



Occupational aspects of irritable larynx syndrome

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Purpose of review

The aim of this article is to provide an update on occupational aspects of irritable larynx syndrome (ILS).

Recent findings

It is being increasingly recognized that ILS is common amongst certain occupations. This is particularly true of occupations that require frequent voice use such as teachers; where there is exposure to workplace irritants such as World Trade Center responders; or mechanical factors that cause laryngeal dysfunction such as elite athletes. Work associated ILS impacts on quality of life but responds to speech and language therapy focusing on education, vocal hygiene, and laryngeal exercises that reduce cough and treat acute laryngeal obstruction episodes.

Summary

ILS may be caused or exacerbated by many occupational exposures, causes significant symptoms, and impacts on quality of life. It is potentially treatable and may well be preventable. More research in this important area is required.

Keywords

inducible laryngeal obstruction, irritable larynx syndrome, laryngeal dysfunction, occupation, vocal cord dysfunction

INTRODUCTION

The larynx is one of the most highly innervated areas of the body and has a complex range of functions that includes swallowing, phonation, and airway protection including cough [1]. The behavior of the larynx can however become dysfunctional leading to clinically significant symptoms. This syndrome has been called laryngeal dysfunction or irritable larynx syndrome (ILS) [1,2]. ILS has been recognized for many years in different forms and is defined by hyperfunctional laryngeal symptoms [2]. It includes, but is not limited to, inducible laryngeal obstruction (ILO). ILO has previously been known as vocal cord dysfunction, paradoxical vocal fold motion disorder, and, less helpfully, Munchausen's stridor. ILO is the current consensus nomenclature agreed on by the European Respiratory Society (ERS), European Laryngological Society (ELS), and American College of Chest Physicians (ACCP) [3,4]. This nomenclature was chosen as it better describes the changes that occur during acute episodes of ILO that often involve adduction of the laryngeal structures rather than just the vocal cords in isolation. In many patients, the primary trigger associated with laryngeal symptoms originates in the workplace. It is recognized that the workplace is important in ILS both as a cause and exacerbating factor. Work-associated ILS is often difficult to differentiate from

work-associated asthma and adding to this difficulty, these conditions commonly coexist.

SYMPTOMS

The common clinical features of ILS are that of globus pharyngeus (the sensation of a lump in the throat), dysphonia, dyspnea, chronic cough, wheeze, and symptoms of ILO [2]. ILO is characterized by acute onset of dyspnea, inspiratory difficulty, the feeling of choking, and the sensation of obstruction at the level of the throat; these symptoms are often of short duration and self-limited [4]. The symptoms of ILS are largely nonspecific and one of the biggest difficulties is that these symptoms overlap with those in asthma so differentiating the two conditions may be problematic [5]. Adding to the confusion, ILS and asthma commonly coexist.

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KEY POINTS

- ILS includes symptoms of a hyperfunctional larynx that include but is not limited to inducible laryngeal obstruction (vocal cord dysfunction).
- Occupational factors commonly cause and/or exacerbate ILS.
- The epidemiology of occupational ILS is poorly described.
- Distinguishing occupational ILS from occupational asthma may be difficult, particularly as they commonly overlap.
- Treatment of occupational ILS should include trigger avoidance and speech therapy.

Features that are more suggestive of ILS than of asthma are a sensation of inspiratory limitation (rather than expiratory limitation), tightness in the throat (not chest), upper airway wheeze, rapid onset, and resolution and improvement in symptoms without salbutamol (Table 1) [6].

EPIDEMIOLOGY

Apart from ILO related to a few specific groups, the epidemiology of nonoccupational ILO is difficult to describe. In children, it is thought to occur in up to 14% admitted with asthma and 75% with ‘difficult asthma’ [7]. In adolescents, it is thought to affect about 5% of the general population [8]. In adults presenting with respiratory symptoms between 2.5 and 22% will have ILO depending on the population and definitions used [9,10]. ILO appears to be more common in females with a 2–3:1 ratio [7,11].

The epidemiology of work associated ILS is poorly described because of the lack of industry-based studies and considerable variation in diagnostic criteria utilized. There are only case series and small cohort studies to inform in this area and these

are heavily biased by referral patterns [12,13]. Hoy *et al.* [12] found that of 340 patients referred with occupational respiratory symptoms, 9% had work-related irritable larynx syndrome. Morris *et al.* [13] found 15% of soldiers on active duty who had exertional dyspnea had an underlying diagnosis of ILO. In a study of elite athletes, 5% had inspiratory stridor on significant exertion suggestive of an underlying diagnosis of ILO (but not confirmed) [14]. Irritable larynx symptoms including cough are also common in athletes [15,16[■]]. In World Trade Center responders, 18.6% had spirometry consistent with ILO with flattened flow volume loops [17]. ILO is commonly thought to occur frequently in healthcare workers although this has not been confirmed in population studies [18,19]. Teachers appear to be excessively affected with ILS and this has been associated with poorer quality of life [20[■]]. Gadepalli *et al.* [21[■]] surveyed teachers in the United Kingdom and compared them to non-teacher controls, finding 30% of teachers compared with 9% of nonteachers reported voice symptoms and 12.8% (versus 2%) had missed work because of voice problems. ILS is also more common in other occupations that require frequent laryngeal use such as performers, telemarketers, sports coaches, and wind instrumentalists [22,23[■],24].

PATHOGENESIS

Inhalation of exogenous noxious agents stimulates laryngeal nerves that activate the involuntary cough reflex to protect the airway. Stimulation of sensory nerve endings by inhaled irritants may also induce laryngeal closure [25,26]. This stimulation may lead to a sensitization of nerve endings resulting in a hyperfunctional state where a lesser irritant or normally innocuous stimulus leads to laryngeal dysfunction and symptoms [2,4]. Therefore, usually innocuous workplace stimuli may trigger symptoms including the odors from cleaning products or perfumes and irritants [12]. Irritants are common in the workplace and may cause and/or perpetuate ILS [25]. There is evidence that there is a variable latency between exposure to the workplace trigger and the onset of ILS that may range from immediate to up to 24 h [25]. ILO may occur after a single irritant exposure [25]. Cold air is a common laryngeal irritant, particularly in elite athletes. Inspiratory stridor suggestive of ILO has been noted to be significantly more common in outdoor athletes who are exposed to cold air than indoor athletes [14].

Mechanical factors are also important, particularly in exercise-related ILO, where laxity of laryngeal structures or laryngomalacia may lead to ILO [27,28] Mechanical factors are also likely to be

Table 1. Symptoms of irritable larynx syndrome versus asthma

Irritable larynx syndrome	Asthma
Inspiratory difficulty	Expiratory difficulty
Throat (or upper chest) tightness	Chest tightness
Upper airway wheeze	Lower airway wheeze
Rapid onset	Subacute onset
Rapid resolution	Gradual resolution
Exercise-related symptoms: peak during exercise	Exercise-related symptoms: peak 20 min following completion of exercise

important in wind instrumentalists who have unique mechanical forces on their larynx [23[¶]]. Furthermore frequent voice use, such as that occurring with teachers and singers appears to be a factor in the development of ILS [21^{¶¶}].

CLINICAL FEATURES

Work-associated ILS may be caused or exacerbated by work although in practice these entities can be difficult to distinguish.

Work-induced ILS refers to the onset of ILS because of a specific workplace exposure. Those who have existing ILS occupational factors may exacerbate these symptoms via irritant exposure [29]. Exacerbation of ILS may additionally be because of the occupation causing other conditions that may exacerbate ILS such as occupational rhinitis, occupational asthma, and occupational sinusitis [30–33,34[¶],35–37].

Occupational irritants may be varied but may include chemicals such as chlorine, perfumes or other strong smells, and pollutants [29,38,39]. There are specific occupations that have been frequently implicated in ILS including elite athletes where the combination of high-stress environment with extreme physical exertion is thought to induce ILS in susceptible individuals [14,40]. Defense force personnel are also at high risk because of the combination of high stress and physical exertion as well as exposure to irritants when deployed [13,41]. Similarly, responders to the World Trade Center disaster had a high incidence of ILS likely as a result of similar psychological, physical, and irritant stressor exposure [17,42–44].

DIAGNOSIS

Morrison *et al.* [2] first proposed diagnostic criteria for ILS that included symptoms, major (dysphonia and dyspnea with sensation of airflow limitation at the level of the throat) and minor (globus and chronic cough), a definite symptom-triggering stimulus, and confirmation of laryngeal tension and exclusion of organic laryngeal disease by specialist assessment. These symptoms were further classified by Hoy *et al.* [12] into a ‘probable’ Work-associated ILS (WILS) diagnosis (at least 1 major symptom and presence of a workplace trigger) and ‘definite’ WILS diagnosis (at least 1 major symptom, presence of a workplace trigger and confirmation of laryngeal tension and exclusion of organic laryngeal disease by a specialist clinic). The diagnosis of WILS is particularly difficult because it shares many symptoms with work-related asthma and these two conditions can be hard to differentiate. The ERS/ELS/

ACCP guidelines recommend that the diagnosis of ILO includes a compatible clinical syndrome, identification of triggers, and objective demonstration of laryngeal obstruction via laryngoscopy [4].

The basis of the diagnosis should be a thorough assessment that establishes the key symptoms (variable wheeze, dyspnea, cough, throat tightness) excludes organic disease and ascertains the temporal link between occupational exposures and symptoms. Central to establishing an occupational cause is to take a thorough occupational history including exposure to irritants, occupational environment including ventilation and protective equipment used, and detailing the temporal link between symptoms and workplace exposures including resolution or improvement in symptoms on absence from the workplace. These irritants may include odors, sleep, stress, cold air, wood dust, chemicals such as chlorine [38,39,45,46]. For elite athletes, exercise-induced ILO may be difficult to differentiate from exercise-induced asthma although on history the timing of symptoms in relation to exercise is important. In exercise-induced ILO symptoms tend to occur during strenuous exertion, whereas in exercise-induced asthma the symptoms tend to be maximal up to 20 min after ending the exercise session [4]. The gold standard for diagnosis of occupational asthma is specific inhalational challenges but it is less clear if these challenges should be used for suspected work associated-ILS [32,47–50].

Questionnaires such as the Newcastle Laryngeal Hypersensitivity Questionnaire may assist in the diagnosis of ILS and ILO although these remain unvalidated for detection of work-associated ILS [51].

Investigations should include lung function that aim to identify the presence of asthma. Spirometry may demonstrate flattening of the flow-volume loop although this is neither sensitive nor specific for the diagnosis of ILO [18,52–54]. At 50% forced vital capacity, a maximal inspiratory/expiratory flow ratio of less than 1 is suggestive of ILO. If spirometry is normal in the setting of acute symptoms and bronchial provocation test is negative, there should be a high index of suspicion that ILS is the cause rather than asthma.

The gold standard of diagnosis of ILO is to perform laryngoscopy whilst symptomatic and demonstrate adduction of the vocal folds or laryngeal structures [4,55]. Increasingly provocation laryngoscopy is being utilized whereby a provocation such as perfume, exercise, or bronchial provocation testing is used to increase the likelihood of detection of abnormal vocal fold movements during laryngoscopy [56,57]. For athletes who are suspected to have exercise-induced ILO a continuous laryngoscopy during exercise test may be utilized [58,59].

MANAGEMENT

Management of ILS is best done with a multidisciplinary approach incorporating explanation and education regarding the condition, speech therapy, and medical therapies where appropriate.

Specific therapy

The mainstay of specific therapy for ILS is that of speech and language therapy which aims to reduce symptoms including cough and control acute episodes via laryngeal exercises and breathing techniques [53,54,60–63]. There is evidence in those whose occupations require frequent voice use (amongst whom voice disorders are common) education and interventions to improve vocal hygiene are effective in prevention and management of throat symptoms [22]. Meier *et al.* [64^{***}] examined the response to voice training amongst a cohort of 286 German teachers, 65% of whom had voice problems. They found that three months after voice training the majority of teachers had implemented these voice strategies in their workplace and this led to improved vocal capacity, reduced throat clearing, less throat symptoms, and better vocal performance [64^{***}].

Neuromodulating medications with or without speech therapy have been shown to be of benefit in chronic cough although they have not been studied specifically in ILS [65,66]. A single-arm nonrandomized, nonblinded study showed benefit of low-dose amitriptyline in the treatment of ILO, although more evidence in this area is required [67].

Avoidance and/or treatment of associated triggers and comorbidities

After establishing potential workplace triggers for ILS the physician must assess whether it is possible to limit the exposure to the triggers or irritants whilst continuing the same occupation. It may be possible for the individual to change roles, implement low-odor workplace environment, or manage irritant exposures by improved ventilation or personal protective equipment [68,69]. In the instances where these triggers are not able to be adequately controlled, an alternative occupation or workplace may be required.

Other identified associated factors such as asthma, rhinitis with postnasal drip, gastroesophageal reflux disease, and psychological issues should be diagnosed and managed although evidence supporting this approach is limited (see below) [5,70].

Asthma

There is a clear association between asthma and ILS although the pathological mechanism remains

unclear [5,71,72]. Additionally, the two conditions may mimic one another. Occupational exposures may cause both asthma and ILO [29,50,71]. Therefore, objective investigations that aim to differentiate ILS from asthma (or confirming both diagnoses) in situations where they are suspected to be work-associated is necessary [19]. This may include bronchial provocation testing where spirometry is normal but asthma is suspected. For suspected occupational asthma, the diagnosis can be confirmed in more than 80% of patients with serial peak flow (or FEV₁) measurements showing a significant decrease at work compared with periods of work absence [47]. Allergy to high molecular weight allergens can be confirmed with skin prick or serum specific immunoglobulin E testing [47]. Bronchial provocation testing that includes provocation with the suspected occupational trigger is the gold standard in suspected occupational asthma but lacks standardization and availability [47]. Unfortunately, those with ILO may have difficulty performing lung function leading to confusion between these diagnoses [19,73].

Rhinitis with postnasal drip

Postnasal drip is thought to play a role in the development of ILS in some individuals because of irritation of the larynx causing increased laryngeal sensitivity and hyperresponsiveness [57]. There is also a theory that changes to olfaction perception may lead to increased chemosensory sensitivity and, in turn, allow ILO to occur at a lower odor threshold [74,75]. Following treatment with antibiotics and nasal corticosteroids Bucca *et al.* [57] found a reduction in laryngeal hyperresponsiveness. Rhinitis is commonly caused by occupational factors and therefore detection and management of occupational rhinitis are likely to be important when addressing occupational ILS although studies on this specific intervention are lacking [44,76–81].

Gastroesophageal reflux

Gastroesophageal reflux is a very common disease and is thought to be a frequent trigger or exacerbating factor for ILS. Studies have shown that reflux leads to altered laryngopharyngeal sensitivity and a lesser stimulus needed to induce ILO [2,82–84]. There are no randomized studies evaluating the treatment of reflux in patients with ILS but in those with chronic cough proton pump inhibitors have a variable effect and are no longer recommended as sole therapy but may be considered as a trial of therapy together with lifestyle modifications [85].

Psychological disease

Occupations that are associated with ILS tend to have high levels of associated occupational stress including military personnel, elite athletes, and teachers [2,12,29]. Comorbid psychological diagnoses are common in those with ILS with one large cohort study showing 93% of cases with ILO had a coexistent psychiatric diagnosis [86]. Detection and treatment of psychological conditions in those with ILO are recommended [87,88].

CONCLUSION

ILS causes significant symptoms and is likely to be underrecognized. Occupational factors commonly cause or exacerbate ILS, but more studies in this area are needed.

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Conflicts of interest

There are no conflicts of interest.

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- of special interest
- of outstanding interest

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