Work-associated irritable larynx syndrome

R. F. Hoy1, M. Ribeiro1, J. Anderson2 and S. M. Tarlo1

1Division of Respiratory Medicine, Toronto Western Hospital, Toronto, Ontario, Canada, 2Department of Otolaryngology, St Michael’s Hospital, Toronto, Ontario, Canada.

Correspondence to: R. F. Hoy, Suite 47, Cabrini Medical Centre, 183 Wattle Tree Road, Malvern, Victoria, Australia 3144. Tel: +61 3 9509 2242; fax: +61 3 9005 2895; e-mail: drryanhoy@gmail.com

Background Work-associated respiratory symptoms may be caused by disorders of both the lower and upper respiratory tract. We propose that occupational exposures may initiate and/or trigger recurrent hyperkinetic laryngeal symptoms, predominantly episodic dyspnoea, dysphonia, cough and sensation of tension in the throat—work-associated irritable larynx syndrome (WILS).

Aims To examine characteristics of individual and work-related factors that are associated with WILS, occupational asthma (OA) and work-exacerbated asthma (WEA).

Methods Subjects with WILS, OA and WEA were identified from an occupational lung disease clinic. A review of 448 charts of patients attending the clinic between 2002 and 2006 was undertaken, with information entered onto a standardized abstraction form.

Results Fifty subjects were identified with OA, 40 with WEA and 30 with WILS. Subjects with the diagnosis of WILS were more likely to be female and more frequently reported symptoms of gastro-oesophageal reflux. The most common triggers of workplace symptoms in the WILS group were odours, fumes, perfumes and cleaning agents. Fourteen patients with WILS identified a specific precipitating event at the workplace at the time of the onset of their symptoms and five of these subjects presented to an emergency department within 24 h of the event.

Conclusions Dysfunction of the upper airway is an important cause of work-associated respiratory symptoms. The identification and management of WILS requires a multidisciplinary approach with a focus on modifying work-related and intrinsic factors that may perpetuate symptoms.

Key words Irritable larynx; laryngeal dysfunction; occupation; occupational asthma; work-exacerbated asthma; work related.

Introduction

Work-associated respiratory symptoms may be caused by disorders of both the lower and upper respiratory tract. Laryngeal dysfunction is an important cause of episodic respiratory symptoms and may be difficult to clinically differentiate from lower respiratory tract disorders such as asthma as it produces similar symptoms such as shortness of breath and wheeze [1–3]. It also generally includes symptoms of dysphonia, difficulty more during inspiration than expiration and tightness in the lower neck or upper chest. Symptoms are often provoked by odours that usually would not be associated with asthma exacerbation (e.g. colognes and other scented products and gasoline fumes). Symptoms usually start immediately on exposure and often clear quickly on leaving and are not usually controlled by asthma medication, even at high doses.

Morrison describes recurrent hyperkinetic laryngeal symptoms triggered by sensory stimuli such as odours and irritants, as the ‘irritable larynx syndrome’ (ILS) [4]. Symptoms of ILS include dyspnoea due to vocal cord dysfunction (VCD), dysphonia due to laryngeal muscular tension, globus (sensation of tension in the throat or neck) and chronic cough [4]. Workers are often exposed to irritants and strong odours; therefore, the workplace may initiate and/or trigger symptoms of ILS in susceptible people. We refer to this condition as work-associated irritable larynx syndrome (WILS).

We have reviewed our clinic population to identify the frequency of WILS and to compare features of these patients with occupational asthma (OA) and work-exacerbated asthma (WEA).

Methods

The Research Ethics Board of the University Health Network and St Michael’s Hospital provided study approval.
A retrospective review of 448 patient files of a secondary/tertiary referral occupational lung disease clinic was conducted. A single reviewer entered file information onto a 94-item abstraction form. Occupational groups were allocated based on the job description abstracted from the clinic chart and the Statistics Canada ‘National Occupational Classification for Statistics (NOC-S) 2006’ classification system for Canadian jobs [5].

All subjects were initially assessed at the author’s centre between 2002 and 2006 for evaluation of potential work-associated respiratory conditions. The clinic is a general occupational lung disorders clinic with a known expertise in the diagnosis and management of OA. A single clinician (S.M.T.) evaluated all patients using the same diagnostic approach. The diagnostic approach and criteria for ‘definite’ and ‘probable’ OA and WEA have been previously described [6,7].

Primary and when required, secondary diagnoses were abstracted, with an assessment of the likelihood of the diagnosis (definite, probable, possible) based on the clinical information provided in the patient file. To confirm the accuracy of the first review’s identified diagnoses, a second reviewer independently abstracted final diagnoses from patient files. A third reviewer resolved any discrepancies between the first and second reviewers abstracted diagnoses.

WILS patients were diagnosed based on a history of episodic laryngeal symptoms associated with a triggering stimulus present at the workplace (Table 1). Triggers and symptoms may have been present in environments outside the workplace; however, work association of symptoms was the primary reason for referral to the occupational lung clinic.

WILS patients were included if the clinic chart documented a diagnosis made by the clinic physician of ILS or VCD as the primary diagnosis and included reference to episodic laryngeal symptoms, work association and descriptions of a specific workplace trigger. The diagnostic approach of the treating physician required patients with possible WILS to undergo pulmonary function testing, including methacholine challenge when appropriate, and evaluation at a multidisciplinary specialist voice disorders clinic.

At the voice disorders clinic, an otolaryngologist (J.A.) and speech therapist examined referred patients. Evaluation included assessment of history, physical examination and laryngoscopic examination. The diagnosis of ILS was excluded if organic laryngeal pathology, other than non-specific laryngeal oedema, was identified.

For inclusion in the study, patients were defined as ‘definite’ WILS if they underwent a voice disorder clinic assessment and documentation of the assessment was present in the file confirming the diagnosis of WILS. If documentation was not present but other features of the condition were identified, patients were classified as ‘probable’ WILS (Table 1).

### Table 1. Modified Morrison’s criteria for WILS [4]

| 1. Episodic symptoms attributable to laryngeal and/or supraglottic tension: |
|---------------------------------|--------------------------|
| Major symptoms                 | Dysphonia (muscular tension dysphonia) |
| Minor symptoms                 | Dysoena with sensation of airflow limitation at the level of throat |
| 2. Presence of a ‘workplace’ sensory trigger: |
| Airborne substance, odour      |
| 3. Confirmation of laryngeal tension and exclusion of organic laryngeal pathology by specialist Voice Disorders clinic. |
| ‘Probable’ WILS = 1 (at least one major symptom) + 2 |
| ‘Definite’ WILS = 1 (at least one major symptom) + 2 + 3 |

The diagnosis of gastro-oesophageal reflux was based on symptoms or previous doctor diagnosis. Confirmatory gastroscopy or oesophageal pH monitoring was not performed.

Statistical analysis was performed using a statistical software package (SAS Institute Inc., Cary, NC, USA). We used the chi-square test or the Monte Carlo estimate for the exact test to determine if there were differences between categorical variables, such as gender and smoking history. Analysis of variance was utilized to assess variance between the groups in terms of age and duration of symptoms. P values of <0.05 were considered statistically significant.

### Results

Four hundred and forty-eight alphabetically consecutive files from the occupational lung disease clinic were reviewed. Three hundred and four subjects were newly referred to the clinic for evaluation of work-associated respiratory symptoms during the 5-year period. Fifty subjects were identified with OA (25 definite, 25 probable, including 4 with irritant-induced OA), 40 with WEA (19 definite and 21 probable) and 30 patients with WILS (14 definite and 16 probable). Five patients had concurrent diagnoses of WILS and work-related asthma (two OA and three WEA). Insufficient information was present for 54 (17%) subjects with possible OA, WEA or WILS to assign more definitive diagnoses. Respiratory tract irritation without ILS or asthma was the primary diagnosis in 31 (10%) of subjects (Table 2).

Common symptoms in the WILS group were dysphonia (86%) and cough (76%). Laryngeal stridor was an unusual feature (1%). Primary work association of these symptoms was noted in 76% of subjects. The duration of WILS symptoms at the time of initial clinic assessment was highly variable, with a median duration of 2.5 years (minimum 0.3 years to maximum 20 years). The median
duration for the OA group and WEA group was 2.5 years.

In the WILS group, subjects were spread across processing and manufacturing (n = 11), sales and service (n = 7), business and administration (n = 5) and transport and equipment operator (n = 5). The business and administration group was notable for having more WILS patients (n = 5) than WEA (n = 2) and OA (n = 0) (Figure 1).

No subjects were identified from primary industries, such as forestry, nor from farming which may in part represent the referral characteristics of the location of the clinic in a southern Ontario city.

There were differences in the workplace agents noted to induce respiratory symptoms in the three groups. The most common causes of symptoms in the OA group were diisocyanates, baker’s flour/dust and wood dust. In the WEA group, common agents were airborne dusts and exhaust fumes. In the WILS group triggers included odours, fumes, perfumes and cleaning agents (Table 3).

Fourteen patients with WILS identified a specific precipitating event at the workplace at the time of the onset of their symptoms and five of these subjects presented to an emergency department within 24 h of the event. The mean age was 49 years (SD 10 years), 86% were women and the median duration of symptoms was 1.5 years. The characteristics of these 14 patients did not significantly differ from the WILS patients with no initial specific triggering exposure at work. Respiratory investigations of these 14 subjects included methacholine challenges in 10; 5 of the 10 had provocative concentration causing a 20% fall in FEV1 (PC_{20}) < 8 mg/ml. These five subjects

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**Table 2. Characteristics of subjects with OA, WEA and WILS**

<table>
<thead>
<tr>
<th></th>
<th>OA definite (n = 25)</th>
<th>OA probable (n = 25)</th>
<th>WEA definite (n = 19)</th>
<th>WEA probable (n = 21)</th>
<th>WILS definite (n = 14)</th>
<th>WILS probable (n = 16)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age–mean (SD)</td>
<td>44.2 (9.6)</td>
<td>45.6 (12.3)</td>
<td>47.0 (9.3)</td>
<td>45.8 (11.7)</td>
<td>50.6 (11.0)</td>
<td>45.9 (6.4)</td>
<td>NS^a</td>
</tr>
<tr>
<td>Gender–female (%)</td>
<td>48</td>
<td>24</td>
<td>47</td>
<td>52</td>
<td>79</td>
<td>81</td>
<td>&lt;0.01^b</td>
</tr>
<tr>
<td>Actively working (%)</td>
<td>83</td>
<td>60</td>
<td>74</td>
<td>62</td>
<td>64</td>
<td>81</td>
<td>NS^b</td>
</tr>
<tr>
<td>Ongoing exposure to suspect agent (%)</td>
<td>67</td>
<td>40</td>
<td>58</td>
<td>43</td>
<td>36</td>
<td>50</td>
<td>NS^c</td>
</tr>
<tr>
<td>Workers compensation claim (%)</td>
<td>88</td>
<td>80</td>
<td>53</td>
<td>52</td>
<td>38</td>
<td>50</td>
<td>&lt;0.01^b</td>
</tr>
<tr>
<td>Symptomatic GORD (%)</td>
<td>32</td>
<td>32</td>
<td>21</td>
<td>33</td>
<td>77</td>
<td>60</td>
<td>&lt;0.05^b</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>20</td>
<td>24</td>
<td>5</td>
<td>20</td>
<td>7</td>
<td>6</td>
<td>NS^c</td>
</tr>
<tr>
<td>Use of asthma medications at time of initial clinic assessment (%)</td>
<td>21 (87)</td>
<td>24 (96)</td>
<td>18 (95)</td>
<td>19 (90)</td>
<td>9 (64)</td>
<td>10 (62)</td>
<td>&lt;0.05^c</td>
</tr>
<tr>
<td>Use of PPE at work (%)</td>
<td>12 (48)</td>
<td>7 (28)</td>
<td>6 (32)</td>
<td>6 (30)</td>
<td>1 (7)</td>
<td>3 (19)</td>
<td>NS^b</td>
</tr>
<tr>
<td>Positive routine SPT (one or more, %)</td>
<td>56</td>
<td>52</td>
<td>68</td>
<td>76</td>
<td>57</td>
<td>69</td>
<td>NS^c</td>
</tr>
</tbody>
</table>

NS, nonsignificant; GORD, gastro-oesophageal reflux disease; PPE, personal protection equipment; SPT, skin prick test.

^a Analysis of variance.

^b Chi square.

^c Monte Carlo estimate for the exact test.

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**Table 3. Suspected agents in subjects with WILS**

<table>
<thead>
<tr>
<th>Exposure agent</th>
<th>Definite WILS</th>
<th>Probable WILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fumes/odours (other than perfumes and exhaust)</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Perfumes</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Exhaust fumes</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cleaning agents/bleaches/fresheners</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Wood dust</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Paint fumes</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Airborne dust</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>
had pre-existing asthma, with two having a concurrent diagnosis of WEA. Four subjects who did not have a methacholine challenge performed demonstrated normal spirometry without a bronchodilator response and normal serial peak flow recordings.

Discussion

We identified upper airway dysfunction with work-associated respiratory symptoms in 10% of subjects referred to a specialist occupational lung disease clinic. In comparison to work-related asthma, subjects with WILS were more likely to be female and have gastro-oesophageal reflux symptoms. They reported dysphonia and cough frequently, and common workplace triggers included fumes and odours such as perfumes.

Data from our retrospective chart review were subject to the limitations imposed by the extent and accuracy of data present in subjects’ files. Occupational exposures were based on patient histories, therefore subject to recall bias and inaccurate reporting.

Another limitation of our study was the lack of psychological assessment. Testing using the Minnesota Multiphasic Personality Inventory (MMPI-2) has suggested conversion disorder as the cause of VCD in a subset [8]. A study of laryngeal hypersensitivity in a non-occupational population demonstrated oral breathing to be associated with milder laryngeal symptoms, supporting the importance of olfaction and possibly psychological conditioning in symptoms [9]. There appears to be a variable degree of psychological overlay in patients with laryngeal dysfunction; however, research has not determined whether this is a cause or effect.

The respiratory tract is often exposed to irritant substances at work. Clinicians must differentiate ‘normal’ responsiveness of the respiratory tract from dysfunctional laryngeal behaviour and occupational lung diseases, such as OA. Laryngeal dysfunction is poorly understood with inconsistencies in terminology and diagnostic approaches. Laryngeal symptoms range from cough alone through to VCD [10]. Morrison proposed the term ‘irritable larynx syndrome’ to describe hyperkinetic laryngeal dysfunction manifested by a combination of VCD, dysphonia, globus pharyngeus (sense of lump or tension in the throat due to laryngeal muscular tension) and chronic cough [4,11].

We propose that in some individuals occupational exposure to airborne substances and/or odours at the workplace may be the predominate trigger of ILS symptoms, resulting in recurrent work-associated respiratory symptoms: ‘Work-associated irritable larynx syndrome’. Triggers include odours, perfumes, exhaust fumes and cleaning products. These differ from exposures associated with OA (diisocyanates, baker’s flour and wood dust), but are similar to WEA (dusts, exhaust fumes and environmental factors).

The pathophysiology of laryngeal dysfunction and VCD remains unknown. It has been proposed that changes in the number and/or regulation of upper airway sensory nerve endings lower the threshold for initiating the glottic closure reflex. This results in episodic stimulation of the laryngeal reflex at inappropriately low levels of exposure, in or out of a workplace [4,11–14]. It has been speculated that inflammatory insult to the upper airway through intrinsic factors such as gastro-oesophageal reflux, upper respiratory tract infection and postnasal drip, or external factors such as occupational irritants, may initiate this change in neurological control [4,12]. Perkner et al. [15] first described the condition of ‘irritant-associated VCD’. In our study, 14 WILS patients identified a specific incident of exposure to a respiratory irritant at the onset of their symptoms, and 5 of these patients presented to the emergency department following this event. The 20 patients that did not identify a specific workplace event had an average of 8.8 years of exposure to the offending agent before the onset of symptoms. Reasons for the change in tolerance are not clear, however they may be due to changes in intrinsic factors.

Similar to the general VCD literature, we identified a considerable predominance of women with WILS [1,11,14,16]. Women have a more sensitive cough reflex than men, as demonstrated by inhaled capsaicin

Box 1. Illustrative case
A 40-year-old nurse developed the sudden onset of upper retrosternal chest tightness, cough, wheeze, dysphonia and facial flushing while assisting in cardiac catheterization. On leaving the area, her symptoms resolved within 10 min except for dysphonia, which cleared after 24 h. Subsequently she had recurrence of these symptoms whenever there was exposure to alcohol swabs or alcohol rinse in the hospital. There were no other environmental triggers to her symptoms, skin tests including prick tests with the alcohol preparations were negative and pulmonary function tests were normal, including methacholine challenge. Physician documentation of an episode showed severe facial flushing, stridor and dysphonia. Except for the dysphonia there was resolution spontaneously within 5–10 min when away from alcohol and no airflow limitation on spirometry at 10 min. Laryngoscopy findings were consistent with gastro-oesophageal reflux disease (GORD) and laryngeal muscle tension. Symptoms with alcohol exposure persisted despite speech therapy and treatment for GORD, and she had to stop work in the hospital as she could not be provided with work that would completely avoid alcohol exposure.

See Table 1 for a summary of the results.
challenges but the reason for the difference is currently speculative [17].

Laryngeal dysfunction can be difficult to clinically differentiate from asthma and the conditions can co-exist [16,18]. Five patients in our study had concurrent WILS and work-related asthma (two OA and three WEA). Dyspnoea due to VCD rather than asthma tends to be rapid in onset and resolution and is poorly responsive to escalating asthma therapy. Patients may indicate their throat or upper chest as the site of maximal tightness. Work-related dysphonia was also common in our patients with WILS.

Diagnosis of WILS is currently based on clinical assessment that is multidisciplinary, involving physicians (primary care, occupational, pulmonary), otolaryngologists and speech pathologists [2,11,19,20].

The approach used in our voice disorders clinic involves neck examination, nasal endoscopy and indirect laryngoscopy with or without provocation testing. Neck palpation and observation during phonation and respiratory tasks are done to ascertain increased tension in extrinsic laryngeal muscles. Flexible endoscopy is performed to observe the larynx ‘at rest’ and during respiratory tasks including sniffing, panting and pursed lip exhalation. In a hospital setting, a provocation test may also be performed. With consent, the patient sniffs chemicals such as perfumes and cleaning solutions and if possible one or more of the occupational triggers. An abnormal test may include observation of inappropriate vocal cord adduction during inhalation or early expiration, supraglottic hyperfunction, increased posterior tongue base movement and increased mucus production. In the setting of an appropriate clinical history, the observation of laryngeal hyperresponsiveness after exposure to a triggering irritant is strongly supportive of the diagnosis of WILS.

Management should involve early intervention commencing with careful explanation of the cause of symptoms, possibly aided by viewing laryngoscopic videotape. Our approach involves modifying factors that may perpetuate laryngeal hyperresponsiveness, such as gastro-oesophageal reflex and post-nasal drip. Unnecessary medications, such as inhaled corticosteroids, should be discontinued after asthma has been excluded. Hydration therapy may be useful, especially if symptoms of chronic cough and throat clearing are present. We also recommend limiting exposure to occupational and non-occupational triggers. This may include the introduction of a ‘low-scent’ workplace policy or use of respiratory protection at times of exposure to stimulating agents. Psychological care, particularly work-related stress management, may also be warranted.

Key areas of needed research include establishing the pathophysiological mechanism of ILS and VCD, in particular the role of altered balance in the control of the larynx’s lung protective reflexes and psychopathology. A standardized and validated diagnostic approach is required for optimal management and for workers’ compensation. Prospective studies are required to investigate the natural history, impact on quality of life and effectiveness of interventions.

In summary, WILS is a condition of work-related hyperkinetic laryngeal symptoms primarily triggered by occupational exposures such as irritants and odours. The identification and management of WILS requires a multidisciplinary approach with a focus on modifying work-related and intrinsic factors that may perpetuate symptoms.

### Key points

- Work-associated irritable larynx syndrome is a condition manifested by recurrent hyperkinetic laryngeal symptoms primarily triggered by workplace exposures, such as respiratory irritants and strong odours.
- Ten percent of subjects with work-associated respiratory symptoms at this clinic described symptoms consistent with WILS.
- Individuals with WILS were more likely to be female and describe symptoms of gastro-oesophageal reflux.

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### Conflicts of interest

None declared.

### References


