Episodic Laryngeal Breathing Disorders: Literature Review and Proposal of Preliminary Theoretical Framework

***Adrianna C. Shembel, †Mary J. Sandage, and *Katherine Verdolini Abbott,** **Pittsburgh, Pennsylvania, and †Auburn, Alabama*

Summary: Objective. The purposes of this literature review were (1) to identify and assess frameworks for clinical characterization of *episodic laryngeal breathing disorders* (ELBD) and their subtypes, (2) to integrate concepts from these frameworks into a novel theoretical paradigm, and (3) to provide a preliminary algorithm to classify clinical features of ELBD for future study of its clinical manifestations and underlying pathophysiological mechanisms.
Study Design. This is a literature review.
Methods. Peer-reviewed literature from 1983 to 2015 pertaining to models for ELBD was searched using Pubmed, Ovid, Proquest, Cochrane Database of Systematic Reviews, and Google Scholar. Theoretical models for ELBD were identified, evaluated, and integrated into a novel comprehensive framework. Consensus across three salient models provided a working definition and inclusionary criteria for ELBD within the new framework. Inconsistencies and discrepancies within the models provided an analytic platform for future research.
Results. Comparison among three conceptual models—(1) *Irritable larynx syndrome*, (2) *Dichotomous triggers*, and (3) *Periodic occurrence of laryngeal obstruction*—showed that the models uniformly consider ELBD to involve episodic laryngeal obstruction causing dyspnea. The models differed in their description of source of dyspnea, in their inclusion of corollary behaviors, in their inclusion of other laryngeal-based behaviors (eg, cough), and types of triggers.
Conclusion. The proposed integrated theoretical framework for ELBD provides a preliminary systematic platform for the identification of key clinical feature patterns indicative of ELBD and associated clinical subgroups. This algorithmic paradigm should evolve with better understanding of this spectrum of disorders and its underlying pathophysiological mechanisms.
Key Words: Episodic laryngeal breathing disorders–Paradoxical vocal fold motion–Vocal cord dysfunction–Irritable larynx syndrome–Periodic occurrence of laryngeal obstruction.

INTRODUCTION

Episodic laryngeal breathing disorders (ELBD) are a spectrum of respiratory disorders, with no known etiology. Included in this spectrum are the so-called *paradoxical vocal fold motion/movement disorder* (PVFMD), *vocal cord dysfunction* (VCD), *irritable larynx syndrome* (ILS), *exercise-induced laryngeal obstruction*, laryngospasm, Munchausen stridor, and an additional 88 or more terms implying functional laryngeal respiratory pathology.[1–13] The hallmark symptoms of putative ELBD are recurring, sudden paroxysmal dyspnea and respiratory distress.[4,6,7,14–19] These symptoms are attributed to inducible intermittent, variable laryngeal airway obstruction that may be observed on laryngoscopy during the inspiratory phase of the respiratory cycle.[6,13–15,17,20–23] However, it is unclear whether this clinical presentation within the larynx is the underlying issue in ELBD or whether this paradoxical laryngeal movement is indicative of other underlying systemic influences. Nonetheless, episodes are thought to be triggered by various systemic or environmental stimuli specific to individuals.[6,7,10,12,15,19,22–24] These sudden episodes are often frightening and alarming, and can have considerable adverse effects on quality of life for affected patients.[5,12,25–29] Pathologies of anatomical, organic, or known origin, such as tracheomalacia/laryngomalacia, laryngeal edema/lesions, and laryngeal dystonia, respectively, are considered exclusionary for ELBD.[15,21,23,30]

Previous studies have shown that individuals ultimately diagnosed with ELBD are initially misdiagnosed in as many as 80% of cases over protracted periods (average of 4.8 years).[5,6] Erroneous diagnosis has significant implications not only for quality of life, but also for physical health. For example, ELBD can be misdiagnosed as refractory asthma and treated with prolonged periods of unnecessary, high doses of inhaled corticosteroids, resulting in iatrogenic conditions such as Cushing's disease, obesity, osteoporosis, diabetes, and hypertension.[6,18,31–33] Misdiagnosed patients may also be erroneously intubated, or may undergo an avoidable tracheotomy.[3,25,34] Patients may even be told that they are malingering and that symptoms are "all in their head," which leads to significant psychological repercussions including increased anxiety levels, adulterated self-concept, and self-blame.[35,36] In addition to unwanted side effects, affected individuals may also become noncompliant with treatment, frustrated by previous, ineffective treatments as a result of erroneous diagnosis.[37] Superfluous interventions (eg, steroids, intubation, etc) also lead to substantial financial and resource burdens.[7]

Accepted for publication November 4, 2015.
Financial support: N/A.
Conflict of interest: No financial or personal relationships with other people or organizations have inappropriately influenced the authors' actions.
Level of Evidence: 5.
From the *School of Health and Rehabilitation Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania; and the †Department of Communication Disorders, Auburn University, Auburn, Alabama
Address correspondence and reprint requests to Adrianna C. Shembel, Department of Communication Science and Disorders, University of Pittsburgh Health and Rehabilitation Sciences, 6065 Forbes Tower, Pittsburgh, PA 15260. E-mail: acs130@pitt.edu
Journal of Voice, Vol. 31, No. 1, pp. 125.e7–125.e16
0892-1997

http://dx.doi.org/10.1016/j.jvoice.2015.11.027

Clearly, accurate diagnostic identification of individuals with ELBD is crucial. Unfortunately, the diagnosis of ELBD can be challenging for several reasons. First, although over 200 observations of presumed ELBD have been reported within various bodies of literature over the past 140 years,[38] consensus lacks among clinicians regarding clinical criteria for diagnosis. Thus, what actually constitutes key signs and symptoms of ELBD is largely unknown. As a result, diagnosis of ELBD is by exclusion. Furthermore, the lack of consensus regarding diagnostic criteria creates challenges in attempts to differentiate putative ELBD from common concomitant pathologies such as asthma, chronic cough, muscle tension dysphonia, and anxiety/panic disorders.[4] Last, although there is a plethora of literature on the co-occurrence of asthma and ELBD within the literature,[16,31,35,39–67] other commonly co-occurring conditions with ELBD do not receive the same level of recognition. The result, as noted, is frequent misdiagnosis.

Second, ELBD features have been described across a heterogeneous spectrum of physiological manifestations, involving substantial variations in symptom presentation, laryngoscopic findings, and trigger stimuli.[5–7,10–24] Moreover, the fact that clinical features and physiological manifestations of ELBD do not arise in the same fashion across all individuals suggests that there may be clinical subgroups, or *phenotypes.* Phenotypes in this context refer to clusters of surface manifestations that clinically define a disease and its subsets. The use of this term in this paper borrows from terminology in contemporary asthma and allergy literature,[68–76] and does not imply any genetic basis.

Unfortunately, the current medical literature in ELBD is largely founded on anecdotal observations limited to specialties that may only see one or two of these phenotypic variants. This creates obvious challenges for comprehensive systematic identification and study of phenotypic subgroups. Thus, key characteristics have eluded definition. Additionally, the lack of strong theoretical understanding of ELBD, in general, and bias in anecdotal reporting within the literature, specifically, may lead to preferential interpretations of ELBD presentations and their various manifestations across the spectrum. Stronger emphasis on the objective, quantitative, and systematic study of ELBD can help dispel these clinical interpretation biases. A more interdisciplinary approach within this domain of study can also be fruitful.

Therefore, a literature review was undertaken to identify commonalities and discrepancies across models of ELBD to the end of proposing a *preliminary* theoretical algorithmic paradigm to better our understanding of this spectrum of conditions in general, and identify key clinical features, in particular. The provisional paradigm that emerged from this review can also be used to begin to identify phenotypic subgroups and guide the systematic study of the underlying pathophysiological mechanisms that drive these clinical presentations (ie, ELBD endotypes[a]). The hope is that this first step in the programmatic-driven and analytically driven approach to the study of ELBD will then serve as a springboard for interdisciplinary conversation and further development of phenotypic- and endotypic-based ELBD algorithms. The paper's main point is that we need to come to a consensus about key clinical features of ELBD before we embark on a journey to explore underlying mechanisms, which we hope to pursue in the future.

The methods involved in this present study were twofold. The first was to identify and critically evaluate current ELBD models in the literature, and compare and contrast findings. Specifically, three commonly proposed models were summarized based on a comprehensive literature review across multiple disciplinary domains and medical specialties. The second step was to integrate these models into a single framework (1) to provide a systematic method to identify clinical features indicative of ELBD and (2) to accommodate speculation about ELBD phenotypes. The proposed theoretical framework that emerged is not intended to be seen as theoretical decree. Instead, the intention is to provide a provisional platform from which to work and evolve.

The ultimate goals of this preliminary endeavor is to help (1) identify and categorize key and auxiliary clinical characteristics of ELBD, (2) provide a platform for the identification of phenotypic subgroups within the ELBD spectrum, and (3) better elucidate these patterns for future systematic study of ELBD pathophysiology, etiology, and treatment.

Criteria for considering studies for review

Peer-reviewed literature from 1983 to 2015 pertaining to theoretical ELBD frameworks was identified using Pubmed, Ovid, Proquest, Cochrane Database of Systematic Reviews, and Google Scholar. Search terms in Table 1 were used across the databases, both in isolation and in combination with the following terms: *theoretical*, *theory*, *framework*, *paradigm*, and *model*. Studies were limited to English and included case series, case reports, and retrospective reviews. Bibliographies and references

TABLE 1.
Search Terms for ELBD Literature Review

1. Dysfunctional breathing (disorder)
2. (Episodic) (functional) (paroxysmal) laryngospasm(s)
3. Exercise-induced laryngeal obstruction (EILO)
4. (Extrathoracic) (functional) (inspiratory) (psychogenic) (upper) (variable/variant) Airway Obstruction
5. (Glottic) (laryngeal) dysfunction
6. (Inspiratory) (expiratory) vocal cord (dysfunction) (disorder)
7. Inter-arytenoid Prolapse (IARP)
8. Irritable Larynx Syndrome (ILS)
9. Laryngeal hyperresponsiveness
10. Laryngeal hypersensitivity syndrome
11. Paradoxical vocal (cord/fold) (motion/movement) (disorder/dysfunction)
12. (functional) (psychogenic) stridor

[a]An *endotype* is a subtype of a condition, defined by a distinct functional or pathophysiological mechanism(s).[68,69,71,72,76,77] The context underlying this concept comes primarily from the pulmonary literature.