Irritable larynx syndrome (Internal and external correlates)

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Irritable larynx is a condition of laryngeal dysfunction at which there is abnormal spasmodic closure of both vocal folds during inspiration. Patient complains of many symptoms as stridor, dysphonia, chocking, globus sensation, and dyspnea. These symptoms are not specific for irritable larynx only, but; they are frequently confused with other disorders such as gastroesophageal reflux, asthma, and different causes of chronic cough. The golden method for diagnosis is to visualize both vocal folds abducted during inspiration in acute attack by indirect laryngoscopy. To review recent available literature concerning irritable larynx syndrome to get essential recent data as a primary step for understanding this disorder.

Keywords:
chronic cough, irritable larynx, paradoxical vocal folds motion, stridor

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Introduction

The larynx is a luxuriously innervated structure and in humans plays a basic role in subserving several basic biological functions; such as the facilitation of swallow, communication, and airway protection [1]. Its anatomical site supports its role as a true 'gateway' to the airways and effective complex reflex mechanisms that prepare the larynx to be in a state of readiness for closure, that is as a protective defensive function [2–4].

Different terms have been utilized to describe a syndrome accompanied with hyperfunctional laryngeal behaviors marked by acute upper airway obstruction with coexisting dysphonia, aphonia, dyspnea, dysphagia, cough, laryngeal stridor, laryngeal muscle tension patterns, and a host of several other physical and nonphysical symptomatology as paradoxical vocal cord movement [2–4], functional airway obstruction [5], factitious asthma [6], paradoxical vocal cord dysfunction (PVCD/VCD) exposed as asthma [7], Munchausen's stridor, laryngeal spasm like a bronchial asthma [8], functional upper airway obstruction, exercise-induced laryngospasm, stridor due to vocal fold malfunction related to psychological factors [9], psychogenic stridor [2], episodic laryngeal dyskinesia [10], episodic paroxysmal laryngospasm [11], a functional laryngeal stridor [12], and the irritable larynx syndrome (ILS) [13].

Incidence and prevalence

The incidence of VCD in the general population in 1999 was measured at 3%, but rates have been reported as high as 26.9% in 2007 [14]. The VCD patients are typically presented as 20–40 years old and female with multiple life stressors [14,15]. Approximately one-third of cases among adolescents are males [16]. Prevalence has been reported to range from 2.5% of patients seeking asthma clinic to up to 22% of patients with recurrent emergency department visits for dyspnea [17,18].

Pathophysiology

Vocal folds normally abduct during inspiration, expanding the glottis (opening between the vocal folds) and adduct during exhalation. Glottis size is controlled by voluntary and reflex acts, with the fundamental task of defensing the airway. Vocal folds permit air to reach the lungs during inspiration [19]. The pathophysiology of VCD is not sufficiently studied but is thought to be a consequence of laryngeal hyperresponsiveness and paradoxical vocal fold closure during inspiration and may be worsened by psychological tension [18]. In VCD, the vocal folds adduct or close during inspiration, decreasing entered inspired air and producing an inspiratory stridor basically over the larynx [18,20].

Once thought to be an essentially psychogenic disease, the ILS becomes presented as a functional disorder that may be relevant to the role of glottis closure in securing the trachea and lungs. Neural malfunction presented as abnormal laryngeal hypersensitivity and reflux,

motor neural dysfunction, inflammatory process, and neuroplastic changes to brain stem governing center of larynx have been proposed as mechanisms leading to the ILS. In spite of the fact that there is a group of patients in whom paradoxical vocal fold motion (PVFM) likely represents a conversion disorder, most patients suffer from other medical conditions, for example, asthma, irritant exposures, gastroesophageal reflux disease, exercise intolerance, and viral illness [21].

Etiology (poorly understood)

Psychogenic causes, conversion reaction (70%) and functional, idiopathic, and nonorganic causes have been proposed by researchers to explain functional stridor, laryngeal muscle tension patterns, aphonia [2,4,9,22–25], and dysphonia. Some authors relate the onset of paradoxical vocal cord movement and ILS with upper respiratory viral infections [3,13].

Over the previous decade, more confirmation has been set on distinguishing other likely precipitating or exacerbating organic etiological variables associated with this syndrome manifestations allergic phenomena, gastroesophageal reflux disorder (63–80%), respiratory type of laryngeal dystonia, drug-induced laryngeal dystonic reactions as neuroleptic drugs like haloperidol, chlorpromazine, and thiopental and other neurologic pathophysiological mechanisms (that affect brain stem as Chiari malformation, hydrocephalus, meningomyelocele, cerebrovascular accidents, and severe closed head injuries) [2].

Upper esophageal inflammation resulting from acidic reflux activates mucosal chemoreceptors, superior laryngeal innervation of larynx, and vagus-mediated nerve networks [2].

Clinical presentation and diagnosis

Symptoms

Patients report a sudden onset of symptoms as shortness of breathing, cough, throat tightness, change of voice, wheezing, chocking sensation, heaviness, globus sensation (lump in the throat), and dyspnea on exertion. These symptoms usually occur as episodes or recurrent attack and sudden onset [16,19,26].

Triggers

Fumes, dust, chemical products, smoking, psychological tension, and strenuous exercise [15,16,18,27].

Laryngoscopic examination

During attack

(1) No organic disease.
(2) Vocal fold adduction during inhalation:
    (a) Mild: minimal movement.
    (b) Moderate: vocal folds go to midline without touch.
    (c) Severe: vocal folds touch.
(3) A posterior 'diamond-shaped chink' on examination with a laryngoscope [28]. With laryngoscopy, vocal fold adduction can be seen on inspiration [16,29].
(4) Lateral constriction.

In between attacks

No abnormality detected.

Voice abnormalities in ILS according to auditory perceptual assessment of voice, stroboscopy, acoustic analysis, and aerodynamic measurement.

As regard auditory perceptual assessment

Dysphonia, strained irregular, and low pitched voice [30].

Stroboscopic finding

Using stroboscopy there is decreased mucosal waves and phase asymmetry [31].

Acoustic assessment

Reduced harmonic to noise ratio and increased jitter [32].

Aerodynamic measurements of voice

Maximum phonation time is much shorter than normal [32,33].

Additional investigations

(1) Pulmonary Function Test.
(2) The Pittsburgh Vocal Cord Dysfunction Index.
(3) Methacholine Challenge Test.
(4) Exercise Provocation.
(5) Laboratory studies may be indicated to exclude other diagnoses including:
    (a) Eosinophil count.
    (b) Eosinophilia.
    (c) Serum immunoglobulin E assay.
    (d) Arterial blood gases.
    (e) C1 inhibitor and C4 levels.
(6) Chest radiography.
(7) Allergy skin testing.

Differential diagnosis is shown in Table 1. [13,34,35]

Work-associated irritable larynx syndrome

Workers usually are subjected to laryngeal stimuli and strong fumes; therefore, the workplace can precipitate symptoms of ILS in exposed humans [13].

Modified Morrison's criteria for work-associated irritable larynx syndrome

Acute manifestations owing to laryngeal and/or supraglottic spasm:

(1) Major symptoms:
   (a) Dysphonia.
   (b) Inability to take a breath.

(2) Minor symptoms:
   (a) Foreign body sensation at the level of throat.
   (b) Chronic cough (CC).

(3) Presence of a 'workplace' irritant stimuli:
   (a) Airborne chemicals and fumes.
   (b) Confirmation of laryngeal spasm and elimination of organic laryngeal pathology by phoniatrics clinic.

Probable'work-associated irritable larynx syndrome = 1 (at least one major symptom)+2.

Definite' work-associated irritable larynx syndrome = 1 (at least one major symptom)+2 + 3 [13].

Paradoxical vocal fold motion disorder in children presenting with exercise-induced dyspnea

There are two different forms of paradoxical vocal fold motion disorder (PVFMD): spontaneous and exercise-precipitated. Spontaneous PVFMD occurs suddenly and without any precipitating factors, while exercise-precipitated PVFMD is precipitated by heavy exercise [36]. The spontaneous PVFMD, the diagnosis is based fundamentally on detailed history giving its random and unstimulated course. Further work-up may include direct visualization of the vocal folds, assessment of pulmonary function tests, and speech pathology examinations [37].

Table 1 Differential diagnosis of laryngeal movement disorders

Causes	Description
Psychogenic	Somatoform disorder, conversion disorder, abuse, anxiety disorder, depression
Irritant	Extrinsic (chemical irritants, olfactory stimuli)
	Intrinsic (GERD, laryngopharyngeal reflux rhinitis/postnasal drip, sinusitis)
Laryngospasm	Intubation, airway manipulation, IgE mediated, nocturnal aspiration
Vocal fold paresis/paralysis	Prolonged intubation, recurrent laryngeal or vagus nerve damage during chest or thyroid surgery, idiopathic
Infectious	Epiglottitis, bronchiolitis, laryngotracheobronchitis (croup)
Neoplastic	Head and neck malignancy
Endocrine	Thyroid goiter
Subglottic	Mass

GERD, gastroesophageal reflux disease; IgE, immunoglobulin E.

Clinical presentation

Symptoms during or following exercise include:

(1) Chest tightness.
(2) Cough.
(3) Shortness of breath.
(4) Wheeze.
(5) Underperformance or poor performance on playground.
(6) Fatigue.
(7) Prolonged recovery time from exercise exhaustion.
(8) Gastrointestinal discomfort [28,37–41].

The relationship between chronic cough and paradoxical vocal fold movement

The relationship between CC and PVFM is unclear and may be viewed from several perspectives. First, cough may be considered a symptom of PVFM. Second, there may be a causal relationship between CC and PVFM. Third, CC and PVFM may be considered to be separate but coexisting entities (Table 2) [42].

Laryngopharyngeal reflux/gastroesophageal reflux disease

We should differentiate between these two terms:
(1) Laryngopharyngeal: means a location/site of hypopharynx.
(2) Gastroesophageal: means a motion of gastric content to esophagus, that is, 'directional prescription' [43].

Clinical outcome

Clinical presentations and complications of the two types of reflux are quite different:
(1) The gastroesophageal type has: heart burn, gastritis, erosive esophagitis, esophageal stenosis, precancerous forms; Barrett's metaplasia, and, adenocarcinoma [44].
(2) The extraesophageal laryngopharyngeal/ hypopharyngeal reflux may show:
   (a) Bronchial: asthma with related symptoms, oropharyngeal dysphagia [45].
   (b) Laryngeal: this is sometimes coined as 'reflux laryngitis' [46].

Table 2 Comparison of chronic cough and paradoxical vocal fold movement[42]

Features	CC	PVFM
Associated symptoms		
Cough	√	√
Dysphonia	√	√
Globus	√	√
Dysphonia	√	√
Dyspnea	X	√
Associated medical conditions		
Asthma	√	√
Gastroesophageal reflux	√	√
ACE inhibitor use	√	X
Postnasal drip	√	√
Postviral	√	√
Other features		
Psychological issues	√	√
Implications for quality of life	√	√
Exercised induced	X	√
Intervention		
Refractory to medical treatment	√	√
Responds to breathing exercises	√	√
Responds to psychological approaches	√	X
Diagnosis		
Anatomic diagnostic protocol	√	X
Nasendoscopy	X	√

CC, chronic cough; PVFM, paradoxical vocal fold motion.

Symptoms

Lump sensation, voice changes [47], hemming, and hawking.

Signs

Redness of both arytenoids, vocal processes, and less frequently contact granuloma [1,48–53].

Irritable larynx syndrome treatment

(1) In acute attacks.
Medical treatment (70% helium and 30% oxygen mixture):
This therapy consists of administration of a helium–oxygen mixture (heliox), which is less dense than air and thus reduces the turbulence in the airway during inspiration.
Heliox inhalation just produces a temporary effect in the emergent management of acute ILS [54].

(2) In between attacks:
(a) Asthmatic treatment.
(b) Proton pump inhibitors.
(c) Antihistaminic medications.
(d) Antianxiety medications, hypnotics.
(e) Organic abnormalities correction.
(f) Psychotherapy.
(g) Reassurance.
(h) Self-awareness of breathing sequence.
(i) Voice therapy (behavioral therapy).
(j) Botox injection [55].

Medical care

A multidisciplinary approach with a physician and speech therapist and a psychiatrist, if needed, is usually effective [55].

Psychotherapy

According to a systematic review of psychological interventions for patients with VCD, techniques such as psychotherapy, behavioral therapy, use of antianxiety, and anti-depressant medications, and hypnotherapy in conjunction with breathing exercises may be effective treatment methods [56].

Anticholinergic agent

Inhaled ipratropium may be helpful treatment in patients with exercise-induced VCD [55,57].

Botulinum toxin

An intralaryngeal injection of botulinum toxin relieves symptoms by blocking acetylcholine release at the motor end plate and creating a laryngeal muscle weakness, thus facilitating inspiratory and expiratory airflow [58].

Topical lidocaine

The mechanism of action is to break the cycle of hyperactive glottal and supraglottic muscle contractions [59].

Voice therapy

The mainstays of treatment for VCD involve teaching the patient vocal fold relaxation techniques and breathing exercises. These procedures have been very successful and are used concomitantly with psychological support in difficult cases [60].

Relaxed throat breathing exercises

Technique

(1) Sip water before and after doing these exercises.
(2) Exercises:
(a) Shoulders down:
This is the cue to relax.
(b) Hands on abdomen:

This helps you focus on easy abdominal breath support (the best and the most relaxed way to breath).

(c) Gentle quick 'sip' of air in (pursed lip 'sip, sip, sip'):
(i) Breathe in through your mouth (using a straw cut to 3' is helpful but just posing your lips can work also).
(ii) Pursed lips around the straw.
(iii) About 1 s for the inhale.

(d) Gentle blow of air out (blow, blow, blow):
  (i) Through the slightly tight lips around the straw.
  (ii) About 2–3 s for the exhale.
  (iii) Breathing both in and out should be easy and relaxed.

(3) Practice 10 breaths five to seven times per day when you are not having symptoms. For example; in the car: when reading, watching, television or before medications. Regular practice when you are feeling well is important.
(4) Be patient when completing the breathing. It may take several minutes to start feeling relief.
(5) Make it automatic and use it at the first sense of throat tightness to prevent or suppress the VCD. You may start with the inhale or the exhale.
(6) If asthma is also a concern, follow your physician's instructions regarding taking an inhaler after completing the breathing exercises.
(7) Use it to 'pre-treat' yourself before known trigger for VCD. Possible triggers be: changing in air temperature, strong odors or perfumes, and exercise.
(8) This technique can be a 'stress buster' too [60,61].

Voluntary resistive breathing

(1) Hold the jaws together.
(2) Pretend to suck through a straw (inhale to the maximum capacity and immediately reverse the procedure to exhale).
(3) Do this procedure at the moment they experience the pre-episode tension in the larynx and neck.
(4) Do the exercise no more than three times and then provide a rest period of no less than 3 min.

Behavioral management of persistent chronic cough and paradoxical vocal fold movement

Vertigan[62] described a treatment program that had four main components, including behavior modification, cognitive adjustment, vocal hygiene, and facilitation of efficient voicing.

Management of laryngo/esophageal reflux disease

PPI is the usual treatment of 'reflux laryngitis.' Despite some recorded positive therapeutic results, this treatment is given on empirical bases [63]. The exclusion of a possible placebo effect cannot be ruled out. The efficacy of such a treatment is not tested [64–67]. Some studies showed that PPI treatment may be inferior to simple measures as modifying life style. The role of noninvasive measures such as behavior readjustment voice therapy is not discussed as a possible line of treatment [68]. Behavior readjustment voice therapy proved to be effective in the management of many of the manifestations attributed to laryngopharyngo reflux disease [69–71].

Summary and conclusion

The larynx plays many roles including respiratory modulation and airway protection. Therefore, it is no wonder that the multifunctioning larynx, when exposed to any number of endogenous and exogenous stimuli, can cause perplexing clinical feature variants.

Adductor spasm of the larynx may be triggered by an excessive response to external and internal airway stimuli such as smoking, dust, fumes, and postnasal discharge.

The clinical history provides a limited opportunity to distinguish between patients with VCD and patients with asthma because both groups present with symptoms of wheezing, cough, and dyspnea. The localization of airflow obstruction to the laryngeal area is an important clinical discriminatory feature in patient with VCD.

Another clinical clue: patients with VCD often have poor response to beta agonists or inhaled corticosteroids.

The hallmark of diagnosis is noted on direct and indirect laryngoscopy; a Glottic Chink is present along the posterior portion of the vocal folds while the anterior portion of the vocal folds is adducted.

Several conditions may deteriorate voice quality in ILS including laryngeal, structural abnormalities neurological impairment, and comorbid diseases, for example, asthma, CC, and reflux.

Most of laryngeal manifestations of laryngopharyngo reflux disease are nonspecific to the claimed causal agent. These symptoms and signs may be a part of other categories of voice disorders where no reflux is encountered.

Voice therapy is a very important measure to be done including breathing exercises. Sometimes, intermittent positive pressure ventilation therapy and respiratory training may give good results in unresponsive patients.

Recommendations

Further researches to reveal the proper pathophysiology to clarify more about this poorly understood topic are needed. Behavioral treatment for ILS is a promising option for patients who have failed medical

management. However, the efficiency of this option for ILS, it requires further exploration using well-defined randomized controlled treatment trials.

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Conflicts of interest
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References

1 Hill RK, Simpson CB, Velazquez R, Larson N. Pachydermia is not diagnostic of active laryngopharyngeal reflux disease. Laryngoscope 2004; 114:1557–1561.

2 Andrianopoulos MV, Gallivan GJ, Gallivan KH. PVCM, PVCD, EPL, and irritable larynx syndrome: what are we talking about and how do we treat it? J Voice 2000; 14:607–618.

3 Martin RJ, Blager FB, Gay ML, Wood RP. Paradoxicvocalcord motion in presumed asthmatics. Semin Respir Med 1987; 79:726–733.

4 Rogers J, Stell P. Paradoxical movement of the vocal cords as a cause of stridor. J Laryngol Otol 1978; 92:157–158.

5 Appelblatt NH, Baker SR. Functional upper airway obstruction: a new syndrome. Arch Otolaryngol 1981; 107:305–306.

6 Christopher KL, Wood RP, Eckert RC, Blager FB, Raney RA, Souhrada JF. Vocal-cord dysfunction presenting as asthma. New Engl J Med 1983; 308:1566–1570.

7 Downing ET, Braman SS, Fox MJ, Corrao WM. Factitious asthma: physiological approach to diagnosis. JAMA 1982; 248:2878–2881.

8 Chawla S, Upadhyay B, MacDonnell K. Laryngeal spasm mimicking bronchial asthma. Ann Allergy 1984; 53:319–321.

9 Kattan M, Ben-Zvi Z. Stridor caused by vocal cord malfunction associated with emotional factors. Clin Pediatr 1985; 24:158–160.

10 Ramirez-R J, León I, Rivera LM. Episodic laryngeal dyskinesia: clinical and psychiatric characterization. Chest 1986; 90:716–721.

11 Gallivan GJ, Hoffman L, Gallivan KH. Episodic paroxysmal laryngospasm: voice and pulmonary function assessment and management. J Voice 1996; 10:93–105.

12 Smith ME, Darby KP, Kirchner K, Blager FB. Simultaneous functional laryngeal stridor and functional aphonia in an adolescent. Am J Otolaryngol 1993; 14:366–369.

13 Morrison M, Rammage L, Emami A. The irritable larynx syndrome. J Voice 1999; 13:447–455.

14 Ibrahim WH, Gheriani HA, Almohamed AA, Raza T. Paradoxical vocal cord motion disorder: past, present and future. Postgrad Med J 2007; 83:164–172.

15 Wilson JJ, Wilson EM. Practical management: vocal cord dysfunction in athletes. Clin J Sport Med 2006; 16:357–360.

16 Koester MC, Amundson CL. Seeing the forest through the wheeze: a case-study approach to diagnosing paradoxical vocal-cord dysfunction. J Athl Train 2002; 37:320–324.

17 Klopper EM. Vocal cord dysfunction secondary to paroxysmal vocal cord movement. Phy Assist 2001; 25:43–48.

18 Newsham KR, Klaben BK, Miller VJ, Saunders JE. Paradoxical vocal-cord dysfunction: management in athletes. J Athl Train 2002; 37:325.

19 Koufman JA, Block C. Differential diagnosis of paradoxical vocal fold movement. Am J Speech Lang Pathol 2008; 17:327–334.

20 Rhodes RK. Diagnosing vocal cord dysfunction in young athletes. J Am Assoc Nurse Pract 2008; 20:608–613.

21 Coderre TJ, Katz J, Vaccarino AL, Melzack R. Contribution of central neuroplasticity to pathological pain: review of clinical and experimental evidence. Pain 1993; 52:259–285.

22 Aronson AE. *Clinical voice disorders: an interdisciplinary approach*. New York: Thieme; 1990.

23 Little FB, Kohut RI, Koufman JA, Marshall RB. Effect of gastric acid on the pathogenesis of subglottic stenosis. Ann Otol Rhinol Laryngol 1985; 94:516–519.

24 Morrison MD, Nichol H, Rammage LA. Diagnostic criteria in functional dysphonia. Laryngoscope 1986; 96:1–8.

25 Roy N, Leeper HA. Effects of the manual laryngeal musculoskeletal tension reduction technique as a treatment for functional voice disorders: perceptual and acoustic measures. J Voice 1993; 7:242–249.

26 Vlahakis NE, Patel AM, Maragos NE, Beck KC. Diagnosis of vocal cord dysfunction: the utility of spirometry and plethysmography. Chest J 2002; 122:2246–2249.

27 Pavord ID, Cox G, Thomson NC, Rubin AS, Corris PA, Niven RM, *et al*. Safety and efficacy of bronchial thermoplasty in symptomatic, severe asthma. Am J Respir Crit Care Med 2007; 176:1185–1191.

28 Sullivan MD, Heywood BM, Beukelman DR. A treatment for vocal cord dysfunction in female athletes: an outcome study. Laryngoscope 2001; 111:1751–1755.

29 Vertigan AE, Gibson PG, Theodoros DG, Winkworth AL. The role of sensory dysfunction in the development of voice disorders, chronic cough and paradoxical vocal fold movement. Int J Speech Lang Pathol 2008; 10:231–244.

30 Vertigan AE, Theodoros DG, Winkworth AL, Gibson PG. Perceptual voice characteristics in chronic cough and paradoxical vocal fold movement. Folia Phoniatr Logop 2007; 59:256–267.

31 Treole K, Trudeau MD, Forrest LA. Endoscopic and stroboscopic description of adults with paradoxical vocal fold dysfunction. J Voice 1999; 13:143–152.

32 Vertigan AE, Theodoros DG, Winkworth AL, Gibson PG. Acoustic and electroglottographic voice characteristics in chronic cough and paradoxical vocal fold movement. Folia Phoniatr Logop 2008; 60:210–216.

33 Zelcer S, Henri C, Tewfik TL, Mazer B. Multidimensional voice program analysis (MDVP) and the diagnosis of pediatric vocal cord dysfunction. Ann Allergy Asthma Immunol 2002; 88:601–608.

34 Dunn NM, Katial RK, Hoyte FC. Vocal cord dysfunction: a review. Asthma Res Pract 2015; 1:9.

35 Hicks M, Brugman SM, Katial R. Vocal cord dysfunction/paradoxical vocal fold motion. Prim Care Clin Office Pract 2008; 35:81–103.

36 Doshi DR, MM Weinberger. Long-term outcome of vocal cord dysfunction. Ann Allergy Asthma Immunol 2006; 96:794–799.

37 Mathers-Schmidt BA, Brilla L. Inspiratory muscle training in exercise-induced paradoxical vocal fold motion. J Voice 2005; 19:635–644.

38 Forrest LA, Husein T, Husein O. Paradoxical vocal cord motion: classification and treatment. Laryngoscope 2012; 122:844–853.

39 Rameau A, Foltz RS, Wagner K, Zur KB. Multidisciplinary approach to vocal cord dysfunction diagnosis and treatment in one session: a single institutional outcome study. Int J Pediatr Otorhinolaryngol 2012; 76:31–35.

40 Marcinow AM, Thompson J, Chiang T, Forrest LA, deSilva BW. Paradoxical vocal fold motion disorder in the elite athlete: experience at a large division I university. Laryngoscope 2014; 124:1425–1430.

41 Altman KW, Mirza N, Ruiz C, Sataloff RT. Paradoxical vocal fold motion: presentation and treatment options. J Voice 2000; 14:99–103.

42 Vertigan AE, Theodoros DG, Gibson PG, Winkworth AL. Voice and upper airway symptoms in people with chronic cough and paradoxical vocal fold movement. J Voice 2007; 21:361–383.

43 Tobey NA, Hosseini SS, Caymaz-Bor C, Wyatt HR, Orlando GS, Orlando RC. The role of pepsin in acid injury to esophageal epithelium. Am J Gastroenterol 2001; 96:3062.

44 Andrus JG, Dolan RW, Anderson TD. Transnasal esophagoscopy: a high-yield diagnostic tool. Laryngoscope 2005; 115:993–996.

45 el-Serag HB, Sonnenberg A. Comorbid occurrence of laryngeal or pulmonary disease with esophagitis in United States military veterans. Gastroenterology 1997; 113:755–760.

46 Qadeer MA, Swoger J, Milstein C, Hicks DM, Ponsky J, Richter JE, *et al*. Correlation between symptoms and laryngeal signs in laryngopharyngeal reflux. Laryngoscope 2005; 115:1947–1952.

47 Šiupšinskienė N, Adamonis K. Diagnostic test with omeprazole in patients with posterior laryngitis. Medicina 2003; 39:47–55.

48 Castellanos P. Changes in the hypopharynx may suggest supraesophageal reflux disease. Am J Manag Care 2000; 6 (16 Suppl):S883–S885.

49 Hickson C, Simpson CB, Falcon R. Laryngeal pseudosulcus as a predictor of laryngopharyngeal reflux. Laryngoscope 2001; 111:1742–1745.

50 Karkos PD, Yates PD, Carding PN, Wilson JA. Is laryngopharyngeal reflux related to functional dysphonia? Ann Otol Rhinol Laryngol 2007; 116:24–29.

51 Koufman JA. The otolaryngologic manifestations of gastroesophageal

reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24 hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope 1991; 101(Suppl 53):1–78.

52 Li YM, Du J, Zhang H, Yu CH. Epidemiological investigation in outpatients with symptomatic gastroesophageal reflux from the Department of Medicine in Zhejiang Province, east China. J Gastroenterol Hepatol 2008; 23:283–289.

53 Milstein CF, Charbel S, Hicks DM, Abelson TI, Richter JE, Vaezi MF. Prevalence of laryngeal irritation signs associated with reflux in asymptomatic volunteers: impact of endoscopic technique (rigid vs. flexible laryngoscope). Laryngoscope 2005; 115:2256–2261.

54 Fitzpatrick T. Vocal cord dysfunction is becoming a significant syndrome. RT-Marina Del Rey 2001; 14:34–40.

55. Sataloff RT. *Professional voice: the science and art of clinical care, 3-volumeset*. San Diego, CA: Plural Publishing; 2017.

56 Guglani L, Atkinson S, Hosanagar A, Guglani L. A systematic review of psychological interventions for adult and pediatric patients with vocal cord dysfunction. Front Pediatr 2014; 2:82.

57 Varney V, Parnell H, Evans J, Cooke N, Lloyd J, Bolton J. The successful treatment of vocal cord dysfunction with low-dose amitriptyline–including literature review. J Asthma Allergy 2009; 2:105.

58 Baxter M, Uddin N, Raghav S, Leong P, Low K, Hamza K, *et al*. Abnormal vocal cord movement treated with botulinum toxin in patients with asthma resistant to optimised management. Respirology 2014; 19:531–537.

59 Dworkin JP, Meleca RJ, Simpson ML, Garfield I. Use of topical lidocaine in the treatment of muscle tension dysphonia. J Voice 2000; 14:567–574.

60 Reitz JR, Gorman S, Kegyes J. Behavioral management of paradoxical vocal fold motion. Am Speech Lang Hear Assoc 2014.

61 Martin S. *Working with voice disorders*. Vol. 47. Taylor & Francis; 2017. p. 135-146.

62 Vertigan A. Speech pathology management of chronic cough. Acquiring Knowledge Speech Lang Hear 2001; 3:62–66.

63 Tauber S, Gross M, Issing WJ. Association of laryngopharyngeal symptoms with gastroesophageal reflux disease. Laryngoscope 2002; 112:879–886.

64 Ford CN. Evaluation and management of laryngopharyngeal reflux. JAMA 2005; 294:1534–1540.

65 Karkos PD, Wilson JA. Empiric treatment of laryngopharyngeal reflux with proton pump inhibitors: a systematic review. Laryngoscope 2006; 116:144–148.

66 Malfertheiner M, Malfertheiner P, Costa S, Pfeifer M, Ernst W, Seelbach-Göbel B, *et al*. Extraesophageal symptoms of gastroesophageal reflux disease during pregnancy. Z Gastroenterol 2015; 53:1080–1083.

67 Noordzij JP, Khidr A, Desper E, Meek RB, Reibel JF, Levine PA. Correlation of pH probe–measured laryngopharyngeal reflux with symptoms and signs of reflux laryngitis. Laryngoscope 2002; 112:2192–2195.

68 Steward DL, Wilson KM, Kelly DH, Patil MS, Schwartzbauer HR, Long JD, *et al*. Proton pump inhibitor therapy for chronic laryngo-pharyngitis: a randomized placebo-control trial. Otolaryngol Head Neck Surg 2004; 131:342–350.

69 Bassiouny S. Efficacy of the accent method of voice therapy. Folia Phoniatr Logop 1998; 50:146–164.

70 Kotby M, El-Sady S, Basiouny S, Abou-Rass Y, Hegazi M. Efficacy of the accent method of voice therapy. J Voice 1991; 5:316–320.

71 The Accent Method of Voice Therapy Pap/Cas by M.Nasser Kotby (ISBN: Paperback: 109 pages; Publisher: Singular Publishing Group Inc.; Pap/Cas edition (1 Jan. 1995); Language: English; ISBN-10: 1565930908; ISBN-13: 978.