulmonary Clinic at the University of Iowa from 1989 to 2002 with a diagnosis of VCD were identified.

Study Design
Medical records of the patients were reviewed to identify demographics, clinical characteristics, previous diagnoses and treatment, criteria for diagnosis of VCD, procedures performed, and treatment recommendations, both before and after the diagnosis. The diagnosis of VCD was based on direct laryngoscopy, reversible inspiratory airflow obstruction with spirometry during observed symptoms, or a convincing history of episodic inspiratory stridor that was rapid in onset and rapidly reversible in the absence of any other findings. Clinically apparent comorbidities, including asthma, gastroesophageal reflux disease, and psychological disorders, were identified. An attempt was made to contact all patients by telephone; if the patient (and parent for those younger than 18 years) consented, a structured interview over the telephone was used to obtain information regarding outcome. The study was approved by the institutional review board.

Pediatric Allergy and Pulmonary Division, University of Iowa College of Medicine, Iowa City, Iowa.
No external funding was required for this study.
RESULTS

Diagnosis

The diagnosis of VCD was established in 49 patients seen in the Pediatric Allergy and Pulmonary Clinic at the University of Iowa between 1989 and 2002. VCD was confirmed by laryngoscopy while symptomatic in 24 of the 49 patients. Symptoms were observed in another 8 patients but were not present long enough for visualization of the vocal cords by laryngoscopy. Flattening of the inspiratory portion of the flow-volume loop when symptomatic, with normal spirometry results when asymptomatic, was the basis for the diagnosis in those patients. In the other 17 patients, the symptoms were not directly observed as a result of either spontaneously occurring VCD (SVCD) or as exercise-induced VCD (EIVCD). These patients received their diagnosis based on a convincing history of recurrent sudden onset of inspiratory stridor followed by rapid cessation after minutes or hours without treatment or associated sequelae.

Forty-one of 49 patients had been diagnosed as having asthma as a cause of their symptoms before the diagnosis of VCD was established in our clinic. Asthma as a comorbidity was confirmed by us in only 12 of those patients. Asthma was excluded in the remaining patients based on history, physical examination, pulmonary function testing, and response to prior therapy. There was no evidence of exercise-induced asthma in any of the patients with EIVCD. Neither gastroesophageal reflux nor psychiatric illness was apparent from the medical history or our evaluation during the visit to our clinic.

Phenotypes

Two distinct patterns or phenotypes of VCD were identified based on the history of recurrent symptoms. One phenotype involved symptoms of VCD that were limited to being exercise induced (EIVCD). The other phenotype was associated with a sudden onset of symptoms occurring without any inciting factors or triggers (SVCD).

Of the 49 patients with VCD, 29 had only EIVCD. Twenty patients had SVCD, only 4 of whom had symptoms also brought on by exercise in addition to the episodes that occurred spontaneously. The median age at the time of diagnosis for those with exclusive EIVCD was 14.9 years (range, 9–20 years); the age of those with SVCD averaged 13.5 years (range, 8–25 years). The female:male ratio demonstrated a higher number of female patients affected in each group (1:6:1 in the EIVCD group; 2:2:1 in the SVCD group).

Outcome of VCD

An attempt was made to contact all 49 patients by telephone. Twenty-eight patients were successfully contacted by telephone and agreed to answer our questions a median time of 3 years after the diagnosis in our clinic (range, 0.5–12 years; interquartile range, 1.3–8.5 years). Consent from a parent also was obtained for those younger than 18 years.

Of the 28 patients we were able to contact, the median onset of EIVCD was 12 months before our diagnosis (range, 3 weeks to 7 years) (Table 1). For SVCD, the median onset was 6 months before our evaluation (range, 1 week to 4 years). Seventeen of the 28 patients (10 female and 7 male) had only EIVCD. Eleven of the 28 patients (8 female and 3 male) had SVCD, with 2 of them (both female) additionally experiencing EIVCD. The median time until resolution of symptoms was 5 and 4 months for EIVCD and SVCD, respectively, although with a great deal of variability, ranging from 1 week to 5 years, irrespective of intervention. Once symptoms were reported as stopped, no recurrences were described.

In patients with EIVCD, a trial of an anticholinergic aerosol metered-dose inhaler (Atrovent oral inhaler), ipratropium bromide, was prescribed for 7 patients to be used before exercise as an attempted preventive measure. All 6 who filled the prescription indicated that the ipratropium bromide prevented EIVCD when used before exercise.

Of the 17 patients contacted with EIVCD, 16 were asymptomatic at the time of contact without any ongoing treatment. One remained symptomatic but continued to use ipratropium bromide before exercise with prevention of symptoms. Speech therapy had been recommended in all patients with SVCD. The 8 who attended speech therapy reported performing the recommended breathing exercises for acute symptoms with cessation of symptoms when they occurred. All but 1 of the 11 patients with SVCD had become asymptomatic by the time of our telephone call. The one patient with continued SVCD when contacted was among the 6 who had attended speech therapy.

At the time of telephone contact with EIVCD patients, 5 reported that they had subsequently received additional diagnoses, 2 with depression, 1 with sleep apnea requiring tonsillectomy, 1 with gastroesophageal reflux disease, and 1 with allergic rhinitis. Among the patients with SVCD, 8 reported new diagnoses, 4 with allergic rhinitis, 2 with gastroesophageal reflux disease, 1 with obstructive sleep apnea, and 1 with anxiety. No attempt was made to identify the basis for or validity of these subsequent patient-reported diagnoses.

DISCUSSION

Two distinct clinical patterns or phenotypes of VCD were seen in our population. Most of those with SVCD did not have it precipitated by exercise, and most of those with VCD limited to exercise had no symptoms other than with exercise. Although more than 80% of our patients had been diagnosed previously as having asthma, that diagnosis was confirmed in fewer than a fourth of the patients in our specialty clinic. As with previous reports, techniques taught by a speech therapist were effective in providing relief of symptoms once they occurred. A trial of an anticholinergic aerosol, ipratropium bromide, was reported by the 6 for whom it was prescribed as successful in preventing the exercise-induced symptoms when used before the activity.

The long-term outcome of VCD overall in our population demonstrated eventual resolution of symptoms in 26 of the 28 contacted patients, irrespective of whether or not they at-
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Abbreviations: EIVCD, exercise-induced vocal cord dysfunction; MDI, metered-dose inhaler; PFT, pulmonary function testing; SVCD, spontaneous vocal cord dysfunction; VCD, vocal cord dysfunction.

* Asthma diagnosed before VCD diagnosis/confirmed as comorbidity.
tended speech therapy. At the time of telephone contact, 2 patients remained symptomatic, 1 with EIVCD and 1 with SVCD. The patient with EIVCD was successfully controlling symptoms by using ipratropium bromide before exercise. The symptomatic patient with SVCD continues to follow up with speech therapy regularly.

Some previous reports have associated symptoms of VCD purely with exercise. This observation of exercise and symptoms was noted in a report by McFadden and Zawadski that described 7 elite athletes, ages 15 to 32 years, with EIVCD. A larger study by Rundell and Spiering evaluated 370 developing or elite athletes for symptoms consistent with inspiratory stridor and exercise-induced bronchospasm. Their findings showed 19 patients (5%) (18 female) with symptoms consistent with EIVCD.

Several previous studies have suggested that a spontaneous onset of VCD is often associated with underlying psychiatric disorders. Psychiatric consultation for further therapy and consideration of underlying somatoform disorders has also been recommended. In a report by Selner et al, 3 patients were described as having spontaneous onset of symptoms attributed to psychological factors, and a psychological evaluation was recommended for patients with VCD. Another study by Gavin et al described 12 patients with VCD occurring only at times of anxiety with no relationship to activity or exercise. Newman et al reported a previous psychiatric diagnosis in 73% of patients with VCD. This observation has also been noted in other studies, suggesting a higher incidence of VCD in female patients with an underlying psychological condition. Stress and emotions, as well as times of increased panic or anxiety, have been suggested as triggers for VCD. Social stressors were also described in 12 of 22 pediatric patients with VCD, particularly in those involved with organized sports, hypnosis, heliox, and injection of botulinum toxin also have been previously used for patients who have failed speech therapy or have more severe symptoms, although evidence demonstrating their efficacy on the clinical course is lacking.

The association of VCD and underlying psychological disorders was not apparent in our population to the extent that has been previously described. Of the 28 patients contacted, only 3 patients (11%) reported anxiety and depression after the diagnosis of VCD. Spontaneous symptoms of VCD occurred at various times of the day, with several patients experiencing symptoms during classes. This may suggest that stress or anxiety may play a role in spontaneous symptoms, but support for an underlying psychological disorder or panic attacks was not apparent from our evaluation.

The predominance of females among our patients was consistent with previous reports as was the frequent misdiagnosis of asthma. Distinguishing characteristics from asthma include an upper respiratory tract inspiratory “wheeze,” which is actually a high-pitched stridor, rather than the typical polyphonic expiratory wheezing of asthma. Spirometry demonstrates the upper airway obstruction by a markedly decreased inspiratory flow rate during a maximal inspiratory effort rather than the decreased expiratory flow associated with active asthma. The usual ratio of the forced inspiratory flow at 50% of vital capacity to forced expiratory flow at 50% of expiration is approximately 1, whereas this is markedly decreased during symptomatic VCD but not during symptomatic asthma, where the ratio is likely to be increased. When not symptomatic, spirometric values for patients with VCD will be normal, which distinguishes this entity from other causes of upper airway obstruction such as vocal cord paralysis or paresis, subglottic stenosis, or other fixed abnormalities of the upper airway. Patients with VCD in the absence of active asthma present at the time of symptoms generally have normal pulse oximetry, chest radiographs, and arterial blood gas values. On rare occasions, VCD may have central neurologic factors as the primary cause.

Additional diagnoses reported but not confirmed by us were reported in 12 of the 28 contacted patients. However, since the symptoms of VCD had resolved for most by the time of our telephone interview, the subsequent diagnoses did not appear to be related to the VCD.

Speech therapy, relaxation, biofeedback, and breathing techniques are interventions that have been described previously for treatment of VCD. Christopher et al described improvement in symptoms 3 to 21 months after speech therapy in 5 patients. In our population, 8 of 11 contacted patients followed our recommendations for speech therapy. Although the patients reported that the techniques taught by our speech therapist enabled them to control symptoms when they occurred, the subsequent duration of recurrences varied from a week to 12 months among them. Of the 3 who did not follow our recommendation for speech therapy, recurrent symptoms persisted for 4, 12, and 60 months.

Only one previous report described the long-term outcome of patients following the diagnosis of VCD. In that report, resolution of symptoms within 8.2 months was described in 5 patients by Murry et al. A previous outcome study by Sullivan et al described teaching 20 female athletes “coordinated thoracic-abdominal breathing exercises” when symptoms of VCD occurred during exercise, with 19 of the 20 indicated as being able to control their symptoms after 6 months. However, it was not clear whether complete resolution of the problem had occurred in any. In our patients with EIVCD, symptoms generally subsided with a decrease or cessation of exercise. Since procedures such as those described by Sullivan et al would require disruption of the athletic activity, the breathing exercises successful for spontaneously occurring VCD were judged by us as being unrealistic during the typically vigorous peak levels of exercise, often during competitive athletics, that precipitated the symptoms of EIVCD.

The use of ipratropium bromide MDI to prevent EIVCD has not been previously described. The use of an anticholinergic inhaler was considered in patients with VCD based on our speculation that a vagally mediated reflex was the mechanism. Six of our patients with EIVCD for whom ipratropium bromide metered-dose inhaler was prescribed and used re-
ported prevention of symptoms associated with exercise, whereas an albuterol metered-dose inhaler had been previously ineffective in the 4 who had been previously diagnosed as having asthma. Of interest, 6 patients with EIVCD for whom the ipratropium metered-dose inhaler was not prescribed indicated when contacted that they had quit the competitive athletic activity that had been associated with their symptoms.

Support for the rationale of using an anticholinergic agent to prevent EIVCD is found in 2 recent case reports that describe prolonged stimulation of the vagal nerve by vagal nerve stimulators, used in patients for intractable seizures, causing VCD as a complication.29,30 Laryngopharyngeal dysfunction, coughing, and voice changes were also reported in these patients. A recent editorial has also suggested an altered autonomic balance as a cause of VCD, since true and false vocal cords derive motor innervation from the vagus nerve.31 A limitation of our study is its retrospective nature. Our assessments in several patients with VCD were also based entirely on history. Since our study went back to 1989, 21 of the 49 patients were lost to follow-up despite attempts to contact them. Several patients moved without forwarding addresses or telephone numbers, and some changed their names after getting married. Our observation of preventing EIVCD with pretreatment ipratropium bromide is generally results in cessation of the symptoms, the outcome desired is for the patient to be able to perform the activity. Although stopping the exercise generally results in cessation of the symptoms, the outcome desired is for the patient to be able to perform the activity. Our data suggest that the use of ipratropium bromide may be a safe and effective measure for treating EIVCD and warrants a double-blind, placebo-controlled clinical trial.

ACKNOWLEDGMENTS

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REFERENCES


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