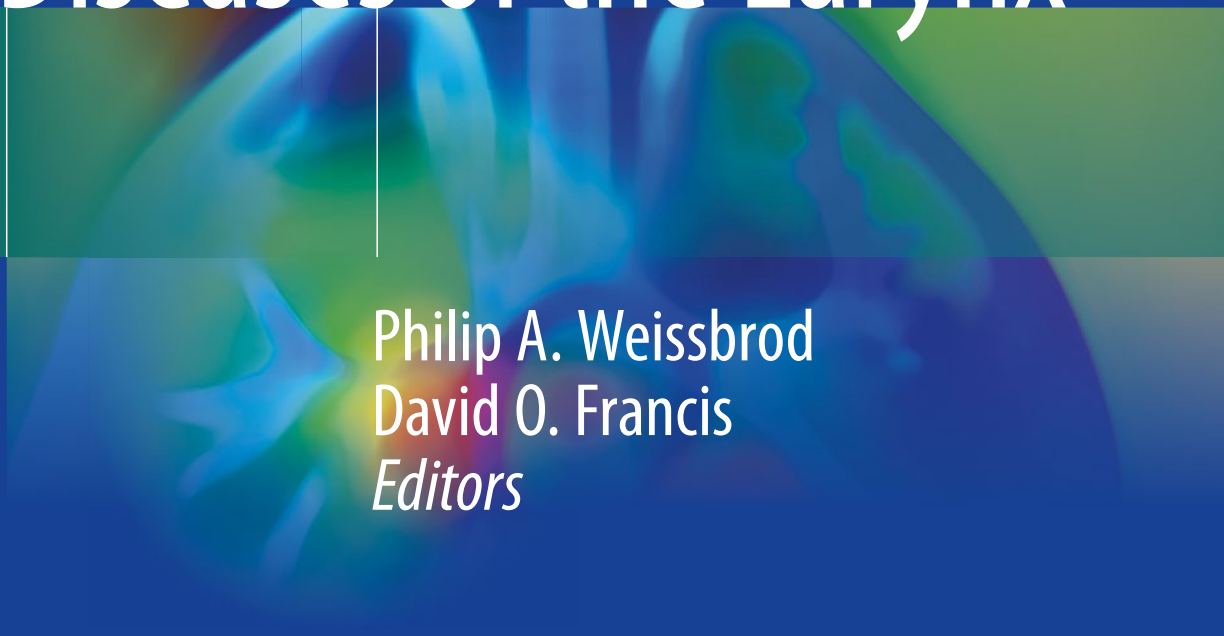
Neurologic and Neurodegenerative Diseases of the Larynx



Philip A. Weissbrod
David O. Francis
Editors

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To Caro, Izzy, and Nina for being my inspiration and motivation and making even bad days bright.
To my parents for a lifetime of unwavering support.
To my mentors and colleagues for your teaching, guidance, and friendship.
To my patients, for it is only through your experience that we can improve the lives of others.

Philip A. Weissbrod

To my wife, Jackie, and little Evie for their unwavering support, for making me laugh, and for making me a better husband, father, and doctor. You are my world.
To my parents who were my first editors and always pushed me to see beyond the horizon.
To my many mentors who fostered a sense of exploration, curiosity, and integrity.
To my patients who have taught me more about medicine and humanity than any professor could.

David O. Francis

Foreword

The larynx is a busy organ. Every natural breath, every soaring aria, and every hotdog eating contest are regulated to spectacular precision by the wonder that is the larynx. Books on this subject are full of feats and amazing facts of anatomy and physiology; to me, the larynx deserves special recognition in the pantheon of organs due to this versatility and precision. All of this magic is due to the elegant neuromuscular function of the larynx.

We have work to do, you and me. The mechanics and sensory processing that begin with hearing transduction, for example, have deservedly captured the enthusiasm and amazement of investigators for a century or more. In contrast, the larynx has as yet unplumbed depths of complexity in health and disease as it relates to sensory and motor function.

In this volume, expertly curated and edited by Drs. Weissbrod and Francis, today and tomorrow's leading authors have presented the first truly comprehensive text of the twenty-first century on this topic. This book will set the stage for the next 20 years of conversation about neurologic function and dysfunction as it relates to the larynx.

If that uncanny bargain between author and reader works out as it should, you will emerge from this book both with more knowledge and yet somehow with even more questions to ponder. The future of caring for laryngology patients depends on our commitment to educating ourselves, other physicians, our allied health partners, and, of course, our patients. *Neurologic and Neurodegenerative Diseases of the Larynx* from Weissbrod and Francis will undoubtedly be a mark on the map for both existing and emerging generations of students of the larynx.

Seattle, WA, USA
July 1, 2019

Albert L. Merati, MD

Preface

For most providers, how neurologic and neurodegenerative disease affect the upper aerodigestive tract is somewhat of a black box. The interplay between these types of diseases and dysfunction of this complicated area of the body is difficult to understand even for laryngologists and speech-language pathologists who focus all their attention on it. Disease presentations can range from subtle to profound, disease course can be progressive, and treatment options can seem limited. Even for experienced providers, care for these patients is difficult and outcomes can be bleak, depending on diagnosis. As we have both gained experience in working with these populations, we have recognized that even in the most difficult of patients, there are options for voice, airway, and swallowing intervention that can lead to improvement in quality of life. It was this concept that inspired us to curate this text.

The objective of this book was to create a common source that summarizes what is known about the myriad of different neurological conditions that cause dysfunction of communication, swallowing, and breathing as it relates to the upper aerodigestive tract. It is critically important to understand that this knowledge is not under the auspice of any particular specialty and that most clinicians, at some point in their careers, encounter the described conditions and manifestations of disease. We recruited the foremost minds and experts in these conditions from a broad spectrum of medical specialties in order to create a book that is inclusive of diagnostic and therapeutic considerations that clinicians should think about when caring for patients with these conditions.

As a community of clinicians and scientists, we are constantly learning how to better diagnose and characterize disease and to improve our management of patient symptoms and concerns in order to maximize both quality of life and longevity. We have both been deeply affected by the patients we have cared for in our practices over the years. Their stories and experiences were our ultimate motivation to put this text together and to push our field forward. These diseases afflict both young and old, and most of us have had friends and relatives who have personally been touched by these pathologies. It is our duty to continually learn and advance scientific discovery to improve the lives of future patients.

We believe this book provides clinicians and scientists at all levels of experience a practical and thorough review of these diseases, their manage-

ment, and frontiers in science. It is our intention for this book to act as a resource to guide our practices and research endeavors. We hope the work herein will help clinicians from various fields better recognize the subtle and not-so-subtle voice, swallowing, and airway manifestations of these diseases so that we can develop a more efficient, evidence-based, and patient-focused multispecialty approach to managing these complex and challenging patients.

Madison, WI, USA — David O. Francis, MD, MS
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Part I

Evaluation

Anatomy from the Inside Out

1

Reed C. Gilbow and James J. Daniero

Introduction

The upper aerodigestive tract is one of the most complex areas of the human body due to its tripartite role in communication, deglutition, and breathing [1]. Understanding the true interplay of each process requires intimate knowledge of these dynamic physiologic processes. Therefore, laryngeal anatomy is of paramount importance when attempting to understand laryngeal physiology and pathology. However, the normal layered transcervical view by which laryngeal anatomy is described in many textbooks and atlases does not correspond to the way most clinicians encounter it in clinical practice. This can make it particularly difficult for less experienced clinicians to apply their anatomic knowledge when viewing the larynx in clinic or in the operating theater. Flexible and rigid laryngoscopy are the most common methods by which otolaryngologists examine the larynx [1]. For this reason, the modern clinician must also consider the various anatomic areas, muscles, cartilages, vascular, and neural structures from this viewpoint. We endeavor to describe laryngeal anatomy from the perspective by which most it is most frequently encountered.

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This chapter is organized systematically. First, we review the location of the bone and the six cartilage structures that make up laryngeal skeleton. Second, we identify and discuss anatomic areas used in head and neck oncology for staging purposes. Third, we discuss surface anatomy from the supraglottic view. Finally, we review vascular and neural structures. These last points are especially important when planning and performing endoscopic microlaryngeal surgery.

The Laryngeal Skeleton

Hyoid Bone

The hyoid is a horseshoe-shaped, free-floating bone that articulates with the superior horns of the thyroid cartilage and is suspended in the neck by a muscular and ligamentous sling attached to the root of the tongue [2]. The hyoid bone provides structural support for several functions related to swallowing and phonation. Beginning at the base of tongue on endoscopy, the hyoid bone can be understood as the origin of the hyoglossus and insertion of the geniohyoid muscles [2, 3]. Unseen on endoscopy are the other suprahyoid muscles—the mylohyoid, stylohyoid, and digastric muscles. Likewise, the infrahyoid muscles, which include the sternohyoid, thyrohyoid, and omohyoid muscles, are unseen on endoscopy but important in understanding the move-

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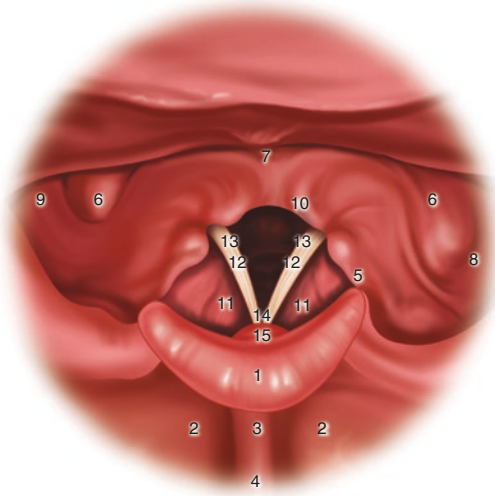

Fig. 1.1 Normal flexible laryngoscopic exam. Pertinent anatomical landmarks of the oropharynx and structures surrounding the supraglottis include: (1) epiglottis, (2) valleculae, (3) hyoepiglottic ligament, (4) base of tongue, (5) aryepiglottic folds, (6) pyriform sinus, (7) post-cricoid region, (8) greater horn of the hyoid bone, and (9) internal surface of the thyroid lamina. Laryngeal structures include: (10) arytenoid cartilages, (11) false vocal folds, (12) true vocal folds, (13) vocal processes, (14) anterior commissure, and (15) petiole of the epiglottis

ment of the larynx physiologically. The median hyoepiglottic ligament, a common finding on endoscopy, serves as an anatomic marker for locating the body of the hyoid endoscopically [1] (Fig. 1.1). The greater horns of the hyoid bone can also be identified in the lateral pharyngeal wall, especially in thin patients (Fig. 1.2).

Laryngeal Cartilages

The laryngeal skeleton is comprised of six primary cartilage structures. Each is discussed sequentially beginning with the thyroid cartilage and moving inferiorly.

Thyroid Cartilage The thyroid cartilage, derived from the Latin word for "shield," is an aptly named cartilaginous structure providing protection and support to the vocal folds [4]. It articulates superiorly with the greater horn of the hyoid bone and is connected to the hyoid along its superior extent by the thyrohyoid membrane, which runs the length of the hyoid. The membrane has three condensations, two

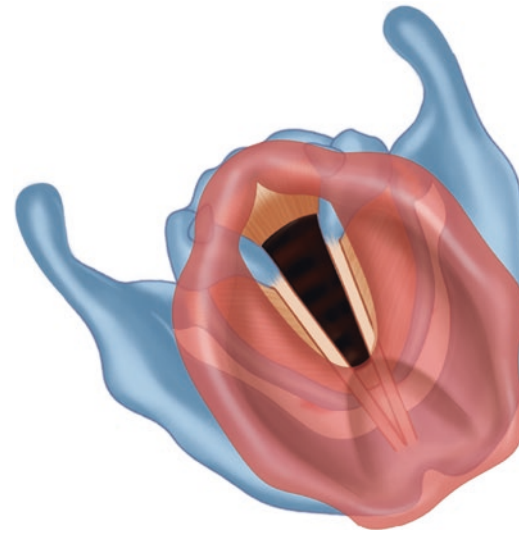

Fig. 1.2 Normal flexible laryngoscopic exam (seen in Fig. 1.1) with an anatomical rendering of the underlying cartilaginous skeleton

lateral and one medial, which are termed the medial and lateral thyrohyoid ligaments [2, 4]. Specifically, the medial ligaments connect the body of the hyoid with the superior thyroid

notch while the lateral ligaments connect the superior horn of the thyroid with the greater horn of the hyoid. Importantly, it is through this membrane that the internal branch of the superior laryngeal nerve and the superior laryngeal artery pass into the internal surface of the larynx laterally [5]. The thyroid cartilage itself is composed of two broad, flat laminae that are fused together anteriorly in the midline. The thyroid cartilage also has inferior horns which articulate with the cricoid cartilage at the cricothyroid joint, which is critical to pitch modulation [6]. The majority of the thyroid cartilage cannot be seen on endoscopy except for the internal surface of the posterior laminae, which can be seen through the anterior pyriform sinus mucosa (Fig. 1.2).

Epiglottis The epiglottis is a broad, leaf-shaped fibrocartilaginous structure which extends superiorly from a stem, or petiole [4]. The epiglottis is connected to multiple laryngeal structures including the hyoid bone, thyroid cartilage, and arytenoid cartilages via the hyoepiglottic, thyroepiglottic, and aryepiglottic ligaments, respectively [7]. Furthermore, a sheet of fibroelastic tissue termed the quadrangular membrane extends from the aryepiglottic ligament inferiorly onto the surface of the false vocal fold, creating the familiar endolaryngeal slope of the supraglottis when viewed on flexible laryngoscopy [1, 8]. It is through these interactions that the epiglottis closes over the airway during swallowing. The epiglottis is a prominent structure easily noted during laryngoscopy; often the laryngoscopist will need to carefully maneuver around the epiglottis in order to fully view the glottis, as this structure contains dense sensory fibers from the internal branch of the superior laryngeal nerve [9]. This is can be more easily accomplished by placing the patient into "sniffing position" by tilting the chin up, flexing the head forward while extending the neck [10]. This position displaces the larynx anteriorly to better align the larynx and trachea with an oral or transnasal endoscopic approach.

Arytenoid, Corniculate, and Cuneiform The prominent laryngeal cartilages of the posterior larynx—and frequently queried structures by patients—are the arytenoid cartilages. They are located in the posterior supraglottis and are oriented vertically with the muscular process located on the lateral surface (not visible on laryngoscopy) and the vocal process medially positioned and attached to the vocal ligament, serving as a prominent landmark of true vocal fold anatomy [1, 10]. The aryepiglottic folds extend from the arytenoid cartilages to the epiglottis. The corniculate and cuneiform cartilages, if present, may be visible at the superior aspect of the arytenoid cartilage or partially extending into the aryepiglottic fold [8]. The vocal process marks the beginning of the posterior one-third of the true vocal fold and is the origin of the thyroarytenoid muscle [11]. The cricoarytenoid joints are complex diarthrodial joints—filled with synovial fluid—located at the superior edge of the cricoid plate. These joints allow the arytenoid cartilage to internally and externally rotate, glide medial and lateral, as well as pitch superiorly or inferiorly in a rocking motion atop the cricoid cartilage. The overall structure is reinforced with several surrounding ligaments to prevent anterior or posterior dislocation. However, in rare cases external trauma can force the arytenoid cartilage beyond the elastic capacity of these ligaments and result in dislocation requiring transoral approach for closed reduction. Closely observing its rotational movement is essential to isolate cricoarytenoid joint and recurrent laryngeal nerve function in the setting of suspected vocal fold mobility impairment [12].

Cricoid The final cartilage to discuss is the cricoid cartilage which is located at the inferior aspect of the larynx and is connected to the trachea via the cricotracheal ligament, connecting the cricoid ring to the first tracheal ring [8]. The cricoid is the only complete cartilaginous ring in a normal airway, presenting a potential choke point of luminal narrowing. It is a signet ring-shaped structure that is short anteriorly and lengthens into a tall, flat lamina posteriorly, upon which the arytenoid cartilages sit. The anterior cricoid ring can be viewed in the anterior subglottis on flexible laryngoscopy as an offset between the cricoid and the trachea below. This natural shelf can be confused for narrowing of the airway due to an oblique viewing angle during indirect laryngoscopy and an inade-

quate view of the trachea inferiorly. The cricoid cartilage is attached anteriorly to the inferior border of the thyroid laminae by means of the cricothyroid membrane and has a condensation in the cricothyroid ligament, which is a more dense fan-shaped structure in the midline [1, 8]. This ligament (not visible on laryngoscopy) serves as a reliable landmark of midline during open laryngeal surgery.

Regional Laryngeal Anatomy and Subsites

In this section we define the regions of the oropharynx, hypopharynx, and supraglottis. We also aim to define the subsites of the larynx—the supraglottis, glottis, and subglottis—and how can they be readily identified on endoscopy. We explore these distinctions sequentially in a superior to inferior manner.

Pharyngeal Subsites The oropharynx is defined by its multiple subsites included in the American Joint Commission on Cancer (AJCC) 8th edition staging guidelines for head and neck cancer [13]. The subsites include the anterior and posterior tonsillar pillars, tonsillar fossae, valleculae, base of tongue, posterior pharyngeal wall, soft palate, and uvula [3, 13]. The boundary between the oropharynx and supraglottis is naturally developed as the lingual surface of the epiglottis, aryepiglottic folds, and the mucosa overlying the arytenoid cartilages.

The borders between the oropharynx and nasopharynx and hypopharynx are less obvious. The boundary between the nasopharynx and oropharynx is defined as an imaginary axial plane through the superior-most surface of the soft palate [14]. Delineating the hypopharynx is a bit more complex, as the boundary between the oropharynx and hypopharynx is an imaginary axial plane defined by the superior surface of the hyoid bone, which demonstrated previously is less readily identifiable, except for key endoscopic landmarks [14].

Laryngeal Subsites Finally, we must differentiate the various subsites of the larynx. The supraglottis is defined as the laryngeal structures superior to the glottis, and this boundary is usually defined as the lateral most aspect of the laryngeal ventricle, where the mucosa transitions from respiratory epithelium to stratified squamous epithelium [15]. Supraglottic structures include the epiglottis, aryepiglottic folds and quadrangular membranes, arytenoid cartilages, and the false vocal folds. The glottis is comprised of the superior and inferior surfaces of the true vocal folds and is defined to be 1 cm in vertical dimension [15]. The subglottis is defined as extending from the glottis to the inferior border of the cricoid ring. This is typically 1 cm below the vocal fold edge anteriorly and 5 mm below the vocal fold posteriorly due to the taller posterior height of the cricoid. It is important to comment on the term "infraglottis." It is not an official laryngeal subsite, but when used refers to the undersurface of the true vocal fold as they descend toward the conus elasticus and cricoid.

Supraglottic, Glottic, and Subglottic Surface Anatomy

Supraglottis The supraglottis is defined by the arytenoid cartilages posteriorly, the aryepiglottic folds laterally, and the epiglottis anteriorly [3, 15]. The aryepiglottic folds are continuous with the quadrangular membrane, which extends inferomedially to support the false vocal fold. Respiratory epithelium continues around the free edge of the false vocal fold and into the ventricle, where it transitions to stratified squamous epithelium inferiorly at the junction of the ventricle and the true vocal fold [15]. Posteriorly, a small sulcus is usually found between the arytenoid cartilages, known as the interarytenoid sulcus, which extends inferiorly until the interarytenoid muscle is encountered. The petiole of the epiglottis is encountered inferiorly in the supraglottis and articulates with the thyroid cartilage immediately superior to the anterior commissure of the glottis.

Glottis The true vocal folds are normally white bands of tissue located in the glottis that extend from the vocal process of the arytenoid cartilage

to the anterior commissure where the thyroarytenoid muscles insert onto the thyroid cartilage to create a V-like appearance on laryngoscopy [1, 11]. The mucosa overlying the true vocal folds is nonkeratinized stratified squamous epithelium. When viewed from above, the true vocal folds appear as two-dimensional shelves extending medially. However, the true vocal folds are composed of laminated soft tissue structures that give them their unique physiologic and biomechanical properties [16]. It should also be noted that the true vocal fold gradually continues inferiorly to the cricoid ring as the conus elasticus [16]. On the surface of the true vocal folds, blood vessels normally orient in a longitudinal fashion. Torturous or horizontal blood vessels are notable and may represent a response to an acute, chronic, or past injury.

Subglottis The view of the subglottis is somewhat limited on flexible laryngoscopy during assessment for subglottic stenosis and/or masses. However, in our experience lifting the chin can pull the epiglottis forward to obtain a better view of the glottis and tucking the chin down can better align the trachea with the larynx to obtain a view of the subglottis and often several tracheal rings. The subglottis can be more definitively explored using rigid telescopes during operative laryngoscopy.

Laryngeal Musculature

The intrinsic muscles of the larynx are divided into three basic groups: adductors, abductors, and tensors [1, 16]. While the actions of many of these muscles cannot be directly observed on laryngoscopy, a three-dimensional understanding of their actions is critical.

Adductors The thyroarytenoid (TA) muscle exists within the substance of the true vocal fold and consists of two main parts: internal and external. The external segment extends from the anterior commissure to the lateral surface of the arytenoid cartilage and principally serves to adduct the true vocal fold [1, 8, 11]. The internal segment, also known as the vocalis muscle, extends from the anterior commissure to the vocal process and acts by foreshortening and tightening the true vocal fold.

Another adductor is the lateral cricoarytenoid muscle (LCA). This muscle originates along the superior lateral border of the cricoid ring and inserts on the anterior aspect of the muscular process of the arytenoid cartilage. Contraction of the LCA muscle results in the arytenoid rotating internally and caudally, which translates into downward and medial movement of the vocal process [1].

The last major adductor is the interarytenoid (IA) muscle. This muscle consists of two defined groups: horizontal and oblique. The horizontal group inserts on the substance of the arytenoid cartilage and serves to narrow the laryngeal inlet and close the posterior glottic gap [8]. The oblique fibers insert on the apex of the arytenoid cartilage [8]. Some of the muscle fibers of the oblique group extend past the apex along the aryepiglottic fold and are known as the aryepiglottic muscle.

Abductors The posterior cricoarytenoid (PCA) muscle is the sole abductor of the true vocal folds. It extends from the broad surface of the posterior surface of the cricoid cartilage to the muscular process of the arytenoid cartilage. The paired muscles of the PCA are innervated by the abductor branch of the ipsilateral recurrent laryngeal nerve [17]. Importantly, the function of this muscle rotates the arytenoid cartilage externally and cephalad, causing the vocal process to be displaced superiorly and laterally. The PCA muscle has a medial (horizontal) and lateral (vertical) segment [17]. The medial segment serves as a true abductor while the lateral segment principally serves to elevate the vocal process and maintain the arytenoid cartilage in an upright position.

Tensors The cricothyroid muscle serves as a tensor of the true vocal folds. These paired muscles extend from the anterior aspect of the cricoid ring and insert on the thyroid laminae. This muscle is made of two separate components, the pars recta and pars obliqua [8]. The pars recta is situated more anteriorly and serves to depress the

thyroid cartilage. The pars obliqua inserts on the inferior horn of the thyroid cartilage and acts to displace the thyroid cartilage anteriorly. By performing this action, the cricothyroid muscles also serve as secondary laryngeal abductors [8].

Extrinsic Laryngeal Muscles

The extrinsic laryngeal muscles are comprised of infrahyoid and suprahyoid muscles. The infrahyoid muscles include the sternohyoid, sternothyroid, thyrohyoid, and omohyoid muscles, while the suprahyoid muscles include the digastric, mylohyoid, geniohyoid, and stylopharyngeus. The principal manner by which they affect laryngeal physiology is by changing the position of the hyoid bone and the larynx within the neck. The infrahyoid muscles can compress the laryngeal skeleton resulting in supraglottic medialization and also cause some vocal fold adduction. This can occur as a maladaptive response to a variety of laryngeal insults or compensation for incomplete glottic closure. Overuse of these paralaryngeal muscles during voice production often results in voice change, vocal strain, neck pain, and dysphagia [18, 19]. Palpation of the thyrohyoid space will often reveal exquisite tenderness as a result of chronic musculoskeletal tension.

Blood and Lymph

The laryngeal blood supply is of particular relevance to otolaryngologists that perform microlaryngeal surgery. Our discussion will identify the usually paired arteries and veins of the larynx from superior to inferior. Finally, we discuss laryngeal lymphatic structure and drainage patterns from each subregion, which normally cannot be identified on endoscopy or gross examination.

Blood Supply

The principal blood supplies to the endolarynx are the superior and inferior laryngeal arteries, which are branches of the superior and inferior thyroid arteries (arising from the external carotid and subclavian artery, respectively) [8, 19]. The superior laryngeal artery normally branches from the superior thyroid artery at approximately the level of the hyoid bone in the neck, from which it courses medially with the internal branch of the superior laryngeal nerve [19]. These structures then pierce the thyrohyoid membrane approximately 1 cm anterior and superior to the superior horn of the thyroid cartilage. The superior laryngeal artery has three commonly noted branches: the epiglottic artery which courses through the aryepiglottic fold to the epiglottis and a common trunk which gives rise to the anteroinferior and posteroinferior arteries, which course over the internal surface of the thyroid cartilage to supply the supraglottis and glottis [19]. Multiple anastomotic networks exist between these arteries as well as between these arteries and branches of the inferior laryngeal artery (Fig. 1.3).

By contrast, the inferior laryngeal artery branches from the inferior thyroid artery and

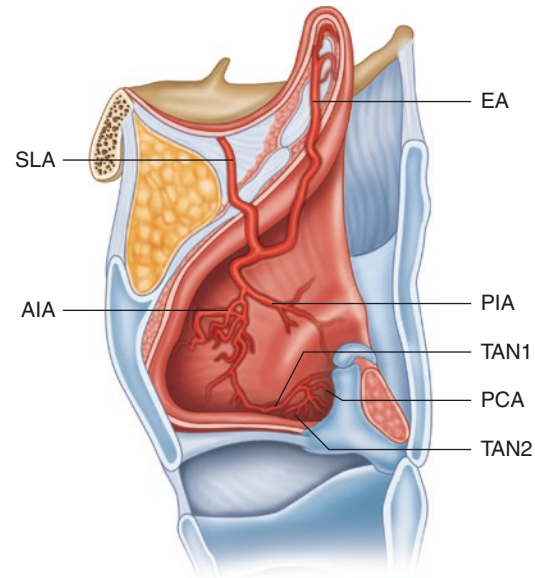

Fig. 1.3 Drawing of a right hemilarynx with tissue removed to reveal the branching of the superior laryngeal artery into the (1) epiglottic artery (EA), (2) anteroinferior artery (AIA), and (3) posteroinferior artery (PIA). The anteroinferior branch also gives off the thyroarytenoid branches (TAN1, TAN2) and the posterior cricoarytenoid branches (PCA)

courses superiorly with the recurrent laryngeal nerve [8, 19]. It has multiple branches that run deep to the inferior constrictor muscle into the larynx that then anastomose with the branches of the superior laryngeal artery. The cricothyroid artery is also a branch of the inferior laryngeal artery, which courses along the superior external surface of the cricothyroid membrane, supplying the cricothyroid muscle. This artery is noted in cadaveric studies to pierce the cricothyroid membrane approximately 2–3 mm from the midline and anastomose with branches of the anteroinferior branch of the superior laryngeal artery [19]. In all areas, the venous blood supply mirrors the arterial supply.

Lymphatics

Lymphatic drainage of the supraglottis is complex, but primarily drains to jugular nodes and deep cervical lymph nodes. The glottis itself has relatively little lymphatic drainage due to the isolation provided by the thyroid cartilage. In the rare case that metastasis occurs from a glottic cancer, it generally tends to involve prelaryngeal, pretracheal, and paratracheal lymph nodes in addition to the deep cervical chains (levels II-IV) [15]. The subglottis normally drains into paratracheal and inferior deep cervical lymph nodes [15].

Innervation

Both sensation and motor innervation of the larynx derive from the vagus nerve. In the neck, the vagus nerve descends in the carotid sheath after exiting the skull via the pars nervosa of the jugular foramen. The vagus nerve has three principal branches in the neck: a pharyngeal branch, the superior laryngeal nerve, and the recurrent laryngeal nerve (Fig. 1.4) [20].

The superior laryngeal nerve emerges from the carotid sheath and divides into an internal and external branch. The internal branch courses with the superior laryngeal artery through the thyrohy-

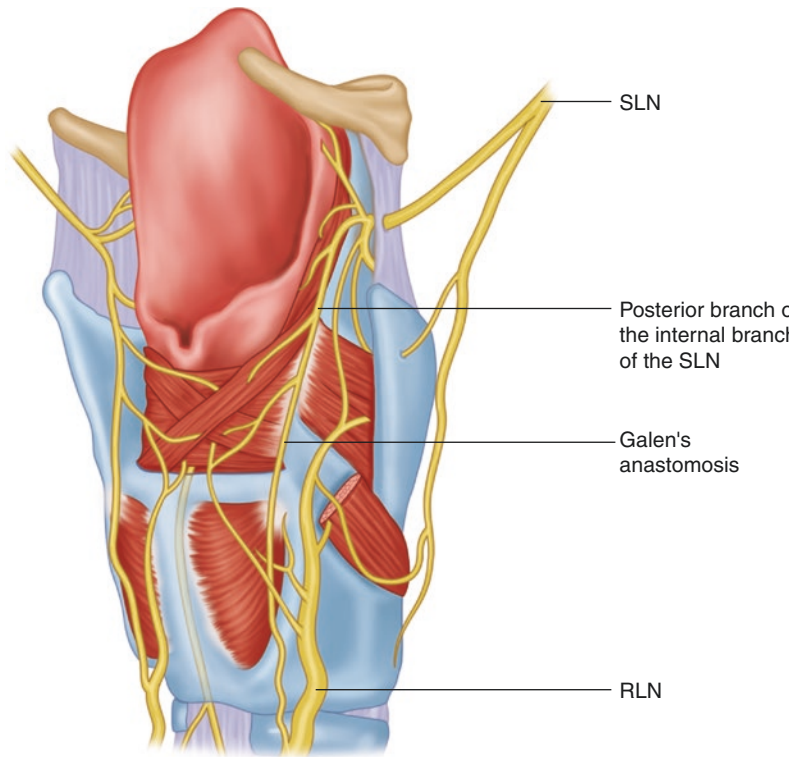

Fig. 1.4 Artist rendering of the larynx with mucosa removed. Noted structures include (1) superior laryngeal nerve, (2) posterior branch of the superior laryngeal nerve, (3) recurrent laryngeal nerve, (4) posterior branch of the recurrent laryngeal nerve, and (5) Galen's anastomosis

oid membrane, as discussed previously, to provide sensory innervation to the supraglottis and the superior portion of the glottis. Importantly, it is known that the internal branch of the superior laryngeal nerve and the endolaryngeal portion of the recurrent laryngeal nerve have a sensory anastomosis [21]. The external branch of the superior laryngeal nerve courses over the external surface of the larynx in close proximity to the superior lobe of the thyroid to innervate the cricothyroid muscle [22].

The recurrent laryngeal nerve emerges from the vagus nerve in the chest and loops from anterior to posterior around the aorta (left) or the right subclavian artery (right) before ascending to the larynx within the tracheoesophageal groove. Rarely (0.7% of the time), the right RLN does not descend, usually secondary to the presence of a retroesophageal (aberrant) right subclavian artery. This anatomic variant leads to the nonrecurrent laryngeal nerve (NRLN) entering the larynx horizontally and places it at great risk during thyroid surgery [23]. The paired nerves course into the endolarynx at the cricothyroid joint to provide sensory innervation to the subglottis and inferior glottis as well as motor innovation to all intrinsic laryngeal muscles except the cricothyroid muscle. It should be noted that motor anastomoses between the RLN and the SLN occur including Galen's anastomosis between the posterior branches of the internal branch of the superior laryngeal nerve and the recurrent laryngeal nerve [24]. Galen's anastomosis normally was found on the posterior surface of the interarytenoid or posterior cricoarytenoid muscles [24].

Conclusion

The anatomy of the pharynx and larynx is particularly complex but provides the basis for our understanding of the complex physiology of the upper aerodigestive tract. The discussed anatomy is from the perspective of the laryngoscopist, which is how most practicing clinicians in the modern age examine the larynx. This applicable anatomy provides the basis for a deeper study of the physiology of the upper aerodigestive tract with regard to airway protection, swallowing, and phonation as well as a greater understanding of the effects of laryngeal pathology on these important functions.

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Laryngeal Physiology

2

Sid M. Khosla and Hayley Born

Vocal fold vibration and intraglottal geometry In order to phonate, the thyroarytenoid, lateral cricoarytenoid, and interarytenoid muscles adduct the folds. These muscles in addition to the cricothyroid and strap muscles (among others) are responsible for pre-phonatory conditions including vocal fold length and tension. When the folds are close enough, flow going through the vocal folds produces vibration. This is an example of a phenomenon known in engineering as a flow-structure interaction; a flag waving in the wind is another example. Flow going through the folds modulates intraglottal pressures, which alters the shape of the glottis. Changes in shape produce different airflow patterns that, in turn, modify intraglottal pressure; thus it changes the glottal shape and so on. To understand the nature of the flow-structure interaction, it is necessary to know the geometry of the glottis, the material properties of the vocal fold, and the intraglottal pressures at different time points in the phonation cycle.

Most of the movement during vibration occurs in the cover. The cover is defined as the mucosa and the superficial layer of the lamina propria. The body is defined as both layers of the ligament and the thyroarytenoid muscle. At higher amplitudes, the ligament and muscle can also vibrate. The rhythmic movement of the cover—the mucosal wave—can travel in three directions: medial-lateral, inferior-superior, and anterior-posterior. The anterior-posterior wave is less common, but this wave and the medial-lateral wave can be seen during videostroboscopy. The superior-inferior wave produces a convergent shape of the glottis during the opening phase and a divergent glottis during the closing phase. The glottis is convergent when the coronal section of the fold is narrower superiorly and wider inferiorly. The glottis is divergent when the superior aspect of the fold is wider than the inferior aspect. This vertical mucosal wave can be seen in Fig. 2.1 [1], which shows a coronal section of the glottis and the corresponding flow rate exiting the glottis. Frames 1 and 2 show the converging glottis during opening. Frame 3 shows a straight glottis during maximal opening and frames 5–7 show a diverging glottis during closing. Frames 8–10 show a fully closed glottis.

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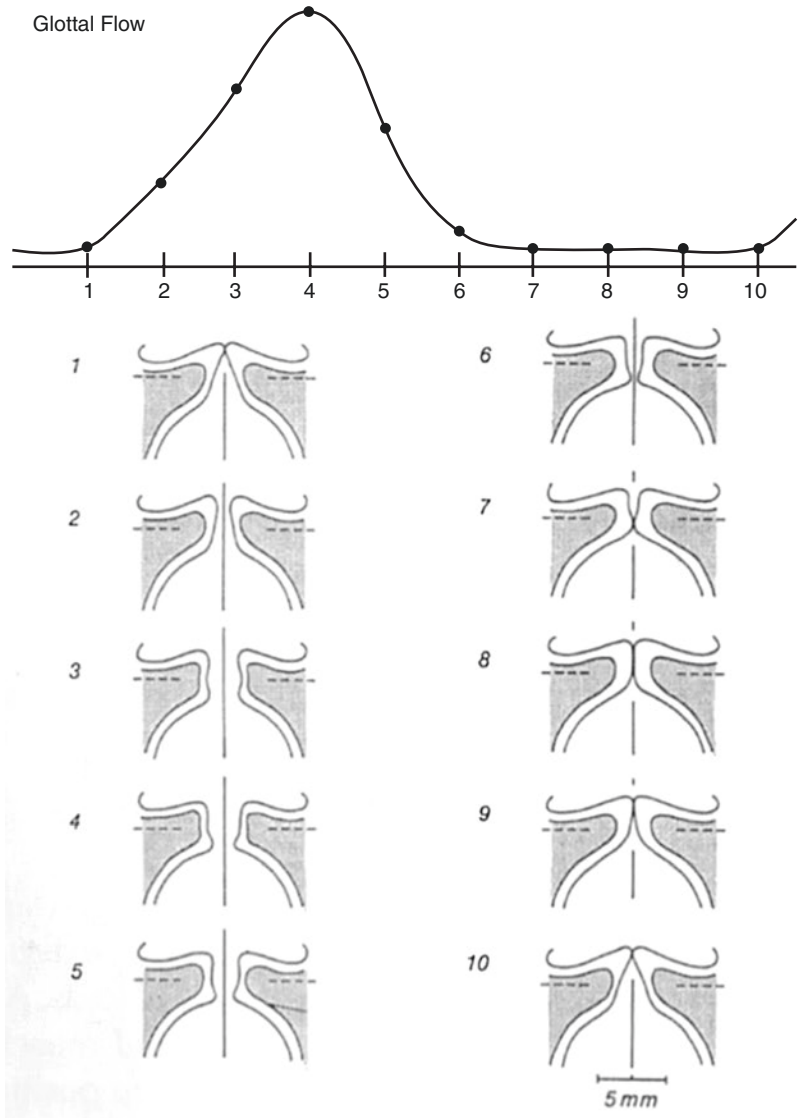

Fig. 2.1 Glottal flow waveform and corresponding glottal motion. The specific phases of the vertical mucosal wave are specified in the glottal waveform. (Adapted with permission from Hirano [1], with permission)

Flow Rate and Source of Sound

Flow rate (Q), which is called glottal flow in Fig. 2.1, is defined as the volume of air that exits the glottis per unit time and is equal to the velocity times area (Q = va). In the classic source filter theory, Fant says the source of sound is due to the change in flow rate (dQ) per time (dt) or dQ/dt and that the vocal tract acts as a filter to increase the intensity of certain frequencies and decrease others [2]. From Fig. 2.1, dQ/dt is the slope of the flow rate per time curve. The flow rate usually skews to the right, meaning that the decline of Q during closing is faster than the increase in Q during opening. The maximum slope of Q during closing is known as the maximum flow declination rate (MFDR). MFDR is highly correlated with acoustic intensity [3]. Since Q is equal to the velocity times the area, MFDR can be increased by increasing the rapid closure of the glottis or by increasing the rapid velocity deceleration of the flow exiting the glottis. The majority of the acoustic energy is produced during this rapid flow shutoff [4].

It is important to note that the source of sound, unlike in a loudspeaker, is not due to vibrations alone. Instead the source of sound is the change in flow rate at the glottal exit. Sound is a pressure wave or wave with constantly varying pressure. In laminar flow, pressure (P) is equal to the flow rate (Q) times the resistance (R) or $P = QR$. Thus, a constantly changing flow rate as is seen in Fig. 2.1 will produce a pressure wave. The area change is directly determined by the vibrations and can be seen by videostroboscopy. We do not currently have any clinical way to measure the velocity, which is one reason why a strobe can be normal with abnormal voice and vice versa. As Verneuil et al. [5] say: "For example, vocal folds with a normal appearance and no demonstrable physiologic deficit may produce poor vocal quality. Conversely, inflamed irregular vocal folds may produce surprisingly good voice. Information about the glottal energy source is required to improve our understanding of the relationship between laryngeal physiology and acoustics in normal and diseased states." The term "glottal energy source" refers to the glottal flow rate waveform. The flow rate can be measured clinically by an indirect method that uses a Rothenberg mask placed over the mouth and nose. This method uses assumptions that have not been validated and the Rothenberg mask is used mostly in research.

Strictly speaking, the acoustic intensity is not proportional to the amplitude of the mucosal wave but to the rapid closing of the mucosal wave, although these two properties are likely related. However, amplitude is only one factor related to rapid closing. To understand the other factors, one has to understand the patterns and causes of vibration.

In the original aerodynamic-myoelastic theory of phonation, the closing of the glottis is attributed to Bernoulli forces [6]. The Bernoulli law, which assumes inviscid flow, says that pressure and velocity are inversely proportional. The law of conversation in fluid mechanics says that in steady flow, area × velocity is a constant. For example, in a constricted hose, the area decreases, the velocity increases, and the pressure will decrease. During opening the glottis is convergent. At the superior aspect of the glottis, the area is the smallest, the velocity is the highest, and the pressure is the lowest. During closing, the glottis is divergent; at the superior aspect, the area is the highest and the velocity is the lowest. By the Bernoulli law, the pressure will be the highest at the superior aspect of the glottis; however, the opposite is seen in experiments (Table 2.1).

Table 2.1 Description of terms

Concept or formula	Description
$Q = Av$	In steady flow in a pipe the flow rate is constant. If the area of the pipe increases, the velocity will decrease and vice versa
$P + ½\,\rho\, v^2 = \text{constant}$	The Bernoulli law. P is the pressure, ρ is the density, and v is the velocity. This law states that if pressure decreases, velocity will increase and vice versa
Change in area of a pipe	If the area increases, velocity will increase and pressure will decrease and vice versa

Intraglottal Pressures

Intraglottal pressures have been measured experimentally in an excised canine larynx using a hemilarynx preparation [7, 8]. The canine larynx is the most similar larynx to the human in terms of anatomy and size. There is not a well-defined ligament in the canine, but behavior of the mucosal waves are very similar. In the hemilarynx preparation, all tissue is removed from the vocal folds. Then one-half of the thyroid cartilage and the adjacent paraglottic tissue and vocal fold are removed. The remaining vocal process, arytenoid, and anterior thyroid cartilage are sealed to a plexiglass plate. Two 1 mm large pressure transducers are placed in the plexiglass plate, one in the superior glottis and one in the inferior. The canine glottis is typically 3 mm high. Measured pressures are shown in Fig. 2.2. The x-axis refers to the phase of vibration where 0° marks the point of opening and one cycle is 360°. The dark lines represent pressures measured in the canine hemilarynx in our lab [7]. The lighter lines are

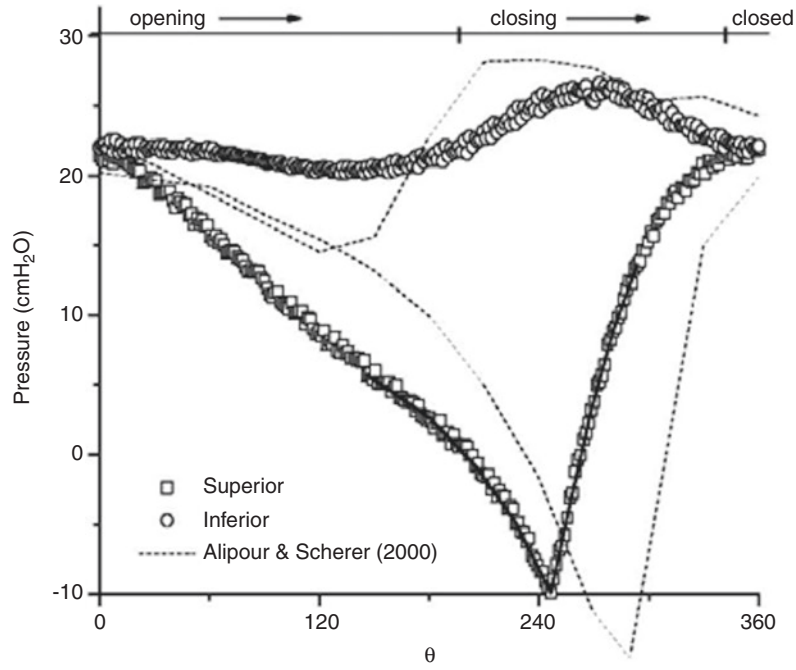

Fig. 2.2 Measured pressures in the canine hemilarynx model. The top lines are taken from the inferior glottis. The lines with negative pressures are taken from the superior glottis. The phase of vibration is on the *x*-axis, where one vibration cycle is equivalent to 360°. (From Alipour and Scherer [7], with permission. The dashed lines represents data from that source)

from another team and general trends are similar. The pressure on the *y*-axis is relative to atmospheric pressure. In the superior glottis, the pressure is actually negative during the latter part of closing; this is opposite of predictions made by the Bernoulli law. Negative pressure means that the pressure is lower than atmospheric pressure and will cause a suction force.

To understand the origin of the negative pressures, one needs to understand the velocity fields in the divergent glottis during closing. Velocity has a magnitude and a direction and is therefore a vector. A picture showing the direction of the vector at selected points is known as a field, and the lines connecting the vectors are known as streamlines. The closer the streamlines are, the higher the velocity and the lower the pressure. Until relatively recently, the velocity fields inside the glottis during vibration were not measured experimentally, so assumptions were made. The three main assumptions are shown in Fig. 2.3. Figure 2.3a shows that the flow stays attached to the wall, which in this case is the medial aspect of the folds. Figure 2.3b shows the flow separating from the

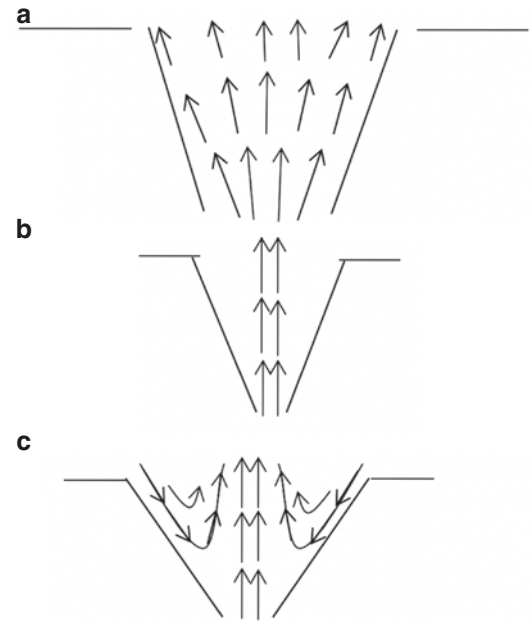

Fig. 2.3 Velocity fields in the divergent glottis during closing (see text). (**a**) Flow follows walls of divergent duct. (**b**) Flow separates from wall, no vortices. (**c**) Flow separates from wall—vortices form

wall, which is a phenomenon known as flow separation. There are many physical flows that have separation, but this occurrence is known to occur in a divergent duct. Vortices, or areas of rotational motion, normally form between the wall and the separated jet of flow, but vortices are more complicated to model computationally, so an assumption has been made to ignore them. Figure 2.3c shows the vortices. These vortices will produce negative pressures. As previously noted, a negative pressure is lower than atmospheric and will produce a suction force. This suction force assists in the glottis closing faster. A faster closing will result in an increase in MFDR and, therefore, an increase in acoustic intensity.

Figure 2.4 shows an example of the intraglottal velocity fields between the folds during closing. Flow can be seen entering and exiting the sides of the glottis on both sides. This rotational flow produces the measured negative pressures in the hemilarynx. Even greater negative pressures are produced in the full larynx. It can be seen that the flow separates from the medial surface of the fold. As mentioned previously, this negative pressure is not predicted by the Bernoulli equation. This is because the Bernoulli equation does not apply when there is flow separation. We will refer to this intraglottal rotational motion as flow separation vortices. In physical divergent ducts, flow separation will occur for a divergence angle greater than 7°. As the angle increases up to a certain point, the vortex strength and thus the negative pressure will also increase. This negative pressure creates a suction-like force that helps close the glottis.

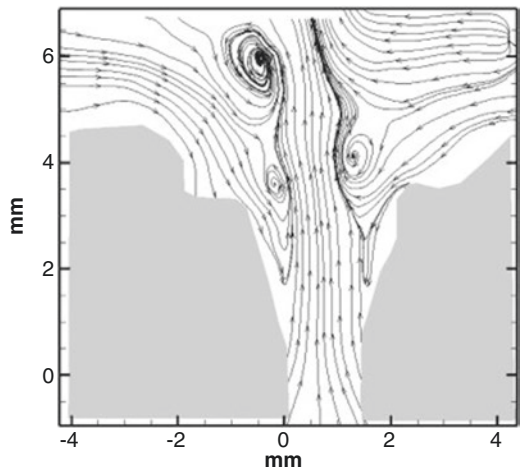

Fig. 2.4 Velocity fields in a divergent glottis during closing in an excised canine larynx

Material Properties of the Vocal Fold

One possible reason for the divergent shape during closing is due to the material properties of the fold. Chettri et al. [9] used an indentation test to measure Young's modulus of the medial surface in the superior and inferior aspect of the fold. A 1 mm probe was used. The probe was displaced various amounts in the lateral direction, the fold was locally compressed by the probe in a direction perpendicular to the medial surface of the fold, and the force for each displacement was recorded. From these measurements, stress-strain curves were calculated. Similar measurements were made in our lab [10]; an example is shown below in Fig. 2.5. At low strains, or displacements, the superior edge is about as stiff as the inferior edge. However as the displacement becomes greater, the inferior edge becomes much stiffer. This means that at similar intraglottal pressures, the superior aspect of the glottis will displace more laterally. The hypothesis for this

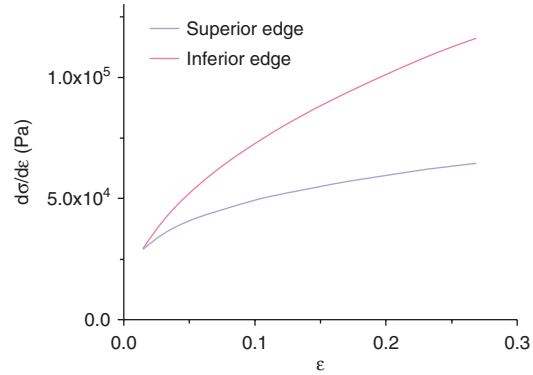

Fig. 2.5 Stress strain curves for the inferior 1 mm and superior 1 mm of the canine vocal fold. The fold is more stiff inferiorly than superiorly

stiffness gradient proposes that the insertion of the conus elasticus on the inferior edge produces the increases stiffness, especially as displacement increases and the conus is stretched more. Increasing subglottal pressure will increase displacement; thus it is expected that increasing subglottal pressure will increase the divergence angle, which is what is seen experimentally. A greater divergence angle is associated with stronger vortices and greater negative pressures; this results in a stronger suction force during closing which produces a higher MFDR and a louder voice.

This difference in elasticity is known as the vertical pressure gradient and varies as the subglottal pressure varies. Figure 2.6a shows the distance or displacement between the folds as a function of phase for three different subglottal pressures. Since the length of the folds is constant, the displacement is proportional to the area between the folds. At low subglottal pressures, the curve is fairly symmetric. On the other hand, the displacement curves are skewed to the right for moderate and high subglottal pressures. At low subglottal pressures, the divergence angle is minimal and there are no vortices and therefore no negative pressures causing additional closing forces. On the other hand, at higher subglottal pressures, there are vortices and the associated negative pressures cause rapid closing of the area curve or skewing of the curve to the right. The velocity curves are shown in Fig. 2.6b. The negative pressures in the superior glottis are also shown as dashed lines. Since the low subglottal pressure does not produce a divergent glottis, and therefore no vortices, there is no associated negative pressure. The negative pressure produces an additional pressure gradient between inferior and superior aspects of the fold. This increased gradient results in increasing velocity. The velocity suddenly decreases because the folds close rapidly. Both the increase and decrease contribute to the skewing of the velocity curve. Since flow rate is equal to velocity times the area, skewing of both velocity and area curves will cause skewing of the flow rate curve and an increase in MFDR. Thus, increasing divergence angle is one way of increasing SPL (sound pressure level, correlated with the perception of loudness) and the amount of higher harmonics. Opera singers can produce higher SPL at similar subglottal pressures compared to music theater singers, and it is also shown that opera singers produce a higher divergence angle [11].

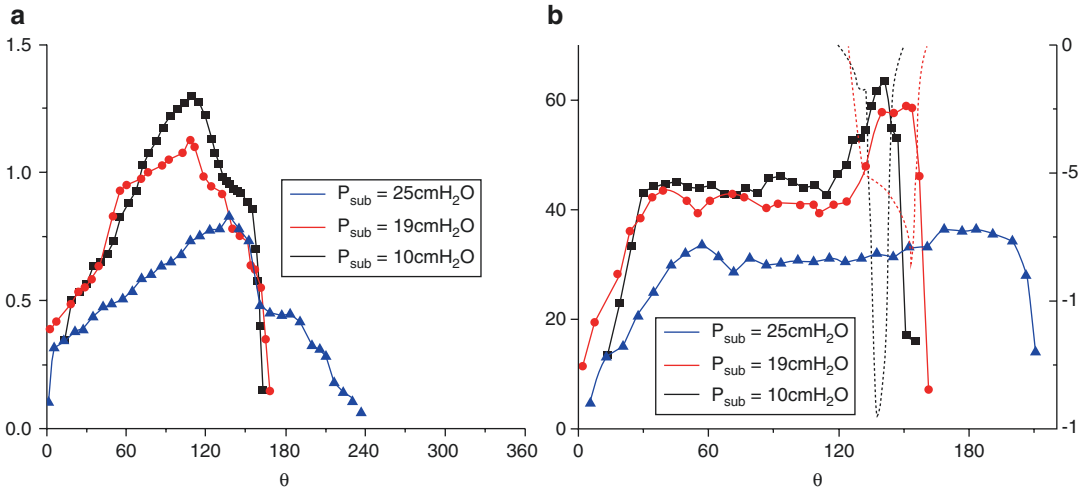

Fig. 2.6 (**a**) Displacement (mm) between folds halfway between the anterior commissure and vocal process at three different subglottal pressures. Note skewing of the wave at moderate and high subglottal pressures. (**b**) Velocity (m/sec) on the left vertical axis and negative pressures in the superior glottis (cm H_2O) for three subglottal pressures. There are no negative pressures for the low subglottal pressure. Note a second peak in velocity associated with the negative pressures for the moderate and high subglottal pressures

Titze [12] notes that in order to sustain vibration, the intraglottal pressures during closing do not have to be negative but they have to be less than the pressures during opening. As previously discussed, two types of forces producing this pressure differential are the positive inferior intraglottal pressures during opening and the negative superior pressures during closing. Two additional forces are due to vocal tract inertance and elastic recoil.

Forces Involved During Vocal Fold Closing

The air in the glottis and vocal tract primarily acts as a mass of air that is accelerated during opening and decelerated during closing; this phenomenon is known as inertive vocal tract loading. During opening, the air column in the vocal tract and glottis is being accelerated requiring a positive intraglottal and glottal exit pressure. During deceleration, the mass continues its forward momentum causing a reduced or negative intraglottal pressures. This effect is increased with increased vocal tract constrictions (such as caused by false fold compression). This effect does not occur without a vocal tract. The experiments previously described in excised canine larynges do not have a vocal tract.

Vocal folds have been modeled as a combination of mass, damper, and spring components. Elastic recoil specifically refers to the spring element. During opening, the vocal fold moves laterally and the spring is compressed. During closing the spring will lengthen due to elastic recoil of a compressed spring. This lengthening causes the fold to move medially. The greater the subglottal pressure, the more the spring will be compressed, and the greater the elastic recoil. However, because of friction, the forces available for closing will always be less than the force required to compress the spring; thus the skewing of the area curve cannot be explained by the elastic recoil forces.

Properties of Sound Produced

The sound produced at the glottal exit is composed of a fundamental frequency and multiples of the fundamental frequency. These multiples are known as harmonics. Acoustic energy at frequencies other than the fundamental or harmonics is perceived as noise. This noise is often perceived as a roughness or breathiness and can be seen in multiple conditions including glottic insufficiency, turbulent airflow, and irregular vibrations. Acoustic measures, such as the signal-to-noise ratio, measure the amount of acoustic energy in the harmonics relative to the energy between the harmonics. The amount of acoustic energy in the higher harmonics will increase as the MFDR increases, and these higher harmonics are important for intelligibility in noise.

The fundamental frequency will be increased by increasing the length or tension of the vocal fold cover or by decreasing the area. Lengthening the fold has much greater effects on increasing tension. Cricothyroid activation will lengthen the vocal fold, decrease the area, and increase the tension of the cover, all changes that will increase frequency. The effect of the thyroarytenoid depends on how much of the fold is vibrating. At low amplitudes of vibration which predominantly involve the cover (which includes the endothelium and superficial lamina propria), thyroarytenoid contraction reduces the length and tension of the cover and will lower the fundamental frequency. If the amplitude is larger and involves the vocalis muscle, contraction of the thyroarytenoid increases tension of the muscle and frequency will be increased [13].

The vocal tract has different resonances depending on the size of cavities and constrictions. Resonance refers to an increase in the acoustic energy of a specific harmonics. The specific harmonics are referred to as formants and vowels and consonants are often associated with specific formants.

Summary

This chapter focuses on two main questions. First, what are the mechanisms for vocal fold vibration? Second, what is the mechanism for sound production? The mechanisms for vibration include positive pressure and Bernoulli forces during opening and elastic recoil and suction forces produced by vortices during closing.

Actual measured pressures in the excised canine hemilarynx show that the Bernoulli law does not apply during the closing phase of vibration. As displacement increases, the vocal fold becomes stiffer inferiorly relative to the superior aspect of the folds. Vocal fold vibration does not directly produce sound. Instead the vibration produces changes in the flow rate exiting the glottis. This modulation of flow produces sound, which is then modified by the vocal tract. The majority of the sound is produced during the latter part of closing and can be characterized by the maximum flow declination rate (MFDR). Higher MFDR will produce greater acoustic intensity and more energy in the higher harmonics.

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Neuroanatomy of Voice and Swallowing

3

Nicole Y. K. Li-Jessen and Chelsea Ridgway

Introduction

The sensorimotor integration of vocalization and swallowing share an intertwined neuroanatomy of the larynx. A precise coordination of the central nervous system (CNS) and the peripheral nervous system (PNS) is integral to proper voice and swallowing functions. The CNS is part of the nervous system located inside the cranium and the vertebral column. The CNS includes the cerebral cortex, the cerebellum, subcortical structures, the brainstem, and the spinal cord. Within the CNS, volitional motor controls of voice production and swallowing involve the activation of cortical and subcortical substrates. In particular, the laryngeal motor cortex within the region of the primary motor cortex (M1) is responsible for controlling the movement of laryngeal musculature for voice and swallowing in humans. The central generation of movement patterns specific to voice and swallowing musculature is now recognized via a collection of interneurons (i.e., nuclei) at the brainstem level (Fig. 3.1).

The PNS is located outside the cranium and vertebral column that connects the CNS to sensory receptors, muscles, and glands of the human body. The PNS includes 12 pairs of cranial nerves and 31 pairs of spinal nerves emerging respectively from the brainstem and various segments of the spinal cord. A peripheral nerve comprises a group of nerve fibers. Each nerve fiber is a long projection of a neuron, i.e., a nerve cell. Neurons can be classified as sensory (afferent) or motor (efferent). Afferent neurons relay nerve impulses from sensory receptors, such as mechanoreceptors in laryngeal joints and superficial mucosae, to the CNS. Efferent neurons transmit motor impulses from the CNS to effector organs such as striated muscles and salivary glands. Most cranial nerves carry a mixture of sensory and motor neurons. In particular, cranial nerves V, VII, IX, X, XI, and XII are involved in sensory, special sensory, and motor functions of voice and swallowing control, in which their cranial nuclei are located in various segments of the lower brainstem (Fig. 3.2). In this chapter, both neuromotor and somatosensory systems specific to the laryngeal control for voice and swallowing functions are reviewed.

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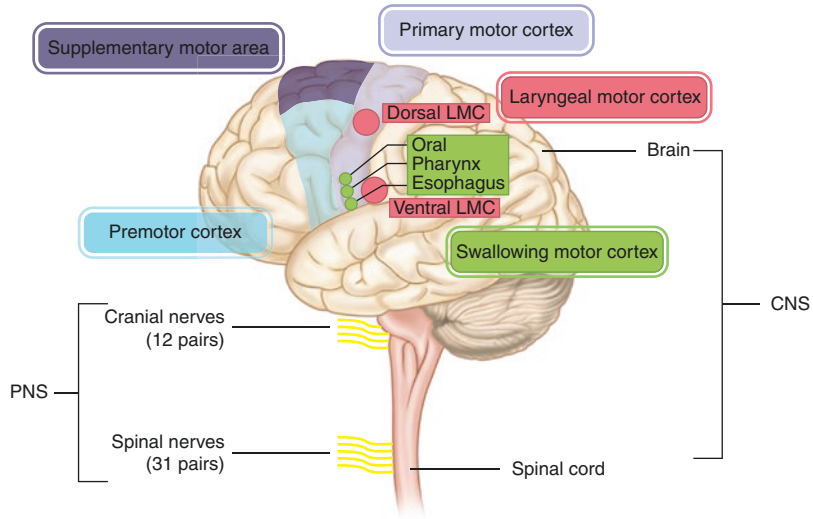

Fig. 3.1 Lateral view of the central and peripheral nervous systems. The central nervous system (CNS) is composed of structures from the brain to the spinal cord. The peripheral nervous system (PNS) is composed of 12 pairs of cranial nerves and 31 pairs of spinal nerves. Specific locations such as the laryngeal motor cortex and the swallowing motor cortex within the primary motor cortex are illustrated. The laryngeal motor cortex (LMC) is important for both human vocalizations and airway protection. Within the LMC, the dorsal laryngeal motor cortex (dLMC) is hypothesized to be the primary region providing motor controls of voice production, whereas the ventral laryngeal motor cortex (vLMC) is hypothesized to be involved in unspecified aspects of voice control. The swallowing motor cortex is the primary region that provides motor control of oral, pharyngeal, and esophageal phases in swallowing. The vLMC is also involved in swallowing since it controls important movements of the larynx for airway protection

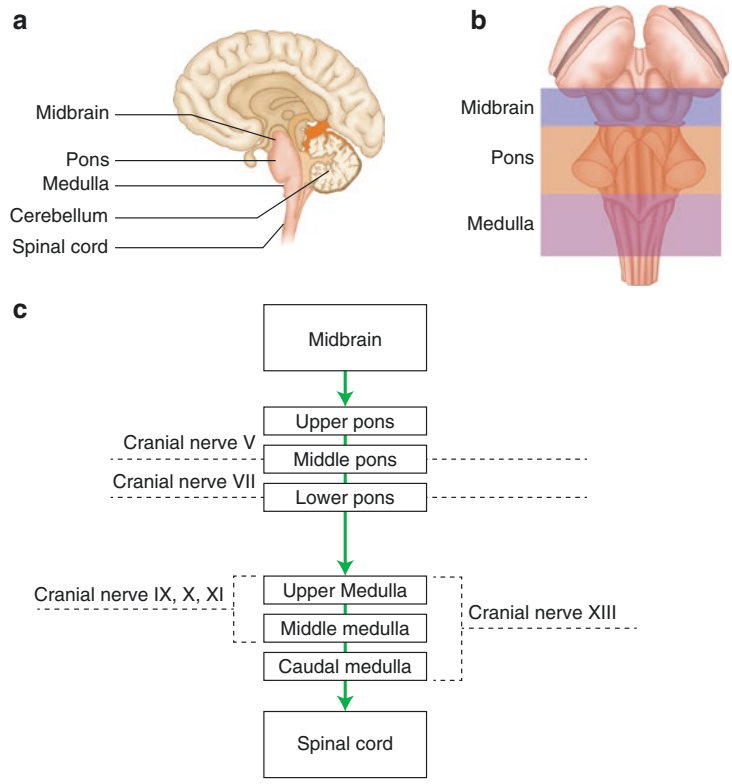

Fig. 3.2 The neural organization of human brainstem. (**a**). The sagittal view of the brainstem in correspondence to the location of the cerebellum and the spinal cord. (**b**). The dorsal view of the brainstem shows the location of midbrain, pons, and medulla. (**c**). A schematic diagram showing cranial nerves at distinct levels of the brainstem

Neuromotor Systems of Voice Production

Central Nervous System in Voice Control

Central neural control of human voice production is executed in two parallel pathways for learned and innate vocalizations, respectively. One of them is the *laryngeal motor cortical pathway* that controls voluntary voice production such as speaking and singing. The other one is the *limbic vocal control pathway* that modulates innate nonverbal and emotional vocalizations such as in response to pain and fright. The limbic (emotional) part of the brain, namely, the anterior cingulate cortex (ACC) and the midbrain periaqueductal gray (PAG), is involved in the limbic vocal pathway. Both pathways are organized hierarchically from the lowest level—the brainstem—to the highest level—the laryngeal motor cortex (LMC). At the lowest level, motor nuclei of extrinsic muscles are located near the hypoglossal nucleus, whereas those of intrinsic laryngeal muscles are mainly situated within the nucleus ambiguous (NA) of the brainstem. Within the pons and the medulla, the reticular formation and motor nuclei receive input from the LMC and the ACC-PAG pathways and generate complex vocal patterns for the coordination of laryngeal motor activities. At the level above, the ACC and the PAG are responsible for the voluntary initiation and emotional vocal responses. As the highest level of voice production control, the LMC is responsible for the direct control of highly skilled learned laryngeal movements in human voice production for speaking and singing [1–10] (Fig. 3.3).

The LMC is located in area 4 of the primary motor cortex (M1) in the frontal lobe of the brain [6]. The LMC has direct connections to the laryngeal motor neurons for all laryngeal muscles via the corticobulbar tract wherein a collection of motor neurons projects from the cerebral cortex. In addition, the LMC has an extensive, indirect neural network of cortical and subcortical connections to laryngeal motor neurons in the brainstem. Such subcortical loops modulate vocal motor commands from M1 through structures of putamen, pontine gray matter, globus pallidus, and cerebellum. Subsequently, the modified motor program is sent back to M1 via the ventrolateral thalamus [11, 12]. In addition, two specific regions of LMC, namely, the dorsal laryngeal motor cortex (dLMC) and the ventral laryngeal motor cortex (vLMC), have been proposed for distinctive functions in voice control. The dLMC, which is located between the cortical representation of the lips and the hand in M1, is assumed to be responsible for both auditory and motor responses of vocal pitch control. The vLMC, which is located at the bottom of M1, is now better known as a laryngeal motor control center for swallowing, with unspecific voice controls as well [13] (see Fig. 3.1).

Nearly all laryngeal muscles receive bilateral cortical innervation from the LMC. That is, each half of the larynx is controlled by both left and right LMC. Thus, unilateral lesions to the LMC rarely result in vocal fold paralysis and patients preserve the ability of voluntary voice control. In contrast, CNS-related vocal fold paralysis is mostly seen in patients with lateral medullary stroke syndrome, also known as Wallenberg syndrome [14]. For patients with bilateral injury to the LMC, they may encounter dysarthria and apraxia of speech. Their nonverbal emotional vocalizations would be minimally affected, as the innate vocalization is controlled separately via the ACC-PAG pathway [15]. Emerging evidence suggests that spasmodic dysphonia is due to disturbances at the highest level of central voice control [8]. Patients with spasmodic dysphonia exhibit laryngeal spasms specific to speech tasks, but preserve an innate and emotional expression such as laugh, cry, and shouting [16]. This clinical observation further supports the separate CNS control of voice for speech and of emotional expression in concordance with the paradigm of dual pathways for vocalization [8].

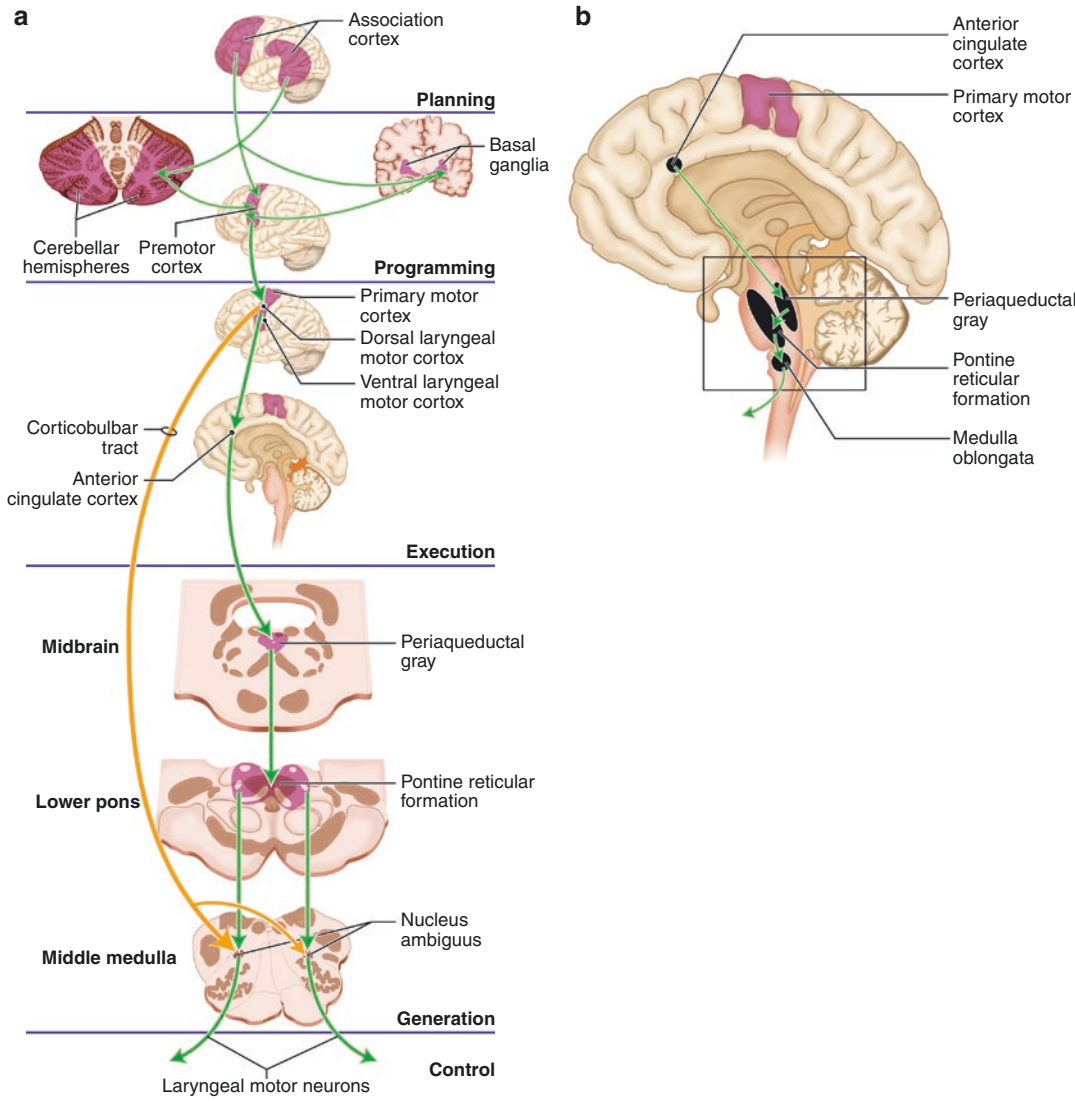

Fig. 3.3 Motor control of voice production in human central nervous system. (**a**) The motor control of voice is initially planned in the association cortex. From there, the cerebellar hemispheres and basal ganglia work in parallel to program the vocalization. The information is then sent to the premotor cortex, which is in turn passed to the dorsal and ventral laryngeal motor cortex within the primary motor cortex. Once the laryngeal motor cortex (LMC) is reached, the information is organized into two separate pathways: the LMC pathway and the limbic vocal control pathway. For the LMC pathway, direct connections from the LMC to the laryngeal motor neurons via the corticobulbar tract are established. For the limbic vocal control pathway, the transmission of information continues from the LMC on to the anterior cingulate cortex (ACC) in the limbic lobe and then into the brainstem to the reticular formation in the pons via the periaqueductal gray (PAG). Signals then travel to the nucleus ambiguus of the medulla where the laryngeal motor neurons are located. (**b**) The sagittal view of the brain demonstrates the limbic vocal control (ACC-PAG) pathway. Specifically, the pathway found in the black box corresponds to the limbic vocal control pathway in the midbrain, lower pons, and middle medulla as illustrated in (**a**)

The Peripheral Nervous System in Voice Control

Two sets of laryngeal muscles, namely, intrinsic and extrinsic, control the movement and posture of human vocal folds and larynx. Intrinsic laryngeal muscles are involved in the adduction, abduction, lengthening, and shortening of the vocal folds. These muscles include thyroarytenoid (TA), lateral cricoarytenoid (LCA), interarytenoid muscles (IA), posterior cricoarytenoid muscle (PCA), and cricothyroid muscle (CT). All intrinsic laryngeal muscles, with the exception of the IA as the only unpaired muscles in the larynx, are supplied by ipsilateral motor neurons. Of note, laryngeal motor neurons receive bilateral *cortical* inputs from the higher level of the brain as discussed in *The Central Nervous System in Voice Control*. Laryngeal muscles are thus always seen as being activated bilaterally [17]. The two branches of the tenth cranial nerve (i.e., vagus nerve), namely, the superior laryngeal nerve (SLN) and the recurrent laryngeal nerve (RLN), provide motor innervations to intrinsic laryngeal muscles. Simply put, the external branch of the SLN (eSLN) supplies motor fibers to the CT, whereas the RLN is the motor nerve for all other intrinsic laryngeal muscles (Table 3.1). There is also evidence of significant neural connections existing between the SLN and the RLN. Galen's anastomosis, for instance, is now recognized as a direct communication nerve between the most inferior portion of the internal branch of the SLN and the posterior division of the RLN [18, 19]. Dual innervation from the RLN and the SLN may thus occur in some intrinsic laryngeal muscles.

On the other hand, extrinsic laryngeal muscles are primarily involved in elevating or lowering the position of the larynx as well as in adjusting the length of the vocal tract, resulting in changes in fundamental frequency and supraglottic resonance of the voice. These muscles include digastricus, mylohyoid, geniohyoid, stylohyoid, hyoglossus, genioglossus, sternohyoid, thyrohyoid, omohyoid, and sternothyroid. Their motor innervation is supplied via cranial nerves (V, VII, XII) and ansa cervicalis, which is comprised of spinal nerves (C1-C3) (Table 3.2).

Superior Laryngeal Nerve The superior laryngeal nerve (SLN) arises from the inferior ganglion of the vagus nerve and receives a branch from the cervical sympathetic ganglion of the sympathetic nervous system (Fig. 3.4). The SLN divides into larger internal and smaller external branches approximately at the level of the hyoid bone. The internal branch of the SLN (iSLN) is about 7 cm long and 1.8–2.0 mm thick [20], whereas the external branch of the SLN (eSLN) is about 8 cm long and 0.2 mm thick [21]. The iSLN carries sensory neurons to the mucosa from the epiglottis to the level of the vocal folds.

Table 3.1 Motor innervation of the intrinsic laryngeal muscles for voice production

Overall roles	Cranial nerves	Branches	Effectors	Functions
Fine motor control of phonatory muscles	Vagus nerve (X)	Superior laryngeal nerve—external branch	Cricothyroid muscle	Adducts and tenses vocal folds
		Recurrent laryngeal nerve	Posterior cricoarytenoid	Abducts vocal folds
			Lateral cricoarytenoid	Adducts vocal folds
			Transverse arytenoid	Adducts vocal folds
			Oblique arytenoid	Adducts vocal folds
			Thyrovocalis (medial thyroarytenoid)	Tenses vocal folds
			Thyromuscularis (lateral thyroarytenoid)	Relaxes vocal folds

Table 3.2 Motor innervation of the extrinsic laryngeal muscles for voice production

Overall roles	Cranial/spinal nerves	Effectors	Functions
Changes vocal tract length and position	Cervical spinal nerves 1, 2, and 3	Sternohyoid	Depresses larynx
		Sternothyroid	Depresses larynx
		Omohyoid	Depresses larynx
	Cervical spinal nerve 1	Thyrohyoid	Elevates larynx
	Trigeminal nerve (V)	Mylohyoid	Elevates larynx
	Facial nerve (VII)	Stylohyoid	Elevates larynx
	Trigeminal nerve (V)—anterior belly of digastrics Facial nerve (VII)—Pposterior belly of digastrics	Digastric	Elevates larynx
	Hypoglossal nerve (XII)	Geniohyoid	Elevates larynx
		Hyoglossus	Elevates larynx
		Genioglossus	Elevates larynx

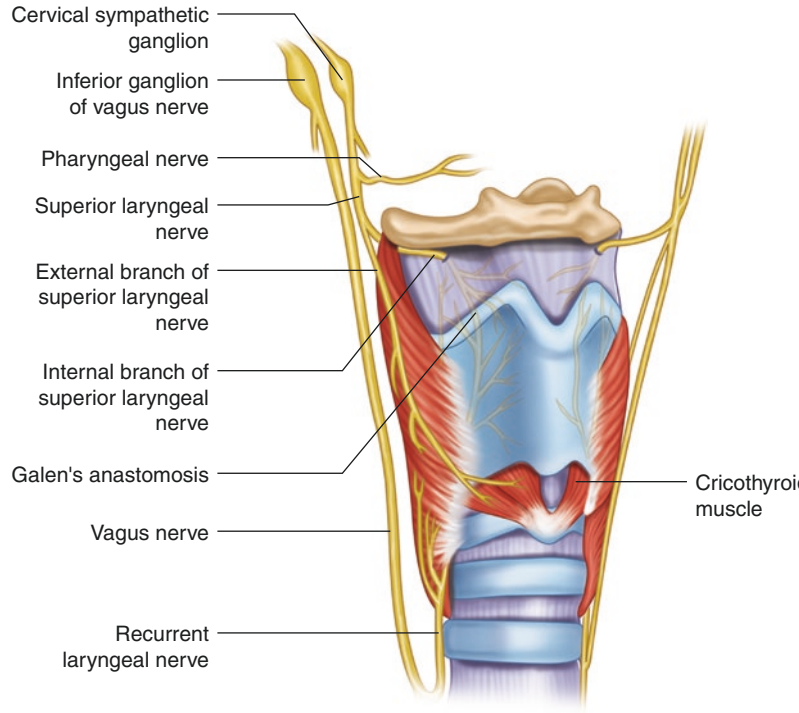

Fig. 3.4 Sensory and motor innervation of the superior laryngeal nerve. The lateral view of the larynx with the internal and external branches of the superior laryngeal nerve. The cricothyroid muscle is innervated by the external motor branch of the superior laryngeal nerve. The internal sensory branch of the superior laryngeal nerve supplies the supraglottic and glottic regions of the larynx. The Galen's anastomosis is also identified as a direct communication nerve between the most inferior portion of the internal branch of the superior laryngeal nerve and the posterior division of the recurrent laryngeal nerve

The details of their sensory functions are presented in *Sensory Components Specific to Voice Control.* The eSLN, which contains mainly motor neurons, travels below the sternothyroid muscle deep to the superior thyroid artery. The eSLN provides motor innervation to the CT primarily but perhaps also to some laryngeal adductors such as the TA [22, 23]. In fact, accumulating data suggests that the motor innervation is more complex than previously thought. A dual motor innervation was reported in some intrinsic laryngeal muscles. The terminal portion of the RLN, i.e., *the inferior laryngeal nerve*, branches off an anterior motor division and a posterior sensory division. Although the eSLN is the primary motor nerve for the CT, a few motor neurons from the anterior division of the RLN may innervate the muscle as well [24].

The adductor IA may also receive a dual motor innervation from the SLN and the RLN in which the iSLN is suggested to provide a secondary motor innervation. Although the iSLN has been thought to comprise purely sensory neurons, emerging anatomical data from canines and human cadavers suggest that the iSLN may comprise a mix of sensory and motor neurons. In particular, two branches from the RLN and up to six branches from the iSLN may contribute to the IA innervation [25–28]. The iSLN along with the eSLN may further contribute to the motor innervation to some muscle fibers within the ventricular folds (false vocal folds) that connect between the epiglottis and the arytenoid. Such neural organization implicates that the SLN may be involved in the activation of supraglottic compensation for phonatory functions after unilateral RLN injuries [29, 30].

An isolated injury to the eSLN is not easy to diagnose due to subtle and unspecific clinical signs and symptoms. Injury to the eSLN during thyroidectomy, reported to be as high as 58%, can result in the paresis or paralysis of the CT [23, 31, 32]. Some patients may not encounter significant complications of the eSLN injury. Professional voice users may, however, experience perplexing problems in manipulating their vocal pitch and registers as well as vocal projection and stamina.

Recurrent Laryngeal Nerve The recurrent laryngeal nerve (RLN) carries several types of fibers, including motor fibers to all intrinsic laryngeal muscles except the CT, sensory fibers to the infraglottis and subglottis, and stretch receptors from the larynx (Fig. 3.5). The sensory component of RLN is reviewed in *Sensory Components Specific to Voice Control*. In terms of laryngeal motor control, the RLN carries motor neurons to adductors (TA, LCA, IA) and the only abductor (PCA) of the vocal folds. The RLN is named as "recurrent" because the nerve descends into the chest, makes a U-turn around the left aorta arch (left RLN) and the right subclavian artery (right RLN), and then travels back up to the larynx. The exact anatomic path of the RLN to intrinsic laryngeal muscles is described in great detail in the seminal review of Orestes and Berke [33]. In brief, both left and right RLN ascend the neck along a groove between the trachea and esophagus before reaching the larynx. The nerve diameter is similar, 1–3 mm, for both sides [34–36]. The left RLN is about 10 cm long and branches off from the vagus nerve in the thorax [37]. The left RLN loops around the arch of the aorta around the level of the fourth and fifth thoracic vertebrae and then ascends into the trachea-esophageal groove. The right RLN, on the other hand, is about 8.5 cm long and loops posteriorly under the right subclavian artery around the level of the first and second thoracic vertebrae [37]. The right RLN ascends alongside the trachea posterior to the common carotid artery. Both left and right RLN have highly variable relations to the inferior thyroid artery. Nonrecurrent laryngeal nerve (NRLN) is an example of anatomical variants that is associated with the vascular anomaly of aortic arch and supra-aortic vessels during embryologic development. Right NRLN is rare, constituting about 0.3–0.8% of general population. Left NRLN is even more rare, constituting about 0.004% of general population [38, 39]. In most NRLN cases, the RLN branches off directly from the vagus nerve at the cervical level and enters directly into the larynx. Given the inherent variability of the RLN structure, particular attention is required if the operative field is close to the inferior pole of the thyroid gland such as during thyroidectomy [40, 41].

When the RLN passes deep to the cricopharyngeus muscle and enters the larynx at the junction between the articulation between the inferior cornu of the thyroid and the cricoid cartilage, the nerve divides into an *anterior motor branch* and a *posterior sensory branch* (see Fig. 3.5). The anterior motor branch further divides into branches to the respective intrinsic laryngeal muscles. The organization of the abductor and adductor nerve fibers is arranged in a relatively loose pattern rather than in a discrete organization of bundles. Also, the RLN innervation to the PCA, IA, and LCA varies greatly between individuals [42]. Generally speaking, the innervation starts at the

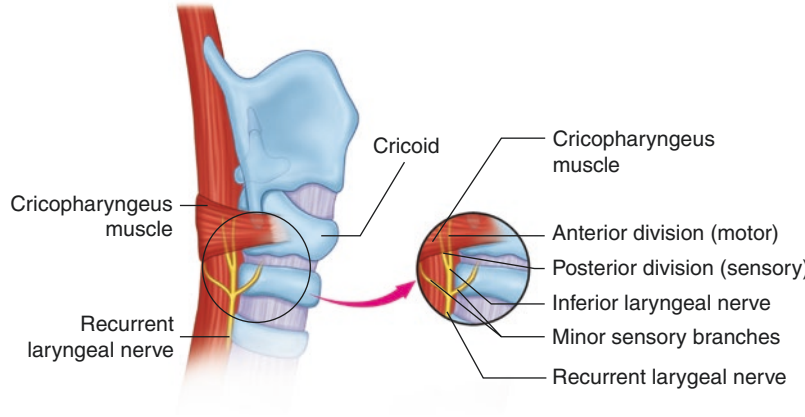

Fig. 3.5 Sensory and motor innervation of the recurrent laryngeal nerve. Two divisions branch off from the interior laryngeal nerve, which is the terminal portion of the recurrent laryngeal nerve. The anterior division provides sensory innervation to the subglottic area of the larynx. The posterior division provides motor innervation to all intrinsic laryngeal muscles except cricothyroid muscles

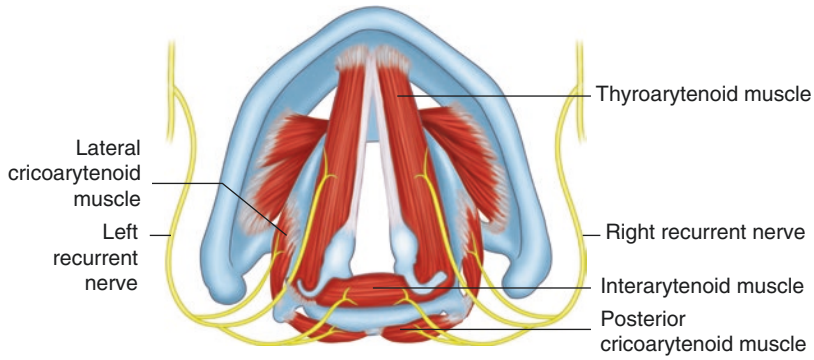

Fig. 3.6 Intrinsic laryngeal muscles innervated by the recurrent laryngeal nerve. The interarytenoid muscle receives a bilateral innervation from both the right and left recurrent laryngeal nerves. The posterior cricoarytenoid, lateral cricoarytenoid, and thyroarytenoid muscles receive an ipsilateral innervation from the recurrent laryngeal nerve

PCA, then the IA, followed by the LCA and the TA distally. Specifically, the nerve travels along the lateral margin of the PCA and crosses the inferior cricothyroid ligament. At this point, the nerve travels deep to the horizontal belly of the PCA as well as gives a branch off to the IA. Of note, IA is the only intrinsic laryngeal muscles receiving bilateral innervation from the RLN, whereas others receive ipsilateral innervation (Fig. 3.6). A complex neural network including some branches forming anastomoses with the iSLN has also been noted in the IA [33, 43–45]. Injury to the RLN can lead to a wide range of voice and swallowing impairments and thus an early detection of RLN paresis or paralysis is critical to provide timely medical care and behavioral rehabilitation [46].

Neuromotor Systems of Swallowing Functions

The Central Nervous System in Swallowing Control

Normal swallowing involves both volitional and reflexive motor acts in response to sensory inputs from the oropharynx, larynx, and esophagus. Simply put, several motor areas of the cerebral cortex initiate both spontaneous and volitional swallowing and direct cortical inputs descending to the brainstem via the corticobulbar tract. From there, motor outputs to the swallowing musculature are modified by central pattern generators

located within the brainstem. The primary cortical control of swallowing in humans is originally thought to lie within and lateral to the face area of the primary motor cortex (M1), whereas oral, pharyngeal, laryngeal, and esophageal muscles are individually represented within the motor cortex [47, 48]. Emerging data show that stimulation of multiple cortical loci could elicit swallowing [49–51], which include:

1. The lateral region of the face in M1
2. An area immediately lateral and anterior to face in M1
3. The lateral region of the face in S1
4. Deep regions in the underlying white matter

The trigger of a swallow often requires a continuous train of stimulations and an integration of multiple sensory inputs from the cortex to evoke the brainstem swallowing system [5, 52–54]. Other cortical and subcortical areas are also involved in optimizing and synchronizing the highly complex swallowing acts. For instance, the ACC may be involved in the premotor and/or attentional processing before the swallow as well as the integration of sensory information during the swallow [51, 55].

Most of aforesaid cortical areas have neural connections between the two hemispheres and descending projections to the motor nuclei within the brainstem. A central neural network at the lower brainstem, now coined as central pattern generators, is proposed to sequentially activate and inhibit at least 25 pairs of muscles within the head and neck throughout phases of swallowing. This brainstem central network is modulated by both central inputs from the cortex and peripheral inputs from mucosal and mechanoreceptors of oropharyngeal muscles.

Specifically, four cranial motor nuclei are involved:

1. The nucleus ambiguus (NA) (with cranial nerves IX, X, and XI)
2. The trigeminal motor nucleus (V)
3. The facial motor nucleus (VII)
4. The hypoglossal nucleus (XII)

Two cranial sensory nuclei are also involved:

1. The nucleus tractus solitarius (NTS—with cranial nerves VII, IX, and X)
2. Specific regions of the trigeminal sensory nuclei (TSN—with cranial nerve V) [52, 56]

On each side of the brainstem, two main groups of interneurons, namely, a dorsal swallowing group (DSG) and a ventral swallowing group (VSG), act as central pattern generators of swallowing (Fig. 3.7). Each phase of swallow is generated by a distinct central pattern generator [52, 56]. Simply put, the DSG is responsible for generating the temporal-sequential rhythm of pharyngeal swallowing muscles. The swallowing command is then transferred to the VSG before distribution to specific motor nuclei. The DSG is situated next to the NTS within the dorsal medullary reticular formation and receives sensory inputs from the SLN of the vagus nerve, the glossopharyngeal nerve, as well as the cortex. The VSG, on the other hand, is situated next to the NA within the ventral medullary reticular formation. The VSG is responsible for relaying swallowing commands generated by the DSG to motor nuclei of cranial nerves V and VII in the pons as well as IX, X, XI, and XII in the medulla oblongata (Fig. 3.8). Lateral medullary lesions such as in Wallenberg syndrome can disrupt the DSG, the VSG, the NA, and the NTS, leading to significant sensory and motor impairments especially in the pharyngeal phase of swallowing.

The Peripheral Nervous System in Swallowing Control

Multiple cranial nerves, including the trigeminal (V), facial (VII), glossopharyngeal (IX), vagus (X), and hypoglossal nerve (XII), provide motor supplies to the swallowing musculature. A summary of anatomical branches, types (sensory vs. motor), innervation location, and functions of these cranial nerves is provided in Table 3.3 (motor functions) and Table 3.4 (sensory functions). Of concern to neuromotor functions, the glossopharyngeal and vagus nerves control the pharynx and

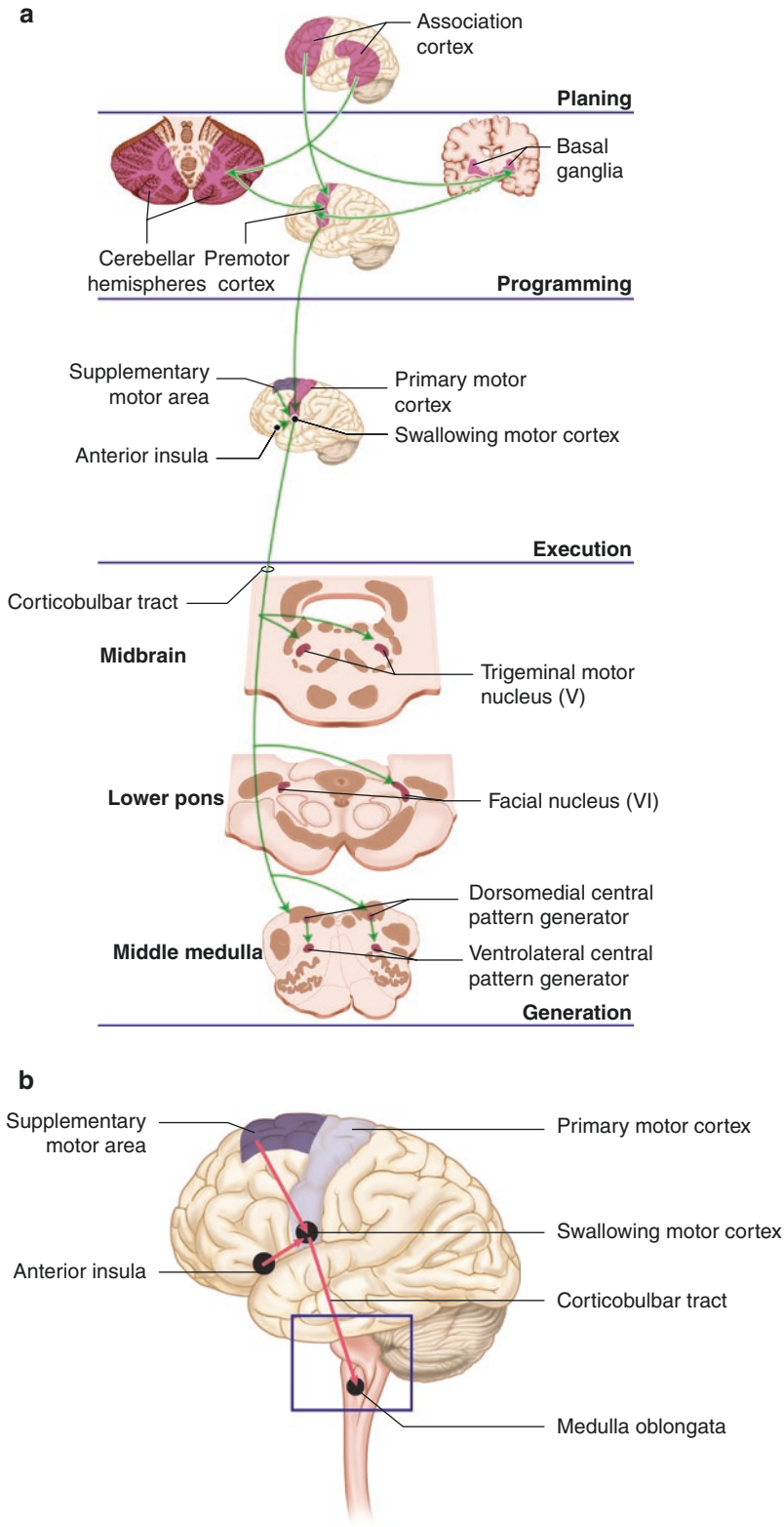
a
Association cortex
Planing
Basal ganglia
Cerebellar hemispheres
Premotor cortex
Programming
Supplementary motor area
Primary motor cortex
Swallowing motor cortex
Anterior insula
Execution
Corticobulbar tract
Midbrain
Trigeminal motor nucleus (V)
Lower pons
Facial nucleus (VI)
Dorsomedial central pattern generator
Middle medulla
Ventrolateral central pattern generator
Generation
b
Supplementary motor area
Primary motor cortex
Swallowing motor cortex
Anterior insula
Corticobulbar tract
Medulla oblongata

Fig. 3.7 Motor control of swallowing in human central nervous system. (**a**) The act of swallowing is initially planned in the association cortex. The cerebellar hemispheres and basal ganglia work in parallel to program the movement of the swallowing musculature and thereafter transmit this information to the premotor cortex. The premotor cortex passes this information to the swallowing cortex, which is located in the primary motor cortex. The swallowing motor cortex also receives input from the supplementary motor area and the anterior insula. Motor signals are then sent through the corticobulbar tract to ipsilateral and contralateral dorsomedial central pattern generators within the medulla oblongata. Signals are then further transmitted to the ventrolateral central pattern generators also within the medulla oblongata. The ventrolateral central pattern generator then distributes motor outputs to cranial nerves V and VII found in the pons and cranial nerve IX, X, XI, and XII in the medulla. The corticobulbar tract may also directly send information to the cranial nerve nuclei. (For the sake of simplicity, the diagram shows only one side of the pathway and ends with the ventrolateral central pattern generator.) (**b**) The lateral view of the left hemisphere demonstrates the overall motor pathway of swallowing. Specifically, the pathway found in the purple box corresponds to the pathway of the middle pons, lower pons, and middle medulla as illustrated in (**a**)

Fig. 3.8 Location of motor nuclei related to swallowing-related functions. (**a**). Cranial nerve nuclei V and VII are found within the pons, whereas cranial nuclei IX, X, XI, and XII are found within the medulla oblongata. The nucleus ambiguus is the location of motor nuclei for cranial nerves IX, X, and XI. (**b**). The sagittal view of the brain shows cranial nerve nuclei at various levels of the pons and medulla as illustrated in (**a**). (**c**). The dorsal view of the brainstem shows the location of corresponding cranial nerve nuclei residing in the pons and medulla oblongata

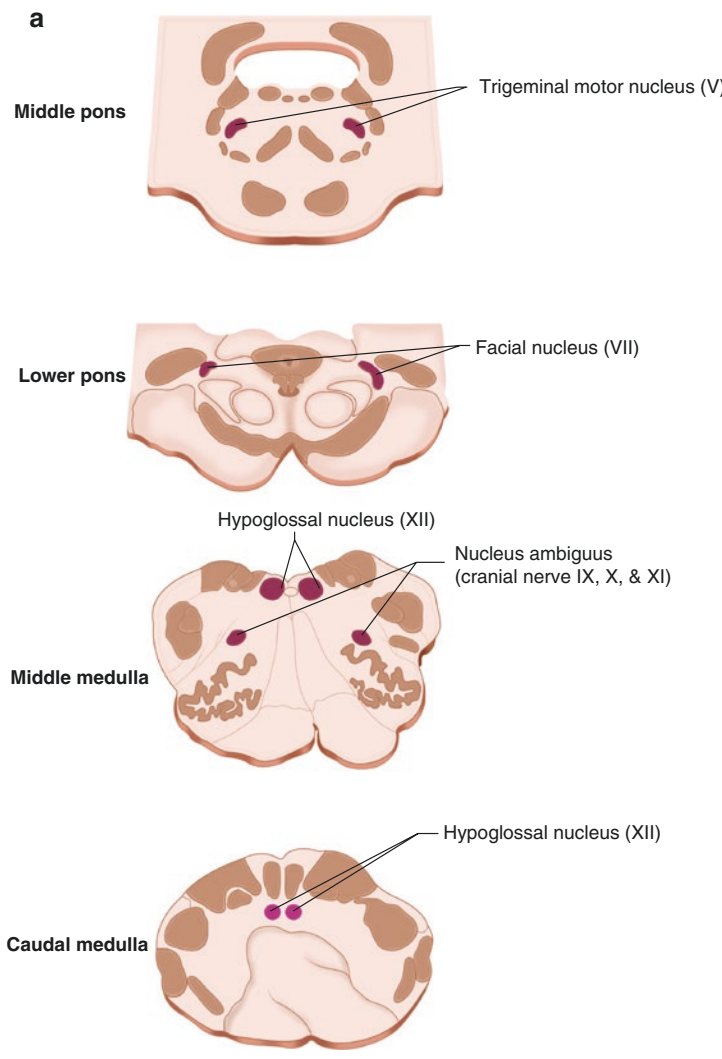

Fig. 3.8 (continued)

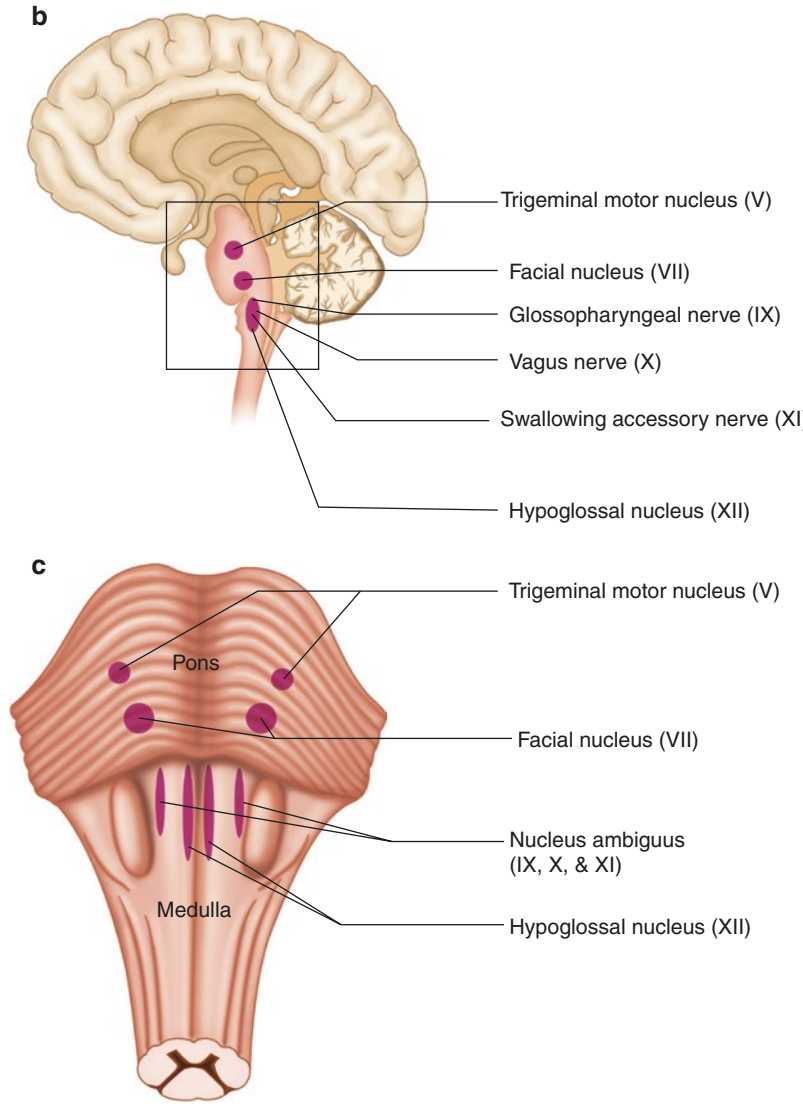

Table 3.3 Motor innervation of the cranial nerves important for swallowing

Cranial nerves	Types	Branches	Effectors	Functions
Trigeminal nerve (V)	Special visceral efferent	Mandibular division: deep temporal nerve, masseteric nerve, pterygoid nerves	Muscles of mastication: temporalis, masseter, medial and lateral pterygoid	Mastication
		Mandibular division: the mylohyoid nerve branch of the inferior alveolar nerve	Oral floor muscles: mylohyoid and anterior belly of digastric	Elevates hyoid bone and tongue
		Mandibular division: Medial pterygoid nerve	Pharyngeal muscles: tensor veli palatini	Tenses soft palate

Table 3.3 (continued)

Cranial nerves	Types	Branches	Effectors	Functions
Facial nerve (VII)	Visceral efferent	Chorda tympani: glandular branches	Small glands of the hard and soft palate Submandibular and sublingual glands Small salivary glands on the anterior two-thirds of tongue	Salivation
	Special visceral efferent	Stylohyoid branch	Stylohyoid	Draws hyoid bone backward to elevate tongue
		Digastric branch	Posterior belly of the digastric	Elevates hyoid bone
Glossopharyngeal nerve (IX)	Special visceral efferent	Pharyngeal branches	Constrictor muscles of pharynx	Pharyngeal branches join the vagus nerve to form the pharyngeal plexus
		Stylopharyngeal branch	Stylopharyngeus muscle	Elevates the larynx and pharynx Dilates the pharynx
	General visceral efferent	Tympanic nerve	Parotid gland Buccal and labial glands	Salivation
Vagus nerve (X)	Special visceral efferent	Pharyngeal branches	Pharyngeal muscles Muscles of the soft palate and uvula: levator veli palatine	Protects airway from foreign objects to enter the lungs
		Superior laryngeal nerve supplies cricothyroid Recurrent laryngeal nerve supplies other laryngeal muscles	All laryngeal muscles	Protects airway from foreign objects to enter the lungs
	General somatic efferent	Pharyngeal branch	Palatoglossus muscle of tongue	Elevates posterior tongue Closes oropharyngeal isthmus
Hypoglossal nerve (XII)	General somatic efferent—purely motor	N/A	All intrinsic and extrinsic muscles of the tongue except for the palatoglossus	Manipulates tongue movements

Table 3.4 Sensory innervation of the cranial nerves important for swallowing

Cranial nerves	Branches	Types	Receptors	Senses
Trigeminal nerve (V)	Lingual nerve	Somatic afferent	Anterior two-thirds of tongue	Touch, pain, temperature
Facial nerve (VII)	Chorda tympani (gustatory fibers)	Special visceral afferent	Taste buds in anterior two-thirds of tongue	Taste
Glossopharyngeal nerve (IX)	Lingual branch	Somatic afferent	Posterior one-third of tongue Soft palate Pharyngeal mucosa Tonsils (for gag reflex)	Pain, temperature, touch
	Lingual branch (gustatory fibers)	Special visceral afferent	Taste buds in posterior one-third of tongue	Taste

(continued)

Table 3.4 (continued)

Cranial nerves	Branches	Types	Receptors	Senses
Vagus nerve (X)	Gustatory fibers	Special visceral afferent	Taste buds on epiglottis	Taste
	Pharyngeal branches Superior laryngeal nerve—internal branch Recurrent laryngeal nerve	General visceral afferent	1. Mucosa of lower pharynx at junction with esophagus 2. Laryngeal mucosa above (1) and below (2) the glottic aperture	Touch, pain, temperature

larynx to protect the airway from liquid and solid bolus. During respiration, the pharynx needs to maintain a certain basal tone to prevent the upper airway from collapsing while the larynx remains in an open position for airflow. During swallowing, multiple pharyngeal and laryngeal acts are evoked, including the dilation of the pharynx, the elevation of the larynx, the approximation of ary-epiglottic folds and false vocal folds, as well as the adduction of the glottis. This motor response effectively helps direct the bolus from the pharynx toward the esophagus while closing off the larynx for airway protection [57–59].

In particular, the glossopharyngeal nerve has both sensory and motor components. The motor innervation to the base of the tongue and the lateral pharyngeal wall is part of the reflexive act of the pharyngeal swallow. Also, the glossopharyngeal nerve contributes to the pharyngeal plexus that controls the movement of pharyngeal constrictors in bolus propulsion and clearance. Moreover, an activation of parasympathetic fibers stimulates secretory cells within the parotid gland for the salivary response. An isolated glossopharyngeal nerve paresis or paralysis is uncommon; most cases are in combination with the vagus nerve and others.

On the other hand, the vagus nerve has various significant roles in the pharyngeal phase of swallowing. Three branches of the vagus nerve, namely, (1) the pharyngeal branch, (2) the SLN branch, and (3) the RLN branch, work in concert to facilitate the pharyngeal swallowing and airway protection. Specifically, the pharyngeal branch is the principal motor nerve of the soft palate and the pharynx that supplies all striated muscles except the tensor veli palatini (by the trigeminal) and the stylopharyngeus (by the glossopharyngeal nerve). Its motor innervation of the levator veli palatini is important to close off the nasal cavity from the oral cavity, preventing nasal regurgitation during the oral transit of the bolus. Its motor innervation of all pharyngeal constrictors (superior, middle, and inferior) is also important to dilate the pharynx for bolus transition. In addition, the motor innervation of the salpingopharyngeus, palatopharyngeus, and palatoglossus helps control the shape of the pharynx for swallowing.

On the other hand, the SLN branches distally to the pharyngeal branch and descends laterally to the pharynx. The eSLN is the primary motor nerve of the CT muscle for vocal pitch control with limited roles in swallowing. At the same time, the iSLN transmits the visceral and general sensory information from the supraglottic and glottic areas to cortical and brainstem centers for important swallowing control (see *Somatosensory Systems in Voice and Swallowing Control*). Lastly, the RLN branch also has both sensory and motor components. The sensory component of RLN is reviewed in *Somatosensory Systems in Voice and Swallowing Control*. At the same time, motor fibers of the RLN innervate all intrinsic laryngeal muscles, with the exception of the CT muscle, and are essential to vocal fold adduction as part of the airway protection mechanism in bolus transition and cough reflex. Injuries to the RLN can lead to dysphagia, weak voice, and poor cough associated with vocal fold paresis or paralysis.

Somatosensory Systems in Voice and Swallowing Control

Sensory components related to voice and swallowing functions are less well known compared to those of neuromotor components. Simply put, the iSLN provides sensory innervation to the supraglottic and glottic regions, whereas the RLN supplies infraglottic and subglottic sensation within the larynx. Other cranial nerves such as the trigeminal (V) and glossopharyngeal (IX) nerves may also be involved in the sensory innervation of the pharynx and larynx especially for the sensory integration of swallowing functions [60]. These nerves project to respective sensory nuclei within the brainstem, and sensory signals are further processed at the higher cortical level involving the thalamus, the insula, and the limbic system as well as the somatosensory cortex.

The sensory nerves to the larynx from the iSLN and the RLN are highly variable and their distribution is assumed to overlap greatly. The iSLN is the primary sensory nerve to the supraglottic larynx and the vocal folds. The iSLN courses along the superior laryngeal artery and pierces the thyrohyoid membrane to enter the larynx laterally between the hyoid bone and the superior cornu of the thyroid. The iSLN divides into a series of terminal sensory branches that provide innervation to the posterior part of the tongue base, the epiglottis, the aryepiglottic fold, and the vocal folds. These sensory neurons project to the interstitial subnucleus of the nucleus tractus solitaries (NTS) within the medulla oblongata [61]. The posterior part of the vocal folds, especially the posterior commissure and the arytenoids, was found to have abundant sensory innervation [62]. The epiglottis was also found to have a dense distribution of sensory fibers that were highly sensitive to touch, heat, and chemical stimuli in a canine model [63]. Stimulation of the iSLN nerve endings in the supraglottic region was also shown to induce protective closure of the glottis, known as polysynaptic involuntary reflex [62]. As such, the highly dense distribution of the sensory nerve endings within the epiglottis and the laryngeal mucosa further highlight the key role of the laryngeal adductor reflex or laryngeal closure reflex to protect the upper airway from bolus penetration and aspiration. On the other hand, the course and distribution of sensory fibers from the RLN to the larynx is not well documented to date. Generally speaking, the RLN divides off the main trunk to a significant number of sensory fibers that are distributed to the esophagus and trachea before entering the larynx. At the terminal portion of the RLN, the posterior branch of the inferior laryngeal nerve was found to contain sensory fibers and form the Galen's anastomosis with the iSLN [33, 64, 65].

Chemoreceptors and mechanoreceptors, which are innervated by the iSLN, are important in modulating the motor activity of vocalization and swallowing as well as protecting the airway from external stimuli. Both mechanoreceptors and chemoreceptors are found on the surface of the mucosa for external stimuli. In addition, articular and muscular mechanoreceptors are found in the laryngeal joints and muscles [59, 66–68]. Chemoreceptors generate nerve impulses when they are stimulated by chemical substances. A large number of taste-bud-like structures have been observed in the larynx, but their functions are different from those on the tongue. The chemoreceptors in the larynx respond only to pH, tonicity, and water but not to taste stimuli as do those in the oral cavity [69]. On the other hand, mechanoreceptors generate nerve impulses when they are deformed by mechanical forces such as pressure, touch, stretch, and vibration. Surface and deep mechanoreceptors are located near the surface of the laryngeal mucosa and at the laryngeal joints and muscles, respectively. These receptors are highly sensitive to the displacement of laryngeal structures and the contraction of laryngeal muscles during inspiration and phonation [60, 70].

Sensory Components Specific to Voice Control

The exact type and role of receptor involved in laryngeal somatosensory feedback during human phonation are still debatable. Repeated adduction-abduction movements by laryngeal muscles are necessary to bring the vocal folds to the midline for phonation. As such, a reasonable speculation is that the deep mechanoreceptors within laryngeal muscles would play a dominant role in providing proprioceptive feedback to the CNS for voice control [71]. Research data, however, show that spindle fibers (stretch receptors) are found only within the IA and are sparse or absent in the TA, LCA, CT, and PCA. Furthermore, no studies have demonstrated the corresponding physiology of stretched human laryngeal muscles [72–75]. At the same time, animal data show that sensory fibers from the iSLN are more sensitive to mucosal deformation than to muscle stretch. When the phonatory cycle is initiated, the vocal fold mucosa is under continuous mechanical deformation subjected to the flow of air from the lung. Human studies show an initiation of laryngeal adduction by applying air puffs to the surface of laryngeal mucosae [76–78]. Research data thus far seems to support the view that surface mucosal mechanoreceptors are more dominant in providing the sensorimotor feedback in voice control compared to those deep in laryngeal muscles.

Sensory Components Specific to Swallowing Control

Sensory inputs affect multiple descending motor pathways to trigger a swallow, modulate motor outputs, and simultaneously activate ascending sensory pathways, which in turn reflexively adjust the motor output throughout the swallowing sequence. In particular, sensory feedbacks can influence cortical activity and direct motor outputs to swallowing musculatures via the central pattern generator in the brainstem. Abundant sensory receptors are distributed within the mucosae along the oral, pharyngeal, and laryngeal structure for an array of sensations including but not limited to touch, pressure, proprioception, taste, temperature, and pain. During the process of mastication, sensory inputs of touch and pressure are mostly carried by the maxillary and mandibular divisions of trigeminal (V) sensory fibers. The touch and pressure receptors in the tongue and palate also transmit sensory information regarding the texture, shape, and size of the bolus to the CNS for facilitating the oral preparation. The integrated sensory information in turn modulates the shape and propulsive forces of the tongue to modify the bolus consistency and transport it toward the pharynx. Multiple modalities, including taste, water, touch, pressure, and possibly temperature from boluses, are normally involved in triggering the pharyngeal swallow and modulating the duration and intensity of the swallowing musculature.

The pharyngeal epithelium is heavily innervated with sensory fibers with the highest density of pharyngeal sensory receptors at the junction of the naso- and oropharynx. The epiglottic and laryngeal epithelia are also distributed with free nerve endings, with the greatest density of sensory receptors in the supraglottic mucosa near arytenoid cartilages. The cell bodies for these sensory fibers are located in the sensory ganglia of glossopharyngeal, iSLN, and other branches of vagus nerves with the NTS at the brainstem [5, 79–83]. Interestingly, mechanoreceptors in the pharynx and the larynx were found to play a significant role in triggering the pharyngeal swallow compared to other sensory nerves within the oropharynx [84–86]. Research shows that electrical stimulation or mechanical air stimulation of iSLN could lead to fictive coughing, glottal closure reflex, or respiratory apnea for airway protection in swallowing (for comprehensive reviews, see Ludlow [5, 81, 87]). An integrated summary of somatosensation and taste sensation related to swallowing is shown in Tables 3.5 and 3.6, respectively.

Table 3.5 The neuroanatomic hierarchy in somatosensation related to swallowing

Higher cortical level	Brainstem level	Cranial nerves (CN)	Sensory nerve endings
Thalamus, primary and secondary somatosensory cortex, insula, limbic system	Trigeminal sensory nucleus (TSN)	Trigeminal nerve (V3)	Anterior two-thirds of tongue Lower teeth/gums Soft palate Lower lip/jaw
		Trigeminal nerve (V2)	Nasopharynx Hard palate Soft palate Upper teeth/gums
	Nucleus of the solitary tract (NTS)	Glossopharyngeal nerve (IX)	Posterior one-third of tongue Oropharynx Anterior and posterior fauces
		Pharyngeal plexus (CN IX & X)	Pharynx
		Superior laryngeal nerve—internal branch (CN X)	Hypopharynx Epiglottis Larynx above vocal folds Aryepiglottic folds
		Recurrent laryngeal nerve (CN X)	Larynx below vocal folds Inferior pharyngeal constrictor Upper esophagus

Table 3.6 The neuroanatomic hierarchy in special sensation of tastes

Higher cortical level	Brainstem level	Cranial nerves	Sensory nerve endings
Thalamus, gustatory cortex (insula and frontal operculum), limbic system	Nucleus of the solitary tract (NTS)	Facial nerve (VII)—chorda tympani branch	Anterior two-thirds of tongue
		Glossopharyngeal nerve (IX)	Posterior one-third of tongue Oropharynx
		Vagus nerve (X)	Epiglottis

Summary

Understanding the neuroanatomic substrates and sensorimotor integration is pivotal to the clinical diagnosis and evaluation for neurologic and neurodegenerative diseases of the larynx. The human larynx is composed of a complex structure of mucosa, cartilages, and muscles that are innervated by a sophisticated network of sensory, motor, and communication nerve fibers. Central neural control involving premotor cortex, limbic areas, and brainstem central pattern generators provide volitional and reflexive actions of voice and swallowing musculatures. Somatosensory substrates of voice and swallowing are less understood compared to those of neuromotor systems. The integrity of sensory components, however, should be considered as part of the standard clinical evaluation. Quantitative measurements for accurate diagnoses of sensory reductions and hypersensitivity are necessary to fully apprehend the complexity of neurolaryngology in voice and swallowing.

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The Complete Neurologic Exam

4

Patrick A. Delaney and Dominic A. Ferrey

Overview

Laryngeal dysfunction is often due to disorders of the neurological system, and a detailed neurological exam can clarify the extent of neurological involvement. A quick glance at the Table of Contents for this book will confirm the wide range of neurological disorders that can impact laryngeal function. Subsequent chapters will deal with many of these conditions. Therefore, the focus here will be on the neurological exam and its diagnostic utility.

The goal of the neurological exam is to use physical findings to identify an anatomic localization for the patient's symptoms. Accurate localization will help narrow the differential diagnosis and lead to a more precise and appropriate workup and treatment plan. The complete neurological examination, as discussed in this chapter, includes the following components: examination of mental status, cranial nerves, motor system, somatosensory system, reflexes, coordination, and posture/gait [1–3]. When learning the neurological exam, it is best to proceed in a standardized routine to avoid accidental omission of any of the individual components.

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In general, the exam begins with surveying all of the subject's neurological systems, exploring any abnormalities detected, and then proceeding to an in-depth exam of the presenting problem. The rationale for this approach is to derive the full scope of the derangement. The neurological exam can elucidate not only whether the nervous system is involved at all, but which subsystems are compromised. The fundamental neurological disease patterns include: upper motor neuron (corticospinal) dysfunction, lower motor neuron (peripheral nervous system) dysfunction, cerebellar dysfunction, neuromuscular junction/muscle disorders, and extrapyramidal disorders [4–6]. Exam findings will be discussed in the context of these disease patterns after reviewing how to perform the exam.

Components of the Neurological Exam

The Mental Status Exam

The mental status exam can be broken down into cognition and language. Aspects of cognition include: level of alertness, attention, orientation (time, place, person, and situation), memory (immediate and delayed recall), visuospatial function, calculation, and reasoning [1–3, 7]. Many of these functions overlap, and deficits in one may lead to deficits in another. For example, the comatose patient is unable to regard an

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interviewer, let alone identify their location or perform complex calculations [8].

The components of language include: naming, comprehension, repetition, spontaneity, fluency, and reading. As opposed to purely mechanical difficulty with enunciation and clarity of speech (dysarthria), these qualities can be used to differentiate between true aphasias. While each of these components should be considered individually, they can be assessed simultaneously. The patient should name an object and its parts. Asking the patient to perform simple tasks such as "point to the window," via auditory and written instruction, allows the examiner to gauge comprehension. The ability to initiate speech, spontaneity, is investigated by open-ended questioning. While fluency can be assessed by evaluating the patient's speaking, prosody and tone can be assessed. The ability to write is part of the reading assessment [1–3, 7].

Much information about the patient's mental status can be determined during the patient interview. However, formal evaluation may illuminate subtle abnormalities often missed in a limited first encounter or in casual conversation. It is also important to establish the reliability of the information that is received [1–3, 7, 8]. Various tools, such as the Mini-Mental Status Exam (MMSE) or the Montreal Cognitive Assessment (MoCA), exist to assist with evaluation of mental status.

Cranial Nerves

Cranial nerve testing represents not only assessment of the individual nerves but also interrogates brainstem function, as well as midbrain, diencephalic, and cortical projections [9–12] (Table 4.1). It is important to note that end organ dysfunction need not only be due to an isolated lesion of its corresponding cranial nerve. For example, while hypoglossal nerve dysfunction can cause tongue weakness that leads to dysarthria or dysphagia, so can a focal mass at the base of the tongue or a widespread process such as anterior horn cell disease [9, 11].

While testing sense of smell (olfactory nerve) may be intuitively straightforward, this is not the case with the visual system. Beyond visual acuity, examiners use either finger motion or finger counting to assess the visual quadrants—first separately and then simultaneously [1–3]. Deficits detected can be highly localizing, with fibers from the superior visual fields coursing laterally through the temporal lobes on their way to the occiput and inferior fibers running medially through the parietal region. In general, the more similar (congruent) the visual defect in the two eyes, the more posterior the lesion in that pathway [5, 6, 9–11]. Testing the pupillary reflexes both with light and as the object distance varies (accommodation) allows assessment of both the ophthalmic nerve (II) (afferent) and oculomotor nerve (III) (efferent) function. Fundoscopic examination allows visual inspection of the optic nerve head, retina, and associated vessels. Ocular motility testing involves asking the patient to follow the examiner's finger through the full range of ocular excursion, allowing for assessment of the oculomotor (III), trochlear (IV), and abducens nerves (VI) [1–3]. This testing yields information about the course of these nerves through the skull base, the horizontal gaze center in the pons, and the structures for vertical gaze in the midbrain. Careful testing of facial sensation allows assessment of the trigeminal nerve (V) and its nuclei in the mid pons. Assessment of facial symmetry and muscle strength affords ready bedside information as to whether a lesion is peripheral or central, as well as some information about the pontomedullary junction. The facial nerve (VII) provides innervation to the muscles of facial expression, lacrimal and salivary glands (with exception of the parotid), and taste to the anterior two-thirds of the tongue. Wrinkling of the forehead, strong eye closure, and cheek puff strength assess the motor components of the facial nerve [5, 6, 9].

The vestibulocochlear nerve (VIII) subserves both hearing and balance. The two portions of the nerve course through the internal auditory meatus to the cerebellopontine angle, where they enter the brainstem. Hearing is facilitated by the cochlear portion of the nerve. This information is relayed to the ventral and dorsal cochlear nuclei within the inferior cerebellar peduncle. Damage

Table 4.1 Cranial nerves

Nerve	Function	Testing/evaluation
Olfactory (I)	Smell	Smell at each nostril tested separately
Optic (II)	Sight	Visual acuity, visual fields, fundoscopy Pupillary light reflex (sensory) Accommodation reflex (sensory)
Oculomotor (III)	Innervation to all extraocular muscles except for lateral rectus and superior oblique muscles Innervation to iris sphincter muscle	Pupillary light reflex (motor) Accommodation reflex (motor) Extraocular motility except eye abduction and eye intorsion Vestibulo-ocular reflex (motor)
Trochlear (IV)	Innervation to superior oblique muscle	Eye intorsion Vestibulo-ocular reflex (motor)
Trigeminal (V)	Somatic sensation to the face Innervation to the muscles of mastication	Facial sensation in V1,V2, and V3 distributions Palpate temporalis and masseter muscles with jaw closure Corneal reflex (sensory) Jaw jerk (motor and sensory)
Abducens (VI)	Innervation to lateral rectus muscles	Eye abduction Vestibulo-ocular reflex (motor)
Facial (VII)	Innervation to muscles of facial expression, stapedius muscle, and salivary/lacrimal glands. Taste	Wrinkle forehead, close eyes, puff cheeks, taste to anterior two-thirds of tongue Corneal reflex (motor)
Vestibulocochlear (VIII)	Auditory, balance	Hearing at each ear, Webber test, Rinne test, vestibular system evaluation Vestibulo-ocular reflex (sensory)
Glossopharyngeal (IX)	Sensation to the pharynx, taste, innervation to the parotid gland	Taste to posterior one-third of tongue, gag reflex (sensation)
Vagus (X)	Innervation to the laryngeal and pharyngeal muscles	Gag reflex (motor) Phonation, elevation of the palate, swallowing
Spinal accessory (XI)	Innervation to the sternocleidomastoid and trapezius muscles	Lateral rotation of the head and shoulder shrug
Hypoglossal (XII)	Motor innervation to the tongue	Tongue movements Inspect for fasciculations

at this level of the nervous system results in unilateral deafness. The fibers ascending from this level are both crossed and uncrossed, and central lesions thus result in bilateral (but not unilateral) hearing deficits [1–6, 9]. Basic testing for the presence of hearing is accomplished by the examiner rubbing fingers in proximity to each ear. The Weber test is helpful in discriminating conductive versus sensorineural hearing loss. A tuning fork is placed either atop the head or on the forehead, in the midline. This should result in the sound appearing equally loud in the normal patient's ears. If there is a conductive loss on one side, the sound will seem louder in that ear to the patient. If instead there is sensorineural loss on one side, the sound will be louder in the normal other ear. This lateralization can be clarified with the Rinne test. A low frequency (256 or 512 Hz) tuning fork is applied to the mastoid bone and then held over the external ear canal. In a normal ear, air conduction should be greater than bone conduction of sound. The vestibular portion of the VIIIth nerve provides for equilibrium and also three-dimensional orientation in space [2–4]. The semicircular canals, utricle, and saccule comprise the receptor portion of the labyrinth. Clinical examination of this system is complex, because balance functions facilitated by proprioception (the dorsal column-medial lemniscus system), cerebellar function, and the visual system need to be teased away. When cerebellar and proprioceptive deficits have been excluded,

motion-sensitive balance impairment related to vestibular dysfunction can be demonstrated by the development of a torsional nystagmus induced by head movement, and that has the qualities of both latency (delayed onset) and extinction (fatigability with repeated testing). Unilateral lesions tend to create such nystagmus toward the dysfunctional side [1–6, 9]. This is most commonly tested with the Dix-Hallpike maneuver, in which the patient quickly moves to a supine position with the head turned to one side and over the edge of the bed at thirty degrees. This has the effect of neutralizing one semicircular canal at a time and is commonly employed for demonstrating the posterior semicircular canal dysfunction in benign paroxysmal positional vertigo (BPPV). There are a variety of other bedside tests that can yield useful information about vestibular function, including the Selvant test, Fukuda test, the head thrust maneuver, caloric testing, and others.

It is not common or practical to test the glossopharyngeal nerve (IX) in isolation. Disorders such as glossopharyngeal neuralgia affect this nerve discretely, manifested primarily as an intermittent, sharp pain of the palate or tongue base. Diphtheria can also involve this nerve in isolation. By contrast, lesions of the medulla and cerebellopontine angle compromise the IXth nerve in combination with eighth nerve and with the Xth and XIth nerves at the jugular foramen.

With respect to laryngeal function, however, the most critical of the cranial nerves is the vagus nerve (X). This nerve supplies smooth and striated muscles in the larynx, pharynx, and even the tongue (palatoglossus). It also has visceral sensory afferents to the larynx, trachea, and esophagus (among others) and general sensation from the external acoustic meatus and back of the ear [5, 6, 9]. A unilateral lesion of the vagus nerve at the skull base can lead to a hypernasal hoarse voice and dysphagia. There may be an ipsilateral decreased elevation of the soft palate and deviation of the uvula toward the unaffected side during palate contraction. High vagal injury or recurrent laryngeal nerve injury can lead to hoarseness from ipsilateral paralysis of the vocal cords [13, 14]. Lesions of the superior laryngeal nerve thus result in impaired high pitch phonation [15, 16]. Please see Chap. 2 for a more detailed discussion.

Clinically, for the non-otolaryngologist, the glossopharyngeal (IX) and vagus nerves (X) are usually tested together with the gag reflex [1–3]. This is accomplished by first appreciating the tonality and clarity of the patient's speech. Asking the patient to sip and swallow water from a glass can allow useful observation of the throat during swallowing as well as elicit any signs of dysphagia. Observing the posterior pharynx through an open mouth can reveal an asymmetry of the palatal arch. A prolonged "ahhh" from the patient should elicit contraction and elevation of the arches, with the uvula remaining midline as it elevates. The gag reflex is elicited by contacting each of the palatal arches with a tongue blade, resulting in brisk involuntary elevation of the soft palate and contraction of the pharynx [1–3]. Note that contacting the soft palate, as opposed to the palatal arches, with the tongue blade can result in similar involuntary muscle response that actually tests sensation via the trigeminal nerve (V) rather than the glossopharyngeal nerve (IX) [1–3, 15, 16].

Bedside testing of the spinal accessory nerve (XI) is accomplished through strength testing of the sternomastoid and trapezius muscles [1–3]. Weakness isolated to these muscles can be the result of lower motor neuron damage, which sometimes occurs during neck dissection [9–12]. Trauma, such as from a heavy luggage strap over the shoulder, can also create this lesion. Often the affected shoulder has a visible droop; there may be a winged scapula and difficulty with forward elevation of the shoulder.

Lastly, the hypoglossal nerve (XII) supplies all the intrinsic and extrinsic muscles of the tongue except for the palatoglossus. This is typically tested at the bedside by asking the patient to protrude the tongue. Damage to the hypoglossal nerve results in ipsilateral tongue weakness with deviation to that same side [1–3]. The hypoglossal nerve also receives feedback of taste and tactile information via the nucleus of the tractus solitarius, facilitating the swallowing, sucking, and chewing reflexes [5, 6, 11].

The Motor System

The evaluation of the motor system should begin with observation. Visualization of muscles is important when gauging muscle bulk and whether atrophy or fasciculations are present. To assess tone, the limbs should be in a relaxed and neutral position. The examiner should move the limb across its joint and determine if spasticity, rigidity, or hypotonia is present [17–19]. Spasticity is the involuntary tightening of muscles that is provoked with movement of those muscles. Rigidity is an inflexibility of passive movement not related to the speed of movement. Muscles can then be tested individually and compared to their contralateral counterpart for formal strength assessment. Scoring systems such as the Medical Research Council grading system (https://mrc.ukri.org/research/facilities-and-resources-for-researchers/mrc-scales/mrc-muscle-scale/) exist to standardize the strength assessment; however, it is important to consider inter-rater variability (Table 4.2). Examiners should place themselves in a position of mechanical advantage to accurately assess each muscle. For example, evaluating for triceps strength with the arm completely extended at the elbow places the examiner at a mechanical disadvantage. The examiner may not be able to overcome the triceps in this position even if weakness is present. Starting with the arm flexed at the elbow and then asking the examinee to extend their arm at the elbow would offer a more accurate evaluation. The plane of gravity needs to be considered when assessing a patient's strength [1–3, 17–19]. Compound motor tasks will assess groups of muscles working together. For example, subtle weakness of the hip flexors may be revealed when a patient struggles to stand from a seated position with their arms crossed preventing the arms from pushing off to assist [18–20].

Table 4.2 Medical Research Council scale for muscle strength

Grade	Description
0	No contraction
1	Flicker of contraction
2	Full range of activation, out of the plane of gravity
3	Active movement against gravity
4	Active movement against resistance
5	Normal power

The Sensory System

Much time spent neurologically examining patients is often devoted to careful peripheral sensation testing, typically in the feet. With respect to laryngeal dysfunction, however, the utility of the sensory exam is often best focused on the cranial nerves, described above.

Somatosensory testing includes pinprick/temperature, light touch, and proprioception/vibration modalities. Pinprick/temperature can be assessed by gently pressing a disposable pin onto the surface of the skin, outlining any areas of deficit to pin sensation. Care should be taken not to injure the patient. A similar technique can be applied to light touch by using a cotton swab instead of a pointed edge. Vibration assessment can be done by applying a 128 Hz tuning fork to the distal interphalangeal joints of the fingers and toes. Proprioception evaluation can be gauged by deflecting a patient's toe caudal or cephalad [1–3, 17–20]. The patient should have eyes closed during much of the sensory testing to remove visual cues. Thus, it is important to explain each step to the patient before proceeding.

Physical exam findings created by damage of cortical sensory processing include extinction, denial, and neglect, among others. Extinction is ascertained by finding that only a unilateral sensation is noticed when both sides are simultaneously tested. Denial is a loss of perception that a body part is one's own. Neglect represents loss of awareness of entire aspects of the perceived world [4–6, 9–11].

Reflexes

The spectrum of reflex responses extends from sustained clonus (hyperreflexia) to a complete loss of a reflex (arreflexia). Clonus is a rhythmic oscillation across a joint induced by passive movement or by tendon reflex testing. To test a

Table 4.3 Deep tendon reflex scale

Grade	Description
0	Absent reflex
1+	Trace reflex
2+	Normal reflex
3+	Brisk reflex, self-limited clonus
4+	Sustained clonus

Table 4.4 Common deep tendon reflexes tested

Deep tendon reflex	Nerve root (s)
Biceps	C5–C6
Brachioradialis	C5–C6
Triceps	C6–C7
Quadriceps (knee jerk)	L3–L4
Gastrocnemius (ankle jerk)	S1

reflex, the examinee should be in a relaxed state. Voluntary tension applied by the examinee to the muscle in question may obscure the response. To maximize the yield of a deep tendon reflex, the examiner should manipulate the muscle into a position of slight passive tension and then proceed with a hammer strike onto the tendon itself (Tables 4.3 and 4.4) [1–3, 17, 21].

Common tendon reflexes tested in the upper extremities include the biceps, triceps, and brachioradialis tendons (Table 4.5). In the lower extremity, standard evaluation includes the quadriceps and gastrocnemius tendon reflexes as well as extensor plantar response testing (Table 4.6). The presence of pathologic reflexes such as the jaw jerk may be important in the right clinical context. The presence of a jaw jerk reflex suggests upper motor neuron injury in the distribution of the trigeminal nerve (V). This pathologic reflex can be seen in diffuse motor neuron diseases such as amyotrophic lateral sclerosis. Furthermore, it can be particularly suggestive of this diagnosis when it is seen in combination with lower motor neuron injury in the same body segment (e.g., tongue atrophy from injury to the lower motor neurons in the hypoglossal nerve). Upper motor neuron and lower motor neuron signs are further discussed below. Another pathologic reflex is the extensor plantar response, seen as dorsiflexion of the big toe following application of noxious stimulation to the sole of the foot [1–3, 17, 21]. The chronic version of this finding is colloquially referred to as "hitchhiker's toe." A "cortical thumb" is the analogous chronic finding noted in the hands.

Table 4.5 Common upper extremity muscle testing

Action	Muscle(s)
Shoulder abduction	Deltoid
Lateral rotation of the arm	Infraspinatus
Elbow flexion	Biceps, brachioradialis
Elbow extension	Triceps
Forearm pronation	Pronator teres
Forearm supination	Supinator
Wrist flexors	Flexor carpi radialis, flexor carpi ulnaris
Wrist extensors	Extensor carpi radialis
Finger flexors	Flexor digitorum profundus, flexor digitorum superficialis
Finger extensors	Extensor digitorum communis, extensor indicis proprius
Finger abduction	Dorsal interossei of the hand
Finger adduction	Palmar interossei of the hand
Thumb abduction	Abductor pollicis brevis

Table 4.6 Common lower extremity muscle testing

Action	Muscle(s)
Hip flexion	Iliopsoas
Hip extension	Gluteus maximus
Knee flexion	Hamstrings
Knee extension	Quadriceps
Ankle dorsiflexion	Tibialis anterior
Ankle plantar flexion	Gastrocnemius and soleus
Ankle inversion	Tibialis posterior
Ankle eversion	Peroneus longus, peroneus brevis
Toe extension	Extensor hallucis longus, extensor digitorum longus
Toe flexion	Flexor hallucis longus, flexor digitorum longus

Coordination Function

Coordination testing surveys cerebellar function. Both finger-to-nose and heel-to-shin testing look specifically for dysmetria or corrective move-

ments occurring at a right angle to the vector of movement [1–3]. Often these are most readily discerned at the end of movements, where smaller, weaker muscles are employed. The latter sometimes results in the misinterpretation of tremor for dysmetria [22]. Practitioners also have patients walk a straight line to assess for midline (cerebellar vermis) dysfunction, which can also be detected as truncal ataxia or overcorrection of trunk stabilization. Some forms of nystagmus also occur with either midline or hemispheric cerebellar lesions [1–3, 23]. Acute unilateral cerebellar lesions can also result in hypotonia of the limbs on the same side as the lesion. This can sometimes be detected in the outstretched arms of a patient by tapping forcefully downward on both limbs at the same time. Both limbs will drop slightly; however the hypotonic limb will rebound excessively (Stewart-Holmes sign).

Posture/Gait

Walking and stance are complex motor tasks that require successful integration of the complete nervous system with musculoskeletal components. It requires an expert observer to visually tease these apart. When evaluating gait particular attention should be given to stance, symmetry, and fluidity of movement. Stride length and speed are also assessed [1–3, 24]. With respect to laryngeal dysfunction, it is easiest to consider these findings in respect to the subsystems discussed above.

Neurological Disease Patterns

Upper Motor Neuron Dysfunction

Broadly speaking, central nervous system (CNS) control is top down. Higher levels inhibit lower systems. When damage occurs within the CNS portion of the motor system, restraint of those lower systems is interrupted. Initially, these lower motor controls can lose activity, as when a side of the body becomes weak immediately following a stroke. With time, however, the lower systems power back up, now unrestrained by higher levels of control. That same stroke patient develops stiffness and spasticity where there was initially only weakness [4–6, 9–12]. The motor system below the chronic lesion will generally display increased muscle tone, brisk reflexes, and pathological signs such as clonus and extensor plantar responses [21]. In general, the more severe the upper motor neuron damage, the more prominent the extensor tone in the legs. It is a different case in the arms, where upper motor neuron lesions below the red nucleus in the midbrain result in extensor posturing and lesions above that level result in a stiff flexion of the arms. Gait may also be affected, and these patients often circumduct and externally rotate an affected leg when walking. If both legs are affected, there may be an additional scissoring component to the gait, which could suggest a lesion of bilateral primary motor cortices along the vertex or potentially a myelopathy [4–6, 9–12]. Sensory and other exam components need not be affected at all if the lesion is sufficiently discrete. However, it is often the damage to adjacent systems (sensory, cerebellar, cranial nerve, etc.) that best localizes the level of the lesion.

Upper motor neuron lesions can create harsh or strained articulation known as spastic dysarthria [4–6, 9–12, 25]. Surveying the rest of the nervous system in such cases will help determine the site of dysfunction within the nervous system. For instance, spastic dysarthria in combination with unilaterally increased muscle tone and reflexes in the limbs would suggest damage to the contralateral corticospinal tract of the brainstem, diencephalon, or cerebral cortex. If the upper motor neuron findings are bilateral, then a midline lesion or bilateral lesions would be more likely [4–6, 9–12]. Of note, dysarthria in isolation is notoriously poorly localizing.

Upper motor neuron lesions in the cervical spine can result in many of the aforementioned findings (typically bilaterally) but are less considered here because the innervation of the larynx exits the central nervous system above that level [4–6, 9–12].

Table 4.7 Upper motor neuron and lower motor neuron signs

Upper motor neuron	Lower motor neuron
Increased muscle tone: spasticity or rigidity	Decreased muscle tone
Atrophy limited to disuse with otherwise normal muscle bulk	Prominent muscle atrophy and decreased muscle bulk
Fasciculations are absent	Fasciculations can be present
Deep tendon reflexes are hyperreflexic	Deep tendon reflexes are diminished or absent

Lower Motor Neuron Dysfunction

Visualize a large motor nerve in the arm, severed by trauma. Downstream sensation may be lost immediately. The victim can no longer move the muscles supplied by that nerve, and the limb goes flaccid. Over the ensuing weeks, the muscles wither and atrophy from lack of nerve stimulation. Fasciculations—involuntary contractions of select muscle fibers within a muscle—may begin to manifest. If damage is at the level of a spinal nerve root or more distal, tendon reflexes may also be diminished. With respect to laryngeal function, dysphonia can result from focal injury to the recurrent laryngeal nerve, as can occur with carotid endarterectomy, aortic arch aneurysms, and enlarged paratracheal lymph nodes. Damage to the vagus nerve itself can cause hypernasality secondary to velopharyngeal insufficiency, hoarse breathy voice from vocal fold paralysis, and dysphagia via a variety of mechanisms (see Chap. 19). Keep in mind that there are also disorders capable of causing both upper and lower motor neuron exam findings, such as with amyotrophic lateral sclerosis [4–6, 9–12]. Upper motor neuron and lower motor neuron signs are summarized in Table 4.7.

Cerebellar Dysfunction

The cerebellum plays a large role in coordinating smooth, voluntary motor movements. It serves as an adjunct to the primary motor system by coordinating acceleration and deceleration of movements via the select activation of agonist and antagonist muscles. Motor tasks such as finger-nose-finger testing are used to interrogate cerebellar function. Normal cerebellar function allows an individual to repeatedly land a finger onto the tip of their nose and then back out onto the examiner's finger in one smooth and coordinated movement. In cerebellar dysfunction, clumsy uncoordinated movements develop, and the patient's finger may overshoot and hit the bridge of the nose or undershoot and miss the face entirely. This is known as dysmetria. Oscillation of the finger around the target, or an intention tremor, can be seen. Similarly, eye movements may overshoot or undershoot a target. Disturbances in cerebellar function can also result in ambulation abnormalities [4–6, 9–12, 23, 25]. Such individuals may demonstrate a wide base, feet set apart beyond the shoulder width, and display irregular cadence and stride length. In severe disease these patients may veer off course and in milder cases may simply step to one side when attempting to walk in a straight line [9–12, 23–25].

Ataxic dysarthria, also known as cerebellar dysarthria, results from cerebellar dysfunction. Patient's with ataxic dysarthria may use scanning speech, a distinct pattern of speech where words and phrases are communicated in a deconstructed manner, articulating individual syllables with frequent and irregular pauses. Ataxic dysarthria may also result in fluctuations in prosody. Given the resulting variability and clumsiness, this dysarthria is also sometimes described as "explosive" speech [9–12, 23–26].

Lesions of the lateral cerebellar hemispheres can produce clumsiness of the limbs ipsilateral to that lesion. Dysfunction of the cerebellar vermis can result in difficulty with truncal stabilization. Titubation, a nodding movement of the head or torso, is another form of truncal ataxia. Of note, truncal ataxia may not be as obvious to the examiner when the examinee is seated in a supported position [4–6, 9–12]. This underscores the importance of having your patients stand and walk when performing the neurological exam.

In the setting of acute cerebellar dysfunction, a loss of muscle tone can be seen in the affected body region. Over time there will be a restoration

of tone, and hypotonia may not be as evident in chronic cerebellar lesions [4–6, 9–12].

Neuromuscular Junction/Muscle Dysfunction

The neuromuscular junction converts electrical impulses of the nervous system into skeletal muscle contraction via the release of the neurotransmitter acetylcholine. Intuitively, disorders of the neuromuscular junction and muscle do not result in sensory abnormalities [18–20].

In presynaptic terminal diseases such as Lambert-Eaton myasthenia syndrome, repeated stimulation of the nerve terminal is required to overcome limitations in the release of acetylcholine. Clinically, this manifests as weakness that improves with repeated activation. In postsynaptic terminal diseases such as myasthenia gravis, larger amounts of acetylcholine are required to produce a muscle contraction. Repeated stimulation eventually leads to depletion of nerve terminal acetylcholine stores. Clinically, this manifests as weakness that develops with repetitive activation of a muscle. These activity-dependent fluctuations in muscle strength suggest neuromuscular junction dysfunction and are unexpected in muscle disease. A dynamic motor exam can be used to thoroughly interrogate the neuromuscular junction [18–20].

Muscle disease tends predominantly to affect proximal shoulder and hip girdle musculature, whereas neuromuscular junction disease has a predilection for cranial nerve innervated as well as proximal musculature [4–6, 9–12, 18–20]. Double vision that results from reading, drooping of an eyelid as the day progresses, and loss of speech volume are common symptoms of neuromuscular junction dysfunction such as myasthenia gravis. Fatigability and return of function with rest are key features of these symptoms and signs. Sustained up gaze for a few minutes during the exam may reproduce these findings. In regard to laryngeal function, neuromuscular junction disorders and muscle disease can produce a nasal speech. In the early stages of both neuromuscular junction and muscle disorders deep tendon reflexes may be preserved. However, as the disease processes progress, they may disappear. Autonomic disturbances are not uncommon in presynaptic neuromuscular junction dysfunction but are absent in postsynaptic neuromuscular junction and muscle disease. As such, the pupillary light response can be affected in botulism toxicity but should be spared, even in the setting of dense ophthalmoplegia, in conditions such as myasthenia gravis or chronic progressive external ophthalmoplegia [18–20].

Extrapyramidal Dysfunction

The pyramidal (corticospinal) motor system receives extensive modulation or feedback from numerous brain structures generically referred to as the extrapyramidal system. Pathology isolated to the extrapyramidal system may leave the subject with no actual weakness and normal reflexes, including the plantar responses. Such patients may have difficulty with initiating movements, completing them at normal speed (bradykinesia), or may develop excessive or involuntary movements (tremor, choreoathetosis, and ballismus). Because these circuits modify motor system controls that can be unilateral or bilateral, extrapyramidal disorders can likewise affect the right, left, or both sides of the body [9–12, 23–25, 27].

In extrapyramidal dysfunction almost all aspects of motor function can be involved. These multifaceted disorders range from focal dystonias to Parkinson disease, corticobasal ganglionic degeneration, and many others. The dysfunction can include not only fine control of the larynx, breathing, and speech but also eye movements. In Parkinson disease, a slow, shuffling gait and a false center of gravity may develop, leading to falls. However, the most telltale physical findings often occur in the limbs. There is increased limb tone that can be further accentuated with additional task performance (termed augmentation, or reinforcement). During sleep or at rest, limb tone can normalize since the abnormal extrapyramidal feedback occurs predominantly when the motor system is active [9–12, 23–25]. An essential tremor resulting from

dysfunction in the ventromedial thalamus shakes at the same rate as the subtle corrective movements in a normal subject, although the amplitude of the tremor increases during movement. By contrast, a Parkinsonian tremor resulting from substantia nigra dysfunction will have a lower rate of shaking, and the amplitude remains unchanged during movement [23–25]. The entire pattern is important as well. While essential tremor can afflict the head, hands, or voice, this is not the case in typical Parkinson disease, where instead the patient may develop a low volume, indistinct vocal pattern, but no vocal tremor. These physical exam findings are nuanced and are best considered in the context of other physical findings and patient symptoms. Thus, in Parkinson disease, while tremor can be one of the earliest motor symptoms, the neurologist will also note a progression of slowness and stiffness of movement [9–12, 23–25].

Disorders of the extrapyramidal system can also result in excessive and involuntary movement. Choreoathetotic movements are continuous writhing movements of the limbs that can be reflective of a relative excess or imbalance of dopaminergic effects within the nervous system. Similarly, in late Parkinson disease, involuntary repetitive movements termed dyskinesias can be the result of chronic use of the very medications that have been mitigating the patient's motor stiffness. Ingested agents that cause dopamine blockade (e.g., older antipsychotic medications) can also result in chronic involuntary tongue and mouth movements (tardive dystonia) or involuntary posturing of the limbs and similar phenomena. Such reactions can also develop acutely in susceptible individuals [9–12, 23–25].

Summary

In this very brief chapter we have attempted to provide an overview of how the basic neurological exam can be employed to localize and diagnose problems presenting as laryngeal dysfunction. The various types of disorders resulting in this presentation each have a unique pathophysiology, natural history, and management strategy, elucidated by our colleagues in the accompanying chapters.

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5 Evaluation of Neurogenic Voice Disorders

Christina Dastolfo-Hromack and Erin Walsh

Introduction

The larynx is a complex organ contributing to physiologic processes of phonation, respiration, and deglutition. Neurogenic disorders can disrupt some or all of these functions. Evaluating focal and systemic voice disturbance is best accomplished through a holistic blend of perceptual, aerodynamic, acoustic, and instrumental assessments. This chapter offers a physiologic approach to expose common pathway disruptions. Laryngologists and voice-specialized speech-language pathologists have expertise evaluating disease nuances, providing accurate diagnoses and managing symptoms. Collaboration among providers is paramount as individuals with laryngeal symptoms often consult with numerous medical specialties in pursuit of answers.

Neurologic input to the larynx is critical for vegetative functions and communicative processes. Vocal intent begins in the central nervous system. It then courses through the peripheral nervous system to lower motor neurons and engages the larynx. Healthful voice production requires intact neurologic input to the lungs, larynx, pharyngeal, and oral cavities. Vocal motor control remains a source of ongoing investigation [1–3]. Evidence supports activation of a feedback loop among the sensorimotor cortex, auditory cortex, basal ganglia, cerebellum, and periaqueductal gray matter [4, 5]. The tenth cranial nerve, the vagus nerve, is essential for voice production. Pertinent branches for vocal function include pharyngeal, superior laryngeal, and recurrent laryngeal nerves. The superior laryngeal nerve innervates the cricothyroid muscle for pitch control and supplies sensation to the laryngeal mucosa. The recurrent laryngeal nerve controls all other intrinsic laryngeal muscles [6]. As air expels from the lungs, the vocal folds close and oscillate. The vibration then filters through pharyngeal, oral, and nasal cavities to trademark a unique sound. Details of voice physiology are covered in more depth in other chapters.

Noninstrumental Assessment

Behavioral evaluation of neurogenic dysphonia will reveal task-specific disease hallmarks. Differential diagnosis hinges on physiologic trait recognition and vocal patterns. Perceptual features of functional disorders may masquerade as a neurological condition. Gradations of compensatory muscle tension also commonly overlap

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Table 5.1 Self-rating scales

Voice Handicap Index [7]
Singing Voice Handicap Index [8]
Voice-Related Quality of Life Index [9, 10]
Spasmodic Dysphonia Attributes Inventory [11]
Unified Spasmodic Dysphonia Rating Scale [12]
Voice Symptom Scale [13]
Voice Activity and Participation Profile [14]
Dyspnea Index [15]
Eating assessment Tool-10 [16]

Table 5.2 Interview

When did symptoms begin? Were the changes sudden or gradual?
Can you correlate these to any medical, medication, or personal events?
Do you have changes in swallowing, articulation or breathing?
Are the symptoms stable, worsening or getting better?
What are your vocal demands?
Are your symptoms always present?
Can you discern triggers or anything to suppress your voice issue?
Does your voice improve with alcohol?
Do you sing? Is there change to your singing voice?
Does your voice ever sound normal?
Do you find it takes excess effort to use your voice or speak?
Do you have prior history of voice issues?
Does anyone in your family have a voice problem or history of neurological disease including tremor?
Have you noticed tremor in your hands or other body parts?

and confound neurogenic presentations. Varying phonatory contexts is often revealing: voiced vs. voiceless sounds, loud vs. soft phonation, pitch variation vs. monotone, sustained phonation, singing, emotionally mediated speech, and vegetative sounds. This diversity illuminates compensatory, functional, and/or neurologic pathophysiology. In some cases, repeating tasks for potential fatigability may be a lone subtle sign of neurogenic dysfunction. An individual's perception of the disorder complements the objective clinical interaction. A variety of self-rating scales, a few of which are referenced in Table 5.1 [7–16], uncover the precise nature of voice dysfunction and reflect patient perception. The Dyspnea Index [15] and Eating Assessment Tool-10 [16] are also useful because voice disorders, particularly of neurologic origin, have higher incidence of confounding respiratory and swallowing dysfunction [17].

During the initial patient interview, questions targeting timelines and comorbidities aid diagnostic precision (Table 5.2). Symptom onset and time course of disease provide valuable insight. For example, vocal fold paralysis and paresis are more likely to have a sudden onset and then stabilize or resolve [18], whereas phonatory weakness or asthenia presents gradually in the setting of degenerative neurologic disease. Laryngeal and respiratory dystonia begin suddenly without overt provocation or insidiously over time. Dystonia has been associated with preceding viral illness, history of extensive voice use, symptom onset in middle ages, and female dominance [19, 20]. Neurologic conditions sometimes manifest with sensory abnormalities as well including laryngeal hyperresponsiveness, cough, paradoxical vocal fold movement, and functional dysphagia. The most concerning circumstances of voice change are those that are progressive and encompass the entire speech and swallowing mechanism. This could be early presentation of serious neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), multiple system atrophy (MSA), Parkinson disease (PD), and multiple sclerosis (MS). In these diseases, laryngeal, pharyngeal, and oral anomalies may present initially before other systemic ailments are apparent. As voice and swallowing clinicians are often the initial medical encounter, they must be vigilant to expediate consultation with a neurologist.

Familiarity with common perceptual features of neurogenic voice disorders will unearth clues of etiology. Breathy vocal quality is typically associated with hypofunctional voice disorders such as unilateral vocal fold paralysis/paresis, PD, and vocal fold atrophy. Incomplete glottic closure underpins this profile. Strained quality occurs with adductor spasmodic dysphonia, laryngeal spasticity, and bilateral vocal fold paralysis [21]. A non-neurological voice disorder, muscle tension dysphonia, can manifest with similar perceptual features and should be differentiated given its significant symptom overlap [22]. Strained vocal quality, also referred to as spastic dysphonia, may

be a sign of broader dysarthria, such as ALS [23] or MSA [24]. The other common trait surfacing among neurogenic profiles is tremor. Voice tremor evolves from unintended rhythmic fluctuations of pitch and loudness between 4 and 5 Hz [25]. While tremor can be isolated to the larynx, often other anatomic subsites are involved [26]. When tremor is distinct from other neurological processes, such as Parkinsonian tremor, it is called essential tremor [26]. Severe tremor can provoke complete phonatory arrests [27]. This should be differentiated from laryngeal dystonia as it can co-occur with tremor. In sustained phonation, essential voice tremor will persist [28, 29], while laryngeal dystonia more typically occurs only with sound initiation.

Instrumental Assessment

Instrumental assessment of voice production involves acoustic analyses, aerodynamic function, and endoscopic laryngeal imaging. Guidelines were developed by the American Speech-Language-Hearing Association in 2018 in attempt to standardize acquisition, synthesis, and reporting of these measures [30]. The benefit of regulated intake processes is multifold. When evaluation procedures become consistent across healthcare institutions, patients are more likely to be assigned accurate diagnoses. Furthermore, consistency in symptom profiles allows for effective communication in research and treatment design.

Acoustic and Aerodynamic Analysis

Evaluation of sound and airflow patterns are essential for determining the appropriate diagnosis and treatment recommendations. Neurogenic pathology can disrupt single and multilevel physiology. Acoustic and aerodynamic measurements help distinguish normal from pathological vocal physiology, inform treatment plans, and objectify therapeutic outcomes. Assessment of neurogenic voice disorders is based on pattern recognition of symptoms. These objective measurements compliment perceptual assessment for a comprehensive view of vocal behavior.

Vocal frequency and intensity are basic acoustic measurements that can be obtained with low technology recording equipment and sound level meters. They roughly correspond to a person's vocal pitch and loudness. Quantifying vocal quality involves more sophisticated equipment to detect degrees of noise in the acoustic signal. Normal voices vibrate at regular periodic intervals with acoustic energy organized around the fundamental frequency (F_0). Maintenance of stable F_0 requires fine motor control of the laryngeal muscles. Researchers are developing an acoustic measurement to capture this control called relative fundamental frequency – RFF [31, 32]; however, it is not currently used in clinical practice. In a disordered voice, noise energy is disorganized and distributes across multiple frequencies in an aperiodic manner. This aperiodicity may occur across an entire speech task or occur in a specific context (i.e., on voiced sounds like "w," but not unvoiced sound like "s" in spasmodic dysphonia). Consider the context of the speech sample gathered during assessment and how it reflects on speech patterns in the patient's daily life. Samples that require patients to speak in phrases or sentences are valuable to estimate dysphonia in daily speech; however, these connected speech samples cannot be used to extract acoustic values reliant on stable F_0, such as variations of pitch (jitter), loudness (shimmer), and noise to harmonic ratio [33], which require recordings of a sustained vowel.

One recently developed approach to measuring vocal quality uses the cepstrum, which can be extracted from connected speech samples [34, 35]. This method of analysis is not time-based and does not rely on a stable F_0, rather, it is completed on the frequency structure (harmonics) of the acoustic sample. A normal voice has a well-organized harmonic structure, while a disordered voice demonstrates disorganization. The peak, cepstral peak prominence (CPP), describes this structure and is of high value in normal (organized) voices and low in disordered (unorganized) voices. It is especially sensitive to the perception of breathiness. Specific descriptions of all acoustic measurements can be found in Table 5.3 [34–49].

Table 5.3 Common acoustic and aerodynamic measurements used to quantify vocal disorders are listed below. Please note that the normative values listed are only a sample of available references and not exhaustive

	Measurement	Stimuli	Definition/construct measured			
Acoustic	Fundamental frequency (F0)	Connected speech or sustained vowel	F_0 captures the lowest frequency at which the vocal folds are vibrating. This roughly corresponds to the pitch we hear. F_0 can be sampled from sustained phonation, although is most relevant during connected speech. *Normative values*: Torre and Barlow 2009 [36], 60–89 years of age, gathered from a connected speech sentence context			
					Male	**Female**
			Fundamental frequency (Hz)		122–142	164–180
	Intensity	Sustained vowel or connected speech	Measures overall energy in the acoustic sample and is helpful to sample vocal loudness and prosodic variation in speech. Measured in dB SPL or root mean square (RMS). Normative values are highly dependent on speech context.			
	Cepstral peak prominence (CPP)	Connected speech or sustained vowel	Measures general dysphonia severity, gathered from the voice cepstrum, and is particularly sensitive to changes in breathiness. *Normative values*: Heman-Ackah et al. [34], gathered from "Marvin Williams" passage; Watts and Awan 2011 [37], gathered from second sentence of "Rainbow Passage"; Iranian norms: Hasanvand et al. [38]			
					Male and female grouped together	
			CPP-smoothed [34] (dB), Marvin Williams passage		4.77 ± 0.97	
			CPP(dB) [37] rainbow passage		5.42 ± 1.38	
			CPP(dB) [37], sustained /a/		11.08 ± 1.91	
	Cepstral-spectral index of dysphonia (CSID)	Connected speech or sustained vowel	Measures overall vocal severity. It is an algorithm consisting of multiple acoustic measures of dysphonia (i.e., CPP and L/H ratio) and is intended to objectively quantify dysphonia similar to clinician perception *Normative values*: Awan et al. [35], gathered from the second and third sentences of the "Rainbow Passage"			
				Male	**Female**	**Male and Female Grouped**
			CSID	28.63 ± 23.82	28.23 ± 17.74	
	Jitter	Sustained vowel only	Captures cycle to cycle changes in fundamental frequency. Requires that voices be rated as type I (nearly completely periodic) or type II (mostly periodic with subharmonics) [39] and carries reliability concerns [40] *Normative values*: Spazzapan et al. 2018 [41], ages 50–60, gathered from sustained "ah"			
				Male	**Female**	
			Jitter	0.92 ± 0.54	0.79 ± 0.61	
	Shimmer	Sustained vowel only	Captures cycle to cycle changes in intensity. Requires that voices be rated as type I or type II [39] and carries reliability concerns [40] *Normative values*: Spazzapan et al. 2018 [41], ages 50–60, gathered from sustained "ah"			
				Male	**Female**	
			Shimmer	5.29 ± 2.4	4.04 ± 1.64	
	Noise to harmonic ratio (NHR)	Sustained vowel only	This ratio captures the energy in periodic vs. aperiodic regions of the signal and relates to overall severity of the voice disorder [42]. It is limited by reliability issues [43]. *Normative values*: Spazzapan et al. 2018 [41], ages 50–60, gathered from sustained "ah"			
				Male	**Female**	
			NHR	0.16 ± 0.06	0.14 ± 0.02	
	MDVP tremor profile (FTRI, Fftr)	Sustained vowel	This group of measurements is available in the KayPENTAX multidimensional voice profile (MDVP) software package. It is intended to capture slow modulations (i.e., tremor) in frequency and amplitude of the signal. *Normative values*: Maccallum et al. [44]			
				Male and female grouped together		
			FTRI (%)	0.157 ± 0.25		
			Fftr (Hz)	1.154 ± 1.46		

Aerodynamic	Maximum phonation time	Sustained vowel	Maximum phonation time (MPT) is an indirect measurement of respiratory function. It is thought to describe how the body uses airflow or "airflow consumption." It is taken by having the patient inhale as deeply as possible and sustain a steady vowel for as long as possible *Normative values*: Joshi 2019 [45] gathered from sustained "a"'; Zraick et al. 2012 [46] gathered from healthy older adults aged 60–89 years		
				Male	**Female**
			Max phonation time (seconds)	24.16 ± 6.14 [45] 19.94 ± 6.79 [46]	18.92 ± 4.97 [45] 20.02 ± 6.58 [46]
	S/Z ratio	Sustained speech sounds	This ratio compares the maximum amount of time the patient is able to sustain an /s/ divided by the time to sustain a /z/. it compares ventilatory to phonatory function *Normative values*: Joshi 2019 [45]; Gelfer and Pazera 2006 [47]		
				Male	**Female**
			S/Z ratio	1.07 ± 0.37 [45] 1.01 ± 0.2 [47]	1.09 ± 0.25 [45] 1.06 ± 0.27 [47]
	Rainbow passage: Breaths and time	Connected speech, reading	The rainbow passage is a text that samples voice production in varying phonetic contexts. The number of breaths and time to read the passage relates to aerodynamic performance in patients with glottic incompetence. *Normative values*: Lewandowski et al. [48]		
				Male	**Female**
			Breaths	5.08 ± 1.72	4.75 +/−1.76
			Time	23.42 seconds ± 3.23	22.63 seconds ± 0.17
	Psub (subglottal pressure) and laryngeal resistance	Repetitive productions of /pa/	Subglottal air pressure measures the pressure immediately below the glottis during phonation (indirectly for clinical purposes), which is the energy needed for speech production. Psub requires precise neuromuscular control of the vocal folds and is the basic physiology control mechanism for pitch modulation and phonation maintenance. Laryngeal resistance is the accompanying description of the subglottal pressure divided by the flow rate, and it measures respiratory driving force. *Normative references*: Joshi et al. 2019 [45]; Zraick et al. 2012 [46] (ages 60–89 years); Matheron et al. 2017 [49]		
				Male	**Female**
			Psub (cm H20)	6.9 ± 2.53 [45]	5.84 ± 1.95 [46]
				8.5 ± 0.18 [49][a]	
			Laryngeal resistance (cm H20/L/s)	55.45 ± 60.64 [45] 137.31 ± 221.5 [46]	50.43 ± 28.83 [45] 79.05 ± 52.05 [46]
	Phonatory airflow (glottal flow)	Sustained vowel or connected speech	This is the average volume of air expended per second during a speech sound *Normative reference values*: Lewandowski et al. 2018 [48]; Joshi 2019 [45]		
				Male	**Female**
			Phonatory airflow (rainbow passage) [48]	0.16 L/sec ± 0.05	0.14 L/sec ± 0.001
			Glottal flow [45] (sustained vowel)	0.14 L/ sec ± 0.10	0.17 L/ sec ± 0.06

[a]Values include both male and female participants, gathered from phrase "buy pop or pop a papa," mean age 68.9 years

Aerodynamic assessment complements acoustic analyses, as it quantifies the physiologic force underpinning healthy vocal fold vibration. Specific tasks are designed to evaluate multiple components of airflow, such as speech level breathing patterns, average airflow used during voicing, or the estimated glottic air pressure generated during vocal fold vibration. Aerodynamic assessment can be accomplished with limited equipment using maximum phonation time, S/Z ratio, and a spirometer [50]. Alternatively, the Phonatory Aerodynamic System TM (KayPENTAX, Lincoln Park, NJ) sophisticates this process by calculating airflow and pressures during functional speech. Aerodynamic patterns may arise and correspond to a specific neurological dysfunction. Examples include patients with PD disease presenting with low transglottal airflow [51], whereas patients with vocal fold paralysis can exhibit high transglottal airflow [52].

While neurologic disruptions vary, disease-specific commonalities are likely to surface across acoustic and aerodynamic measures. A variety of identifying pathways are provided in Figs. 5.1 and 5.2 [48, 52–54], and see Table 5.3. Examples include reduced pitch range, monotone, and low-volume output in PD. Isolated vocal intensity disruption may be due to discrete glottic insufficiency from a vocal fold paralysis. Strained quality combined with elevated subglottal air pressures may be indicative of dystonia. If disease features are nebulous, pair measures with perceptual ratings, self-ratings, and the patient interview. Diagnostic voice therapy is often a favorable adjunct to complement acoustic and aerodynamic measures across linguistic and behavioral contexts.

Endoscopy and Videostroboscopy

Laryngeal visualization evaluates for co-occurring anatomic irregularities, provides opportunity to scrutinize movement patterns, and permits observation of vibratory characteristics. This process leads to identification of periphery nerve insults encompassing the superior laryngeal nerve, recurrent laryngeal nerve, or both. When the abnormalities are multilevel, consider central nervous system involvement. The examination is performed with an endoscope inserted into the oral cavity (rigid endoscopy) or nasal cavity (flexible endoscopy). Neurologic disease unfolds most clearly during flexible endoscopy whereas rigid endoscopy highlights discrete mucosal abnormalities. Transnasal endoscopy is well tolerated [55], depicts velopharyngeal integrity, and provides gestalt function during speech and respiration. A small subset of larynges may demonstrate elevated hypersensitivity leading to endoscopic intolerance. Sensory neuropathy may underpin this and have concurrent evidence of motor dysfunction depending on the involved nerve [56]. During endoscopy a still light is used to examine broad movement features and positioning while stroboscopic light depicts vibratory characteristics. Otolaryngologists and voice-specialized speech-language pathologists routinely perform these procedures.

Specific movement attributes are evaluated during endoscopy, including vocal fold opening, closing, and lengthening. The anticipated laryngeal movement under normal circumstances involves complete and symmetric opening and closing of both vocal folds during inhalation and phonation. Disruption of this process implicates recurrent laryngeal nerve or vagal dysfunction, especially if the movement deficit is unilateral. This is best elicited when prompting patients to alternate “sniffing” and “eee” postures in sequence. Irregularities range from obvious immobility to subtle sluggish movements of one or both vocal folds [57]. There may also be deviation of the glottic axis [58], uneven vocal fold height [59], insufficient arytenoid rotation [60], and fatigability [61]. Observe vocal fold lengthening at rest and during pitch glissandi spanning the entire stimulable range. Inability to control pitch and loudness suggests superior laryngeal nerve injury. Pitch range extremes are useful to evoke asymmetric postures compensating for abnormal neurologic input. Capturing continuous speech and sustained modal pitch is equally telling to correlate perceptual, aerodynamic, and acoustic physiologic disruptions.

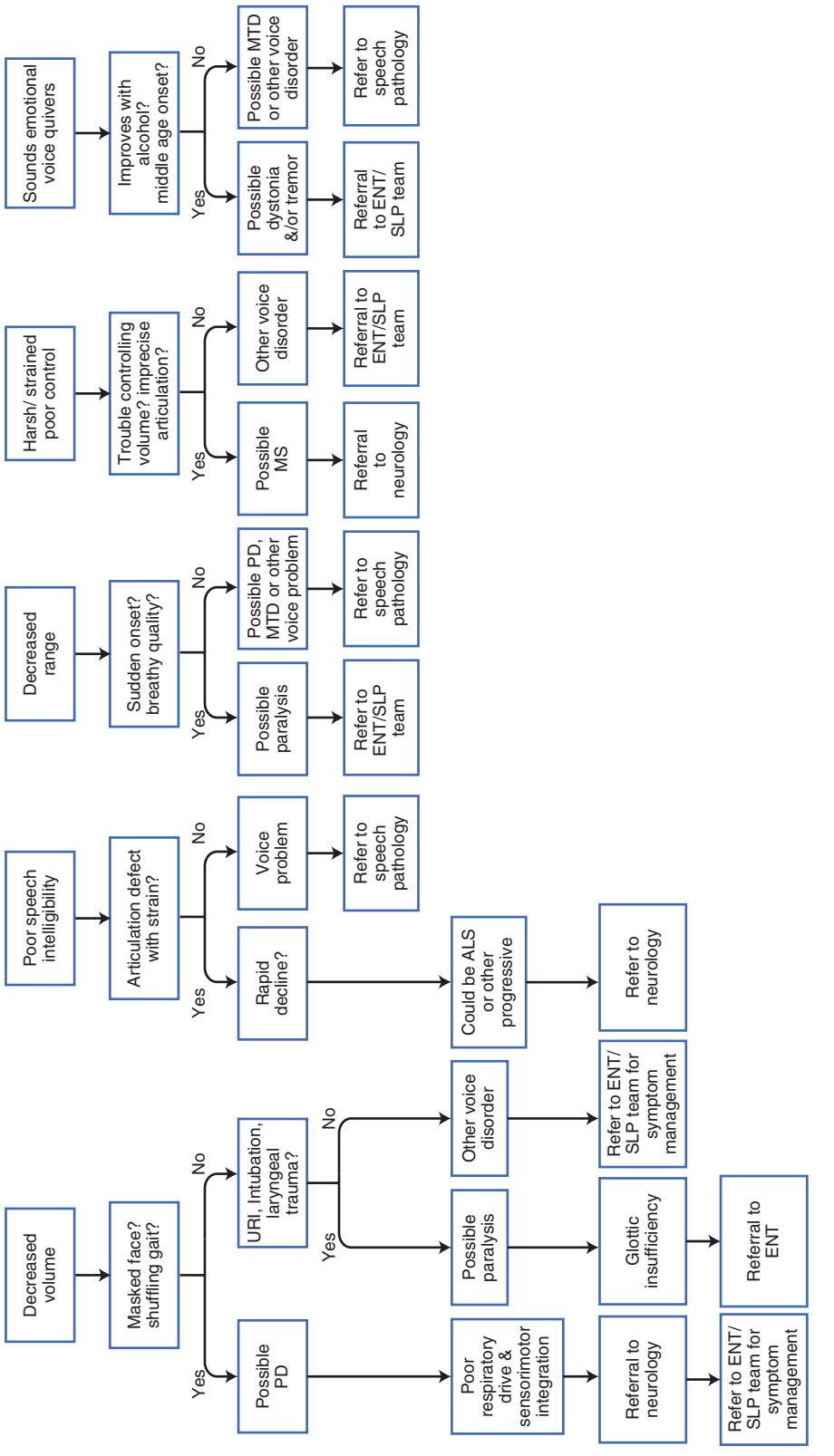


Fig. 5.1 Algorithm used by authors to obtain neurologic profile

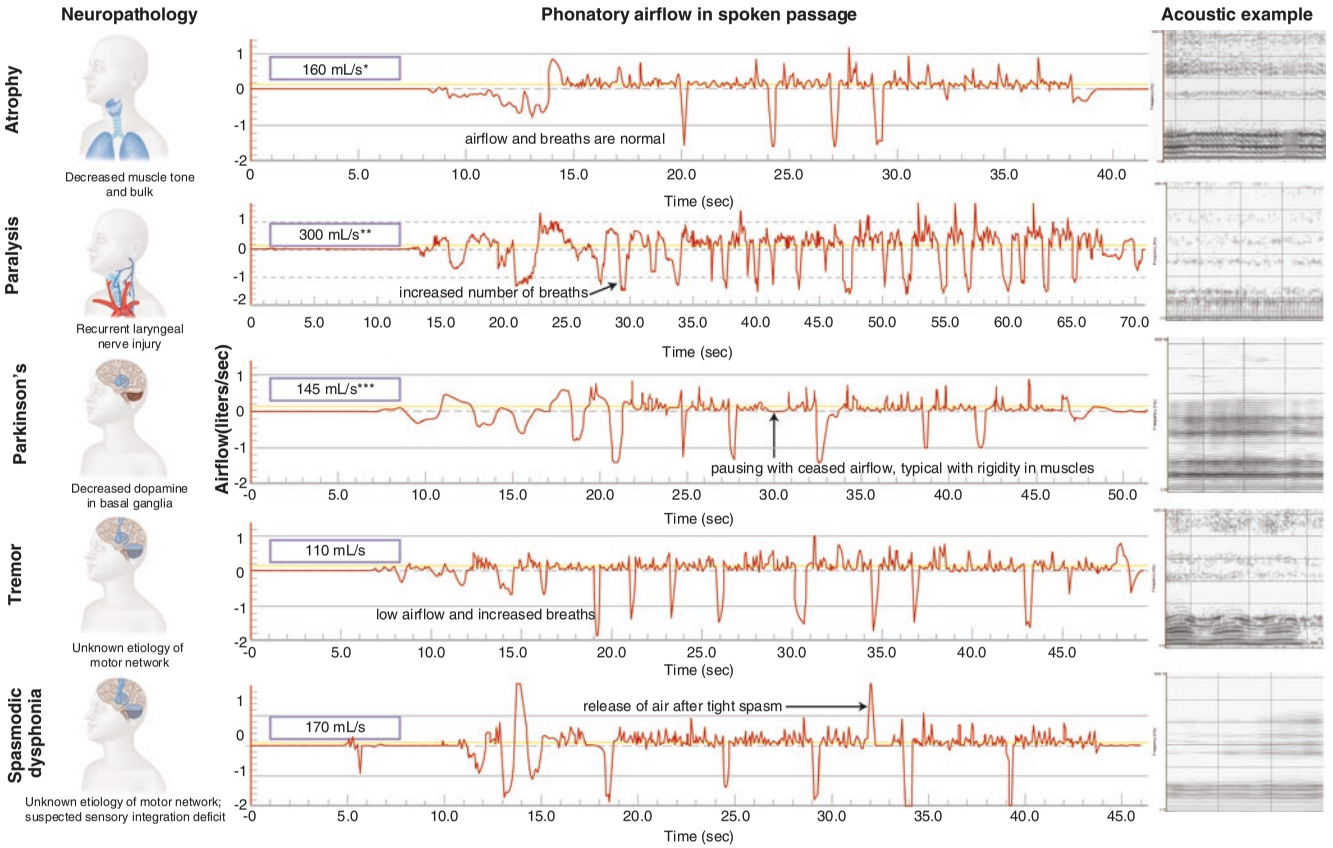


Fig. 5.2 Example acoustic and aerodynamic measurements from select patients are shown in the above diagram for the corresponding neurological disorder. These samples were chosen to depict salient features of each disorder. Red tracings depict phonatory airflow while reading the Rainbow Passage; see Gartner-Schmidt et al. ([52]) for protocol details. Average phonatory airflow is given in the box on the left; asterisk indicates normative value. Measurements for tremor and spasmodic dysphonia do not reflect normative information. Example spectrograms on the right side reflect example acoustic patterns during sustained vowel production and correspond to the same patients with airflow tracings. Varying degrees of harmonic organization can be noted in the horizontal stripes, which represent different frequencies (Hz) (i.e., paralysis – horizontal lines are not clear/disorganized). The tremor spectrogram depicts rhythmic variation in intensity (*dark* vs. *light shading*) and frequency. References: (∗Goodwin et al. [53]; ∗∗Lewandowski et al. [48]; ∗∗∗Dastolfo-Hromack et al. [54]). Measures were taken using the Phonatory Aerodynamic System (PAS) and acoustic spectrograms were generated using the Analysis of Dysphonia in Voice (ADSV) software package; both tools are created by KayPENTAX®

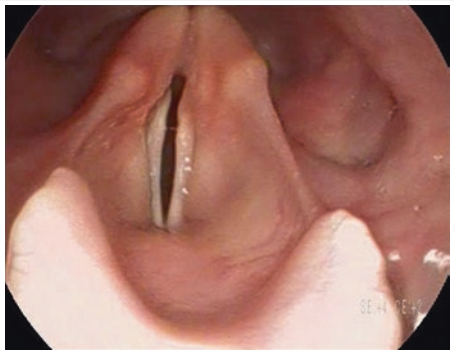
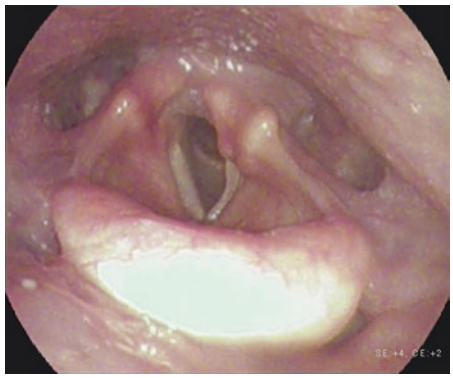
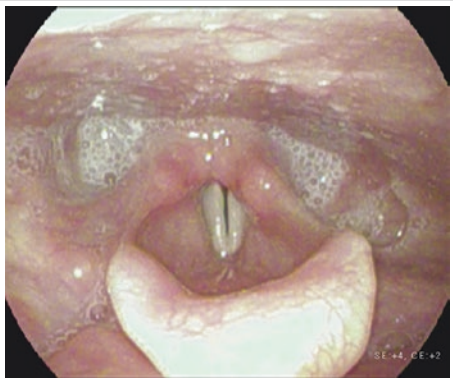
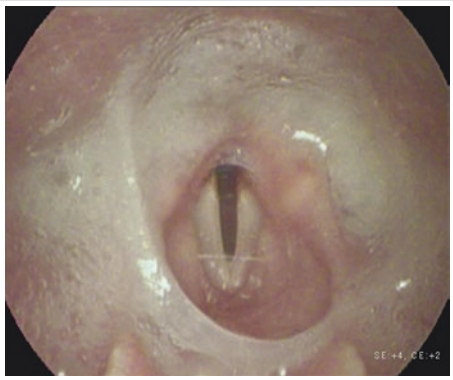
Unveiling tremor is performed in a systematic manner. The *Vocal Tremor Scoring System* was designed for endoscopic evaluation of vocal tremor. It aims to quantify affected structures including the palate, tongue base, pharyngeal walls, larynx, supraglottis, and true vocal folds [62]. This metric eases therapeutic planning and has demonstrated prediction of treatment outcomes. If tremor surfaces only with voicing, it is called a dystonic tremor. When observed within unvoiced contests, it may represent essential voice tremor. Close collaboration with neurology colleagues will facilitate the most accurate profile of tremor disorders, each of which reveals a unique pathophysiology. Researchers found the unvoiced phoneme /s/, continuous whistling, and falsetto a means of distinguishing between essential and dystonic tremor syndromes [63]. Tremor may be isolated, coexisting with dystonia or part of broad neurological disease such as PD.

Laryngeal dystonia has distinct features that are identifiable during laryngoscopy. There are a number of passages laden with voiced and voiceless phonemes that can highlight or trigger dystonic features. Examples of tasks to elicit adductor dystonia include passages such as "I'll roll you away" and "Good dogs beg in bed" [64]. Abductor spasms, the less common laryngeal dystonia variant, will become apparent with abnormally long pauses during voiceless passages such as "Hal hurt his heavy heart" and "Pick up a tasty cake" [64]. In either condition, the vocal folds may demonstrate intermittent or persistent freezing in adduction or abduction. More subtle variations of laryngeal dystonia may not be reflected during laryngeal visualization. These cases will typically surface during thorough perceptual, aerodynamic, and acoustic testing. If the tension is not contextual, consider primary muscle tension dysphonia.

Transitioning from still to stroboscopic light permits observation of vibratory function. Videostroboscopy illuminates progressive positions of the vocal cords throughout the vibratory cycle. The interaction of video and these discrete positions reveals a composite image that mimics real-time vibration. While there are limitations to gaps in vibratory function, examination of each cycle with high-speed imaging typically does not change the diagnostic impression [65]. Advantages of high-speed imaging include greater refinement of the mucosal wave, vibratory amplitude, and glottal closure patterns. This technology is cost prohibitive and not readily integrated into most voice clinics. The cyclic waves course along medial to lateral planes and are evaluated based on pliability, wave propagation, and symmetry [66]. Neurogenic anomalies may impose reduced oscillation due to poor respiratory drive, vocal fold atrophy, immobility that limits free edge contact, and vibratory asymmetries. There is also potential of discovering comorbid mucosal disturbances that further complicate the underlying disorder limiting glottic competence.

Disease-specific trends can be observed throughout the endoscopy, including hypomobility, paradoxical vocal fold movement, tremor, spasm, and dysphagia when secretions are poorly managed. These are outlined in Table 5.4. Consider that many of the individuals undergoing evaluation are in later decades of life. A wide range of dysphonia incidence occurs in the elderly, between 12% and 47% [67], and laryngoscopic incidental findings are common [68]. This can encompass vocal fold atrophy, mucosal imperfections, and inflammation. These discoveries may warrant treatment because they will likely exacerbate a neurogenic communication handicap and can obscure diagnostic symptomatology. Strategies to dissect neurological signs from potential physiological aging effects include a detailed temporal depiction of symptom presentation and associating disease-specific trends. Finally, endoscopy may be abnormal without unifying disease traits. In these circumstances initiating therapy services with a speech-language pathologist is advised. Repeating the exam at a later date can allow a disease to unfold over time and optimize complementary behavioral observations.

Table 5.4 Laryngoscopic findings commonly found in neurolaryngologic voice disorders

Neurological sign	Description of finding	Common disorders
	Incomplete glottal closure. May not close in spite of effort. Prominent vocal processes. Bowed configuration. If paired with asymmetric movement or hypokinesia, could be Parkinson disease	Atrophy, Parkinson disease
	Immobile or partially immobile vocal fold. Challenge with sniff "eee" combination and pitch manipulation.	Paresis, paralysis
	Complete or partial fixation of both vocal cords. Voice may sound normal or strained. Listen for stridor and probe respiratory complaints.	Bilateral paralysis, post radiation, multiple systems atrophy
	Hypopharyngeal pooling	Sensory deficit, dysphagia

Conclusion

The larynx is a complex organ intimately tied to human expression. Neuropathology involving this structure can be identified early by a varied roster of medical care providers, depending on symptom constellation and evaluation acumen. One such example includes a pulmonary consult for severe dyspnea in the setting of bilateral vocal fold paralysis. Another involves patients with PD referred by general practitioners to speech pathologists for seemingly idiopathic voice weakening and eventually meeting with neurology for systemic diagnosis. All practitioners have a unique opportunity to initiate appropriate care pathways based on perceptual voice impression. Skilled physiologic evaluation, with subsequent coordinated treatment among appropriate providers, greatly improves care and patient outcomes. Whether the disease lies centrally or peripherally, opportunity exists to assess integrity of this multilevel system involving respiration, phonation, articulation and deglutition.

A comprehensive neurological voice evaluation ought to involve four components: thorough history, self-rating scales, laryngeal visualization, and behavioral evaluation with acoustic, aerodynamic, and perceptual measures. Disease onset characteristics, demographics, and epidemiologic factors provide vital clues for diagnosis. Varied performance in speech and nonspeech tasks and responsiveness to technique modifications are important to disambiguate neurogenic disease from psychopathology. It also improves sensitivity to categorize the type of neurological voice disturbances. The included diagrams and questionnaires in this chapter are intended to mold and sequence interactions with patients whose case is suspect for a neurogenic laryngeal disorder. Isolating the condition as focal (paralysis, paresis, dystonia, tremor) or systemic (PD, ALS, MS, MSA) is a critical piece of this intake. Referrals to speech-language pathology, laryngology, and neurology can then refine and synthesize the symptoms with endoscopy, aerodynamic, acoustic, and perceptual analyses. Ultimately, patients will benefit when all clinicians are well-educated on laryngeal symptoms and the neurological pathology from which they originate.

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Evaluation of Speech

6

Nancy Pearl Solomon

Introduction

Disorders of the central and/or peripheral nervous systems can lead to a variety of communication disorders, including aphasia, apraxia of speech, and dysarthria. To differentiate among and between these disorders, speech-language pathologists (SLPs) are trained to identify problems involving cognitive-linguistic functions (aphasia), motor speech planning (apraxia of speech), and motor speech execution (dysarthria), as well as disorders of swallowing (dysphagia).

This chapter focuses on dysarthria in adults. There are several types of dysarthria (collectively referred to as "the dysarthrias"), corresponding to the site or sites of lesion (Table 6.1). It is important to note that impairment of any of the subsystems of speech, not only the articulators, can result in a dysarthria despite the root of the word ("arthron," n., Greek) meaning "joint" or "articulator." Technically, any aspect of speech that is affected by a neurologically based etiology is a dysarthria. In fact, neurogenic disorders involving only the voice (e.g., spasmodic dysphonia (see Chap. 16, Laryngeal Dystonia), vocal tremor (Chap. 17, Essential Tremor), unilateral vocal fold paralysis (Chap. 19, Iatrogenic Injuries to Nerves of the Larynx and Pharynx), etc.) can be considered focal dysarthrias.

Table 6.1 Types of dysarthria, site(s) of lesion, and common etiologies

Type of dysarthria	Site of lesion
Flaccid	Lower motor neuron
Spastic	Upper motor neuron, bilateral
UUMN	Upper motor neuron, unilateral
Ataxic	Cerebellar control circuit
Hypokinetic	Basal ganglia control circuit
Hyperkinetic	Basal ganglia control circuit
Mixed	Any combination

The dysarthrias can also present as complex impairments involving multiple speech production subsystems. Take, for example, the hypokinetic dysarthria that often accompanies Parkinson disease (see Chap. 12, Parkinson Disease and the Larynx). Although not all people with hypokinetic dysarthria will sound similar, there are common features that make it recognizable and distinguishable from the other dysarthria types. When the most prominent characteristics involve the voice, such as quiet, monotonous, and breathy phonation, the dysarthria is sometimes termed hypophonia, but this simplifies the extent of the problem. Articulatory and prosodic issues such as imprecise, blurred consonants, and fast rate are also prevalent. Furthermore, people with Parkinson disease often present with reduced facial expression, giving their communication

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partners few cues to determine, for instance, if they are joking. A skilled SLP is trained to parse out these features and determine an overall diagnosis, prognosis, and management plan for individual patients.

Goals of Motor Speech Assessment

There are four overall goals for the assessment of motor speech disorders (in particular, the dysarthrias in adults) according to the American Speech-Language-Hearing Association [1]:

1. Describe perceptual characteristics of the individual's speech and relevant physiologic findings.
2. Describe speech subsystems affected (i.e., articulation, phonation, respiration, resonance, and prosody) and the severity of impairment for each.
3. Identify other systems and processes that may be affected (e.g., swallowing, language, cognition).
4. Assess the impact of the dysarthria on speech intelligibility and naturalness, communicative efficiency and effectiveness, and participation.

Goals 1, 2, and 4 represent complementary approaches to this topic and will be considered in turn. Goal 3 is beyond the scope of this chapter but reminds us that the SLP conducts a comprehensive evaluation of all aspects of communication and swallowing when examining any patient. It is common for people with neurogenic speech disorders, such as someone with Parkinson disease in the example above, to have concomitant problems with cognitive function, language use, and swallowing because of the shared mechanisms and underlying substrates. Screening these functions will determine the need for more extensive assessments.

Motor Speech Examination

A motor speech examination includes physical and functional examination of the speech production mechanism with the structures at rest and while the patient is asked to perform a variety of nonspeech, speechlike, and connected speech tasks. Table 6.2 lists common tasks and observations included in the motor speech examination.

Physical Examination

Physical examination of the motor speech mechanism is often called an "oral-peripheral mechanism exam" but in fact surveys the entire speech production system. SLPs will examine the face, lips, teeth, tongue, jaw, hard palate, velum, pharyngeal walls, neck, and chest wall. A key purpose of this examination is to evaluate relevant peripheral nerve function (see Chap. 5 Evaluation of Neurogenic Voice Disorders for cranial nerve evaluation). Observing orofacial muscles at rest while holding postures, during reflex testing, and while moving for nonspeech and speech purposes informs site of lesion and reveals limitations and abilities of the speech production musculature.

Motor signs of flaccidity or spasticity can contribute to the differential diagnosis of the dysarthrias (see Table 6.2). Evidence of lower motor neuron (LMN) lesions includes muscle atrophy, fasciculations, and postural asymmetry and can often be observed in the tongue. Upper motor neuron (UMN) damage presents as slow, labored movements with reduced range of motion. In addition, testing reflexes relevant to the speech mechanism can reveal primitive reflexes or hyperreflexia. Clinical sources claim that orofacial muscle tone can be inferred from observing resting postures, speed, and extent of movement, but there do not appear to be valid subjective or objective measures at this time [2].

Paresis can occur with both LMN and UMN lesions and may be distinguishable by the pattern of weakness. For example, hemifacial weakness suggests ipsilateral CN VII damage but weakness of the lower face with forehead sparing implicates contralateral UMN damage. The threshold for the functional impact of orofacial muscle weakness is unknown, although it is generally agreed that speech will be impacted if weakness is severe [3–6]. In general, decades of clinical wisdom and converging evidence suggest that

Table 6.2 Common tasks and observations from a motor speech examination

Task	Feature/function	Abnormal observations	Disorder category
Resting	Structure	Muscle atrophy, asymmetry	Flaccid
	Stability	Fasciculations	Flaccid
		Tremor	Hypokinetic
		Irregular abnormal movement	Hyperkinetic (chorea, ballism, tics, dyskinesia)
		Regular abnormal movement	Hyperkinetic (tremor, myoclonus)
		Twisting, writhing movements	Hyperkinetic (dystonia, athetosis)
Reflexes	Suck, snout, jaw-jerk, gag, palmomental	Positive response (pursed lips, jaw movement)	Spastic
Strength	Weakness	Low resistance to opposing force	Flaccid, spastic
Range of motion	Extent, speed, direction	Reduced extent and speed	Spastic, flaccid
		Asymmetric	Flaccid, UUMN
		Excessive, dysmetric	Hyperkinetic
Prolonged vowel	Stability of pitch, loudness, and quality	Continuous breathiness, loudness decay	Flaccid, hypokinetic
		Continuous strain, harshness	Spastic
		Inconsistent quality, tremor, myoclonus, voice stoppages	Hyperkinetic
Diadochokinesis: Alternating motion rates (AMRs) (speech AMRs: syllable repetitions)	Rate, rhythm/ regularity, precision/ accuracy	Slow, regular, imprecise	Spastic or flaccid
		Continuous voicing (e.g., /b/ for /p/)	Spastic
		Slow, irregular, imprecise	Ataxic
		Fast, regular, imprecise	Hypokinetic
		Variable rate, rhythm, and precision	Hyperkinetic
Diadochokinesis: Sequential motion rates (SMRs) (repeating a sequence of syllables)	Order, precision	Similar deficits as for AMRs	Dysarthria
		Sequencing errors, syllabic errors, halting	Apraxia of speech

nonspeech and speechlike tasks are informative for the diagnostic process but may not directly inform speech impairments.

Functional and Maximum Performance Tasks

Disorders involving the cerebellar and basal ganglia motor control circuits are often revealed through tasks that require postural stability or coordinated activation of opposing muscle groups. For a motor speech examination, stability is best evaluated during a prolonged vowel sound. Many protocols call for maximum duration of phonation, but most characteristics of interest for a motor speech or voice assessment only require 5–10 s. The diagnostically important information is the ability to maintain a steady phonation. Unsteadiness or irregularities in the signal are suggestive of a hyperkinetic dysarthria. This task is also helpful for assessing voice quality without the interference of other speech movements. Maximum phonation duration is normally ~20 s and is considered clinically important if it is less than 10 s. This task is often used as a clinical estimate of adequate respiratory support (lung volume, alveolar pressure, airflow) for speech, but the relationship between these variables is complicated and may not be directly interpretable [7–9].

Diadochokinetic (DDK) tasks, also called alternating motion rate (AMR), are useful for evaluating speed, coordination, and accuracy of

movement. Nonspeech oral DDKs include tasks such as alternating lip protrusion and retraction (pucker and smile) or side-to-side tongue movements. Speechlike DDKs, or fast repetitions of the syllables "puh," "tuh," and "kuh," are normally produced at a rate of ~6 syllables/s [10]. Laryngeal diadochokinesis can be tested as well with the syllables "huh" and "uh" and average ~5 syllables/s [11]. Speech DDK performance differs qualitatively between the dysarthria types as well as apraxia of speech, making this an informative test for differential diagnosis (see Table 6.2).

Despite their diagnostic utility, the relevance of maximum performance tasks such as maximally sustained phonation, speech DDK, or orofacial strength testing is commonly questioned because results may not necessarily correlate with speech impairments [12, 13]. Difficulty establishing this relationship relates to the redundancy in the speech production mechanism (e.g., consider the ventriloquist with perfect-sounding speech despite little discernable facial movement), contributions from other articulators or subsystems to the overall speech impairment, and the fact that strength requirements for speech are submaximal.

Typical tasks for eliciting connected speech are oral reading and extemporaneous conversation. The seminal work of Darley et al. [14, 15], which laid the foundation for the differential diagnosis of the dysarthrias, was based on readings of "The Grandfather Passage." This remains the most common text for motor speech evaluations. A new passage titled "The Caterpillar" was designed specifically to elicit features of speech that are expected to assist with the differential diagnosis of motor speech disorders [16].

Tests for Assessment of Dysarthria

There are several formal and informal protocols available for assessing dysarthria in adults, although none are widely accepted for research or clinical use. The Frenchay Dysarthria Assessment [17] is the most commonly cited dysarthria test in the research literature aside from intelligibility tests (reviewed below). It addresses certain reflexive functions; observations about breathing at rest and during speech; functions of the lips, palate, larynx, and tongue; intelligibility of single words, words in carrier phrases, and conversation; and other factors such as speech rate, posture, dentition, and language. Examples of other tests are the Dysarthria Profile [18], the Dysarthria Examination Battery [19], and the Quick Assessment for Dysarthria [20]. These generally take a subsystems approach to assessment, with a variety of additional evaluations including reflexes, sensation, and intelligibility.

Based on the work of Darley et al. [14, 15], Duffy [21] provided a form for rating individual characteristics of connected speech on 5-point ordinal scales. These are grouped into categories of pitch, loudness, voice quality, respiration, resonance, articulation, and prosody, plus items based on speech DDK tasks and unusual characteristics associated with certain types of hyperkinetic dysarthria.

A recent tool, the Bogenhausen Dysarthria Scales (BoDyS) [22], assesses connected speech according to categories or "traits" of breathing, voice (pitch, loudness, and stability), articulation, resonance, speech rate, fluency, and prosodic modulation. Notably, the BoDyS only includes speech tasks (sentence repetition, picture description, reading, conversation), although the tasks used to elicit speech were far less informative than the traits themselves.

Given that no formal assessment of dysarthria has emerged as a clear frontrunner, there is no consensus on which test or tests to administer. Instead, ASHA offers a template for the assessment of motor speech disorders in adults, developed by an expert consensus group [23]. It provides the opportunity to enter information gathered by interview, chart review, direct observation, and formal testing without recommending any particular tests.

Perceptual Characteristics of Speech and Physiological Attributes

The phonatory and articulatory sound sources are filtered by the upper airways to produce the complex acoustic waveform that we recognize as

speech. A practitioner is faced with the task of complex pattern recognition when evaluating speech perceptually. In order to determine the source or sources of a problem when speech is disordered, we attempt to break down this signal auditorily into its component parts. Interestingly, four of the seven categories used by Darley et al. [14, 15] focus on breathing and voice. Clearly, respiratory-phonatory behaviors are highly informative for the differential diagnosis of the dysarthrias.

As is clear from the list of tests in the previous section, most schemes used to characterize speech are grouped according to categories that loosely correspond to the speech production subsystems but also take into account their interdependencies. For example, on Duffy's [21] rating form, items about loudness are listed with phonatory features but loudness is determined primarily by respiratory pressure; and audible inspiration and stridor are included under respiration but are consequences of laryngeal constriction. Nonetheless, these groupings are efficient as the SLP quickly takes stock of the patient's speech characteristics: the voice characteristics (pitch, loudness, quality) are observable during phonation and the respiratory characteristics are observable during breathing-specific events. Table 6.3 lists the most common speech characteristics for each type of

Table 6.3 Common speech characteristics by most likely subsystem(s) for each type of dysarthria

Type of dysarthria	Respiratory	Phonatory	Resonatory	Articulatory	Prosody
Flaccid	Short phrases, low loudness, monoloudness	Breathiness, hoarseness, monopitch, audible inspiration, stridor	hypernasality, nasal emission	Imprecise consonants	Short phrases, monopitch, monoloudness
Spastic	Short phrases, monoloudness, reduced stress, excess and equal stress	Strained-strangled voice, harshness, breathiness, low pitch, monopitch, pitch breaks	Hypernasality, denasality	Imprecise consonants, distorted vowels, slow rate	Slow rate, short phrases, monopitch, monoloudness, excess and equal stress, reduced stress
Ataxic	Monoloudness, excess and equal stress	Harshness, monopitch		Imprecise consonants, distorted vowels, irregular articulatory breakdowns, distorted vowels	Excess and equal stress, prolonged phonemes, prolonged intervals, monopitch, monoloudness, slow rate
Hypokinetic	Low loudness, monoloudness, reduced stress	Low loudness, breathiness, harshness, monopitch, low pitch		Imprecise consonants, "blurred" speech	Fast or accelerating rate, variable rate, short rushes of speech, monopitch, monoloud, reduced stress, inappropriate silences, palilalia
Hyperkinetic	Excessive loudness variation, low loudness, monoloudness, short phrases, excess and equal stress, reduced stress	Variable pitch, monopitch, harshness, strained-strangled voice, voice stoppages, voice tremor	Hypernasality (intermittent)	Imprecise consonants, irregular articulatory breakdowns, distorted vowels	Prolonged intervals, prolonged phonemes, inappropriate silences, short phrases, slow rate, variable rate

dysarthria according to contribution by each subsystem.

By conducting a careful physical examination and auditory perceptual evaluation of speech, the SLP is equipped to contribute meaningfully to a team workup of neurologic conditions by offering speech-related clues to potential etiologies [21].

Motor Speech Production Subsystems

Physically, the speech production system comprises the torso, neck, and head and is usually divided into four subsystems: respiratory, phonatory, resonatory, and articulatory. Although not an anatomical subsystem, prosody is added as a fifth category because it relies on the integration of several subsystems. This section focuses on the structures and neuromuscular functions of each subsystem for the overall purpose of producing speech. In many cases, examinations are conducted in collaboration and consultation with other appropriate clinical providers, including those in neurology, pulmonology, laryngology, and physical medicine.

Respiratory

Examination of the respiratory system for motor speech purposes focuses on the neuromuscular control of the chest wall. Muscles of the rib cage, diaphragm, and abdominal wall are innervated by spinal nerves extending from C1 to L2. Spinal cord injuries, therefore, are expected to lead to speech-breathing problems, with the extent of the speech impairments varying widely between individuals [24]. High spinal cord injuries may require mechanical ventilation or more recently phrenic nerve or diaphragmatic pacing. Part of the speech-breathing assessment involves determining optimal settings of ventilation or stimulation devices for speech while maintaining ventilatory needs [25, 26]. Lower or less extensive injuries, such as those affecting abdominal muscle strength, can affect speaking or singing. Therefore, a thorough examination of the breathing apparatus is merited if speech breathing impairments are suspected [27].

Four parameters can organize the assessment of breathing function for speech: (a) alveolar pressure, (b) lung volume, (c) airflow, and (d) chest wall shape. Functional tasks for these parameters are grounded in their closest perceptual correlates. Vocal loudness depends largely on subglottal pressure. Typical conversational speech is produced with subglottal pressures of about 6–8 cmH_2O. Louder speech is produced with higher pressures, perhaps up to 20 cmH_2O, as the chest wall takes advantage of its natural inherent pressures, and the quietest possible phonation (phonation threshold pressure) hovers around 3 cmH_2O at habitual pitch [28]. The closest perceptual correlate to lung volume during speech is the duration of speech produced on a single expiration, called a "speech breath group." A typical speech breath group lasts about 4 s and uses approximately 0.6–0.8 L of air. Airflow, typically ~0.2 L/s, correlates perceptually to the voice quality continuum of breathy to pressed or strained. Chest wall shape does not have direct auditory perceptual correlates, although a paralyzed diaphragm will lead to an abnormally distended abdominal wall and will be associated with slow, shallow inspirations. Inspirations between speech breath groups normally last 0.5–0.7 s when speaking with a conversational partner [29]. Slow inspirations can disrupt the normal turn-taking during conversational speech.

Phonatory

As noted previously, phonatory characteristics of speech are highly informative for the differential diagnosis of the dysarthrias. Chapter 5 addresses voice assessments that are also relevant for the motor speech assessment of the phonatory system; also see the voice assessment recommendations as outlined in ASHA-sponsored studies [30, 31]. This section, therefore, is brief but highlights two differences in the assessment of phonation as it is approached by voice specialists and motor speech specialists.

The first difference is terminology. Whereas voice experts have mostly settled on the relatively

standard terms of breathy, rough, and strain [32], Darley et al. [14] used the terms breathy, harsh, hoarse (wet), and strained-strangled to describe voice quality. These seemed to characterize the voice qualities of certain disorders – breathiness for flaccid, strained-strangled for spastic, and wet hoarse for the mixed spastic-flaccid dysarthria associated with amyotrophic lateral sclerosis. Over time, these literatures are merging as voice scientists work to improve consistency in terminology and develop acoustic correlates for voice quality. Generally speaking, hoarseness is considered to be a combination of breathiness and roughness, and harshness is considered to be a combination of strain and roughness. Additional terms are common to both literatures, but some such as voice tremor and voice stoppages signal neurogenic voice disorders.

A second feature of laryngeal function that deserves special attention during a motor speech evaluation is that of the laryngeal devoicing gesture. This is the brief vocal fold abduction that occurs during a voiceless consonant, making the difference between, for example, /b/ and /p/ or /z/ and /s/. This quick movement requires precise neuromuscular control of the posterior cricoarytenoid muscle and the opposing laryngeal adductors. Failure to execute this gesture results in voiceless phonemes sounding voiced, a feature called "continuous voicing," which is salient for spastic dysarthria.

Resonatory

Hypernasality in neurogenic speech disorders results from weakness or incoordination of the velopharyngeal muscles. Innervation is from the pharyngeal plexus, including CNs IX, X, and possibly XI, as well as CN V and CN VII that innervate the palatal tensor and levator, respectively. The perception of hypernasality results from greater nasal acoustic energy than nasal impedance. This can occur from an incompletely closed velopharyngeal port, but that does not necessarily ensure perceptible hypernasality. Audible nasal emission during oral consonants is a valid indication of velopharyngeal incompetency.

Perceptual characteristics of resonatory abnormalities can be salient to differential diagnosis. Hypernasality and nasal emissions indicate weakness consistent with flaccid or spastic dysarthria, denasality (denasalization of nasal consonants, such that, e.g., /m/ sounds like /b/) can reflect reduced speed and range of motion consistent with spasticity, intermittent hyponasality can occur with ataxia, and intermittent hypernasality can be a sign of hyperkinesias [33, 34].

Acoustic assessments of nasal resonance can be practical and useful. Determined during nasometry measurement, *nasalance* is the ratio of nasal to total acoustic energy during nonnasal speech utterances. Nasalance measures are moderately correlated with the perception of hypernasality in children with cleft palate when using a reading passage with no nasal consonants [35]. In addition, a one-third octave spectra method has been used to identify abnormal resonances in adults with dysarthria. This method examines spectral changes, typically during a prolonged vowel /i/ ("ee"), based on increased nasal resonances at about 1 kHz and reduced energy at about 2.5 kHz in speakers with resonance disorders [33, 36, 37].

Physiologic measures of velopharyngeal function are also available, including visualization via nasendoscopy, nasal airflow, velar kinematics, and a combination of accelerometry (contact microphone to sense nasal tissue vibration) and acoustics [38].

Articulatory

The cranial nerves most important to speech articulation are CNs V, VII, and XII, generally for mandibular, facial, and lingual movement, respectively. In addition to the oral mechanism examination, assessment tasks for speech articulation for the dysarthrias include repeating or reading words, sentences, or paragraphs and conversational speech. Specific speech sound inventories, used with children with disorders of speech articulation, are not necessary or appropriate in most cases. Rather, the examiner will listen for imprecision and distortion of conso-

nants and vowels and whether these deficits are consistent or inconsistent. As noted in Table 6.3, articulatory features of dysarthric speech contribute to the differential diagnosis. In addition, impaired articulation is considered to be the primary (but not only) contributor to reduced speech intelligibility [39, 40].

Acoustic analysis of speech can add to the assessment of articulation by measuring the frequency components and temporal features of various segments of the speech signal. These types of analyses can provide quantitative data regarding positioning and movements of the speech articulators, particularly the tongue and lips [41, 42]. Although SLPs generally have not embraced such acoustic analyses in clinical settings, clear potential exists for them to contribute to automated analysis of disordered speech and to generate clinically interpretable indices of the type and severity of dysarthria [43].

Physiologic measures of speech articulation are available and, like acoustic measures, are primarily used for research purposes despite their potential utility to identify early stages of dysarthria [44]. Articulatory kinematics typically rely on methods involving electromagnetic articulography [45] and ultrasound [46]. As technology continues to advance, we can expect these methods to become clinically practical.

Prosody

Prosody can be described as the "melody" of speech and is often considered to be the primary contributor to the perceived naturalness of speech. It incorporates changes in loudness, pitch, and timing to convey lexical or emphatic stress, intonation, and rhythm. Traditionally, prosody was considered to be "overlaid" onto the meaningful segments (e.g., consonants, vowels, words) of the message. It is now recognized as the scaffolding upon which speech sounds are bound [47]. Nonetheless, expert clinicians have long recognized prosody as a therapeutic gateway to improved speech in patients with nonfluent expressive aphasia. Melodic intonation therapy [48] uses exaggerated prosody ("intoned speech") to help patients regain fluent speech, most likely by treating the motor aspects of their disorder [49].

Ten separate auditory perceptual terms are included in the Mayo Clinic assessment of prosody, as listed in Table 6.3. The BoDyS [22] devotes three of its nine traits to prosodic aspects: articulation rate, fluency, and prosodic modulation. Using confirmatory factor analysis to examine relationships between the traits, Ziegler et al. [22] demonstrated that prosodic features correlate with respiratory and articulatory factors, suggesting a dependence of prosody on the integrity of the other speech production subsystems. The Prosody-Voice Screening Protocol was designed to systematically classify prosodic characteristics of speech during a variety of tasks in children and adults [50]. However, the test protocol requires extensive training and experience.

Acoustic analysis is well suited to the evaluation of pitch, loudness, and temporal aspects of speech. Acoustic features of intonation and stress can be determined by measuring slope and peak values from F0 and intensity contours of speech utterances. Stress patterning can be assessed by comparing the peak F0 and intensity values from emphasized words or syllables to those from less emphasized words or syllables. Recent resources provide overviews and approaches for quantifying rhythm and intonation in speech [51, 52].

Overall Speech and Its Impact

To capture the general impact of a motor speech disorder, we must consider its overall severity and its impact on communicative effectiveness and efficiency. The overall severity of a dysarthria is based on a composite judgment of individual speech characteristics and is usually described as mild, moderate, or severe. There are no formulae or reference values, and it can be biased by the SLP's listening skills and experiences with disordered speakers. Automated assessments of dysarthria severity based on acoustic features of connected speech are emerging in the literature [53].

Speech intelligibility is measured or estimated as the amount of speech that is understood by lis-

tening to the speaker. Clinicians usually estimate conversational intelligibility as a percentage, choosing this informal method over a more quantitative and time-consuming method of transcribing speech and calculating the percentage of words understood [54]. The estimation method is less reliable and tends to underestimate actual intelligibility. Attempts to quantify overall ratings of intelligibility while maintaining clinical efficiency have used scaling or rating methods [54–56].

The most common formal assessment of speech intelligibility is the Sentence Intelligibility Test (SIT) [57]. Sentences are recorded and transcribed by one or preferably multiple listeners who are unfamiliar with the patient or their circumstances. In addition to the percentage of correctly identified words, the SIT can be used to determine efficiency of speech production by dividing the intelligibility score by the duration of speaking. Eventually, the use of speech recognition technology should partially automate the scoring of intelligibility and efficiency tests, greatly reducing the burden on the clinician.

Although intelligibility is a functional indicator of speech, it does not capture the overall "goodness" of speech. Consider a patient who is entirely intelligible yet has a marked case of spastic dysarthria because of slow rate, harsh voice quality, and monopitch and monoloudness. In this case, intelligibility alone overestimates the patient's speaking abilities and can be an insensitive measure of impairment. Therefore, an assessment of overall speech impairment should include ratings of overall severity and interaction abilities in addition to specific characteristics attributed to the speech production subsystems [6, 39, 58].

A person's reduced participation in communication opportunities can be the most devastating impact of motor speech disorders. Even people with excellent speech intelligibility may have communication problems in their day-to-day activities [59]. The International Classification of Functioning, Disability, and Health provides a scheme to classify health-related function and disability. This can provide important indicators of functional impairments and the need for services. The Communicative Participation Item Bank is a survey instrument for the functional impact of overall communication problems [60]. Other scales that assess the psychosocial impact of dysarthria are the Dysarthria Impact Profile [61], Living with Neurologically Based Speech Difficulties [62], and Communicative Effectiveness Survey [63].

Conclusion

As is evident from this overview of speech assessment, SLPs mostly rely on their trained ears to diagnose and differentiate the various types of dysarthrias. Using auditory perceptual ratings alone is the most common approach, although acoustic and physiologic measures provide useful corroborating evidence. The motor speech examination addresses the respiratory, phonatory, resonatory, articulatory, and prosodic aspects of the speech production system separately and as they interact. Recent innovations utilizing automated speech technology, such as feature extraction, are promising for the future development of reliable and objective assessments of speech.

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Evaluation of Swallow

7

Kristen Linnemeyer and Liza Blumenfeld

Introduction

The safe transport of food and liquid from the oral cavity to the esophagus involves precise coordination of both voluntary and involuntary movements involving the oropharyngeal, esophageal, laryngeal, and respiratory muscles. Dysphagia, or difficulty swallowing, can occur as a result of a broad spectrum of acute or chronic medical conditions. Dysphagia, of neurogenic origin, accounts for more than 75% of all reported cases of dysphagia, largely involving deficits in the oropharynx [1, 2]. It results in an array of medical, social, and psychological sequelae that can lead to malnutrition, dehydration, pneumonia, chronic lung disease, and decreased quality of life.

The financial consequences of neurogenic dysphagia are significant. Patel et al. explored the economic and survival burden of dysphagia among hospitalized patients. Patients with dysphagia generated costs that were $6,243 higher than those without dysphagia ($19,244 versus $13,001, $P < 0.001$). Additionally, patients in the dysphagia cohort were 33.2% more likely to be transferred to a post-acute care facility, were 1.7 times more likely to die in the hospital, and had a higher overall length of inpatient stay [3].

The trajectory of swallowing dysfunction varies depending on whether it involves an acute or progressive condition. Therefore, identification of the underlying neurological process driving dysphagia and accompanying comorbidities is critical, as it predicts the nature, urgency, and frequency of assessment. Acute onset conditions (e.g., stroke, head trauma, spinal cord injury) result in transient swallowing dysfunction. For example, dysphagia in stroke resolves in almost 90% of patients within 2 weeks [4]. Degenerative conditions (e.g., Parkinson disease, amyotrophic lateral sclerosis [ALS], Huntington disease, multiple sclerosis, and myasthenia gravis) often result in gradual, insidious, and progressive deterioration of the swallow mechanism and function.

This chapter will describe noninstrumental tools (dysphagia screening and the clinical swallow evaluation (CSE)) as well as instrumental tools (videofluoroscopic swallowing study (VFSS), flexible endoscopic evaluation of swallowing (FEES), and manometry). The intent is to describe the appropriate timing and clinical utility of each and, more importantly, how clinicians can develop a patient- and condition-centric diagnostic workflow.

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Screening

Early identification of dysphagia risk is fundamental in the setting of neurogenic disorders. In the inpatient setting, the genesis of dysphagia management is often a screening performed by nurses. The American Speech-Language-Hearing Association (ASHA) defines swallowing screening as a pass/fail procedure to identify individuals who require a comprehensive assessment of swallowing function or a referral for other professional and/or medical services [5]. While a screening provides little information about dysphagia severity or management, the objective is to differentiate patients who need a more detailed assessment with a SLP, from those who are safe for alimentation, including medications. The most robust information related to screening is found in the stroke literature. This is largely due to criteria for comprehensive stroke-ready certification which mandates facilities to have an evidenced-based, hard-wired screening tool as part of their protocol [6]. Due to inherent limitations in both labor and technological resources, screenings should be easily administered without extensive training, and be time- and cost-effective. Multiple systematic reviews have been published investigating the reliability, specificity, and sensitivity of numerous dysphagia screenings. Two tools that have strong accuracy within the neurogenic population are the Standardized Swallowing Assessment (SSA) [7] and the Toronto Bedside Swallowing Screening Test (TOR-BSST) [8–10] (Fig. 7.1).

Clinical Swallow Evaluation

The clinical swallow evaluation (CSE) is germane to the role of a SLP when managing dysphagia. A CSE does not require expensive or sophisticated technology and can be readily performed at the patient's bedside, as well as in an outpatient setting. The CSE serves to generate a detailed medical history, diagnose oral phase dysphagia, and direct clinical management. This includes diet/texture recommendations, the necessity for further testing via instrumental swallow exams to further investigate pharyngeal function, referrals to other medical specialists, and/or tailored therapeutic intervention.

The CSE begins with obtaining past and current medical history, highlighting comorbidities that affect the swallowing mechanism and function. The patient's pulmonary function, nutritional status (oral feeding versus non-oral nutrition), weight management, and history of past dysphagia assessments and/or therapies are noted. Medications are reviewed, specifically those that are known to cause dysphagia symptoms (e.g., xerostomia, tardive dyskinesia, esophageal dysmotility) [11] (Table 7.1). General observations of the patient's gait, balance, fine motor control, cognitive status, his/her ability to follow directions, and general alertness are considered.

It is crucial to have an understanding of the nature, onset, frequency, severity, and progression of the patient's dysphagia symptoms. Inquiring what types of food and liquid are easy to swallow and which are difficult, having the patient describe a typical meal, and learning how the patient takes his/her pills provide insight to the patient's current function.

Patients with neurogenic disease often present with poor perception and awareness, leaving dysphagia symptoms undetected [12]. Cognitive-communication deficits can also be a confounding factor. Recruiting family members and/or caregivers can be helpful in generating an accurate representation of the patient's swallow function.

Patient-reported outcome measures (PROM) and questionnaires assist in detecting, characterizing, and understanding symptoms. The Swallowing Disturbance Questionnaire (SDQ) was developed and validated for the detection of swallowing problems across a variety of etiologies. Cohen and Manor found that an SDQ score of more than 12.5 is a good predictor of the presence of both known and undiagnosed swallowing disturbances [13]. The EAT-10 is a second self-administered, symptom-specific PROM that can be completed in less than 2 minutes to document and monitor dysphagia severity. The normative data suggest that an EAT-10 score of three or more is abnormal [14].

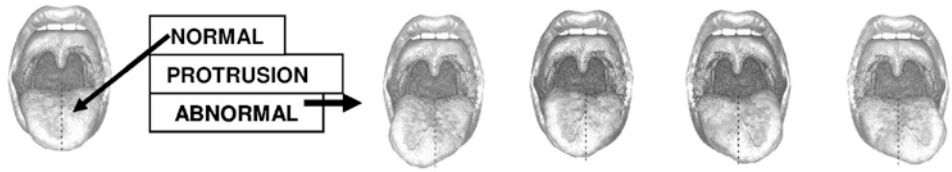
Some Guidelines and Tips for the TOR-BSST©

Before the start of screening, remember to: a) have a cup of water and a teaspoon; b) ensure patient's mouth is clean; and c) ensure patient is sitting upright at 90°.

A. Before water intake:

1. ***"I want you to say "ah" for 5 seconds using your speaking voice."***
   - Model a clear "ah" for the patient.
   - Remind them not to sing "ah" or use a quiet voice.
   - You can ask them to stretch the last syllable of the word *Ottawa*.
   - Remember to take note of the patient's voice when speaking. If his/her voice sounds different when saying "ah" re-instruct the patient to use a normal voice using any of the suggestions above.
   - **You are looking for any breathiness, gurgles, hoarseness, or whisper quality to the voice. If you perceive any of these, even to a mild degree, mark as abnormal.**

2. ***"Open your mouth. Now stick out your tongue as far as it will go. Now move it back and forth across your mouth."***
   - Stick your tongue straight out. If no deviation, model a consistent back and forth motion for the patient.
   - **You are looking for any deviation of the tongue towards one side on protrusion, or any difficulty in moving the tongue to one side. Mark as abnormal if you perceive any of these features.**
   - **If the patient is unable to protrude his/her tongue at all, mark as abnormal.**



B. Water Swallows:

Give the patient 10 X 1 tsp of water. Remind the patient to say "ah" after every teaspoon swallow. If normal, give cup to patient for drinking.

- The patient should always be fed the teaspoon of water.
- Ensure that full teaspoon amounts are given.
- Lightly palpate the throat to monitor for movement of the larynx on the first few swallows.
- **You are looking for any coughing, drooling or change in the patient's voice suggesting wetness, hoarseness, etc. If you perceive this, mark accordingly and stop the water swallows.**
- **If you see what looks like a stifled or suppressed cough, mark this as a cough.**
- **If there is no coughing, drooling, wet voice or hoarseness mark as normal.**

C. Voice after Water Swallows:

- Wait one minute after the end of the water swallows.(You can use this time to clear away the cup etc. and mark the form)
- Ask the patient to say "ah" as in the first part of the screen.

D. Final Scoring:

If you have marked ***any*** of the ***items*** as ***abnormal***, score the patient as ***Failed.***

Fig. 7.1 The Toronto Bedside Swallowing Screening Test ©. (TOR-BSST Courtesy of Rosemary Martino, MA, MSc, PhD, University of Toronto/University Health Network, Toronto, Ontario, Canada)

TOR-BSST©
The Toronto Bedside Swallowing Screening Test©

(addressograph)

DATE: _____ *(mm/dd/yyyy)* TIME: _____ *(hh/mm)*

A) Before water intake:

(Mark either abnormal or normal for each task.)

	Abnormal	*Normal*
1. Have patient say 'ah' and judge voice quality	☐	☐
2. Ask patient to stick their tongue out and then move it from side to side.	☐	☐

B) Water intake:

Have the patient **sit upright** and give water. Ask patient to **say "ah"** after each intake. Mark as abnormal if you note any of the following signs: **coughing, change in voice quality** *or* **drooling.** If abnormal, stop water intake and advance to 'D'.

1) One Tsp Swallows	***Cough during/after swallow***	***Voice change after swallow***	***Drooling during/after swallow***	***Normal***
Swallow 1	☐	☐	☐	☐
Swallow 2	☐	☐	☐	☐
Swallow 3	☐	☐	☐	☐
Swallow 4	☐	☐	☐	☐
Swallow 5	☐	☐	☐	☐
Swallow 6	☐	☐	☐	☐
Swallow 7	☐	☐	☐	☐
Swallow 8	☐	☐	☐	☐
Swallow 9	☐	☐	☐	☐
Swallow 10	☐	☐	☐	☐
2) Cup drinking	☐	☐	☐	☐

C) After water intake:

(Administer at least a minute after you finish Section B.)

	Abnormal	*Normal*
1. Have patient say 'ah' again and judge voice quality.	☐	☐

D) Results:

☐ **Passed** (no abnormal signs)

☐ **Failed → Initiate referral to SLP** (1 or more abnormal signs)

TOR-BSST© Screener's Signature: _____

June 2007 version

Fig. 7.1 (continued)

Table 7.1 Drug-induced dysphagia

Mechanism	Drug/drug classification
Xerostomia (dry mouth)	Anticholinergics Antihypertensives Cardiovascular agents Diuretics Opiates Antipsychotics Antiemetics Antidepressants Muscle relaxants Antihistamines
Reduced lower esophageal sphincter pressure (promoting gastroesophageal reflux)	Theophylline Nitrates Calcium antagonists Anticholinergics Diazepam Morphine
Esophageal injury	Antibiotics Ascorbic acid ASA and NSAIDS Ferrous sulfate Prednisone Potassium chloride Quinidine Theophylline
Extrapyramidal effects (compromising muscle function in the oropharynx and esophagus)	Antipsychotics Metoclopramide Prochlorperazine

From Sokoloff and Pavlakovic [11] with permission Springer-Verlag [11]
ASA acetylsalicylic acid (aspirin), *NSAID* nonsteroidal anti-inflammatory drug

After obtaining a thorough medical history and a comprehensive understanding of the patient's current swallowing status, the CSE can be divided into two parts: collection of noninstrumental measures and trials of food and liquid by mouth (*per oral* or PO).

Noninstrumental Measures

Prior to PO trials, the examiner administers an oral mechanism exam. Key components include:

- Cranial nerve assessment
- Structural assessment of the face, jaw, lips, tongue, dentition, hard and soft palate, oropharynx, oral mucosa and hygiene
- Assessment of muscles and structures used in swallowing, including symmetry, sensation, strength, tone, range and rate of motion, and coordination of movement:
  - The Iowa Oral Performance Instrument (IOPI Medical LLC, Redmond, WA) is a standardized portable device that can be used to objectively quantify tongue and lip strength [15, 16].
  - Tongue strength is measured by asking the patient to use his/her tongue to press a standard-sized air-filled bulb against the roof of the mouth with maximum force.

    Lip strength is measured by placing the same air-filled bulb inside the cheek just lateral to the corner of the mouth. The patient squeezes the bulb against the buccal surface of the teeth by pursing the lips with maximum force. Each task generates a numerical value in kilopascals (kPa), known as peak pressure.
  - Normative data for tongue strength in healthy adults is age-adjusted, while data for lip strength is gender-specific [16].
- Observation of head-neck control, posture, oral reflexes, secretion management, and involuntary movements (e.g., fasciculations, tremor)

Noninstrumental measures also include an informal assessment of speech, voice, and respiration.

Speech

- Connected speech sample observing articulatory precision, speech patterns, rate, and overall intelligibility (e.g., dysarthria, apraxia, dysfluency)
- Diadochokinetic rate (DDK), or a measurement of the accurate repetition of sounds within a designated amount of time

Voice

- Structured tasks and conversational voice sample noting disturbances in the parameters of pitch, intensity, resonance, prosody, and intonation.
- Observation of wet versus dry voice: A wet voice may indicate reduced sensation or

awareness of secretions within the laryngeal vestibule, poor management of secretions, and/or a risk of aspiration [17].
- Cough precision and strength: The strength and quality of the cough does not necessarily indicate that the patient will present with a reflexive cough in response to aspiration, nor that the reflexive cough, if present, is productive.
- Maximum phonation time (MPT) provides insight to glottic competency but is also a test of respiration [17].

Respiration

- Observation of the patient's respiratory rate and breathing patterns (oral or nasal), his/her coordination of respiration during phonation/speech, his/her ability to comfortably hold their breath
- Presence of a tracheostomy tube, cuff status, +/− speaking valve
- Baseline pulse oximetry and observation of oxygen saturation/desaturation during the CSE

Daniels et al. identified six clinical features as being indicative of increased risk of aspiration in acute stroke patients: dysphonia, dysarthria, abnormal volitional cough, abnormal gag reflex, cough after swallow, and voice change after swallow. Results showed that the presence of at least two of the six features has clinical significance in distinguishing patients with moderate to severe dysphagia from patients with mild dysphagia/normal swallowing [18]. These data demonstrate that the above clinical observations can provide objective criteria for the need for instrumental assessment in acute stroke patients.

Per Oral or PO Trials

Trials are administered across a continuum of both texture and volume. When the severity of dysphagia is unknown, and the patient is at high risk for aspiration, ice chips are often trialed first. Additional textures include thin, nectar, and honey-thick liquids, puree, mechanical soft, mixed consistency, and solid. Liquid bolus volumes vary from 1 ml to self-regulated consecutive drinking tasks. Administration can be patient- or examiner-directed and varies from syringe, spoon, cup, and straw.

Information relating to the oral and pharyngeal phases is gleaned from PO trials. Oral phase observations include:

- Oral bolus containment (e.g., labial seal, anterior or suspected posterior spillage)
- Oral prep and transit (e.g., mastication, bolus formation, and bolus manipulation)
- Oral holding, pocketing, and/or residue

While the pharyngeal phase of swallowing cannot be visualized, inferences of pharyngeal function are made via the following observations and tools:

- Palpation – Base of tongue, hyoid, and laryngeal movement can be assessed during the swallow by lightly palpating the area spanning the submandibular area to the inferior aspect of the thyroid cartilage. This provides information regarding timing of the swallow and laryngeal mobility [17].
- Cervical auscultation – Sounds of swallowing, swallowing-related respiration, and secretions in the airway are evaluated with a stethoscope on the lateral side of the neck in the region of the larynx. Distinct differences in acoustic and vibratory signals have been found between non-aspirating swallows from healthy controls and patients with dysphagia [19]. However, there is conflicting evidence for the validity of cervical auscultation, and the reliability of cervical auscultation is insufficient when used as a stand-alone tool in the diagnosis of dysphagia [20].
- Clinical signs and symptoms of penetration/aspiration – Throat clearing, wet voice quality with post-swallow phonation, coughing, choking, watering eyes, shortness of breath.
- Clinical signs and symptoms of reduced pharyngeal clearance – Multiple swallows, patient report of pharyngeal stasis and request for liquid wash.

Compensatory strategies, postural techniques, and swallow maneuvers to improve the safety and/or efficiency of the swallow are referenced in Table 7.2 [17].

Table 7.2 Compensatory strategies/postural techniques/swallow maneuvers and the rationale

Disorder/problem	Compensatory strategy/ posture/maneuver	Rationale
Poor oral bolus containment with premature spillage	Preparatory set	Improves organization and management within oral phase
	Reduced bolus size	
Poor bolus formation (including dentition)	Texture modification	Optimizes bolus manipulation and transit
Inefficient oral transit (reduced posterior propulsion of bolus by tongue)	Head back	Utilizes gravity to clear oral cavity
	Texture modification	Optimizes bolus manipulation and transit
	Reduced bolus size	Improves organization and management within oral phase
Unilateral oral dysfunction	Head tilt to stronger side	Utilizes gravity to divert bolus to intact side
Nasal regurgitation	Reduced bolus size	Compensates for reduced velopharyngeal closure
	Texture modification	
Delay in triggering the pharyngeal swallow (bolus past ramus of mandible, but pharyngeal swallow not triggered)	Chin down	Widens valleculae to prevent bolus entering airway Narrows airway entrance Pushes epiglottis posteriorly
	Supraglottic swallow	Voluntary breath hold closes vocal folds before and during swallow
	Reduced bolus size	Reduces volume burden in the pharynx
	Texture modification (increasing liquid viscosity)	Reduces speed of bolus
Reduced posterior motion of tongue base (residue in valleculae)	Chin down	Pushes tongue base backward toward pharyngeal wall
	Effortful swallow	Effort increases posterior tongue base movement
	Liquid wash	Improves bolus clearance
	Multiple swallows	
Reduced pharyngeal contraction (residue throughout pharynx)	Effortful swallow	Effort increases posterior tongue base movement; improves bolus clearance
	Texture modification (decreasing viscosity)	Promotes ease of clearance
	Reduced bolus size	
	Liquid wash	Improves bolus clearance
	Multiple swallows	
Unilateral pharyngeal weakness (residue on one side of pharynx)	Head rotated to damaged side	Redirects bolus flow to intact side
	Texture modification (decreasing viscosity)	Promotes ease of clearance
	Reduced bolus size	
	Liquid wash	Improves bolus clearance
	Multiple swallows	
Unilateral laryngeal dysfunction (aspiration during swallow)	Head rotated to damaged side	Places extrinsic pressure on thyroid cartilage, increasing adduction
	Texture modification (increasing liquid viscosity)	Reduces speed of bolus; compensates for reduced airway protection and sensation
	Chin down	Places epiglottis in more posterior protective position
	Reduced bolus size	Compensates for reduced airway protection

(continued)

Table 7.2 (continued)

Disorder/problem	Compensatory strategy/ posture/maneuver	Rationale
Reduced or late laryngeal closure (aspiration during swallow)	Chin down	Places epiglottis in more posterior protective position; narrows laryngeal entrance
	Supraglottic swallow	Voluntary breath hold usually closes vocal folds before and during swallow
	Super-supraglottic swallow	Effortful breath hold tilts arytenoids forward, closing airway entrance before and during swallow
	Texture modification (increasing liquid viscosity)	Reduces speed of bolus Compensates for reduced airway protection and sensation
	Reduced bolus size	Compensates for reduced airway protection
Reduced anterior and superior laryngeal mobility	Mendelsohn maneuver	Laryngeal movement opens the upper esophageal sphincter (UES) Prolonging laryngeal elevation, increasing duration of UES opening
Cricopharyngeal dysfunction (residue in pyriform sinuses)	Head rotation	Pulls cricoid cartilage away from posterior pharyngeal wall, reducing resting pressure in cricopharyngeal sphincter
	Mendelsohn maneuver	Laryngeal movement opens the upper esophageal sphincter (UES) Prolonging laryngeal elevation, increasing duration of UES opening
	Texture modification (decreasing viscosity)	Improves bolus clearance
	Reduced bolus size	
	Liquid wash	
	Multiple swallows	

Adapted from Logemann [17], with permission Pro-Ed

Summary of findings, recommendations regarding diet, medication administration, aspiration risk, compensatory strategies, therapy indications, and additional referrals are discussed with the patient and family. Diet texture recommendations including both liquids and solids are prescribed using the International Dysphagia Diet Standardization Initiative (https://iddsi.org/) (Fig. 7.2). This ensures consistent communication between providers and uniform preparation of food.

If the CSE suggests oropharyngeal, pharyngeal, and/or pharyngoesophageal dysphagia, or is inconclusive, instrumental assessment is warranted. See Table 7.3 for additional criteria [5]. Instrumental assessments provide measures to define the nature of dysphagia and determine the trajectory of management. A videofluoroscopic swallowing study (VFSS), also known as a modified barium swallow study (MBSS), and flexible endoscopic evaluation of swallowing (FEES) are widely accepted and utilized. VFSS and FEES each carry unique advantages, disadvantages, and clinical implications. Table 7.4 provides clinical guidance to determine the most appropriate instrumental exam. Pharyngeal manometry is an additional instrumental tool that compliments VFSS and FEES.

Fig. 7.2 The IDDSI framework. © The International Dysphagia Diet Standardisation Initiative 2016 @https://iddsi.org/framework/, with permission

Table 7.3 Criteria for determining whether instrumental assessment is warranted [5]

Yes	No
1. The CSE indicates signs and symptoms of dysphagia or is inconclusive	1. The CSE did not indicate dysphagia
2. Confirmation and/or differential diagnosis of dysphagia is needed	2. The patient is medically unstable and thus cannot tolerate either VFSS or FEES
3. There is a need to identify disordered swallowing physiology to guide management and treatment	3. The patient is unable to cooperate or participate in the CSE
4. Patient's nutrition, hydration, and/or pulmonary health is compromised, and there is question as to whether oropharyngeal function is contributing	4. The instrumental exam would not change management or recommendations
5. The safety and efficiency of the swallow is a concern due to a medical condition or diagnosis associated with a high risk of dysphagia	
6. The patient has previously been diagnosed with dysphagia and a change in swallow function is suspected	
7. A degenerative disease with progression is known, and oropharyngeal function may require further definition for effective management	

CSE clinical swallow examination, *VFSS* videofluoroscopic swallowing study, *FEES* flexible endoscopic evaluation of swallowing

Table 7.4 Videofluoroscopic swallowing study (VFSS) vs. flexible endoscopic evaluation of swallowing (FEES) – selecting the most appropriate instrumental exam

Clinical symptom/indication	VFSS	FEES	Either
Unknown etiology, vague symptoms, or if a comprehensive view is needed	X		
Oral phase dysphagia is suspected	X		
Question of secretion management or suspicion of aspiration of secretions		X	
Complaints of pharyngeal stasis (e.g., food sticking)			X
Esophageal complaints	X		
Extended exam needed/desired for testing of fatigue (e.g., full meal assessment)		X	
Submucosal anatomy is at question (e.g., cervical osteophytes)	X		
Visualization of surface anatomy and/or mucosal abnormalities suspected		X	
Esophagopharyngeal regurgitation	X		
Examination of movement of multiple structures at the height of the swallow (e.g., hyoid movement, laryngeal mobility)	X		
Concern regarding vocal fold mobility, dysphonia, and/or glottic closure		X	
Suspected velopharyngeal incompetence			X
Biofeedback is desired for therapeutic purposes		X	
Question of UES function (e.g., stricture, cricopharyngeal bar)	X		
Aspiration suspected during the swallow	X		
Complaints of globus sensation	X		
Sensory testing is warranted		X	
Radiation exposure issues or if the patient is pregnant		X	
History of epistaxis, vasovagal episodes, laryngospasms, and/or bilateral obstruction of the nasal passage	X		
Obesity, patients wearing a halo, cervical collar, etc., resulting in obstructed fluoroscopic views		X	
Risky transportation to radiology due to medical fragility, mechanical ventilation, transferring precautions, etc.		X	

Videofluoroscopic Swallowing Study

The videofluoroscopic swallowing study (VFSS) has been considered the gold standard for dysphagia assessment for patients demonstrating swallowing dysfunction due to various medical conditions. The technique was initially introduced by Donner and Siegel in 1965 [21]. In the 1970s, Logemann and colleagues revamped the procedure, allowing for accurate and reproducible assessment of oropharyngeal swallow function. This became the impetus for behavioral swallowing rehabilitation [17].

Technique

Fluoroscopic images are captured and recorded during dynamic swallowing. The patient can be in a seated or standing position, whichever allows for maximum comfort, optimal visualization, and safety. Radiopaque material (barium) is administered across a continuum of both texture and volume. Textures may include thin, nectar, and honey-thick liquids, puree, mechanical soft, mixed consistency, solid, and barium tablet. Volumes vary from 1 ml to self-regulated consecutive drinking tasks. Administration can be patient- or examiner-directed and varies from syringe, spoon, cup, and straw. Patients are positioned in both the lateral and anterior-posterior (AP) view in order to capture information regarding safety, efficiency, timing, and symmetry. To optimize swallowing function, stimulability probes including compensatory strategies, postural techniques, and swallow maneuvers are trialed (see Table 7.2) [17]. Dysphagia severity can be classified using the Penetration-Aspiration Scale (PAS) (Table 7.5) [22] and the Dysphagia Severity Rating Scale (Table 7.6) [23, 24].

Table 7.5 Eight-Point Penetration-Aspiration Scale (From Rosenbek et al. [22] with permission Springer-Verlag)

Score	Description
1	Material does not enter the airway
2	Material enters the airway, remains above the vocal folds, and is ejected from the airway
3	Material enters the airway, remains above the vocal folds, and is not ejected from the airway
4	Material enters the airway, contacts the vocal folds, and is ejected from the airway
5	Material enters the airway, contacts the vocal folds, and is not ejected from the airway
6	Material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway
7	Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8	Material enters the airway and passes below the vocal folds, and no effort is made to eject

Key members of the team include an SLP, who directs, performs, and interprets the exam; a radiology technologist, who activates and captures the fluoroscopic images; and a fluoroscopy-certified physician, who supervises the radiation dosing and also provides diagnostic interpretation. Specific roles and personnel vary by institution.

Benefits

Neurogenic dysphagia often includes both discrete and interrelated patterns of motor and/or sensory dysfunction. Table 7.7 delineates common observations within neurogenic populations [17, 25]. One defining benefit of the VFSS lies in its ability to capture not only the morphological features, but the dynamic properties of the oral, pharyngeal, and esophageal phases of swallowing. Another hallmark feature of the VFSS is the ability to visualize aspiration during the swallow in patients with diminished or absent sensory systems. Silent aspiration has been reported to present in 40–60% of patients with dysphagia of neurogenic origin [26]. Figure 7.3 is a still frame from a VFSS highlighting the presence of a cricopharyngeal bar.

Table 7.6 Dysphagia severity rating scale [23, 24]

Rating	Explanation
0	*Normal swallowing mechanism*
1	*Minimal dysphagia* – VFSS shows slight deviance from a normal swallow. Patient may report a change in sensation during swallow. No change in diet is required
2	*Mild dysphagia* – Oropharyngeal dysphagia present, which can be managed by specific swallow suggestions. Slight modification in consistency of diet may be indicated
3	*Mild-moderate dysphagia* – Potential for aspiration exists but is diminished by specific swallow techniques and a modified diet. Time for eating is significantly increased. Supplemental nutrition may be indicated
4	*Moderate dysphagia* – Significant potential for aspiration exists. Trace aspiration of one or more consistencies may be seen via VFSS. Patient may eat certain consistencies by using specific techniques to minimize potential for aspiration and/or to facilitate swallowing. Supervision at mealtimes is required. Patient may require supplemental nutrition orally or via feeding tube
5	*Moderate-severe dysphagia* – Patient aspirates 5–10% on one or more consistencies, with potential for aspiration on all consistencies. The potential for aspiration is minimized by specific swallow instructions. Cough reflex is absent or non-protective. Alternative mode of feeding is required to maintain patient's nutritional needs. If pulmonary status is compromised, "nothing by mouth" may be indicated
6	*Severe dysphagia* – Patient aspirates more than 10% of all consistencies. "Nothing by mouth" is recommended

Limitations

Inherent limitations to the VFSS are mitigated by referencing selection criteria found in Table 7.4. Two limitations warranting further discussion are radiation exposure and the subjective methods of interpretation. Due to the use of radiation, a VFSS is considered an invasive exam. This demands thoughtful and judicious utilization to keep individual and cumulative doses as low as reasonably achievable (ALARA). Due to the

Table 7.7 Videofluoroscopic swallowing study (VFSS) – common findings within neurogenic populations [17, 25]

Swallow phases	What we assess	Common findings
Oral	Lip closure Bolus preparation Bolus containment Premature spillage Oral clearance	Labial leakage (ALS, AD) Tongue dysfunction (CVA, ALS) Poor mastication (ALS, AD) Delayed bolus transit (ALS, AD) Poor bolus manipulation and control (PD) Premature spillage (PD) Oral residue (ALS, AD)
Pharyngeal	Pharyngeal swallow initiation Soft palate elevation Tongue base retraction Laryngeal excursion Anterior and superior hyoid displacement Epiglottic inversion Pharyngeal contraction Pharyngeal transit time Laryngeal closure Penetration/aspiration Pharyngeal clearance Upper esophageal opening Sensation Symmetry	Delayed swallow (PD, ALS, AD) Nasal regurgitation (ALS) Pharyngeal weakness (CVA) Prolonged pharyngeal transit time (CVA) Decreased laryngeal elevation (ALS, AD) Aspiration (CVA, ALS, AD) Silent aspiration (CVA, PD) Pharyngeal residue (PD, ALS)
Esophageal	Presence of osteophytes Presence of diverticulum Presence of narrowing/obstruction Esophageal screening Reflux	Cricopharyngeal dysfunction (PD, CVA) Poor esophageal clearance (PD) Tertiary contractions (PD) Reflux (PD)

ALS amyotrophic lateral sclerosis, *AD* Alzheimer disease, *CVA* cerebral vascular accident, *PD* Parkinson disease

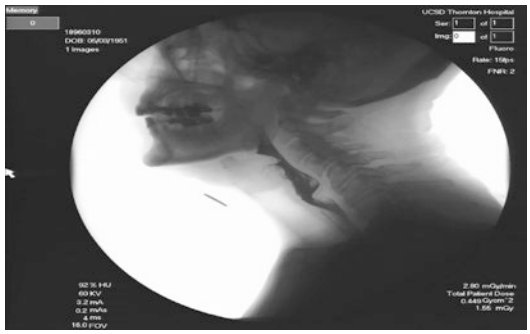


Fig. 7.3 Still frame from videofluoroscopic swallowing study (VFSS) illustrating the presence of a cricopharyngeal bar

nature of neurogenic dysphagia and the need for serial exams, clinicians must perform them at critical time periods and maximize utility during each exam [27]. Careful consideration should be made, especially in the pediatric population, given the lifetime risk of radiation-association malignancy [28].

While the performance of VFSS continues to be widely used in a variety of medical settings, multiple parameters of the exam including protocol design and interpretation methods remain subjective and non-standardized. Lee et al. explored the accuracy of subjective VFSS analysis. Swallow studies were correctly classified as being normal or abnormal only 61.5% of the time. Inter- and intra-rater reliability was found to be variable, further suggesting that subjective interpretation should not stand alone [29]. To reduce dependence on subjective impressions and maximize the potential of the VFSS, Leonard and Kendall designed a novel method, now known as Swallowtail, for collecting objective surrogate measures of timing and swallowing gestures using a standardized protocol. This was not intended to replace the traditional subjective exam, but rather to apply a consistent methodology, supplying quantitative information that can be compared to normative data [30].

Flexible Endoscopic Evaluation of Swallowing

The first description of fiber-optic endoscopic evaluation of swallowing (FEES), and now more often referred to as flexible endoscopic evaluation of swallowing, was published in 1988 [31]. Susan Langmore describes the genesis of FEES as being rooted in the collaborative relationship of the otolaryngologist and SLP during traditional laryngoscopies. She recognized that the larynx, a salient region for detecting aspiration, was beautifully portrayed, thus inspiring her to use this modality to evaluate swallowing [31]. Over the last three decades, FEES has become an established instrumental exam used to evaluate the swallow mechanism and function, implement therapeutic interventions, and make recommendations for safe PO intake [32].

Technique

FEES can be performed at a patient's bedside, as well as in an outpatient setting using a flexible fiber-optic or video endoscope, which is passed transnasally. A FEES exam is comprised of three parts. The assessment begins with a survey of the structural, physiologic, and sensory mechanisms critical to swallowing function. This is accomplished by asking patients to perform non-swallow and voicing tasks. Table 7.8 provides a detailed list of these probes, as well as findings in both normal and neurogenic populations. Evaluation of secretion management is imperative in the neurogenic population and has significant predictive value for aspiration [33]. The Murray Secretion Scale (MSS) is a reliable tool to quantify accumulation of oropharyngeal secretions [34].

The second portion of the exam involves administration of food and liquid boluses. Patients ingest various consistencies, typically dyed with food coloring, with the scope in place. Textures may include: ice chips, thin, nectar, and honey-thick liquids, puree, mechanical soft, mixed consistency, and solid. Volumes vary from 1 ml to self-regulated consecutive drinking tasks. Administration can be patient, family, or clinician-directed and varies from syringe, spoon, cup, and straw. During PO trials, the examiner observes premature spillage of boluses into the pharynx or larynx, assesses airway protection and closure, and localizes residue in the pharynx and hypopharynx. To optimize swallowing function, stimulability probes including compensatory strategies, postural techniques, and swallow maneuvers are trialed (see Table 7.2). Dysphagia severity can be classified using the Penetration-Aspiration Scale (PAS) (see Table 7.5), the Dysphagia Severity Rating Scale (see Table 7.6), and the Yale Pharyngeal Residue Severity Rating Scale – an image-based, five-point ordinal rating scale quantifying residue location (vallecular and pyriform sinus) and amount (none, trace, mild, moderate, and severe) [35].

Part three is described as the intervention portion of the exam. The examiner evaluates stimulability for improved swallowing safety and efficiency. Patients are provided with modifications in postural and/or texture to optimize bolus transit and clearance and eliminate penetration and aspiration.

Both SLPs and otolaryngologists with didactic and hands-on training perform FEES. Criteria for SLPs performing the exam independently vary by state and institution.

Benefits

There are several remarkable attributes of FEES, including utilization at the patient's bedside, direct visualization of the larynx, and the ability to be used repeatedly for therapeutic purposes [32]. One illustration of these benefits is the use of endoscopic biofeedback. Biofeedback is used to learn or improve a motor skill as well as optimize patient engagement and compliance [17]. This is valuable within neurogenic dysphagia, where sensory integrity is compromised. Biofeedback expedites the accurate performance of prescribed compensatory techniques, for example, the supraglottic swallow maneuver, a head turn, or a volitional cough [31]. Manor et al. found that the use of visual assistance in the Parkinson disease pop-

Table 7.8 Non-swallow and voicing tasks prior to trials of food and liquid by mouth

Task	Indication	Normal	Neurogenic findings
"Say pa, pa, pa" "Sustain /s/"	Evaluate palatal function and closure	Full velopharyngeal closure with each syllable and sustained closure during /s/	Unilateral or bilateral velopharyngeal insufficiency
"Stick out tongue"	Visualize vallecular space	Base of tongue moves symmetrically anteriorly to allow visualization of the vallecular space	Pooling of secretions
"Say 'all', with prolonged, exaggerated vowel"	Assess base of tongue movement	Base of tongue moves symmetrically posteriorly and obstructs view of the epiglottis	Reduced or weak retraction of tongue base
"Alternate between an /i/ and a sniff"	Observe true vocal fold abduction and adduction/recurrent laryngeal nerve function	Full adduction (with phonation) and abduction (with inhalation)	Unilateral or bilateral immobility
"Glide on /i/ from high to low"	Assess superior laryngeal nerve function	True vocal folds elongate (with increased pitch) and contract (with decreased pitch); symmetric, lateral pharyngeal wall contraction at peak frequency	Truncated pitch Reduced unilateral or bilateral pharyngeal wall contraction
"Make a dolphin squeal /i/"	Evaluate pharyngeal constriction	Symmetric, lateral pharyngeal wall contraction	Reduced unilateral or bilateral pharyngeal wall contraction
"Count from 1 to 10"	Assess vocal quality and observe coordination between phonation and respiration	True vocal folds adduct for voicing resulting in glottic closure sufficient for phonation	Dysphonia; glottic incompetency; atrophy of the true vocal folds; poor respiratory support
"Hold breath tightly" (Valsalva)	Assess patient's ability to close glottis	True vocal folds adduct, false vocal folds adduct, arytenoids tilt anteriorly to base of epiglottis, completely closing off glottis	Weak or inability to demonstrate Valsalva Reduced duration of breath hold
"Puff out your cheeks like you are blowing a trumpet, but don't let the air out"	Visualize hypopharynx	Pyriform sinuses dilate bilaterally; space between arytenoids and post pharyngeal wall dilates offering visualization of the hypopharynx	Pooling of secretions Inability to perform due to nasal emission/ velopharyngeal insufficiency
"Cough"	Assess airway protection	True vocal folds symmetrically adduct abruptly; any secretions on the vocal folds and/or in the laryngeal vestibule clear	Weak, imprecise, or nonproductive cough
Laryngeal adduction reflex by lightly tapping the right and left arytenoid with the tip of the endoscope	Sensory integrity	Immediate and complete adduction of the vocal folds	Unilateral or bilateral delayed or absent response

ulation improved the understanding and implementation of strategies and enhanced patients' motivation to practice [36].

Despite the invasive nature of the exam, FEES has been found to be a safe procedure with limited incidence of adverse events. In 2016, a report of complications in 2820 FEES exams was published. Subjects included inpatients and outpatients. They reported four cases of epistaxis (0.14%), three cases of vasovagal syncope (0.1%), and two cases of laryngospasm (0.07%), three of which occurred in patients with ALS. All resolved spontaneously [37].

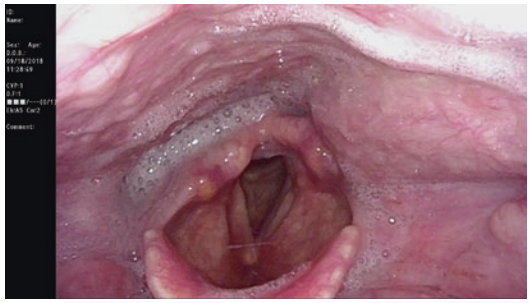


Fig. 7.4 Still frame from flexible endoscopic evaluation of swallowing (FEES) displaying right unilateral pharyngeal weakness

Safety of FEES was also confirmed in a series of 300 exams involving acute stroke patients. There were no reported instances of epistaxis, despite the use of anticoagulant therapy or antiplatelet drugs [38]. Figure 7.4 is a still frame from a FEES highlighting unilateral pharyngeal and laryngeal weakness with associated pooling of secretions.

Limitations

Inherent limitations to FEES are mitigated by referencing selection criteria found in Table 7.4. Three limitations that warrant further discussion are exam tolerance, limited information regarding the oral and esophageal phases, and lack of visualization of aspiration during the swallow. Poor exam tolerance can lead to a truncated exam which limits the acquisition of salient information. Patients may experience minimal discomfort, gagging, or emesis. To avoid these complications, topical analgesics are administered. When compared to VFSS, FEES offers a less holistic view with emphasis on the pharyngeal phase. In addition, events during the swallow, including aspiration, cannot be visualized during the normal white-out period when the combined effect of pharyngeal constriction and epiglottic tilt obscure the view of the larynx.

Manometry

High-resolution manometry (HRM) provides biomechanical swallowing information, which serves to inform both diagnosis and treatment strategies. The technique involves passing a flexible catheter through the nose and into the pharynx and esophagus to capture swallowing-related pressures along the catheter's sensor array [39]. The output of HRM is quantitative information including: the force of the pharyngeal propulsive wave, the squeezing tone of the UES, and the timing of the coordination between the pharyngeal contraction and UES relaxation [40].

Hoffman et al. used simultaneous HRM and videofluoroscopy to determine if results of Modified Barium Swallow Impairment Profile (MBSImP) and penetration/aspiration status could be identified from HRM alone. MBSImP parameters were correctly identified as being normal or disordered approximately 91% of the time. These data suggest HRM provides quantitative functional data at the bedside to supplement and, at times, replace traditional VFSS, thus avoiding radiation exposure [41].

HRM has potential to guide and validate the efficacy of surgical management of the UES (e.g., dilation, Botox, myotomy) and/or therapeutic interventions to optimize swallow strength and coordination. See Chap. 8 "High Resolution Manometry and Its Utility in Patients with Neurological Diseases Affecting the Larynx/Pharynx" for additional information regarding manometry.

Closing

Oropharyngeal dysphagia is a highly prevalent comorbidity in neurogenic disease and presents a serious health threat, which may lead to aspiration PNA, malnutrition, hospitalization, and death. Early identification of risk is fundamental by using a battery of diagnostic tools in a complimentary and timely fashion.

In the context of neurogenic dysphagia assessment, a patient-centric, holistic approach is paramount to maximize quality of life. Optimal outcomes are achieved by a multidisciplinary team, which may include at various stages a neurologist, registered nurse, SLP, otolaryngologist, radiologist, and dietitian.

This chapter highlights a spectrum of noninstrumental and instrumental tools, all of which play a role within dysphagia management. Assessments should be reproducible, sensitive, and specific to the condition and objective when possible. Striving to quantify swallowing disturbance is crucial in order to predict risk, accurately diagnose, and recommend effective intervention.

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High-Resolution Manometry

8

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Clinical Practice Model

Videofluoroscopic and endoscopic imaging of swallowing are standards in viewing and judging swallowing events including lingual-palatal contact, tongue base contact to posterior pharyngeal wall, laryngeal vestibule closure, pharyngeal constriction, and upper esophageal sphincter opening. A limitation of imaging is the inability to gauge pressure generation during these events; thus treatment planning is subjective and highly variable [1]. Patients with complex dysphagia may be underserved by swallow imaging alone.

High-resolution pharyngeal manometry (HRPM) is expanding throughout specialty dysphagia care centers worldwide [2–4]. It has been adapted from esophageal high-resolution manometry and can be used to complement oropharyngeal imaging studies in one of several ways. Concurrent HRPM with a videofluoroscopic swallow study (VFSS), termed "manofluorography," has been traditionally regarded as ideal in acquiring synchronized pressure measurements of recorded swallowing events. In this model, the manometer is inserted under the guidance of VFSS and verified as entering the esophagus. Swallowing images are acquired at the same time as manometric measurements during VFSS barium bolus administration. In swallowing research, precise synchrony of VFSS images with manometric measures is vital to establish validity in measures of swallowing events. The presence of the manometric catheter may affect swallowing, but by applying a systematic protocol for all patients undergoing HRPM, normative data obtained under the same conditions can be used for functional comparison.

In the pragmatic clinical care setting, where the demands for conducting two concurrent procedures in the fluoroscopy suite may exceed available resources, routine manofluorography may not be feasible. Furthermore, HRPM is an invasive procedure that warrants selective application. It is therefore fitting to perform an imaging study first to establish an indication for adding HRPM to the diagnostic workup [2]. HRPM may then be pursued following the imaging study, with visual images providing guidance for interpreting pressure topography and associated pressure measures.

Conventional manometry has been paired with fiber-optic endoscopic evaluation of swal-

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lowing (FEES) in normative swallowing research [5–7]. HRPM combined with FEES is emerging in clinical research [8], and it holds promise for application in clinical settings where access to VFSS may be limited. HRPM can complement FEES by providing measures of the upper esophageal sphincter (UES), as FEES offers direct imaging only to the hypopharynx [9]. Conversely, HRPM is limited to measures of pressure and timing through the pharynx and UES, and it cannot provide direct assessment of airway closure or aspiration.

The HRPM procedure can be safely conducted by speech pathologists with advanced training and verified competency [10]. Adult patients selected for HRPM should be cognitively capable of understanding the rationale for examination and reconciling discomfort during nasal and pharyngeal passage of the manometric catheter. The role for nasal anesthetic in promoting tolerance continues to be investigated. A study comparing comfort and pressure measurements under both anesthetized and non-anesthetized conditions showed no difference in comfort but significantly reduced maximum and mean pharyngeal pressures under the anesthetized condition [11].

After providing informed consent for the procedure, patients are instructed in the steps for manometric catheter insertion. The catheter is lubricated to ease nasal passage and inserted with the patient breathing nasally at rest. When the examiner feels the catheter passing along the posterior pharyngeal wall, the patient is invited to take several consecutive swallows, typically water via straw if deemed safe. For patients who may not demonstrate adequate laryngeal closure or UES opening, instrumental guidance for catheter placement can be used to assure proper placement of the manometric catheter into the esophagus. As the patient swallows, the catheter is advanced until insertion into the esophagus can be visually verified by manometric pressure readings. A period of acclimation to the catheter is monitored over several minutes. Examination protocol typically includes multiple trials each of increasing measured volumes of saline from 1 milliliter to 20 milliliters in volume. Salinity allows for impedance measurement when using an HRPM system with this feature. Other textures may also be presented, including thickened liquids, puree, or solids. The impact of swallowing postures and maneuvers on pressures, timing, and impedance can be analyzed to inform both the clinician and patient. HRPM offers optimal assessment of UES function, thus assisting in planning for medical/surgical and behavioral interventions (Fig. 8.1).

HRPM provides ample data for analysis of pressures, impedance, and timing. Normative measures of pressure and impedance in healthy adults are published [12–14]. Manual analysis of regions of interest within the pressure topography plots can provide peak pressure and duration calculations for normative comparisons. Software analysis platforms are emerging that feature complex algorithms capable of rendering sophisticated calculations of pharyngeal and UES function, promising to bridge HRPM research to clinical practice (Fig. 8.2). Ultimately, even objective measurements require interpretation when generating a dysphagia treatment plan. Imaging studies are essential in validating HRPM interpretation. Identification of HRPM pressure artifact, such as epiglottic contact or cervical spinal osteophyte compression, assures that measurements can be attributed to an associated muscular movement on VFSS or FEES rather than anatomic or technologic anomalies.

Adding HRPM data to the care of the patient provides objective measure, which can reassure both patients and clinicians that therapies are directed to maximize recovery or maintain function. Neurologic disorders tend to be progressive or acute with potential for full recovery; however, in either case swallowing physiology is in flux. The addition of objective measurements can also inform rate of disease progression and/or recovery. Additionally the objective data may provide threshold information to trigger modifications in care, reprioritization of treatments, and the re-stratification of risks.

Dysphagia treatment is plagued by challenges in helping patients discover the volitional control they can achieve in modifying swallowing func-

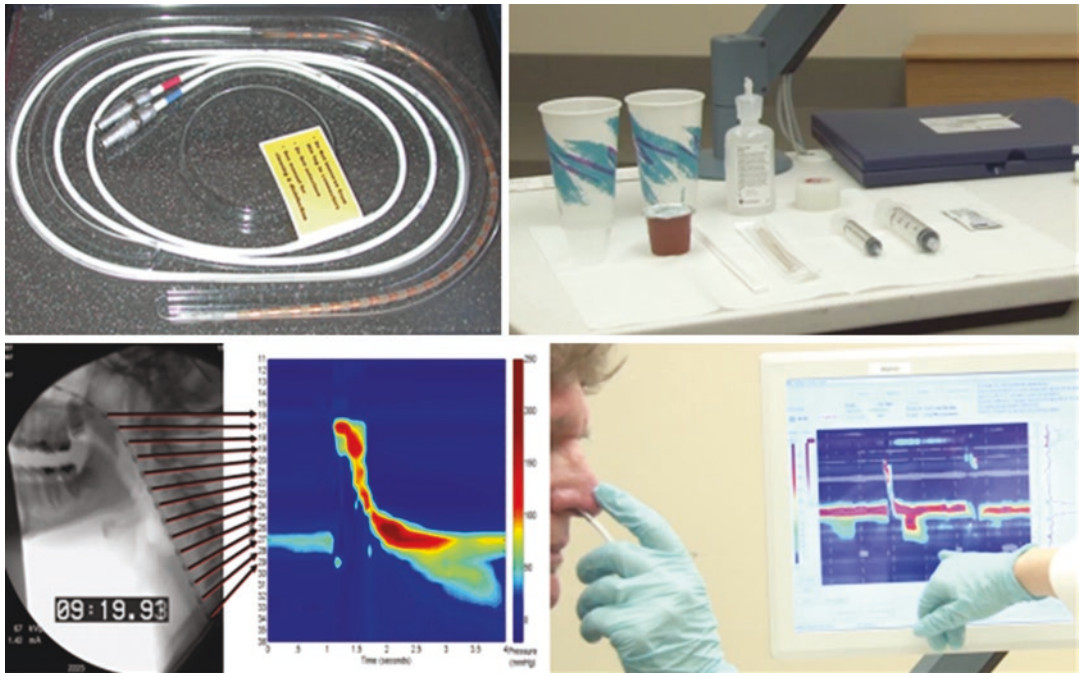


Fig. 8.1 High-resolution catheter, 36 circumferential sensors. Test and insertion materials, two cups of water, 4% lidocaine jelly to anesthetize the nose, cotton swabs to apply lidocaine jelly, lubricant jelly to aid insertion. Tape, saline, and syringes to measure out saline boluses

a

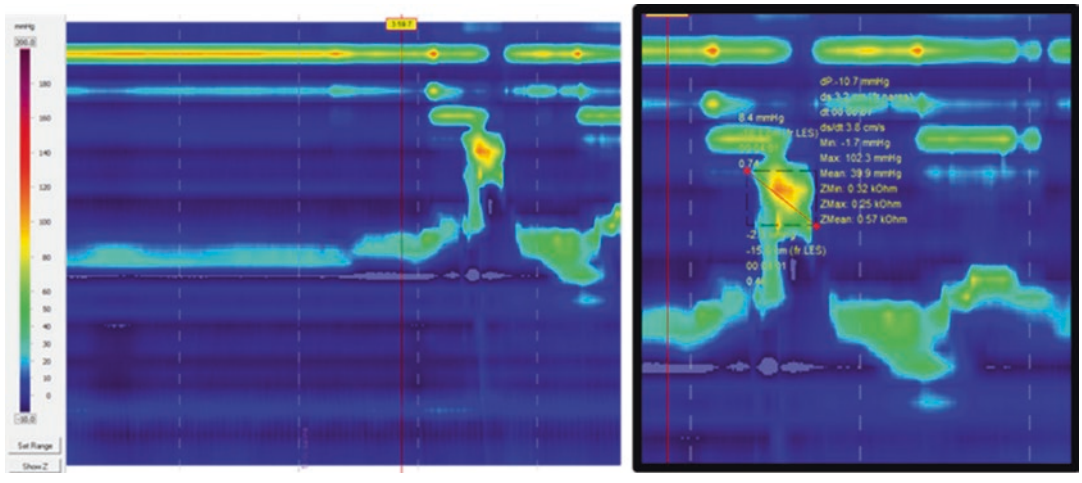


Fig. 8.2 (**a**) A 61-year-old male post-medullary stroke. Smart mouse data analysis ManoScan™ ESO High Resolution Manometry system (Medtronic, Minneapolis, Minnesota) (**b**) High-resolution manometry special temporal plot pressure viewed through convention esophageal analysis software top frame and specialized software lower frame. Video fluorography and multiple swallow pharyngeal high-resolution manometry with summary data and alternative plotting via Wismano software (McCulloch Labs, University of Wisconsin–Madison)

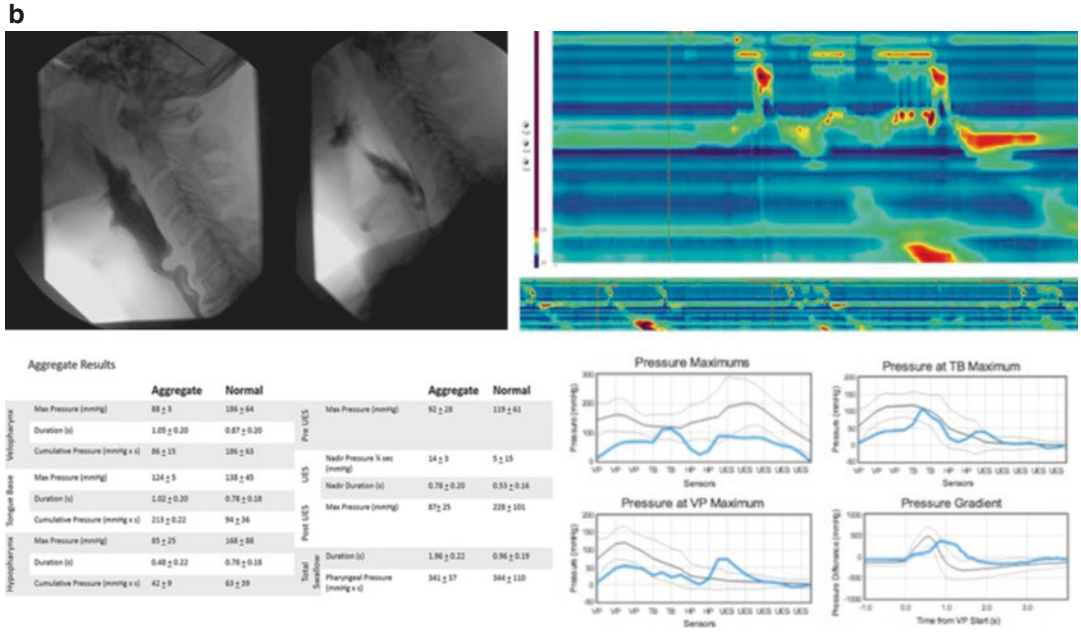


Fig. 8.2 (continued)

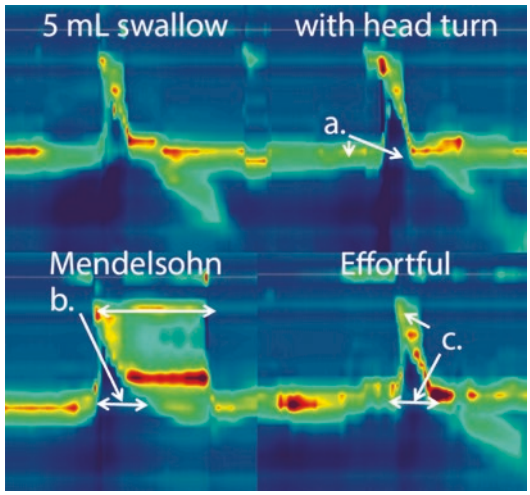


Fig. 8.3 High-resolution manometry with therapeutic maneuvers

Table 8.1 Maneuver and primary high-resolution manometry (HRM) effect

Maneuver	Primary HRM effect	Reference
Head turn	Decrease in pre-swallowing UES pressure, decrease in UES intrabolus pressure	McCulloch et al. 2010 [17]
Chin tuck	Decrease post-swallow UES pressure	McCulloch et al. 2010 [17]
Mendelsohn	Prolongation of velopharyngeal pressure duration, prolongation of UES nadir duration	Hoffman et al. 2012 [18]
Effortful swallow	Increase and velopharyngeal pressure, prolongation of UES nadir duration	Hoffman et al. 2012 [18]

UES upper esophageal sphincter

tion. HRPM plays a role in dysphagia treatment as a biofeedback tool [3]. Pilot studies have shown both healthy adults and patients with dysphagia capable of modifying timing of swallowing events with HRPM biofeedback [15, 16]. Training patients in complex maneuvers such as the Mendelsohn maneuver, targeting increased UES opening, can be facilitated for both the clinician and patient by the visual representation of HRPM. The objective data provided by HRPM is ideal for pre- and post-therapy comparison of pressure and durational measures of physiologic change in response to treatment over time (Fig. 8.3 and Table 8.1) [17, 18].

Stroke

HRPM can serve both evaluation and treatment of pharyngeal dysphagia following stroke. Swallowing impairment is prevalent in patients after stroke, with dysphagia diagnosed in 20.7% of a large sample of hospitalized stroke patients [19]. An impaired pharyngeal phase of swallowing due to stroke may be characterized by delayed onset of the pharyngeal swallowing response, prolonged tongue base contact to the posterior pharyngeal wall, slowed hyolaryngeal excursion affecting UES opening, and impaired pharyngeal constriction [20–23]. These physiologic features of dysphagia contribute to poor bolus transit to the esophagus and risk for aspiration of bolus contents. In ischemic stroke patients studied with HRPM, pharyngeal contractile pressures in the pharynx were significantly lower in patients with bolus residual in the pyriform sinus than those without residual [24]. Furthermore, those patients with aspiration showed shorter UES opening duration, with shortened duration of UES opening as the main risk factor for aspiration. Application of HRPM in patients seeking dysphagia treatment to address aspiration risk not only provides objective measures for treatment planning but also serves posttreatment comparisons to verify functional progress for clinicians, patients and families, and payers.

HRPM may also have an important role in evaluation and treatment of patients following brainstem stroke, which can have a devastating impact on swallowing function. In the large stroke sample referenced above, brainstem stroke accounted for 14% of stroke patients, with 24.4% of patients following brainstem stroke screening positive for dysphagia and 13% showing dysphagia persisting at discharge [19]. Brainstem stroke in the same study comprised 10.8% of patients requiring feeding tube placement after stroke, and 3-month mortality was predicted by severity of dysphagia requiring a feeding tube and brainstem involvement. Lateral medullary infarction of the rostral to middle medulla is associated with ipsilateral paralysis of the velum, larynx, and pharynx, in turn affecting pharyngeal swallowing efficiency and safety [25, 26]. Cognitive abilities typically remain intact for most brainstem stroke patients, which allows for higher complexity of behavioral swallowing strategies and rehabilitation. HRPM can verify physiologic benefits associated with postural strategies, such as head turning strategies typically trained to assist in bolus routing to the stronger side (see Fig. 8.3). HRPM used as biofeedback in training strategies, maneuvers, and exercises can assure that all are performed in a consistent and effective manner.

Patients suffering medullary lesions may exhibit persistent dysphagia that includes both impaired pharyngeal pressures and cricopharyngeal dysfunction [27]. Absence of UES opening during manometry has been associated with impairment of the pharyngeal swallow response in patients with neurologic disease [28]. Two case reports have documented prolonged effects of more than 1 year following Botox injection to the cricopharyngeus in patients after brainstem stroke [29, 30]. Judgments of UES opening on VFSS alone have not been predictive of patient outcomes following interventions including UES dilation or cricopharyngeal myotomy [31]. Studies employing conventional manometry in heterogenous patient populations demonstrated the predictive value of intrabolus pressure measures in the hypopharynx when combined with UES resistance to bolus flow [31–34]. More recently, HRPM with impedance has shown similar promise in the predictive value of hypopharyngeal intrabolus pressures identifying UES strictures in head and neck cancer patients, though peak pharyngeal pressures must equal or exceed 57 mmHg for adequate sensitivity and specificity [35]. There may be a role for HRPM in predicting outcomes following medical/surgical interventions for cricopharyngeal relaxation failure after stroke, though HRPM research to date has not yet defined manometric thresholds in the relationship between pharyngeal and UES pressures to guide patient selection or medical/surgical treatment planning.

Muscular Dystrophy

Muscular dystrophies are genetically inherited diseases characterized by degeneration of muscle. There are several types of muscular dystrophy that may affect swallowing, including Duchenne muscular dystrophy, myotonic dystrophy, and oculopharyngeal muscular dystrophy. Conventional manometry was used in early clinical research investigating the effects of muscular dystrophy on swallowing [36–40]. Patterns of impairment in pharyngeal constriction and UES function in oculopharyngeal muscular dystrophy were recognized, with conventional manometry serving as a modality to assist in predicting outcomes of cricopharyngeal myotomy [41, 42]. Even the less refined conventional manometric measurements provided insight into the delicate balance between pharyngeal pressure generation and UES function, helping researchers to recognize the limited success of cricopharyngeal myotomy when pharyngeal pressure generation is severely impaired. In the clinical setting, HRPM can serve patients with muscular dystrophy to determine likely outcomes from medical/surgical interventions such as cricopharyngeal myotomy. Further research in the utility of HRPM technology is needed to establish the predictive value of specific calculations for selecting patients most likely to benefit from medical/surgical interventions.

Motor Neuron Disease

Swallowing impairment in motor neuron disease, a category of progressive neurologic disorders that includes amyotrophic lateral sclerosis (ALS), relates to the degeneration of upper and lower motor neurons. Upper motor neuron dysfunction causes spasticity of oral, pharyngeal, and laryngeal musculature, manifesting as reduced range and slowed speed of movement. Clinically, patients with spasticity may present with audible clues such as strained/strangled vocal quality or reduced speed of production in rapid repetition of consonant sounds. Slowed oral transit, delayed pharyngeal swallowing response, reduced tongue base contact to the posterior pharyngeal wall, slowed and incomplete laryngeal closure, reduced range of pharyngeal constriction, and impaired hyolaryngeal excursion with impaired UES opening can result from spasticity. Lower motor neuron dysfunction presents as weakness in the bulbar musculature. Telltale clinical signs of flaccidity during oral mechanism examination include fasciculations in the tongue musculature, reduced lingual strength, and velopharyngeal incompetence. Swallowing impairment as a result of lower motor neuron dysfunction may include reduced lingual contact to the palate, reduced tongue base contact to the posterior pharyngeal wall, weakened pharyngeal constriction, reduced hyolaryngeal excursion with impaired UES opening, and incomplete laryngeal vestibule closure. Investigation of pressure abnormalities in ALS patients using conventional manometry showed reduced tongue base peak pressures and prolonged bolus transit [43].

Early signs of motor neuron disease may be more ambiguous, especially in patients exhibiting mild, focal impairments in speech and swallowing without symptoms in upper or lower extremities. It is not unusual for patients to first present to the otolaryngologist or speech pathologist with dysarthria and dysphagia [44, 45]. Older adults may not have motor neuron disease recognized as early due to confounding considerations for dysphagia and weakness [46]. HRPM can offer definitive early baseline measurement of swallowing pressures for comparison over time in patients whose diagnosis may elude their care team. The speech pathologist can combine findings of an oral mechanism examination, isometric tongue strength measures, imaging studies, and HRPM to provide the neurologist an inventory of swallow-

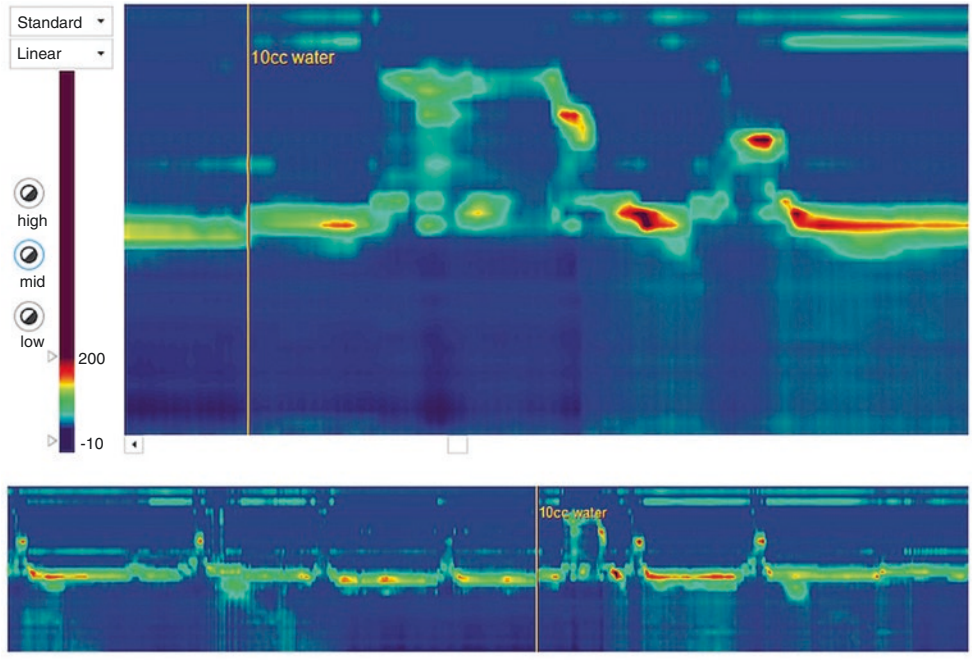
Table 8.2 High-resolution pharyngeal manometry (HRPM) applied during edrophonium testing shows no change in swallow pressures and durations in a patient with mild dysphagia complaints

HRPM measures (normal ranges)[a]	Baseline (0:00)	Placebo injection (9:16)	Edrophonium injection (18:59)
1 mL saline 3	(4:27)	(12:45)	(22:38)
Nasopharynx region (127 ± 29 mmHg)	162.9 mmHg	162.7 mmHg	159.0 mmHg
Tongue base region (337 ± 196 mmHg)	138.2 mmHg	142.4 mmHg	131.4 mmHg
UES clearance pressure (303 ± 147 mmHg)	312.2 mmHg	333.0 mmHg	346.4 mmHg
UES opening minimum (−4.0 ± 9 mmHg)	−7.1 mmHg	−6.6 mmHg	−4.7 mmHg
UES opening duration (0.92 ± 0.17 s)	0.5 s	0.5 s	0.5 s
Total swallow duration (0.81 ± 0.01 s)	1.3 s	1.1 s	1.2 s
10 mL saline ×1	(5:26)	(13:36)	(23:34)
Nasopharynx region (153 ± 50 mmHg)	165.1 mmHg	179.9 mmHg	169.8 mmHg
Tongue base region (267 ± 132 mmHg)	143.8 mmHg	148.3 mmHg	139.3 mmHg
UES clearance pressure (306 ± 111 mmHg)	474.9 mmHg	348.8 mmHg	258.8 mmHg
UES opening minimum (−2.0 ± 7)	−4.3 mmHg	−3.8 mmHg	−4.6 mmHg
UES opening duration (1.11 ± 0.15 s)	0.5 s	0.5 s	0.5 s
Total swallow duration (1.02 ± 0.13 s)	1.3 s	1.2 s	1.1 s

UES upper esophageal sphincter
[a]Normative ranges based on Hoffman et al. 2010 [12]

ing function [47–49]. A pilot study conducted using conventional manometry showed early signs of ALS manifesting in reduced pharyngeal pressures and increased residual UES pressures during bolus passage to the esophagus as compared to healthy adults [50].

In cases where differential diagnoses are being explored, such as myasthenia gravis, HRPM can provide an objective measurement of pharyngeal and UES function across baseline, placebo, and edrophonium conditions (Table 8.2). The standard HRPM examination can be extended based on procedure tolerance to assess muscular endurance over repeated swallowing tasks. The role of HRPM in patients with an established motor neuron disease diagnosis would be reserved for early stages when maintenance exercise may be desired by highly motivated patients and families (Fig. 8.4). Given the invasive aspect of HRPM, indications for its use in more advanced motor neuron disease should be carefully weighed with regard to patient beneficence. While HRPM use in research with more advanced ALS may seek to further understanding of the natural disease course, clinical indications will be limited by the palliative goals of care.



Aggregate Results

		Aggregate	Normal	Diff
Velopharynx	Max Pressure (mmHg)	106 ± 8	144 ± 30	-38
	Duration (s)	0.78 ± 0.54	0.72 ± 0.10	0.06
	Cumulative Pressure (mmHg-s)	84 ± 48	137 ± 51	-53
Tongue Base	Max Pressure (mmHg)	136 ± 43	127 ± 34	8
	Duration (s)	0.37 ± 0.03	0.66 ± 0.21	-0.29
	Cumulative Pressure (mmHg-s)	66 ± 26	63 ± 25	3
Pre-UES	Max Pressure (mmHg)	119 ± 22	101 ± 23	18
Post-UES	Max Pressure (mmHg)	108 ± 27	225 ± 49	-117
UES	Nadir Pressure 1/4 sec (mmHg)	11 ± 6	9 ± 16	1
	Nadir Duration (s)	0.58 ± 0.30	0.49 ± 0.19	0.08

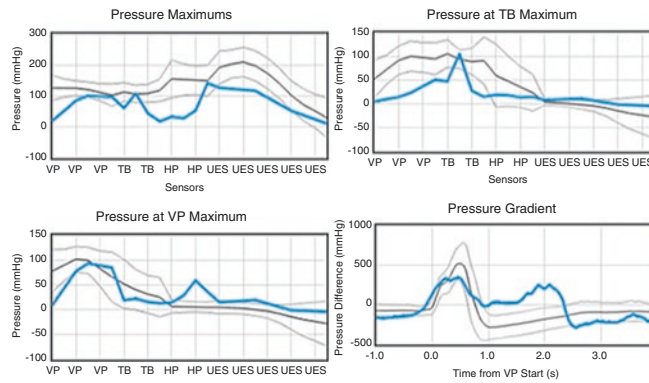


Fig. 8.4 High-resolution manometry in an 80-year-old female with childhood history of bulbar palsy. High-resolution findings included multiple swallow profile, poor upper esophageal sphincter (UES) opening with higher pressure at the UES at tongue base and velopharyngeal pressure maximum pressure time points, preserved gradients, but double hump due to double swallow

Conclusion

HRPM offers unique opportunities for objective pressure, timing, and impedance measures that can serve neurogenic dysphagia populations in both evaluation and treatment applications. Swallowing specialists in speech pathology and otolaryngology are highly qualified to analyze and interpret HRPM for medical/surgical and behavioral treatment planning. In collaboration with neurologists, the dysphagia care team should consider HRPM for selected patients

where pre- and posttreatment measures will inform the patient, provider, and payer of treatment effectiveness.

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9 Evaluation of the Pulmonary System

Jeremy E. Orr and Lisa F. Wolfe

Lung Function Testing

Familiarity with pulmonary function testing is helpful for individuals taking care of patients with neurological disorders, including laryngologists, speech and language pathologists, neurologists, and other professionals. Pulmonary function testing is useful in assessing for (or excluding) pulmonary or respiratory muscle disease and at times for identifying laryngeal pathology. Testing is performed by a trained technologist according to established standards [1] and consists of several distinct maneuvers that assess various aspects of the pulmonary system [2].

Spirometry

Spirometry involves rapid and complete inhalation to total lung capacity followed by rapid and complete exhalation. Measurements include inspiratory and expiratory flows (including forced expiratory volume at 1 second, FEV1) and total volume exhaled (forced vital capacity, FVC). The data is characteristically plotted as a flow versus volume curve (Fig. 9.1). Spirometry is highly useful for assessing the function of the airways, which are abnormal in obstructive lung diseases such as asthma or chronic obstructive pulmonary disease, but measures also reflect the compliance of the respiratory system (lung and chest wall) and strength of the respiratory muscles. Spirometry benefits from being relatively inexpensive and widely available; portable devices allow spirometry to even be performed in the exam room. However, spirometry does require the ability to tightly seal on a mouthpiece and perform repeated forceful maneuvers in a coordinated fashion.

Lung Volumes

Lung volumes are determined by placing the patient in a sealed box (plethysmography) or by dilution of an inert gas (generally helium), utilizing the principles of Boyle's law to determine the amount of air in the lung. Measured volumes include resting lung volume (functional residual capacity, FRC), total gas in the lung at end-inhalation (total lung capacity, TLC), and gas left in the lung after complete exhalation (residual volume, RV). The relationship between these

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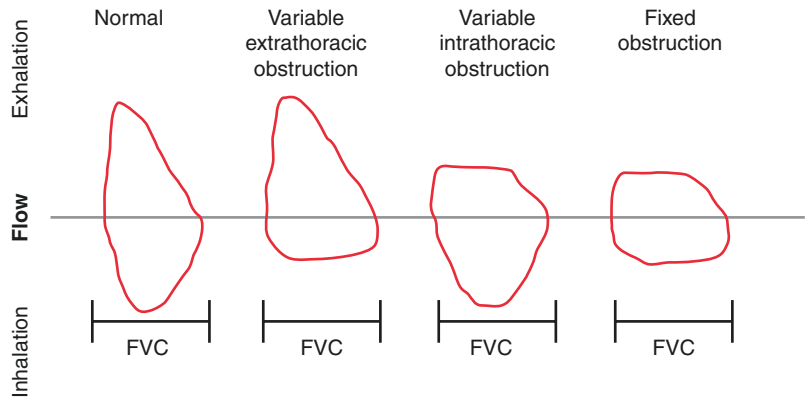

Fig. 9.1 Flow-volume curves derived from standard spirometry. *Normal* flow volume curve. Note that after rapid increase to peak expiratory flow, there is a linear fall in flow throughout exhalation. In contrast, the inspiratory flow is relatively symmetric and bell-shaped. *Variable extrathoracic obstruction*. The peak inspiratory flow is blunted and flattened. The expiratory flow is normal. *Variable intrathoracic obstruction***.** The peak expiratory flow is blunted and flattened. The inspiratory flow is normal. *Fixed large airways obstruction***.** Both the expiratory and inspiratory flows and blunted and flattened

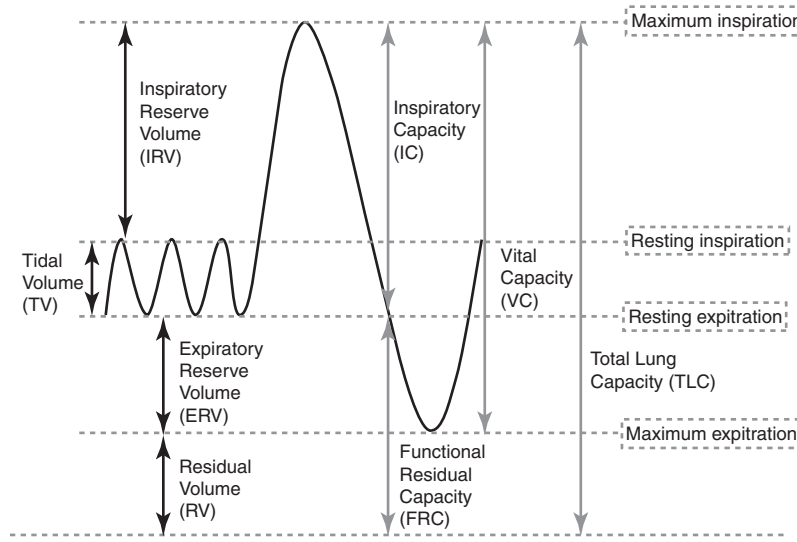

Fig. 9.2 Schematic representing the relationship between the lung volumes and capacities. Note the association with resting and maximal inspiration and exhalation. (From Lutfi [3] with permission)

measures is shown in Fig. 9.2 [3]. Lung volumes are sensitive to disorders affecting the compliance of the respiratory system (lungs and chest wall) but also can assess respiratory muscle function and may be abnormal in airway disease as well. Although the necessary equipment and training is more complex, lung volume measurements are available in pulmonary function labs and some clinics. The ability of the patient to form a tight mouthpiece seal and coordinate relaxed breathing is needed.

Diffusing Capacity

Diffusing capacity (DLCO) measures how readily a rapidly diffusing gas (carbon monoxide) moves from the airspaces into the bloodstream. This measure is a marker of both the surface area available for gas exchange and the distance between the airspace and blood. Diffusing capacity is available in pulmonary function labs and some clinics. The ability of the patient to form a tight mouthpiece seal and perform a breath-hold is needed.

Maximal Inspiratory and Expiratory Pressures

Maximal inspiratory and expiratory pressures (MIP and MEP, respectively) measure the pressure generated by the respiratory muscles. Since the test is performed without airflow (i.e., against a closed shutter), airway resistance and respiratory system compliance do not influence the test, although variable or poor effort can limit the utility. This testing can be performed by most pulmonary function labs but often must be specifically requested. A mouthpiece is often used, but an occlusive nasal probe can be used to transduce inspiratory pressure (i.e., sniff nasal inspiratory pressure (SNIP)) for those with inability to form a mouthpiece seal.

Maximal Voluntary Ventilation

Maximal voluntary ventilation (MVV) is determined by having the patient breathe at maximal effort for 15 seconds and then multiplied by 4 to determine the MVV [4–6]. This test is affected by any lung disease impacting airflow (particularly FEV1) but may be disproportionately low if respiratory muscle endurance is compromised or if effort is low. This testing can be performed by most pulmonary function labs but often must be specifically requested. The ability of the patient to form a tight mouthpiece seal is needed.

Peak Cough Flow

The peak cough flow is measured by having the patient inspire fully and then cough forcibly through mouthpiece attached to a flow meter or spirometer. A mask can be used if unable to form a mouthpiece seal. The test is not standardized, and lung function laboratories may not be familiar with its use.

Laryngeal Disease Mimicking Pulmonary Disease

Episodic dyspnea and abnormal airway sounds are commonly encountered in practice, symptoms which might be due to either laryngeal or pulmonary diseases. The differential diagnosis of laryngeal disease is broad and covered elsewhere in this book. For pulmonary disease, the differential diagnosis of dyspnea and abnormal airway sounds is also broad and includes chronic obstructive pulmonary disease, bronchiectasis, asthma, tracheobronchomalacia, airway lesions, pulmonary embolism, and pulmonary edema.

A classic diagnostic challenge is the patient with paradoxical vocal fold motion (PVFM) versus asthma. Similar to asthma, PVFM affects all ages, and patients present with episodic dyspnea, chest tightness, "wheezing," or cough. Also similar to asthma, episodes may be spontaneous or associated with triggers, particularly exercise, irritant exposures, gastroesophageal reflux, or stress/anxiety. PFVM generally causes obstruction to airflow on inhalation, whereas the obstruction in asthma is on exhalation; this timing difference in symptoms or wheezing/stridor can at times be elicited by history or exam. Another point of potential distinction is that PVFM is generally not responsive to bronchodilators such as albuterol, whereas asthma often does respond, although a significant response to bronchodilators may not be seen in severe asthma. It should be noted that PVFM may co-occur commonly with asthma.

PVFM can be seen in patients with amyotrophic lateral sclerosis (discussed below), and symptoms may be thought to be due to respiratory muscle weakness rather than laryngeal involvement. Episodes of PVFM in ALS are often self-limited, but should be contrasted with sustained issues indicating possible vocal cord paralysis or respiratory muscle weakness. In contrast, PVFM in patients with multisystem atrophy (MSA) may be life-threatening [7].

Laryngoscopy is the gold standard for diagnosis of PVFM; however pulmonary function testing is often performed first in the workup, and findings on pulmonary function testing may be helpful. A blunted inspiratory limb of the flow volume curve (see Fig. 9.1) is suggestive of variable upper airway obstruction (UAO) and can be quantified by the ratio of forced expiratory flow to forced inspiratory flow at 50 percent vital capacity (FEF50/FIF50). The ratio is normally <1; a ratio of >1 is suggestive of variable UAO [8,

9], along with a corresponding reduction in peak inspiratory flow. However, these findings are nonspecific to PVFM (i.e., can be any cause of dynamic upper airway obstruction) and might not be seen due to the intermittent nature of the disorder. Emerging data suggest better utility of other spirometric measures, including a low forced inspiratory volume at 0.5 seconds compared to the total forced inspiratory volume (FIV0.5/FIVC, typically <0.9) [10]. Nebulization of methacholine prior to spirometry, which is used to evaluate for asthma (i.e., will lead to a reduction FEV1 compared to pre-methacholine values in asthmatic patients), may provoke PVFM, with corresponding spirometric findings of UAO. Methacholine testing thus provides particularly useful information for the patient under consideration for asthma or PVFM, but it should be noted that a lack of spirometric UAO with methacholine does not rule out PVFM [11]. Of note, the use of methacholine testing during laryngoscopy may improve the ability to detect PVFM [12]. In the patient with exercise-triggered symptoms, cardiopulmonary exercise testing with pre- and posttest spirometry may be helpful to identify exercise-induced asthma, but the role for PVFM is less clear [13].

Occasionally, severe PVFM may lead to respiratory distress prompting emergent endotracheal intubation. When faced with the patient intubated due to upper airway obstruction, the decision whether to extubate or perform an intervention (e.g., laryngeal botulinum toxin injection or tracheostomy) depends on the degree of clinical suspicion for PVFM versus a more acutely threatening cause of UAO. Ideally, management should be coordinated between the pulmonologist/intensivist and laryngologist to avoid unsafe extubation while also avoiding an unnecessary tracheostomy.

Pulmonary Aspiration Syndromes

Laryngeal dysfunction leads to an increased risk of aspiration due to a failure of the neuromuscular reflexes that normally protect the airways and lungs. There are several manifestations of pulmonary aspiration (see below) that may prompt consideration of laryngeal evaluation, depending on the specific context [14].

Aspiration Pneumonitis

Aspiration pneumonitis is a hyperacute process occurring after aspiration of a large quantity of sterile liquid containing a chemical irritant. Gastric acid appears to key in the pathogenesis of this entity. A precipitating event is almost always known, such as difficult endotracheal intubation with gastric fluid reflux. Within minutes to hours, chemical pneumonitis leads to hypoxemia and often respiratory distress. The syndrome generally resolves with supportive care within hours to days but may progress to acute respiratory distress syndrome and therefore may be fatal. Underlying laryngeal pathology is not requisite.

Anaerobic Lung Infection

Anaerobic lung infection is a subacute process that presents insidiously and nonspecifically with malaise, anorexia, and cough, which may be nonproductive. Chest pain and low-grade fever are variably reported. Aspiration of mixed oral flora leads to pneumonia, which may be characterized as an infiltrate, but may progress to pulmonary abscess and pleural involvement. Patients often have recognized aspiration symptoms accompanied by underlying laryngeal disease, although a specific triggering event may not be identified.

Recurrent Pneumonia

Microaspiration of typical pneumonia pathogens such as *Streptococcus pneumoniae* or *Haemophilus pneumoniae* is thought to be the mechanism for development of bacterial pneumonia [14]. Patients may be colonized with these bacteria and otherwise have pulmonary or immunologic predisposition. However, laryngeal dysfunction is often present in patients with recurrent episodes, which is often subclinical – i.e., "silent" aspiration.

Parenchymal Lung Disease and Fibrosis

Ongoing micro-aspiration (with or without clinically apparent recurrent infections) appears to lead to lung inflammation and fibrosis, which may contribute to other otherwise mimic primary parenchymal lung disease [15]. In addition, micro-aspiration (along with gastrointestinal reflux) in patients with lung transplantation has been implicated in chronic allograft rejection.

Diseases Causing Laryngeal Dysfunction with Frequent Pulmonary Complications

There are a number of neurological diseases affecting the larynx that often lead to pulmonary issues (Table 9.1). Examples that are common and are of specific interest are discussed further:

Table 9.1 Neuromuscular diseases affecting larynx that can also affect the respiratory system

Location/type	Disease
Central nervous system	Multiple sclerosis
	Multisystem atrophy
	Parkinson disease
	Chiari malformation
Motor neuron	Amyotrophic lateral sclerosis
	Spinal muscular atrophy
Neuropathy	Guillain-Barré syndrome
	Charcot-Marie-Tooth syndrome
Neuromuscular junction	Myasthenia gravis
	Botulism
Muscular dystrophy	Duchenne/Becker
	Myotonic dystrophy
	Limb-girdle
	Facioscapulohumeral
	Oculopharyngeal
Metabolic myopathies	Mitochondrial Glycogen Lipid
Congenital myopathies	Central core Myotubular Nemaline
Inflammatory myopathies	Inclusion body myositis Polymyositis/ dermatomyositis

Amyotrophic Lateral Sclerosis (ALS)

Respiratory muscle weakness is common in amyotrophic lateral sclerosis (ALS), although its timing relative to other muscle group involvement (including laryngeal involvement) and rate of progression varies greatly. It should be noted that ALS is relentless – patients will progress to respiratory muscle and bulbar paresis and eventually a "locked-in" state of global paresis. Thus, ongoing assessment and proactive management between pulmonology, speech pathology, neurology, and laryngology are essential for effective and appropriate respiratory management (discussed more below). Patients with ALS may exhibit attacks of laryngospasm/PVFM, which can cause respiratory distress prompting medical attention and may be mistaken for respiratory muscle weakness [16]. Episodes often spontaneously abate, although in some individuals are troublesome enough to warrant treatment and case reports suggest a possible link to sudden death. PVFM may respond to noninvasive positive airway pressure [7] although tracheostomy may be warranted in some individuals. Other treatments for laryngospasm include the use of muscle relaxants such as lorazepam solution as rescue during episodes, which have been minimally studied but are often used based on clinical experience of efficacy among many individuals. Another important point is that with progressive respiratory muscle weakness, symptoms of laryngeal dysfunction (including paresis) may be difficult to distinguish from pulmonary issues, highlighting the need for comprehensive care of these patients.

Muscular Dystrophies

Muscular dystrophies are genetic diseases. These genetic diseases include those beginning in childhood, such as Duchenne muscular dystrophy, and those presenting as delayed as in late adulthood, such as facioscapulohumeral dystrophy. Some forms of muscular dystrophy are known for having earlier bulbar/laryngeal involvement, such as myotonic dystrophy. In other forms such as Duchenne, bulbar involvement occurs much later,

often long after patients have established chronic respiratory failure. Thus, multidisciplinary management (ideally including a neurologist specializing in neuromuscular disorders) is essential to individualize therapy based on the expected course of each specific disease.

Myasthenia Gravis

Generalized myasthenia gravis can involve ocular, bulbar, neck, limb, and/or respiratory muscles. The course is waxing and waning and may progress (sometimes rapidly) to decompensated respiratory failure due to bulbar and/or respiratory muscle weakness. Although treatment (thymectomy, immunosuppression) is effective for many, other patients have suboptimal control and require ongoing evaluation. Given the potential for rapid decompensation, these patients require close multidisciplinary management in both the inpatient and outpatient settings.

Parkinson Disease and Multisystem Atrophy

Parkinson disease (PD) and multisystem atrophy (MSA): Respiratory symptoms are common in these disorders. Respiratory muscle involvement has been documented in the studies of lung function, but the clinical consequences are unclear. Aspiration is particularly common in these disorders, so there should be a low suspicion to evaluate new respiratory symptoms. In addition, laryngospasm and PVFM may be seen in both disorders. Management of PVFM depends on the severity of episodes and symptoms, with consideration that episodes in MSA may be very severe.

Neuromuscular Respiratory Weakness

Weakness of the respiratory muscles is a particularly important consequence of many neurological disease affecting the larynx. The most important muscle of respiration is the diaphragm, but even weakness of "accessory" muscles of breathing (intercostals, abdominals, scalenes) can lead to complications. Loss of supporting muscles can lead to substantial changes in the spine and chest wall (e.g., kyphoscoliosis), which can contribute to reduced pulmonary function. Importantly, as respiratory muscle weakness progresses, airflow through the upper airway is diminished, which may limit the utility of classic signs and symptoms of laryngeal dysfunction. Conversely, respiratory muscle weakness should be suspected when symptoms such as hypophonia are not clearly attributable to laryngeal issues.

Evaluation of Respiratory Muscle Weakness

Substantial respiratory muscle weakness is readily diagnosed on standard lung function testing, although more subtle cases may require more extensive testing. Findings of restrictive lung disease include a reduction in total lung capacity and forced vital capacity, absent a reduction in FEV1/FVC that would indicate obstruction. Such restriction can be seen in the presence of interstitial lung disease; the absence of such disease on imaging and normal diffusing capacity, along with reduced inspiratory and expiratory flows, maximal inspiratory pressures, or maximum voluntary ventilation confirms a neuromuscular etiology. A > 10–20% reduction in FVC in the supine position is seen in the presence of diaphragmatic weakness; diaphragm weakness is generally sufficient but not necessary to result in lung function impairment. In mild disease, the FVC and TLC may be preserved; in this case diagnosis becomes more challenging, but such mild changes are unlikely to be of immediate clinical relevance. Overall, reliance on one test may lead to poor sensitivity and specificity; evaluation of multiple values may provide a better assessment [17]. Gold-standard testing to directly measure respiratory muscle pressures is semi-invasive (requiring esophageal and gastric catheterization) and almost never performed clinically, particularly as the aforementioned testing provides similar information.

Peak cough flow is a test that provides valuable information regarding the integrated function between respiratory muscles and glottic function and thus may be of particular interest when considering the larynx [18]. Poor function of the glottis will lead to a reduced peak cough flow, as insufficient ability to maintain closure during the initial phase of cough (i.e., activation of expiratory muscles with closed glottis) will not allow for intrathoracic pressure generation. Similarly, expiratory muscle weakness and/or low lung volumes precludes the generation of high intrathoracic pressures to "power" high expiratory flows when the glottis opens. Patients with peak cough flows of <270 L/min are at risk for pneumonia, while those with levels <160 L/min are considered at particularly high risk [19–21].

Management of Respiratory Muscle Weakness

Respiratory support has an important role in mitigating the adverse effects of neuromuscular respiratory weakness and can lead to improved quality of life and survival. Regular lung function is essential for assessing risk of chronic respiratory failure and avoiding decompensated disease as the initial manifestation. From a pulmonary standpoint, there are two (related) issues.

Chronic respiratory failure occurs when respiratory muscle function is not sufficient to support adequate ventilation, leading to hypercapnia and hypoxemia. Patients with rapid progression may note shortness of breath, particularly in the supine position (i.e., orthopnea), while in other patients, the onset is more insidious, and dyspnea may be minimal. Nocturnal ventilatory support is offered when patients demonstrate substantial restriction on lung function testing, hypercapnia on arterial blood testing, or symptoms of dyspnea or orthopnea. Advances in noninvasive ventilation technology, including reliable home ventilators and improved mask interfaces, mean that ventilatory support can generally be provided at home without a tracheostomy. This is true even for patients with minimal vital capacity, provided upper airway function is reasonably intact. Noninvasive ventilation has been shown to prolong survival and improve quality of life in a number of neuromuscular disorders, including with randomized clinical trial evidence in ALS [22–25].

Inadequate airway clearance occurs when laryngeal dysfunction leads to aspirated secretions, and/or ineffective cough precludes sufficient clearance of mucus out of the lung. Such at-risk patients are currently best identified with peak cough flow, as above, and regular assessment for symptoms of aspiration and swallow studies. Exam findings of retained secretions might include basilar crackles only if respiratory muscle strength is relatively intact, but abnormal pulse oximetry values (<95%, assuming absence of parenchymal lung disease) are highly useful for identifying inadequate airway clearance. If aspiration is the primary issue, subsequent dietary restriction is advised, and gastrostomy tube placement should be considered alongside "goals of care" discussions. Untreated, inadequate airway clearance leads to pneumonia, and if respiratory muscle weakness is insufficient to overcome the additional mechanical "load" of this infection, patients will develop decompensated respiratory failure. It is important to recognize that neuromuscular patients with acute pneumonia often do not exhibit typical signs of respiratory distress, such as accessory muscle use or tachypnea; these patients are at high risk for unrecognized decompensation and subsequent respiratory arrest. Airway clearance modalities include mechanical insufflation-exsufflation, manually assisted coughing, and hyperinflation maneuvers; these therapies should be provided early and aggressively. For these modalities, glottic insufficiency substantially reduces their effectiveness [26]. Note that other treatments such as nebulized bronchodilators, vibratory vest systems, etc. have minimal effect unless cough is sufficient.

Deciding on an Invasive Approach to Management

With progression of respiratory muscle weakness, noninvasive ventilatory support can be

provided on a continuous basis, including daytime provision of either mouthpiece ventilation or continuous nasal ventilation. This support can provide adequate ventilation for patients with minimal vital capacity. Nonetheless, bulbar weakness leading to glottic insufficiency is particularly challenging for patients with neuromuscular respiratory weakness, as it may limit the effectiveness of the noninvasive respiratory support modalities discussed above. Most often, this manifests as issues with retained secretions or episodes of pneumonia. The decision to abandon a noninvasive approach and proceed with tracheostomy and invasive ventilation should nonetheless not be taken lightly, as it may lead to additional issues with speech, swallowing, respiratory infections, increased caregiver burden, and higher costs [16, 27–29]. In selected patients, tracheostomy can be associated with a good quality of life, although no randomized comparisons with a noninvasive approach have been performed. Given the effectiveness of noninvasive therapies mentioned above, their use should be optimized before considering a change to an invasive approach, particularly in patients with intact or only mild bulbar impairment. It is our practice to maximize noninvasive therapy and only proceed with tracheostomy in the setting of clear failure of these modalities, rather than at a pre-specified earlier time.

Based on these advances in noninvasive treatment modalities and potential burdens of tracheostomy/invasive ventilation, patients may elect to forgo these interventions, particularly when this progression represents end-stage disease with already impaired quality of life. In ALS patients in the USA, for example, only about 10% of patients undergo tracheostomy placement [30]. All patients undergoing tracheostomy should have clear and comprehensive goals of care well before progressing to a locked-in state. Discussions of goals of care, including palliative and hospice care, should ideally involve all treating providers, including neurology, pulmonology/sleep medicine, laryngology, and social work.

Perioperative Pulmonary Considerations

Perioperative pulmonary issues include:

1. Inability to wean from acute ventilatory support
2. Hypoventilation following extubation (which may be poorly recognized)
3. Aspiration combined with ineffective airway clearance leading to pneumonia

Patients with neuromuscular respiratory weakness are highly susceptible to the respiratory-depressant effects of anesthetic agents, neuromuscular blockade, and opioid analgesics. Neuromuscular patients with respiratory muscle involvement should undergo preoperative evaluation by an experienced pulmonologist and anesthesiologist, particularly if planning to undergo general anesthesia. Pulmonary evaluation should include spirometry (measurement of FVC), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), peak cough flow (PCF), oxyhemoglobin saturation, and potentially arterial CO2 measurement [31]. Based on recommendations for patients with Duchenne muscular dystrophy, the authors suggest considering all neuromuscular patients with a FVC < 50% of predicted at increased risk of respiratory complications. Those with an FVC < 30% of predicted are at particularly high risk, and the authors advise initiation of noninvasive ventilation prior to surgery, provided the surgery is not needed urgently. For patients at high risk of ineffective cough, defined in adults by PCF < 270 L/min or MEP < 60 cm H_2O, the authors advise preoperative training in manual and mechanically assisted coughing. It should be noted that clinical risk calculators to assess postoperative risk are unlikely to be sufficiently sensitive for neuromuscular patients [32–34].

Avoidance of general anesthesia for patients with restricted lung function is advisable whenever feasible, including neuraxial and regional strategies. Intraoperative management should include the use of IV anesthetics (e.g., short-

acting agents) and an absolute avoidance of depolarizing neuromuscular blockade. For procedural sedation, ventilatory assistance should be given using the patient's home noninvasive ventilator and should be considered for patients with FVC <50% of predicted. For general anesthesia, noninvasive ventilation should be considered following extubation. Patients should be monitored closely in the postanesthetic care unit (PACU), and strong consideration of admission should be given to each patient. Of note, monitoring oxygen saturation may not detect respiratory issues (which are primarily hypoventilation) in these patients until severe. On the other hand, decreased oxygen saturation is often met with the administration of supplemental oxygen, which in neuromuscular patients does not address the underlying issue of needing ventilatory support and may itself further decrease respiratory drive.

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Electromyography of the Larynx

10

Simon Brisebois and Allen D. Hillel

Introduction

Laryngeal electromyography (LEMG) was first described in 1944 by Weddell et al. in their comprehensive work titled "The Electrical Activity of Voluntary Muscle in Man Under Normal and Pathological Conditions" [1]. Its principles were further elucidated in the 1950s by the work of Faaborg-Andersen and Buchtnal [2]. Significant interest and research into its application has culminated in its recognition as an indispensable clinical diagnostic and research tool. Common clinical applications include differentiating vocal fold paralysis from cricoarytenoid joint ankylosis, confirming subtle paresis, informing the prognosis of neural injury and characterization of laryngeal dystonia. In contemporary practice, the most common use in laryngology is as an aid in guidance for injections of botulinum toxin for laryngeal dystonia.

LEMG is a study of the electrical signal of the laryngeal muscle that reflects innervation from the associated nerve. It has different forms: (1) simple signal guidance for therapeutic injection into the laryngeal muscle, (2) diagnostic needle LEMG, (3) diagnostic fine-wire LEMG, and, less commonly, (4) compound muscle action potential evaluation. Overall, LEMG is a diagnostic test, which is the extension of the neurolaryngeal physical examination that can confirm findings suspected on history and videostroboscopy. It is typically performed by an otolaryngologist without input from an electrophysiologist (neurologist or physiatrist) particularly when using it for therapeutic laryngeal injections. However, its interpretation can be complex, and most otolaryngologists are not familiar with its subtleties when using it for diagnostic purposes. Therefore, collaboration with an electrophysiologist who can help interpret the signals and manage the settings and documentation on the EMG machine is preferable. Interpretation of findings involves visual feedback in the form of waveform analysis and auditory feedback, as audio characteristics of specific motor units are distinct. Thus, the combined real-time evaluation of the visual and audio signals of electrical responses is essential to the interpretation of LEMG.

LEMG is an interactive diagnostic tool that requires constant communication between the clinician and the participant. Objective findings exist, but the clinician prompting muscle activation in a cooperative patient elicits these findings. Thus, the exam is often fluid; that is, the

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progression of an exam often changes depending on the initial findings. As a study, it is less like radiologic or electrocardiographic studies, which have fixed measurable parameters, and more like ultrasound during which the examiner is searching for an answer to a specific question. Therefore, diagnostic LEMG is tailored for the specific questions in consideration, and the information gleaned is predicated on the ability of the patient to cooperate with the study.

In this chapter, we discuss technical aspects of accessing laryngeal muscles and performing the LEMG, highlight normative findings, review scenarios where it is often useful, and discuss pathologic findings seen in various disorders.

Technical Aspects

Candidacy and Preparation

Prior to beginning an LEMG study, the clinician examines the patient's neck anatomy to determine ease of access and rule out any contraindication before proceeding. Relative contraindications include known bleeding disorder, glottic stenosis, or pacemaker (if stimulation studies are done). The procedure can be performed in various clinical settings. In any case, the clinician should be ready to intervene if an airway complication arises during the procedure. This is especially true in a patient presenting with glottic stenosis from bilateral true vocal fold immobility. In these cases, the examination should be limited to the lateral cricoarytenoid muscles only since placing a needle in the TA muscle could cause edema and further compromise the airway.

Positioning

The study is performed with the patient either supine or sitting with a gentle extension of his/her neck to access the cricothyroid membrane (CTM). Depending on the patient's preference, topical anesthesia using lidocaine is injected into the skin overlying the CTM and/or the subglottic airway. It is important to notify the patients that their perception of breathing and swallowing may be altered by the topical anesthesia, as this sensation is anxiety provoking in some individuals. The patient can also be reassured that although he/she will most likely feel some discomfort from the procedure, they should generally not experience significant pain. Indeed, Ferster et al. demonstrated, in a series of 80 patients undergoing LEMG, that the pain level was considered mild to moderate by participants as evaluated by visual analog scale and the McGill Pain Questionnaire administered after the procedure [3].

Needles

There are a variety of needles available for LEMG, the most common of which are the monopolar, bipolar, concentric, and single-fiber electrodes. The *monopolar needle* is insulated except at the exposed tip and needs a reference electrode, which is usually a surface disc on the skin. Injection needles are monopolar electrodes. This type of needle has the advantage of sampling a large number of muscle fibers at one time and provides a more rapid comprehensive evaluation of the muscle. In order to limit volume conduction (responses from other motor units between the needle and reference electrode), the low EMG filter should be set to screen out signals below 300–500 Hz.

The *concentric needle* consists of a hollow steel needle with an internal silver, platinum, or steel wire used as the active electrode, while the outer uninsulated shaft will serve as the reference. This provides a more detailed study (1–2 MUAPs at a single point). The *bipolar needle* consists of a hollow needle with two internal platinum wires which are insulated, except at their tips. Similar to the concentric needle, the ability to record is limited to the area between the two electrodes only (1–2 MUAPS). These electrodes are useful if the examiner is trying to do a more detailed study of individual motor units but takes longer to do a study of the overall muscle.

In the authors' experience, the monopolar needle is the most versatile needle as long as the filters are set to exclude signals below 500 Hz and above 10,000 Hz. Generally, the goal of diagnostic LEMG is to evaluate recruitment and search for abnormal motor units rather than do a detailed study of specific motor units. The filters limit risks of volume conduction, and neighboring motor units, if detected, have a very different sound. It is also essential to note that the audio feedback is as important as visual feedback, because the two need to be congruent. For example, a good visual signal can be misleading if the audio feedback is not crisp.

Approaches

Thyroarytenoid Muscle

The thyroarytenoid muscle (TA) can be accessed by inserting the tip of the needle near the CTM midline. The two approaches include (1) entering the airway and (2) staying submucosal without entering the airway. The authors prefer the former technique in which the needle enters the subglottic lumen and presents an incomplete circuit on the EMG machine when the needle tip enters the airway. After placing the needle in the airway, the needle is angled superiorly and slightly lateral (more so in female) to the entry point and advanced until activity is picked up on the EMG monitor. The underside of the vocal fold then becomes the entrance point of the needle, and this is observed on the EMG machine as a completed circuit (quiet). Using the technique of entering the airway, the authors feel there is more certainty of the location of the needle tip, and then the needle is in the TA muscle. With the second approach, the needle remains submucosal and is placed under the thyroid cartilage without entering the airway. Then, the needle is angled superiorly and slightly lateral to avoid entering the tracheal lumen and advanced until activity is picked up on the EMG monitor. With both techniques, the confirmation task is instructing the patient to make the /i/ sound. However, it should be noted that by not entering the lumen, it may be more difficult to distinguish between the TA and lateral cricoarytenoid muscle (LCA) since there are no specific confirmation tasks that can differentiate between the TA and LCA (see below).

Lateral Cricoarytenoid Muscle

Access to the lateral cricoarytenoid muscle (LCA) muscle is through the CTM at the most lateral point that the space between the thyroid and cricoid cartilages can be palpated by the examiner. The needle remains entirely outside the laryngeal lumen and does not trigger an airway reflex. Therefore, local anesthetic is not necessary in most cases. Again, the positioning can be confirmed by having the patient sustain a /'i:/ sound.

Interarytenoid (IA) Muscle

The needle traverses the CTM and mucosa in the midline into the airway and directed with a cephalad tilt until it encounters the posterior cricoid lamina. The tip of the needle is then displaced upward, feeling for the cartilage, until the superior aspect of the lamina is reached. The IA is slightly above the superior aspect of the cricoid. Again, a sustained electrical activity is measured using sustained phonation. Local anesthesia in the airway is required to examine the IA muscle.

Posterior Cricoarytenoid Muscle

This posterior cricoarytenoid muscle (PCA) is accessible in one of two ways. One can access the muscle laterally by firmly grasping the larynx and rotating it away from the approached side. This will expose the posterior aspect of the posterior cricoid lamina and the overlying PCA. The needle is advanced until the needle passes deep to the posterior edge thyroid cartilage lamina and contacts the posterior cricoid plate. Once this cartilage is encountered, PCA activity can be recorded. It is important to note that all PCA recordings are performed with the tip of the

needle in contact with the cricoid. Confirmation of position is done by instructing the patient to "sniff" two or three times, which activate PCA EMG activity.

If the lateral approach is unsuccessful or not preferred, a transcartilaginous approach can be done. The needle is placed through the CTM in the midline. The needle is advanced through the airway until the anterior plate of the cricoid is palpated. The needle is then withdrawn slightly and tipped laterally toward the PCA muscle. The needle is then firmly advanced through the posterior plate of the cricoid. Once the needle passes through the cricoid, the tip of the needle will be in the PCA muscle. If the needle does not penetrate the cartilage, it can be slowly rotated while pushing. Sometimes, the needle needs to be moved slightly to find a less calcified area of the cartilage. In men, both tables of the cricoid are usually palpated with the needle, while in women, who usually have less calcification, the two tables are usually not noted. This approach, while more direct, can be especially challenging in older patients with calcified cartilages. While using this approach to inject the PCA for abductor laryngeal dystonia, one must also be careful while injecting as a small piece of cartilage may have lodged in the hollow portion of the needle and create significant resistance upon injection. In some instances, the hollow EMG needle must be replaced if the plug cannot be dislodged.

Cricothyroid Muscle

Contrary to the muscles described above, the cricothyroid (CT) muscle is extra laryngeal. It can be reached by puncturing the skin about 5 mm lateral to the midline at the level of the CT membrane. The needle is angled laterally by 30–35° and placed on the surface of the cricoid cartilage. When EMG activity is encountered, positioning can be confirmed by having the patient make a sustained /'i:/ sound from low to high pitch. If positioned in the CT muscle, one would expect an increase in the recorded activity during glide transition to high pitched phonation. In all cases, the patient should be asked to begin to lift their head from the exam table to confirm that the needle is not in a strap muscle.

Laryngeal Electromyography Findings

Normal Conditions

Motor Unit Action Potentials (MUAP) A motor unit represents all the muscle fibers in a specific muscle innervated by a single axon. Contrary to larger muscles which can have a ratio of innervation of more than 1000 fibers/neuron, the laryngeal muscles have a different ratio with fewer motor fibers per motor neuron [4]. During activation, the muscle will produce a motor unit action potential, which can be appreciated on the LEMG. On the EMG machine, the MUAP manifests as a simple electrical deflection that crosses the midline in a single major "spike" that represents the simultaneous firing and contraction of a neighboring muscle fiber (Fig. 10.1). A normal MUAP will usually be of about 5–6 ms in duration and can have an amplitude of 200–500 mV [4].

Insertional Activity Under normal condition, insertional activity will be demonstrated upon entry

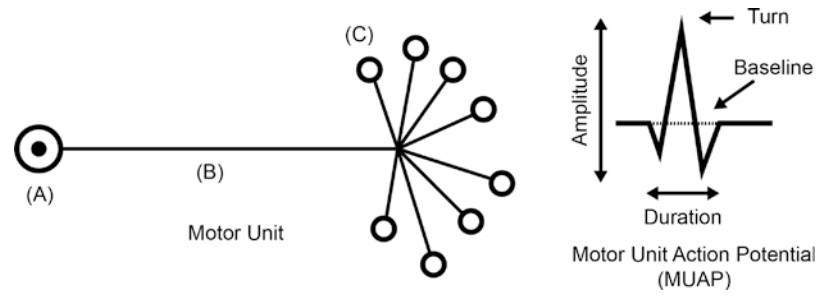

Fig. 10.1 The normal motor unit and motor unit action potential (MUAP). (**A**), Motor neuron; (**B**), Axon; (**C**), Muscle fibers

with a needle in the muscle. This represents a sudden depolarization of MUAPs that are stimulated by the insertion of a needle in the muscle milieu and will usually last a few hundred milliseconds (less than 300 ms). Insertional activity will be present even in a completely denervated muscle if the LEMG study is performed early after an injury. The value of insertional activity is that it stimulates the muscle directly and moving the needle around can allow you to find positive sharp waves and fibrillation potentials. Sometimes polyphasic potentials or large amplitude motor units are seen during insertional activity, although these motor units are also searched for during recruitment. On the contrary, denervation for over a year often will be reflected in a decrease in that type of activity as the muscle may be replaced by fibrosis or fat.

Recruitment corresponds to the amount of total electric signal during voluntary activity of the muscle. During volitional movement, the number of recruited motor units will increase, leading ultimately to what is called a full "interference pattern" formed by the superposition of multiple MUAPs which now become undistinguishable (Fig. 10.2). Recruitment is proportional to the laryngeal activity and will be less prominent with soft phonation compared to a Valsalva maneuver which produces the maximal voluntary recruitment. It is difficult to grade the degree of recruitment more precisely than "full," "diminished," "minimal," or "none." More graduated estimations in percentages tend not to be reproducible among examiners. In the case of LEMG, recruitment is usually measured while the patient is saying /i/. General recruitment, without concern for the specific individual type of motor unit action potential (MUAP), is the primary signal response evaluated during injection for laryngeal dystonia.

Abnormal Conditions

Spontaneous Activity Spontaneous activity at rest during LEMG is not a normal occurrence and is an indication of ongoing severe neuropathic or myopathic injury. This finding is observable about 2–3 weeks after an injury once the denervation has occurred. This is usually an indication of poor prognosis. *Fibrillation potentials* are an example of this type of activity. Single muscle fibers may spontaneously discharge and present as biphasic or triphasic action potentials of several hundred microvolts in amplitude and with a duration of less than 2 ms. They can be seen regularly firing at a frequency of about 1–50 Hz. They are mostly characteristic of denervation. *Positive sharp waves* are another typical finding in this situation. They are represented by a positive (downward) deflection followed by a more prolonged negative deflection. Likewise, they can be found to repeat regularly at a frequency of 1–50 Hz (Fig. 10.3). *Complex repetitive discharge (CRD)*, *although not often found*, is another sign of chronic neural or muscle injury.

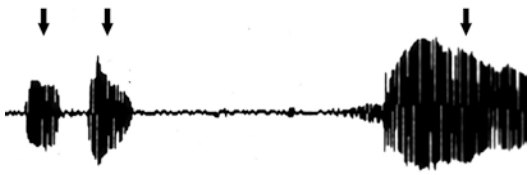

Fig. 10.2 Full recruitment pattern recorded in a patient while saying /'i:/ (indicated by arrows)

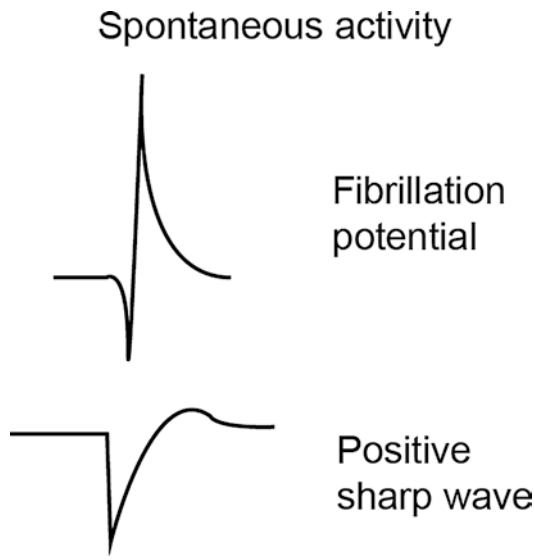

Fig. 10.3 Abnormal spontaneous activity findings in the muscle fibers after a neuropathic injury

They occur through ephaptic activation of a group of muscle fibers that activate in near synchrony at a frequency of 5–100 Hz. The expected amplitude will be between 100 uV and 1 mV. The result is a distinct machine-like sound with abrupt onset and cessation. *Myotonic potentials and fasciculations* are other reported EMG findings, but are rarely found on LEMG.

The findings during insertional activity are most important during diagnostic LEMG. In a normal muscle, a brisk burst of activity is heard and seen when the needle enters the muscle. Relative quiet then ensues. Continued activity with the needle stable can suggest an abnormality. Positive sharp waves and fibrillations can be difficult to detect and sometimes identified by careful listening. Gently moving the needle in the muscle can continue to stimulate activity, and with the EMG machine set to capture MUAPs at a fast recording rate, these indications of denervation can be recorded.

Polyphasic Potentials After denervation has occurred and reinnervation is in process, newer and smaller unmyelinated axons will reform and provide innervation to denervated muscle fibers. Therefore, the size of the motor unit increases as more muscle fibers are innervated by a single nerve fiber (Fig. 10.4). Since the new axons conduct more slowly than mature ones, the EMG signal is longer. Thus, prolonged MUAPs with aberrant waveform morphology named polyphasic potentials will be created. These waveforms can be recognized by their multiple baseline crossing (at least 5). When these new nerve fibers mature, their conduction speed achieves normal rates, and the duration of the EMG signal reverts closer to a normal motor unit, but because it is still a larger unit of muscle fibers, the amplitude of the signal is abnormally large. Over time, when these new sprouts mature, their conduction velocity increases to a normal speed, and the electrical signal when the intact neuron fires shortens to a normal duration. However, since the response now includes more than the original muscle fibers, the signal will have a larger amplitude. These signals are called large-amplitude motor units and are an indication of a previous peripheral nerve injury that has undergone some mature recovery (Fig. 10.5).

Synkinesis During reinnervation, particularly after a more severe mixed nerve injury, sprouting axons can be misdirected to antagonistic muscles, creating synkinesis. One example would be the presence of a burst of electrical activity during a "sniff" maneuver while surveying the TA muscle. As all the laryngeal muscles may present with various levels of activation during phonatory or non-phonatory actions, synkinesis may be difficult to detect. Generally, with the adductor

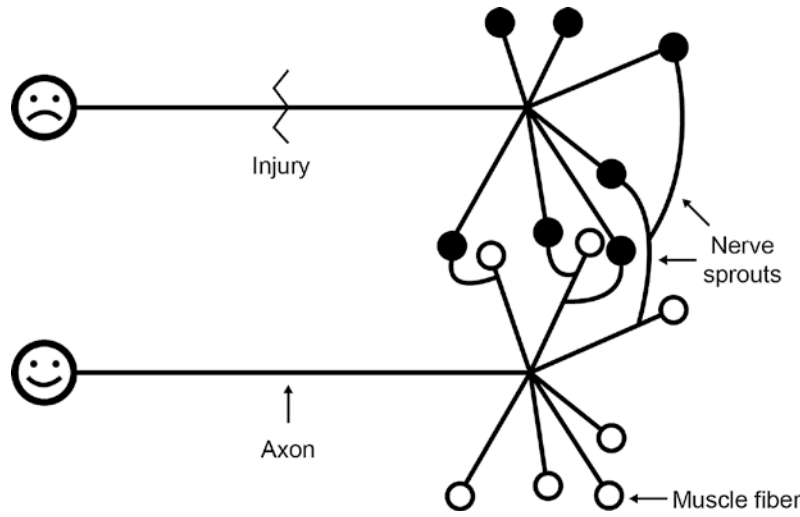

Fig. 10.4 The motor unit after denervation and reinnervation. After a neuropathic injury, nerve sprouts will form from a normal axon to a denervated muscle fiber

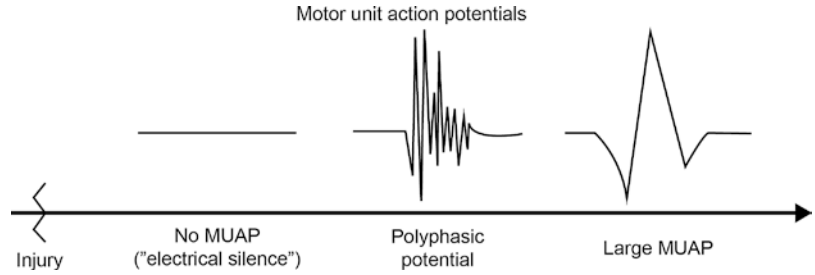

Fig. 10.5 The progression of the motor unit action potential morphology in time during the reinnervation process after a neuropathic injury

muscles, if the response of a "sniff" is equal to, or more than, the response during phonation, that is a sign of synkinesis. With the PCA, if you get more than very minimal recruitment during phonation, that is a sign of synkinesis [5].

Reporting

Typically, the performing clinician immediately uses LEMG results. Nonetheless, it is important to document study results for future reference. Including the indications for the exam is helpful for the reader to understand why certain recordings were performed for the patient. The specific findings for the recordings for each muscle should be listed in an objective format, without interpretation. The impression, summarizing the study, should be offered in simple language so that a reader who is not familiar with EMG terms can understand the test results. Usually this consists of a comment regarding the status of the recurrent laryngeal nerve. Finally, a "disposition" reflecting how the test results help direct the patient's clinical course can increase the usefulness of the LEMG in a written form.

LEMG Applications

Signal Guidance for Therapeutic Injection

LEMG is useful for precise localization and therapeutic injection into laryngeal muscles. The most common use of this technique is for botulinum toxin injections for laryngeal dystonia (e.g., spasmodic dysphonia, tremor). A hollow monopolar needle allows the clinician to localize insertion signal and recruitment of the target muscle. It is the authors' belief that EMG-guided injections may be superior to point-touch technique (i.e., no EMG guidance). One study by Fuller et al. did compare the two techniques done by the same physicians for TA muscle injections. They did not report any differences in the rate of successful injections, but they conclude that excellent results can be achieved in experienced hands using both techniques [6]. However, in the senior author's (ADH) experience, EMG guidance can more accurately position the injection needle closer to the active MUAPs and may allow for improved efficacy with lower doses used and fewer side effects. Using EMG guidance not only allows the examiner to target the TA muscle (point-touch being limited to the TA muscle alone) but also allows for specific delivery of the toxin to the LCA, the IA, and the PCA muscles when indicated. Additionally, using EMG guidance for injections gives the examiner continued experience with the techniques of LEMG that will transfer to increased skills when performing diagnostic LEMGs.

While LEMG guidance for injections can be performed in conjunction with a trained electromyographer, most laryngologists acquire enough experience to do the procedure alone. When the needle in placed, the main response to confirm positioning is the insertional activity and recruitment, which are more global responses. In contrast to diagnostic LEMG, in this setting, there is less concern for the type of motor unit. Nonetheless, it is imperative that the otolaryngologist be trained to identify these general LEMG response patterns. It is important to note that the demonstrated electrical activity may vary across patient population. Therefore, proper documentation of previous

response, such as decreased recruitment, will help for subsequent injection, avoiding unnecessary probing by the physician to find a more significant response, which may not exist in the patient.

Diagnostic Needle LEMG

This form of LEMG is used to examine laryngeal muscles for the presence of abnormal motor units as well as the degree of recruitment. During diagnostic EMG studies, in addition to evaluating recruitment, the actual MUAP morphology is examined. This technique requires careful listening and "capturing" the specific MUAPs to evaluate them in detail. While there are many different morphologies, the primary ones that are examined are fibrillations, positive sharp waves, polyphasic potentials, and large amplitude MUAPs. Fibrillation potentials and positive sharp waves suggest an ongoing or recent injury. Polyphasic potentials generally indicate a nerve recovery phase. Large amplitude MUAPs are a sign of an older peripheral nerve injury that has matured. In addition to the specific morphologies, the examiner will also characterize the pattern of recruitment which can suggest a peripheral (decreased with motor units firing at a rapid rate) or central (decreased with motor units firing at a slow rate) pattern of injury. In most cases, diagnostic LEMG is used to confirm the presence of neurological injury rather than mechanical limitation (e.g., joint fixation, dislocation) in cases of vocal fold motion impairment or to advise on prognosis in such cases. We will discuss its usefulness in evaluating vocal fold motion impairment and for prognosis in the following sections.

Vocal Fold Motion Impairment Vocal fold motion impairment (VFMI) includes hypomobility or immobility of the vocal folds of any etiology, either neurogenic or mechanical. LEMG can be used, for example, to discern between a vocal fold paralysis and a cricoarytenoid joint fixation.

Some studies have tried to quantify how LEMG changes clinical management. In their consensus statement in 2016, Munin et al. meta-analyzed the available literature and found that the clinical care plan could be altered up to 48% of the time because it changed the diagnosis. The most common alternative diagnoses were cricoarytenoid fixation and superior laryngeal neuropathy [7].

Prognosis in Recurrent Laryngeal Nerve Injury Recurrent laryngeal nerve (RLN) injury can have many etiologies, including iatrogenic trauma, most commonly from anterior cervical spine approaches, thyroid surgery, cardiothoracic surgery, and neoplasia, or can be termed idiopathic [8, 9]. Depending on the extent of the injury, recovery, either partial or complete, may occur. As such, available treatment options will be selected on a case-by-case basis with treatment ranging from speech therapy to injection laryngoplasty, to more definitive laryngeal framework procedures or reinnervation. Temporary solutions are often considered early in the process in order to avoid surgery with the hope of spontaneous recovery.

Generally, recovery of peripheral nerve injuries of the recurrent nerve occurs within 8–12 months of onset. During this potential recovery period, the absence of recruitment is not a certain indication that regrowth is not occurring because until some active nerve fibers reach the muscle, no insertional activity or recruitment will be seen. However, as time progresses beyond 6 months, it is possible that LEMG can forecast the odds of recovery. Some studies suggest that it can serve a role in predicting patients with a poor prognosis who will not recover purposeful motion of the vocal fold. This information would be valuable if it allows the laryngologist to move forward with the management and suggest early surgery in some patients. Ingle et al. demonstrated that in their center, the use of LEMG changed of diagnosis in 10% of cases and led to alteration of the treatment plan in 36% and eliminated the observation period before permanent treatment in 26% [10]. The 2016 consensus statement by the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) recommended that if prognostic

information is required in a patient presenting with a suspected vocal fold paralysis, a LEMG should be performed between 4 weeks and 6 months after the injury [7]. However, it is of interest to note that some studies argue that it may overestimate negative prognosis if done before 3 months [11]. In any case, the important time to do a LEMG is just prior to proceeding with definitive procedures since that is when the findings will most affect clinical decisions.

In addition to all this, Lin et al. looked at the LEMG findings in patients with persistent vocal fold immobility of at least 6 months duration. They found that only 3 out of 27 patients presented with electrical silence upon examination, while the rest showed motor unit potentials, with normal configuration (44%) or polyphasic (44%). Adductor synkinesis, referring to misdirected reinnervation after RLN injury, was found in 30% of patients [12]. Indeed, a vocal fold might remain immobile in spite of spontaneous reinnervation due to synkinesis. In many cases, this synkinesis is significant in providing vocal fold tone and would be an indication to proceed with laryngeal framework surgery rather than risk losing the synkinetic reinnervation during a reinnervation procedure [5]. Because of this, including LEMG in the workup prior to laryngeal reinnervation is important [12].

Diagnosis of Neuromuscular Diseases A variety of neurologic conditions can affect the larynx. While rarely used in this setting, LEMG had the potential to aid in the diagnosis of motor neuron diseases like Parkinson disease (PD), multiple system atrophy (MSA), supranuclear palsy, pseudobulbar palsy, amyotrophic lateral sclerosis (ALS), laryngeal tremor, and/or spasmodic dysphonia. For example, in patients with PD, one could expect normal responses during the exam, although it has been shown that some may demonstrate a pattern of hypercontractility at rest, suggesting relaxation difficulty consistent with the muscle rigidity associated with the disease [13]. In contrast, patients with ALS may demonstrate signs consistent with peripheral injury with decreased responses and signs of ongoing denervation with positive sharp waves and fibrillation, as well as polyphasic potentials [14]. MSA patients may exhibit various LEMG patterns including neurogenic change on MUAP analysis of the thyroarytenoid (TA) and posterior cricoarytenoid muscle (PCA), paradoxical activation of the TA muscle during inspiration, and tonic activity of the TA during quiet breathing [15]. Behavioral conditions also need to be considered. Indeed, muscle tension dysphonia, conversion disorder, and malingering may present in a similar fashion, and it may be hard to distinguish among these entities.

The current diagnostic validity of LEMG in a variety of motor neuron disorders affecting the larynx is not defined. Various qualitative or quantitative indicators have been proposed and studied throughout the years, including the qualitative assessment of muscle activity pattern during phonation, but it is unknown if blinded evaluation would allow to properly distinguish between pathologic and normal [16, 17]. Based on a study by Palmer et al. looking at lower and upper motor neuron disorder, LEMG abnormalities were significantly associated with lower, but not upper, motor dysfunction. MUAP recruitment was found to be the most sensitive (82%) and specific (92%) parameter [18]. Table 10.1 presents the common findings on LEMG characterizing upper and lower motor neuron disorders.

Diagnostic Fine-Wire LEMG

The technique of fine-wire electromyography (FWEMG) is most valuable when the examiner is interested in measuring the timing of response rather than the amplitude of recruitment or the morphology of the MUAPs. Hook wires allow the placement of an electrode in a muscle with the confidence that the electrode will remain stable for the recording session. Usually monopolar fine wires are placed. Pairs of fine wires can be used but have not been found to offer any advantages over single wires with a surface electrode [19].

Fine-wire electrodes can be purchased, prepackaged, and loaded in a hollow needle (Wire Electrode Needle Set Male, 1512A-M; Laborie,

Table 10.1 Electromyographic findings in upper and lower motor neuron disorders

		Upper motor neuron disorder	Lower motor neuron disorder
Insertional activity	Normal	Normal	Normal-↑-↓[a]
Spontaneous activity	Absent	Absent	Fibrillation potential Positive sharp wave
Motor unit action potential (MUAP)	Normal	Normal	Polyphasic potential Large MUAP
Recruitment	Full	↓; Slow-firing	↓; Fast-firing

[a]Progression over time

Brossard, QC, Canada). These wires are made of stainless steel and are coated with heavy polyimide insulation except at the last 5 mm of the wire, which acts as the recording electrode. The tip of the wire is bent back at the tip of the needle, allowing the wire to be passed into the tissue. Usually, the uninsulated tip of the "hook" is trimmed with scissors so that only 2–3 mm of the uninsulated wire remains to increase the likelihood that the wire will record from the targeted muscle only. The laryngeal muscles can then be probed with the same approach as with a monopolar needle until the muscle of interest is reached. Once in position, the needle is removed, leaving the wire in place as the barbed tip will maintain it in position. Several wires can thus be positioned to study a series of muscles at the same time using multichannel EMG. Fine wires are technically more difficult to place than simple needle electrodes because the needle can only be advanced forward due to the barb. If the target muscle is not found *during the initial forward movement of the needle*, the entire fine wire/needle must be removed and replaced.

Once the wires are in place, a FWEMG can be performed. Ideally, a multichannel EMG machine can monitor all the wires simultaneously, and one channel can be devoted to a microphone, so the timing of phonation can be seen in comparison with the timing of muscle activity. This technique is valuable to look at patterns of laryngeal dystonia and can indicate which muscle is most involved with dysphonic activity [19]. FWEMG is also the best technique to look for synkinesis because wires can be placed on both the affected side and the normal side, and the timing of muscle activity during tasks can be compared.

Compound Muscle Action Potential

The technique of measuring the compound muscle action potential (CMAP) requires active stimulation of the nerve by the examiner while recording from the destination muscle. Effectively, the recording electrode measures the simultaneous contraction of all the muscle fibers after the nerve is stimulated. CMAP is often used to measure nerve conduction velocity and is also used in some facial nerve studies. CMAP is not often used with LEMG but can be useful in the diagnosis of myasthenia gravis. A hook wire electrode is placed in the muscle to provide a stable recording site while the recurrent nerve is stimulated repeatedly. The recurrent nerve can be stimulated by placing the two probes of the stimulating device with some pressure toward the tracheal-esophageal groove just above the manubrium. Repeated stimulation that results in a diminishing CMAP is suggestive of myasthenia gravis (Fig. 10.6).

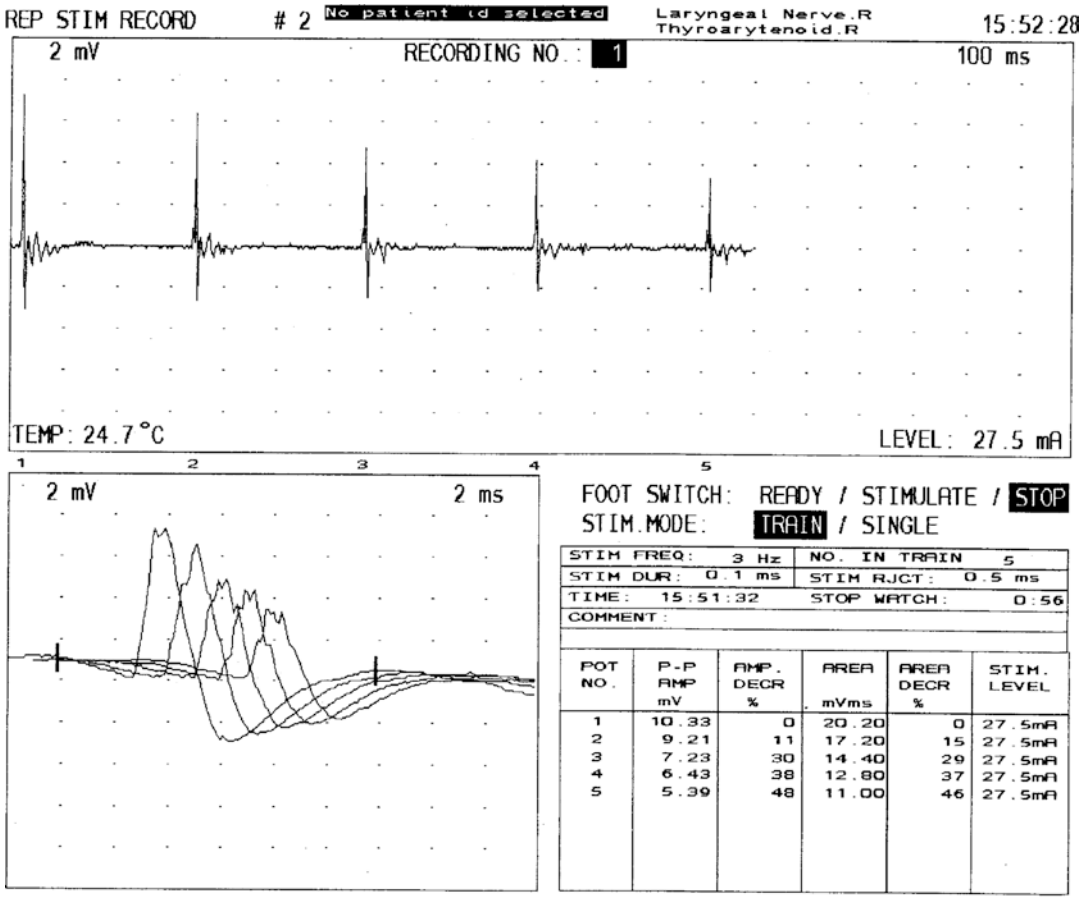

Fig. 10.6 Electromyographic recording showing a decrease in compound action potential with repetitive stimulation in a patient with myasthenia gravis

Summary

Laryngeal electromyography is the only technique that actually examines the innervation of the laryngeal muscles. Until a LEMG is performed, or the nerve is known to have been cut, the term "immobility" is best used to describe a vocal fold that does not move. The terms "paralysis" and "paresis" should be reserved for those cases in which the neurological injury to the nerve has been confirmed. LEMG is a powerful investigative technique for the laryngologist, and its value increases as the examiner gains experience using it in clinical situations.

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Part II

Neurologic Disease

Amyotrophic Lateral Sclerosis and Motor Neuron Disease

11

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Introduction

Motor neuron diseases (MNDs) are a class of progressive neurodegenerative disorders affecting motor neurons resulting in weakness, spasticity, and atrophy of innervated muscles. Most common and familiar of this group is amyotrophic lateral sclerosis (ALS). As a class, MNDs are heterogeneous, occurring at varying rates, ages of onset, and disease severity. Furthermore, most have little to no inheritable contribution, while a minority are genetically linked. Manifestations reflect preferential involvement of upper and/or lower motor neurons and spinal and/or bulbar tracts. Clinical features commonly include limb weakness, poor articulation, swallowing impairment, and breathing derangement. Individualized evaluation and management of MND is important but can be challenging as phenotypes differ among subtypes and invariably fluctuate throughout disease evolution. Because they are uniformly progressive and fatal, early and accurate assessment, open communication, and shared decision-making are imperative.

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Epidemiology

As a class, MNDs are relatively rare, occurring with an incidence of approximately 2 in 100,000 people and affect men slightly more than women, at a ratio of 1.4:1 [1]. The most common MND, ALS, occurs in up to 3 out of 100,000 people, and in some parts of the world, the terms MND and ALS are used interchangeably. Age of onset varies across MND subtypes and also within certain diagnoses. Some features of MND including early age at onset, female gender, and initial presentation with bulbar symptoms (e.g., dysarthria, nasal regurgitation, dysphagia, dysphonia) seem to predict worse disease severity and more rapid progression, particularly in ALS [2, 3]. Awareness of such predictors allows for earlier, prophylactic interventions such as enteral feeding.

The etiology of MND is broad and likely multifactorial. MND may be acquired through environmental exposures, genetic predisposition, or contributions from both. Although no one environmental exposure has been definitively associated with MND, there are several studies associating physical and psychological stress, environmental toxins, cigarette smoking, autoimmune attack, and history of military service with the development of MND [4–6].

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Genetics

MND subtypes can be classified as inherited or largely sporadic (Table 11.1). Inherited forms of MND include spinal and bulbar muscular atrophy (SBMA), spinal muscular atrophy (SMA), and hereditary spastic paraparesis (HSP). Additionally, up to 10% of ALS cases are familial. Sporadic forms of MND include most cases of ALS, primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), and progressive bulbar palsy (PBP).

Pathophysiology

MNDs are a varied group of progressive neurologic disorders characterized by degeneration of upper motor neurons (UMNs), lower motor neurons (LMNs), or a pattern of both. UMNs are either pyramidal or extrapyramidal and originate in the motor region of the cerebrum, specifically along the fifth layer of the cerebral cortex housed in Betz cells [7]. Alternatively, LMNs originate in the alpha motor neurons of the gray matter in the brainstem and spinal cord. UMNs carry out their effect on LMNs, controlling voluntary muscle groups.

Key pathologic features of MND result from involvement of the brain and anterior horn cells of the corticospinal and corticobulbar tracts producing deleterious effects on the neuromuscular skeletal system. Frequently this manifests as unilateral, progressing to bilateral, upper or lower limb dysfunction. The deterioration of corticobulbar pathways to IX, X, XI, and XII cranial nerve nuclei greatly impacts the complex, coordinated control of speech and swallowing. Particularly harmful are impairments of the vagal and glossopharyngeal nerves as they are responsible for the motor and sensory innervation to the larynx and pharynx [8].

Clinical presentation of MND depends on the pattern of motor neuron involvement. When UMNs are affected, muscle spasticity, brisk reflexes, and overall slowing are observed. When LMN involvement predominates, muscle weakness, atrophy, and fasciculations are seen. Many MNDs are characterized by the affliction of both upper and lower motor neurons, thereby manifesting clinical features of both. The most common MNDs and their defining characteristics are detailed in Table 11.1.

Common Motor Neuron Disease

Inherited MND

Spinal and bulbar muscular atrophy (SBMA) or Kennedy disease is an adult-onset X-linked MND affecting bulbar and LMNs. Individuals with SBMA are exclusively male and may present

Table 11.1 Common motor neuron diseases

Motor neuron disease	Classification	Age of onset	UMN	LMN	Bulbar involvement
Spinal and bulbar muscular atrophy (SBMA)	Inherited	15–60 years	–	+	+
Spinal muscular atrophy (SMA)	Inherited	<6 months–30s	–	+	+/–
Hereditary spastic paraparesis (HSP)	Inherited	Across lifespan	+	+/–	+
Primary lateral sclerosis (PLS)	Sporadic	40–60 years	+	–	+
Progressive muscular atrophy (PMA)	Sporadic	Across lifespan	–	+	+
Juvenile amyotrophic lateral sclerosis	Sporadic	<25 years	+	+	+
Progressive bulbar palsy (PBP)	Sporadic	50–80 years	+	+	+
Amyotrophic lateral sclerosis (ALS)	Sporadic 5–10% inherited	40–60 years	+	+	+/–

UMN upper motor neuron, *LMN* lower motor neuron
"+" characteristic; "–" not characteristic; "+/–" sometimes present

with similar phenotypes as their brothers, fathers, or uncles. Common features include slowly progressive bulbar and spinal muscular atrophy resulting in limb and facial weakness, dysphagia, and dysarthria. Less common but a feature unique to Kennedy disease is a propensity for laryngospasm, informally referred to as "dry drowning [9]." The diagnosis of SBMA is confirmed by molecular genetic testing for CAG trinucleotide repeat expansion on the androgen receptor of the X chromosome. Point mutations within the androgen gene receptor confer androgen insensitivity, resulting in infertility, testicular atrophy, and gynecomastia. These features distinguish Kennedy disease from all other MNDs [10].

Spinal muscular atrophy (SMA) is an autosomal recessive LMN disease and is the most common genetic cause of death in children less than 2 years old. The pathogenesis involves the loss of a specific protein, survivor motor neuron 1, which results in poor muscle tone. Proximal muscle weakness is much greater than distal and, in severe cases, results in fatal respiratory failure. There are four types of SMA, defined clinically by age of onset and most advanced motor milestones achieved. The first molecular genetic target for SMA, nusinersen (Spinraza®, Biogen Netherlands, Badhoevedorp, the Netherlands), was approved by the US Food and Drug Administration (FDA) in 2017. Early studies have demonstrated children treated with nusinersen have improved motor strength and manifest a milder disease phenotype. Type I SMA occurs in children less than 6 months old and is also known as Werdnig-Hoffmann disease. Infants with SMA Type I never sit and require gastrostomy tube feeding and tracheostomy to prolong life. SMA Type II, Dubowitz disease, occurs later than SMA Type I, between the ages of 6 and 18 months. These children sit but never stand. SMA Type III is juvenile in onset and known as Kugelberg-Welander disease. These children walk but eventually regress and may require a wheelchair. Type IV is adult-onset SMA, a milder phenotype.

Hereditary spastic paraparesis (HSP) is a primarily UMN disease involving the posterior column of the spinal cord and bladder. The prevalence of HSP is 1.3–9.6 per 100,000, and the inheritance pattern is variable including autosomal dominant, autosomal recessive, or X-linked [11]. Over 15 genes have been associated with HSP; therefore the phenotype can be quite diverse. Key features are progressive lower extremity greater than upper extremity spasticity, weakness, cerebellar ataxia, neurogenic bladder, and peripheral neuropathy [12, 13]. Dysarthria and dysphagia are less common, usually seen in atypical forms of HSP, and the exact mechanism is unknown [14].

Sporadic MND

Sporadic MNDs are a spectrum of mainly adult-onset diseases of which ALS is the most common, accounting for approximately 80% of MNDs [15]. Atypical variants including primary lateral sclerosis (PLS), progressive muscular atrophy (PMA), progressive bulbar palsy (PBP), and juvenile amyotrophic lateral sclerosis are less common and less severe.

Sporadic ALS involves both UMNs and LMNs. It has an incidence of 1–2.6 per 100,000 persons with the average age of onset of 58–60 years [1, 5, 16]. The average survival from symptom onset is 3–5 years with only 20% of patients surviving beyond 5 years and fewer than 10% surviving beyond 10 years [17]. The etiology of ALS is not entirely clear.

The development of ALS is theorized to be multifactorial and acquired through environmental exposures, cellular oxidative stress, excitotoxicity, and mitochondrial dysfunction leading to cell death [5, 16, 18–20]. Up to 10% of ALS cases may have genetic associations. Most commonly, mutations in well-characterized proteins, C9ORF72 and superoxide dismutase 1 or SOD1, are associated with both familial and sporadic forms of ALS. Owing to the increased applications of molecular genetic testing, the genetic influences on sporadic MND will be more transparent in the future.

Symptoms at disease onset include progressive, painless weakness, often with a distinct and predictable spread throughout the body. The initial weakness pattern can be divided into thirds

with approximately one-third bulbar, one-third upper extremity, and one-third lower extremity [21–23]. Bulbar presentation is associated with poorer prognosis [24].

Communication, Swallowing, and Respiratory Findings

Involvement of the corticospinal and corticobulbar tracts, in particular the nuclei of cranial nerves V, VII, IX, X, and XII, yields clinical signs of dysarthria, dysphonia, dysphagia, and dyspnea. Bulbar manifestations may occur in isolation or in combination with limb symptoms. Patients often present to otolaryngologists or other specialists prior to correct disease diagnosis which may result in delayed identification of MND [17]. Diagnosis relies on building a clear clinical impression and may take time, ruling out other possible causes. Ancillary testing including lab work, electromyography (EMG), MRI, and muscle biopsy may confirm a suspected diagnosis. Among MND subtypes, swallowing impairment occurs in up to 100% of patients leading to significant morbidity and mortality [7]. Although dysarthria and dysphonia are also common among MND, the underlying mechanisms are not as clearly defined and are often reticent as compared to respiratory comorbidities. Cognitive abnormalities, depression, and emotional lability commonly coexist with MND with up to 50% of patients demonstrating some degree of impairment which may further contribute to alterations in communication and deglutition [25].

Communication

Communication impairment is a significant source of distress, isolation, and altered quality of life in MND patients. Abnormalities of voice, the sound produced by the larynx, and speech, the sound ultimately modified by the upper airway and oral cavity, are common in MND. In ALS, dysarthria is more common than dysphonia, each occurring in up to 93% and less than 50% of patients, respectively [17]. Table 11.2 highlights features of both dysphonia and dysarthria in MND.

Table 11.2 Features of voice and speech impairment in motor neuron disease

Dysphonia	Dysarthria
Spastic	Slow
Harsh	Labored
Breathy	Disarticulate
Fatiguing	Imprecise
Monotone	Hypernasal

Voice quality varies depending on predominance of the upper vs. lower motor neuron involvement. Spastic dysphonia is a manifestation of UMN involvement with a voice that sounds tight, harsh, and strained which is easily fatigued. LMN disease is accompanied with breathy or weak dysphonia and limited ability for rapid vocal changes resulting in monotonicity or monoloudness [15].

Speech in MND is influenced by both upper and lower motor neuron manifestations. UMN involvement results in stiffening of oral cavity muscles including the tongue and lips. Resultant dysarthria is slowed and hypertonic and lacks precision. LMN involvement may start as unilateral and then progress to bilateral and includes low tone, atrophy, weakness, and fasciculation of oral cavity and oropharyngeal muscles. Tongue fasciculations are one of the most common signs of ALS presenting to otolaryngologists [17]. Dysarthria is characterized by quietness, huskiness, and slurring. Speech may also be hypernasal due to involvement of muscles innervating the soft palate which creates velopalatal insufficiency, though this scenario is not consistent across MND [26].

Swallowing

At onset of most MND, swallowing function is often preserved. However as disease progresses, dysphagia becomes increasingly common, ultimately reported by up to 90% of MND patients [27]. MNDs with initial presentation limited to dysphagia or dysphonia are likely to present first to an otolaryngologist or speech language pathologist. In a large cohort of ALS patients in otolar-

yngology practice, 86% reported dysphagia. In comparison with rates, dysphagia in PBP and PMA were 89% and 45%, respectively [28].

All phases of swallowing are affected by MND. Presenting symptoms may be purely UMN or LMN or a combination of both. With disease progression, both UMNs and LMNs are often affected leading to severe dysphagia, often requiring a gastrostomy tube to meet nutritional needs. Table 11.3 details abnormalities of various components of swallowing observed in MND.

Oral cavity structures affected by MND include the lips, tongue, and masticatory muscles. Muscle atrophy and weakness as well as tongue fasciculations are observed. Oral phase dysfunction may manifest as drooling, difficulty chewing, and mealtime fatigue. Such oral impairments are commonly seen in SBMA but are slowly progressive and may not develop until as late as 10 years after disease onset. In these patients, reduced tongue pressures may be an early indicator of swallowing dysfunction.

Pharyngeal structures involved by MND include the palate, pharyngeal constrictors, and cricopharyngeus muscle (CPM). Clinically, dysphagia to liquids and nasal regurgitation, which are attributed to LMN degeneration, generally arise before difficulty with solids. The typical pharyngeal manifestation of UMN involvement is CPM dysfunction. Pharyngeal phase impairments result in reduced swallowing efficiency and compromised airway protection. In early onset SMA, oropharyngeal weakness leads to dysphagia secondary to impaired pharyngeal clearance evidenced by post-swallow vallecular and hypopharyngeal residue commonly identified during videofluoroscopic swallow study (VFSS). Combined with neck extensor weakness and resultant forward head posture, such patients are predisposed to aspiration pneumonia. Gastrostomy tubes are universally required for these patients to maintain nutrition and mitigate pulmonary disease [29].

Esophageal dysphagia related to MND is less completely described owing to upstream (oral and pharyngeal) deficits which make characterization of esophageal phase impairments challenging. Prolonged esophageal transit has been identified in PBP and PLS and is an isolated finding in patients with PMA [30–32].

Laryngopharyngeal sensory abnormalities, particularly of the supraglottis, magnify the effect motor deficits and have been observed in up to 54% cases of ALS [33]. Undoubtedly such impairment contributes to the well-described and considerable sequalae of swallowing dysfunction in MND including dehydration, malnutrition, pneumonia, social isolation, fear, and anxiety. And for ALS patients, aspiration pneumonia is a leading cause of death [34].

Respiratory

Further compromising lung health is weakening of intercostal and diaphragm muscles leading to respiratory compromise and ineffective cough. For fatal MND, respiratory failure is a frequent cause of demise, and shared discussions surrounding the use of mechanical ventilation or artificial airway (tracheostomy) should take place early in the disease course.

Table 11.3 Features of swallowing impairment in motor neuron disease

Oral phase	Pharyngeal phase	Esophageal phase	Sensation and timing
Drooling	Reduced tongue base retraction	Impaired stripping wave	Delayed swallow trigger
Spillage	Velopharyngeal incompetence	Prolonged transit	Multiple swallows
Poor bolus formation	Decreased hyolaryngeal elevation	Esophageal residue	Orofacial pain
Lingual weakness	Weak pressures		Delayed airway closure
Ineffective chewing	Vallecular residue		Aspiration
Prolonged mastication	CPM dysfunction		Impaired/absent cough
Mandible rigidity	Hypopharyngeal residue		
Oral cavity residue			

CPM Cricopharyngeus muscle

Evaluation and Assessment

Comprehensive evaluation and management of MND patients and the upper aerodigestive manifestations of their disease requires multidisciplinary care. The complete team is comprised of family members or caregivers, physicians (including otolaryngologist, neurologist, pulmonologist), speech language pathologist, dietician, therapist (physical, occupational, respiratory), and mental health professional.

A focused physical exam of MND patients includes a qualitative assessment of voice and speech. Furthermore, attention is paid to the integrity of oral cavity structures and cranial nerve function. Judgement of cognitive impairment is important and factors into decision making throughout the disease course. Indirect laryngoscopy, with stroboscopy when feasible, is performed to evaluate vocal fold motion, contour, and closure as well as laryngopharyngeal sensation, secretion management, and cough strength [15]. Common videostroboscopic findings in patients with MND include incomplete glottic closure, vocal fold bowing, hyperfunction, decreased abduction, pachydermia, and pooling [17]. Aerodynamic and acoustic measurements provide additional information regarding glottic incompetence, subglottic air pressure, velopharyngeal insufficiency, and intelligibility which may help guide appropriate therapies for dysphonia and dysarthria.

Disease- and symptom-specific outcome measures are useful tools for screening MND patients for deficits as well as for disease severity and progression. The most commonly used tool specifically designed for MND is the Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R). It is a four-domain instrument which measures bulbar, fine motor, gross motor, and respiratory function to a maximum score (best function) of 48 [35]. Items assessed include speech, salivation, swallowing, and respiratory insufficiency, and worse scores have been shown to predict laryngeal penetration in patients with ALS [36].

The Eating Assessment Tool-10 (EAT-10) and Swallowing-Related Quality of Life (SR-QOL) are symptom-specific, patient-reported outcomes measuring perceived swallowing function. Among ALS patients, the EAT-10 has high discriminant ability to predict aspiration with reasonable sensitivity and specificity of 86% and 76%, respectively, as well as a superb negative predictive value of 95% [36]. Furthermore, SR-QOL is moderately reduced in patients with ALS with the fatigue and eating duration domains most accurately reflecting degree of swallowing dysfunction [37].

Instrumental tools including VFSS, flexible endoscopic evaluation of swallowing (FEES), and high-resolution manometry (HRM) are well-established, validated methods for assessing swallowing impairment. Each provides valuable information about swallowing anatomy, physiology, efficiency, and safety, but as different assessment modalities, each offers certain advantages and has specific limitations. Table 11.4 reviews the ability of each VFSS, FEES, and HRM to assess swallowing function.

On VFSS, certain features common to MND-related swallowing impairment are well-visualized including incomplete velar closure, reduced tongue base retraction, and post-swallow pharyngeal residue. Furthermore, VFSS is an excellent tool for assessing and measuring hyolaryngeal elevation and its relationship to completeness and timing of laryngeal closure. This is particularly valuable in patients with MND who are at high risk of negative health sequelae related to unsafe swallowing [38, 39].

FEES is uniquely useful for assessing laryngopharyngeal anatomy, sensation, swallow onset, and pooling or residue. In ALS patients, residue on FEES predicts ALS clinical stage as measured by ALSFRS-R [40]. FEES is also a good tool for biofeedback and to evaluate the efficacy of particular swallowing maneuvers or strategies.

HRM, originally used primarily to assess esophageal phase of swallowing, has gained popularity in measuring more proximal, pharyngeal manometric and impedance information. For cases of MND, HRM very accurately detects abnormal pharyngeal pressures and variable CPM tonicity. Furthermore, manometry technology can be used to assess tongue pressure, which, in

Table 11.4 Comparison of instrumental swallowing assessments

Component evaluated	FEES	VFSS	HRM
Vocal fold function and anatomy	++++	++	+
Laryngopharyngeal sensation	++++	+	+
Spillage	++++	++++	+
Aspiration	++++	++++	+
Laryngeal penetration	++++	++++	+
Pharyngeal and vallecular residue	++++	++++	+
Cricopharyngeus muscle function	+	++++	++++
Pooling of secretions	++++	+	+
Objective swallowing parameters	++	++++	+++
Oral cavity	+	+++	+
Laryngohyoid elevation	++	++++	+++
Esophageal phase of deglutition	+	+++[a]	++++

FEES flexible endoscopic evaluation of swallowing, *VFSS* videofluoroscopic swallow study, *HRM* high-resolution manometry

"+" poor ability to evaluate; "++" average ability to evaluate; "+++" good ability to evaluate; "++++" excellent ability to evaluate

[a]with esophageal follow through

MND, shows reduced isometric strength as well as disorganized movement during swallowing.

Electromyography (EMG) and nerve conduction are often used to help confirm the diagnosis of MND. To assess specific components of swallowing or voice, the use of EMG has been largely experimental. EMG in ALS patients has demonstrated longer swallowing duration, variability in cricopharyngeal pause duration, and discoordination between the timing of laryngeal excursion and cricopharyngeal relaxation.

Additional useful tools for assessing the MND patient include spirometry and airflow measures. The finding of irregular voluntary cough airflow and altered respiratory-swallowing coordination predicts aspiration in patients with ALS [41].

Management and Therapies

Presently, there are no cures for MND. Two drugs approved by FDA—riluzole (Rilutek®, Sanofi Aventis, Bridgewater, New Jersey) and edaravone (Radicava®, MT Pharma America, a US subsidiary of Mitsubishi Tanabe Pharma)—have demonstrated small improvements in survival (2–3 months) and reduced clinical decline, respectively. Despite these promising developments, symptomatic management remains the primary focus of treatment for ALS and MND [42]. Because of the degenerative and progressive nature of these conditions, therapeutic approaches focus on patient autonomy and advanced planning toward end of life early in the disease course. Behavioral and lifestyle modifications orchestrated by occupational therapists, speech language pathologists, and respiratory therapists, among others, are mainstays for preserving quality of life and mitigating illness in MND.

Sustaining communication relies on enhancing a patient's own voice and speech or providing an alternative means of expression. Augmentative and alternative communication (AAC) devices are very commonly used in the MND population, and appropriate patients should be referred expeditiously for early integration [43]. On average, patients with ALS use such devices from 25 to 31 months depending on disease subtype. There are a range of devices available including non-keyboard technology (dynamic touch screen, head tracking, and eye tracking) which is often useful in later disease stages. With recent technological advanced, voice banking has emerged as a means to potentially personalize an individual's AAC experience.

In mild or less advanced MND, interventions specifically aimed at improving voice quality may be considered. For predominant UMN manifestations such as harsh voice and spasticity,

voice therapy may be useful for teaching volitional relaxation, breath support, and speech control. However, in LMN involvement and symptoms of hypotonicity, intensive voice therapy may be counterproductive due to increased effort required [26]. In patients who have coexisting glottic insufficiency, vocal fold augmentation may be an appropriate procedural intervention; otolaryngologists should evaluate for candidacy using clinical impression and videostroboscopy.

Appropriate instrumental evaluation of swallowing such as VFSS of FEES should guide interventions for feeding and diet allocation. As previously discussed, these evaluations are critical to establish swallowing safety and efficiency and are the foundation to personalize swallowing care throughout the course of disease. The decision to continue oral diet in patients with MND should be serially reevaluated and based on swallowing function, level of activity, nutritional status, pulmonary clearance, quality of life, and preestablished goals of care.

Commonly recommended diet modifications include mechanically altered foods, limited textures, smaller more frequent meals, supplemental nutrition, and thickened liquids if indicated. Where appropriate, patients are advised to reduce to bolus size, perform multiple swallows, alternate solids and liquids, and avoid distractions during mealtime. For some patients, the addition of enhanced sensory stimuli including thermal, vibratory, and gustatory may be considered. Most patients are recommended a set of compensatory strategies during swallowing to mitigate abnormalities identified during instrumental evaluation. Table 11.5 describes commonly used swallowing maneuvers and positions.

Table 11.5 Swallowing postures and maneuvers

Posture/ maneuver	Description	Therapeutic effect
Chin tuck	Chin is tucked toward the neck during swallow	Narrows entrance to airway by bringing tongue base to posterior pharyngeal wall and arytenoids to the epiglottis
Chin up	Chin is tilted up during the swallow	Facilitates bolus transfer from oral cavity to pharynx
Head turn	Head is turned to either the left or the right side, typically toward the damaged or weak side	Improves glottic closure, diverts bolus away from impaired side
Mendelsohn maneuver	When larynx is maximally elevated during swallow, patient holds larynx in elevated position for 2 seconds and then relaxes	Increases height and duration of hyolaryngeal elevation
Supraglottic swallow	Bolus is held in the oral cavity, and then breath is taken and held, followed by swallowing and then volitional cough	Triggers glottis closure prior to swallow
Super-supraglottic swallow	Similar to supraglottic swallow, except breath is held effortfully with Valsalva prior to initiating swallow	Triggers glottis closure and moves arytenoids anteriorly to close vestibule
Effortful swallow	Patient instructed to swallow as hard as possible, push hard with tongue against hard palate	Improves posterior tongue base movement during swallow

There are several rehabilitative strategies for impaired swallowing in MND. Whereas swallowing exercises are commonly employed across disease states and degrees, use in MND must be cautiously considered and continuously reassessed. In more advanced disease, engaging in effortful, repetitive exercise may hasten fatigue and be counterproductive toward swallowing function. Adjuvant devices (palatal prosthesis) are mainstays of treatment. Strategies aimed at enhancing breathing coordination and cough strength such as expiratory muscle strength training (EMST) have demonstrated improved maximum expiratory pressure, hyoid displacement, and laryngeal penetration and aspiration [44].

Medical and procedural interventions may be appropriate to target specific swallowing impairments. Velopharyngeal insufficiency is common

in ALS and presents a challenge for maintaining pharyngeal competence during swallowing and causes bothersome hypernasality of speech. Palatal interventions such as prostheses (palatal lift) and augmentation procedures improve hypernasality, articulation, and nasopharyngeal regurgitation in most patients with effects lasting longer than 6 months in most cases [45]. For MND patients with excessive drooling or difficulty managing secretions, therapies for saliva management are available. Medical options include anticholinergic drying agents as well as salivary gland botulinum toxin injection. For more severe cases, salivary gland diversion or excision may be considered.

For many with MND, progression of symptoms will render swallowing function unsafe and unable to meet nutritional demands. Enteral nutrition via feeding tube is the most common recommendation across all MND patients [38]. With this in mind, discussions regarding non-oral feeding should take place early so that personal wishes and goals of care may be established [46]. In patients who accept feeding tubes, early prophylactic placement is preferred so that respiratory capacity is maximized at time of surgery. Furthermore, mortality from feeding tube is influenced by degree of weight loss at time of tube placement with those losing >10% of diagnosis weight demonstrating poorer survival. Feeding tube use in MND has been extensively studied. Enteral feeding reduces risk of secondary health consequences, improves and maintains nutritional status, and enhances weight gain [47, 48]. However, whether feeding tubes prolong survival or positively impact quality of life is unknown and controversial [49]. Feeding tube-related complications including leakage, pain, irritation, bleeding, and infection are commonly managed conservatively, and rarely do MND patients undergo feeding tube removal [50].

Similar to the inevitability of enteral feeding for many MND patients, noninvasive ventilation (NIV) and tracheotomy with invasive mechanical ventilation (TMV) are common recommendations and considerations for those with or moving toward advanced disease. NIV improves forced vital capacity (FVC) on pulmonary function testing as well as survival. It may be initiated early (FVC > 80%) and has been demonstrated to offer more benefit to ALS patients without bulbar predominate symptoms [51]. Indications for TMV include respiratory failure (FVC < 50%), improved access for pulmonary clearance, and laryngeal obstruction, most commonly due to bilateral vocal fold immobility [15]. As with feeding tubes in MND, tracheostomy prolongs life and but has equivocal effect on quality of life [52]. Ultimately, fewer than 15% of ALS patients undergo tracheostomy. Morbidity of tracheostomy including mucus plugging, accidental decannulation, bleeding, infection, and airway stenosis dampens enthusiasm for its universal recommendation.

In patients who experience recidivistic aspiration pneumonia despite conservative efforts (enteral feeding, tracheostomy), consideration of functional laryngectomy may be appropriate. In otherwise healthy adults, the procedure is relatively safe, efficient, and completely effective at eliminating aspiration [53]. Appropriateness for laryngectomy should be considered in the context of overall quality of life, future prognosis, post-laryngectomy communication options, and access to psychosocial support.

Conclusion

As a group, MNDs are rare, but because they involve motor neurons of the corticobulbar and spinal tracts, they commonly manifest with disordered communication, deglutition, and respiration. Consequently, clinicians who evaluate and treat upper aerodigestive are anticipated to interface with this population. Symptom severity varies across MND subtype and disease stage with inevitable progression toward complete nutritional and respiratory support in the most advanced cases. Clinical phenotypes reflect the distribution of motor neuron involvement—whether upper or lower, spinal or bulbar. Accurate diagnosis and appropriate assessment rely on a cooperative multidisciplinary team, and it may require multiple evaluations before definitive conclusions can be made. In such cases,

screening tools may be useful in guiding additional testing and workup [54]. It is critical that candid conversations about disease course and expectations take place before significant progression in order to preserve patient autonomy. MND management involves treatment of symptoms when possible, prevention of negative disease sequelae, and, importantly, meeting the psychosocial needs of patients and their caregivers.

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Parkinson Disease

12

Jacqui E. Allen and Anna Miles

Abbreviations

AADC	Aromatic amino acid decarboxylase
AD	Autosomal dominant
AR	Autosomal recessive
BBB	Blood-brain barrier
COMT	Catechol-O-methyltransferase
DA	Dopamine
DJ-1	DJ-1 parkinsonism associated deglycase∗
LRRK2	Leucine-rich repeat kinase 2∗
Parkin	Parkin (PARK2)∗
PD	Parkinson disease
PINK1	PTEN-induced putative kinase 1∗
RLN	Recurrent laryngeal nerve
SNCA	α-Synuclein gene (also called PARK1/4)∗
UES	Upper esophageal sphincter
VF	Vocal folds
VFSS	Video-fluoroscopic swallowing study
∗	Gene names for genes associated with familial Parkinson disease

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Introduction

Parkinson disease (PD) is a progressive neurodegenerative condition of unknown causation, affecting more than 6 million people worldwide [1]. Pathognomonic degeneration of the substantia nigra in the midbrain occurs with loss of dopaminergic neurons [1]. Characterized by bradykinesia, gait instability, and affective change, speech and swallowing are frequently affected, and this may occur at any time in the disease course, even in the earliest stages. Swallow dysfunction remains the leading cause of mortality in people with PD due to aspiration pneumonia [2–8]. Dysfunctional swallowing results in multiple episodes of airway violation which includes aspiration pneumonia [2–7]. Those with dysphagic complaints are most at risk of pulmonary problems as the combination of poor motor swallow control and disturbed timing of swallow kinematics results in enhanced risk of penetration and aspiration [2–7]. Disordered deglutition and hypophonia typically seen with PD are also relatively unresponsive to current treatment paradigms including medical therapies and deep brain stimulation (DBS) techniques [3]. This has led to the development of alternative strategies for managing speech and swallowing problems and a raft of different approaches to management. This chapter will examine the findings and effects of PD on upper aerodigestive function and review the current and potential management regimens to address deficits.

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Prevalence of PD is difficult to determine and also shows geographic and age variation. In the United States alone, there is marked state-to-state difference in prevalence of around 845/100,000 persons in Minnesota to 1780/100,000 in New York in those over 65 years, but a lower rate of 450–668/100,000 in those 45–64 years [9]. Worldwide it is estimated that 6 million people suffer from PD, and this is expected to double by 2040 [10]. With the growing belief that environmental agents trigger late-onset sporadic PD, this number may balloon further. The potential health and economic burden that this may bring is significant and will require planned strategies.

Gender demonstrates a slight predominance toward males on average (1.5:1, M:F) but again varies by location [9]. Alaskan PD sufferers are 62% male, while in West Virginia, there is a 50/50 split of genders [9]. In other countries estimates suggest a 60:40 (M:F) ratio. PD is a disease of the elderly with more than 25% of those diagnosed aged over 85 years [9]. In the USA during 2014, for those over 65 years covered by Medicare, almost 8 billion US dollars was spent delivering services to those with PD [9]. Around $20,000 was spent per patient, plus patients themselves also had to pay an average of between $12,000 and $22,000 in out-of-pocket expenses for their healthcare needs [9]. Cost estimates in Germany, the United Kingdom, and Australia estimated similar expenditure with the large proportion of cost associated with hospitalization [9].

Pathophysiology of Parkinson Disease

The pathologic hallmark of PD is degeneration of the pigmented dopaminergic neurons in the substantia nigra pars compacta (SNpc). The cause of this degeneration has been the subject of research for 50 years. Loss of dopamine results in the motor impact of PD; however, there are additional pathologic changes that occur and modify disease expression which are neither dopamine dependent nor responsive [1]. In 2003, Braak and colleagues suggested that peripheral symptoms predated central symptoms because the disease started in the periphery (due to unknown triggers) and propagated centrally [11]. Identification of transport of α-synuclein through neurons in animal models has lent credence to this theory. Over time, identification of α-synuclein in peripheral nerves and the enteric nervous system and as a component of Lewy bodies that are associated with other dementia disorders suggested a multisystem disease, rather than just one of the central nervous system alone. Tracking of axonal movement of α-synuclein from neurite to neurite supported a caudal-rostral pathway for disease spread again in support of the proposed Braak pathogenetic mechanism and staging system [12, 13].

Other proposed disease mechanisms include mitochondrial dysfunction, oxidative stress, and central nervous system (CNS) inflammation with a lack of capacity to address these insults [1, 14]. Genetic forms of PD offer insight into these pathways and demonstrate mutations in genes largely related to mitochondrial function, biogenesis and repair, or neuronal protection, and animal models of PD such as the PINK1 mice mutant are loss-of-function mutations at these gene loci [1]. Cellular accumulation of damaged or defunct mitochondria allow increased oxidative damage with production of reactive oxygen species (ROS). ROS directly damage mitochondrial elements and DNA and may create a cycle of further mitochondrial injury followed by cellular destruction [1, 14]. Examination of postmortem neural tissue from people with PD demonstrates degeneration of pigmented dopaminergic neurons in the SNpc and inclusions of α-synuclein (Lewy bodies) within the remaining neurons [1, 14]. Furthermore, Lewy bodies have been identified in peripheral muscle and the GI tract of PD sufferers suggesting a systemic involvement. A number of Parkinsonian-like syndromes are recognized with features that mimic PD despite the presence of an alternative primary disease, e.g., Lewy body disease and multisystem atrophy (see Chap. 13). α-Synuclein aggregates also accumulate in these disorders, and they are often referred to as synucleinopathies.

Acknowledgment now that inflammation in the brain also contributes to PD neurodegeneration has led to examination of anti-inflammatory approaches to limit progression and control symptoms [1]. Microglial activation in the brain is a

sign of inflammation and engages a cycle of inflammation through release of further mediators that recruit and activate other microglia [1, 14, 15]. Cytotoxic T-cells are implicated in this process through increased blood-brain barrier permeability and through direct presentation of antigen on neurons and via the mitochondrial antigen presenting pathway [1]. Increased levels of circulating pro-inflammatory cytokines and α-synuclein in the CSF and blood indicate that peripheral activity can also influence central events [1]. A further mechanistic pathway implicated in PD development and speed of progression is glycosylation of CNS tissues. This is enhanced in patients with diabetes mellitus (DM), and epidemiologic study suggests that DM increases speed of PD progression supporting glycosylation as a marker of disease severity [1, 2]. This has led to an "indication-switching" approach whereby drugs designed to target glucose control in type 2 DM have been applied to a PD population [2]. Glucagon-like peptide-1 (GLP-1) receptor agonist exenatide was assessed in a randomized controlled trial in people with PD on levodopa treatment. A modest improvement in motor scores was seen, with no significant side effects [2].

Cross-talk between pathways seems synergistic. For example, glycosylation of α-synuclein increases aggregate formation, induces oligomerization (which forms the aggregates), and activates cell enzymes that trigger neuroinflammation [1]. Glycosylated α-synuclein also triggers formation of reactive oxygen species promoting mitochondrial damage and depletion and activates nuclear transcription factor (NK-κB) with downstream signalling resulting in increased receptor expression for glycosylated α-synuclein [1]. Thus, a positive feedback loop is created with ongoing neural destruction.

Laryngeal Function

In order to understand the impairments that PD can produce in pharyngolaryngeal function, we must understand normal function first. Our larynx plays a crucial function in airway protection. It is primarily a valve that is designed to prevent incursion of material into the lower airway. This is a direct consequence of evolutionary development which has landed the airway in the path of swallowed material. This "crossed" airway results in foodstuffs passing across the laryngeal vestibule region, and as a consequence a number of protective airway reflexes have developed to enable detection, response, and rejection of swallowed material headed toward the airway. This fundamental function of the larynx must be maintained to ensure airway integrity and avoid secondary damage to the lower respiratory tract from aspirated material.

Secondary laryngeal functions include airflow rate control and production of positive end expiratory pressure in the alveoli, due to vocal fold positioning which controls airflow volume and velocity. Finally, the larynx is also a vibrator, producing sound through entrainment of the vocal folds into the airstream from the lungs. Modification of sound by the phonatory tract and skull and articulation by the tongue and palate produces meaningful speech.

Laryngopharyngeal function is controlled by cranial nerves IX and X, with their cell bodies in the brainstem, with interconnections to the cortex, cerebellum, spinal cord, and cervical plexus. Complex sensory function is the control mechanism through afferent pathways that travel in the glossopharyngeal (IX) and vagal (X) nerve afferents. These synapse in the brainstem nucleus tractus solitarius (NTS), relay with interneuron connections and messages from the cortex, and then anastomose with vagal efferents (nucleus ambiguus) to pass back to the laryngeal motor effectors (the vocal folds, false vocal folds, and paralaryngeal muscles). Stimulation of the superior laryngeal nerve, which provides sensory supply to the posterior one-third of the tongue, valleculae, epiglottis, and larynx, triggers airway responses designed to protect our lower respiratory tract. The laryngeal adductor reflex (pharyngoglottal reflex) occurs in response to contact with the epiglottis, aryepiglottic folds (AEFs), or interarytenoid region resulting in true vocal fold (TVF) closure. Much earlier in a swallow though, contact of foodstuffs with the faucial pillars at the watershed between the oral cavity and oropharynx begins a cascade of airway closure-contraction of the laryngeal inlet (AEFs and epiglottic retroversion), false VF constriction,

and closure of the TVFs. Conversely retrograde flow of material in the esophagus also triggers upper airway responses. If flow is rapid or gaseous, there is usually relaxation of the upper esophageal sphincter (UES) with airway closure (esophago-glottal reflex); however if flow is slower and liquid/solid, then there may be a reflexive UES contraction combined with secondary esophageal peristalsis to clear material back to the stomach. Dilatation of the UES also results in airway closure, as is appropriate if there is eructation or a vomiting response.

About 1.5 L of saliva is produced daily and generally swallowed unconsciously throughout the day, either spontaneously (30–40 times per hour) or with food or fluid we ingest. At night this rate drops to around 1–2 swallows/hour as the salivary production rate also decreases. Medications may affect saliva production (usually drying it), as can hydration status and previous radiotherapy.

In PD, several mechanisms are affected in the oral and pharyngolaryngeal complexes as well as in esophageal motility [16]. This includes both motor and sensory deficits and can result in poor oral bolus control, incomplete glottal closure (Fig. 12.1), reduced swallow clearance and increased pharyngeal and esophageal transit times, increased risk of misdirection of food and fluids (penetration and aspiration), poor cough clearance, and gastroesophageal reflux [4]. Spontaneous swallow rate also decreases, which may contribute to anterior loss of saliva (drooling) or pooling within the pharynx. It is likely that the central pattern generator for swallowing (in the brainstem) is affected, thereby reducing swallow frequency, akin to the bradykinetic response in limb musculature [3]. Pathways affected may not be dopaminergic (see below), as with other PD deficits and so will be less responsive to dopamine replacement therapies (widely used in PD treatment) [3, 17, 18].

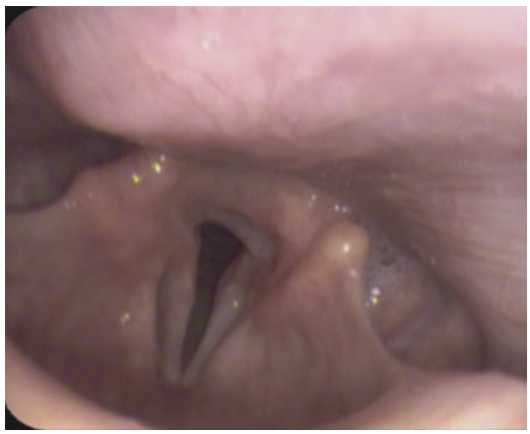

Fig. 12.1 Endoscopic image of glottis of patient with Parkinson disease. Note atrophic vocal fold, posterior pharyngeal wall osteophyte, and small amount of pooled saliva in left piriform fossa apex

Clinical Manifestations of Parkinson Disease

The most common complaints from PD sufferers are slowing and rigidity of movement (bradykinesia), changes in facial expression (affect), gait instability, balance disorders, alterations in voice (Parkinson's hypophonia), and swallowing difficulties (dysphagia). The shuffling gait with head bobbing and limb tremor that are well recognized as signs of PD may be late presenting in the disease process. Over the past two decades, a large range of non-motor symptoms have been identified as indicative of PD and may be the earliest signs of onset. These include loss of smell, disrupted sleep, depression, behavioral disturbances, autonomic dysfunction, constipation, reduced vision, and cognitive impairment such as inability to plan and organize tasks. Non-motor symptoms may precede typical bradykinesia and rigidity by months to years. This "preclinical" or "prodromal phase" is now more commonly recognized which enables early therapy interventions.

Diagnosis

Diagnosis is usually made by a movement disorders specialist neurologist. Diagnostic criteria have been delineated and are set out in the UK Brain Bank Clinical Diagnostic Criteria. Traditional criteria of bradykinesia plus one additional symptom, e.g., tremor, rigidity, or postural

instability, are now outdated with recognition that these symptoms may not appear until Stage 3 Hoehn and Yahr level [19, 20]. Prodromal symptoms may offer the best indication of early onset of PD, with recent work showing the combination of hyposmia, constipation, and rapid eye movement sleep behavior disorder was present in a third of PD cases and produced an odds ratio of 160 for diagnosing PD compared to adults in which these were not concurrently present [21]. Furthermore, mimic syndromes such as cervical dystonia, drug effects (including tardive dyskinesia), or psychogenic disorders may cloud diagnosis, and Parkinsonism is present in PD-variant multiple system atrophy, progressive supranuclear palsy, and corticobasal degeneration [20]. Additional investigations now include diffusion-weighted MRI scan, PET scanning, SPECT scanning, and dopamine trial therapy [20]. Both sporadic and familial forms of PD exist, although the genetic form represents just 10% of cases [1]. Both autosomal-dominant (genes *SNCA*, *LRRK2*) and autosomal-recessive (genes *PARK2*, *PINK1*, *DJ-1*, *ATP13A2*) forms are seen [1]. Proposed disease mechanisms include mitochondrial dysfunction, oxidative stress, and central nervous system inflammation with a lack of capacity to address these insults (discussed above) [1].

Effect on Airway Protection

As the glottis is the last line of defense against airway intrusion by swallowed material, changes at this level increase the chance of penetration and aspiration episodes that may compromise pulmonary function. People with PD tend to have thinner (Fig. 12.2) and weaker vocal folds, with greater presence of incomplete glottal closure (see Fig. 12.1). Hypophonia may result in recruitment of glottic and supraglottic musculature (Fig. 12.3) but is also modified by respiratory drive and output. Under-breathing or poor posturing reduces lung output, thus impairing flow across the glottis. Interestingly, the prodromal non-motor symptoms of PD may also affect airway protective mechanisms. Reduced smell results in lack of preparatory airway closure, and

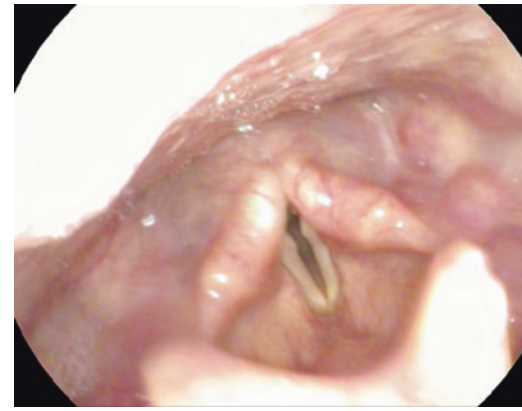

Fig. 12.2 Endoscopic image demonstrating atrophic vocal folds with prominent vocal processes bilaterally and prominent false vocal folds as a compensatory behavior

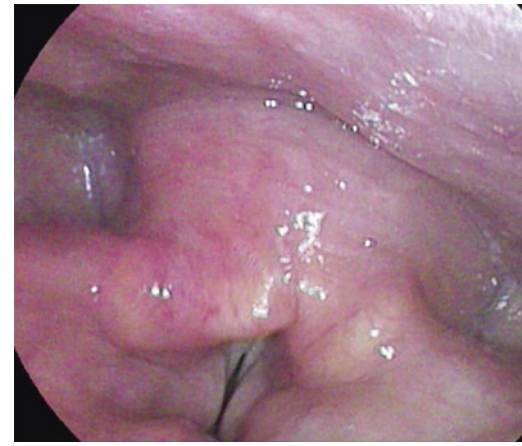

Fig. 12.3 Endoscopic image demonstrating false vocal fold constriction that hoods over the true vocal folds while phonating. This can result in rough voice quality and loss of projection

disturbed sleep is associated with changes in pharyngolaryngeal sensitivity as also occurs in sleep disordered breathing [22, 23]. Sleep disorders are common in PD patients including obstructive sleep apnea [24]. Poor glottal contact also impairs cough strength with weaker clearance of secretions when needed.

Effect on Swallowing

When asked, only 12% of people with PD complain of dysphagia, but on instrumental evaluation

80% demonstrate abnormalities [3]. Complaints from patients usually start as solid food difficulties, with sticking of foodstuffs in the oral and oropharyngeal region, associated with choking or coughing episodes. Cough is a symptom that patients may not connect with a swallowing problem, and it must be enquired about directly. Loss of smell and swallow impairment reduce appetite and willingness to eat, as does low mood. Autonomic dysfunction can affect secretion control, further disturbed by reduction in the spontaneous swallow rate. Drooling is common, with prevalence as high as 75%, and has a significant impact on socialization and mealtime enjoyment [25]. Secretions pool in the hypopharynx (see Fig. 12.1) and may tip into the laryngeal vestibule resulting in sudden cough or choking responses. As difficulties progress there may be stasis of bolus in the oral cavity and oropharynx, regurgitation of material, increased duration of mealtimes, reluctance to eat certain foods, and weight loss. Complaints of mucus retention in the pharynx may also indicate pharyngeal weakness and evolving swallow impairment. This can also delay medication transit, affecting the "on-time" of medication effectiveness [26]. Pathological examination of postmortem specimens has identified α-synucleinopathy affecting pharyngeal muscles and the vagus nerve and its branches feeding the pharynx [27]. Density of α-synuclein aggregates was statistically greater in those with known complaints of dysphagia compared to people with PD without dysphagia complaints [27]. In addition, denervated muscle fibers (in pharyngeal constrictors and cricopharyngeus) and change in myosin heavy chains were seen in people with PD but not control specimens [27]. This confirms peripheral pathological changes that mirror CNS alterations at a molecular level.

When examined systematically on fluoroscopic swallowing studies (VFSS), characteristic findings include abnormal bolus formation, delayed onset of swallow, repetitive swallows or tongue pumping gestures, premature spill of bolus, delayed swallow, reduced hyolaryngeal elevation, presence of valleculae and piriform residue, penetration, aspiration, and poor stripping wave [3, 4, 7]. Tomita et al. proposed a specific new scale – the Parkinson disease VFSS Scale (PDVFS) – said to more specifically incorporate abnormalities most frequently associated with aspiration development in people with PD [7]. This combines mastication, lingual motility prior to transfer, aspiration and total swallow time into one scale with simple ratings (Table 12.1) [7]. On ROC curve analysis using a score of 3 as a cutoff, sensitivity was 92%, and specificity was 82% for development of aspiration pneumonia. Scores above 3 were associated with a poor prognosis and shorter life expectancy [7]. Inter-rater reliability for the overall PDVFS score was 0.82 (moderate) among six speech-language therapists based on a single 3 ml jelly swallow [7]. In this study, being ambulatory also helped protect against aspiration pneumonia (benefit of exercise, see below). Limitations of this scale include lack of generalized validation and the use of a single jelly swallow for VFSS measures, rather than the usual liquid swallowing protocol. Video-fluoroscopic and manometric

Table 12.1 Video-fluoroscopic swallowing study scale for predicting aspiration pneumonia in Parkinson disease

Parameter	Definition	Value	Score
Mastication	Mastication is slow, hesitant, and delayed with ineffectual movements	Intact	0
		Inadequate	4
Lingual motility prior to transfer	Tongue movement assisting mastication and bolus formation	Intact	0
		Inadequate	2
Aspiration	Entry of bolus into lower respiratory tract	Absent	0
		Present	3
Total swallow time	From initiation of mastication until tail of bolus passed through upper esophageal sphincter	≤10s	0
		>10s	3
Total			12

From Tomita et al. [7], with permission

studies suggest pharyngeal weakness with elevation in hypopharyngeal intrabolus pressure – a sign that can be linked to pharyngoesophageal outlet obstruction [28–32]. Esophageal contractility is impaired, with failed peristalsis noted, and appears to respond to subthalamic nucleus (STN) stimulation [31, 32].

It is the same muscular systems involved in phonation and deglutition; therefore function of the laryngopharynx impacts both tasks. Ko et al. examined findings from VFSS compared to voice measures, particularly the maximum phonation time (MPT) [3]. In those with greater laryngeal range of motion (increased elevation range), shorter oral transit time, better oral bolus control, and earlier pharyngeal triggering of swallow, there was a longer MPT [3]. This suggests that improvement in voicing can lead to concomitant improvement in swallow parameters. Early work supports this, and we can use it to our advantage with simple therapeutic strategies to address both symptom complaints [28, 33].

Changes in swallowing have a profound emotional effect on the patient and carers due to fear and anxiety of eating, social isolation, and embarrassment [4]. Reduced self-esteem, reluctance to attend social occasions, and increased depression scores are resultant states that are induced by functional swallowing impairment [4].

Effect on Nutrition

While aspiration pneumonia is considered a significant risk for people with PD, malnutrition is also a consideration. People with PD have significantly lower body mass indices and higher rates of unintentional weight loss than people without PD [34]. This is multifactorial in nature with dysphagia as contributor but alongside a long list of other factors either as a result of the motor and/or non-motor symptoms of PD or as a side effect of medicines: increased energy expenditure (as a result of dyskinesias); apathy; loss of appetite; physical challenges of shopping, cooking, and eating; constipation; nausea; smell and taste alteration; and prescribed texture-modified diet and saliva difficulties [35]. Screening for malnutrition should be routine, and dietitian referrals should be initiated for all people with PD at risk of malnutrition or experiencing swallowing difficulties.

Effect on Phonation

Changes in phonation are well recognized in PD. Often termed Parkinson's hypophonia, common perceptual observations are of low volume, monotonous voicing. Sound imprecision and reduced stress have also been recorded, with levodopa treatment providing no benefit to voice changes despite improvement in limb motor function [17, 18, 36] (Table 12.2).

Management Approach

Comprehensive management of PD requires a multidisciplinary team. Neurology services often coordinate overall care with assistance from neurosurgical colleagues, speech-language pathologists, respiratory medicine, otolaryngologists, gastroenterologists, physiotherapists, specialist nurses, and community-based care support. People with PD often find encouragement and support in meeting other people with PD, and support groups can be a huge assistance in managing day-to-day problems for both the patient and the caregiver. Nationally and globally, support groups advocate for patient treatments, education, social support, and access to services. There are dedicated institutions focused on PD research such as the Michael J. Fox Foundation, Parkinson's Foundation, and David Phinney Foundation plus the PD biomarkers project and World Parkinson's Congress for sharing medical knowledge. World Parkinson's day is marked annually and is an attempt to promote awareness of the conditions and its many facets.

Use It or Lose It – The Role of Exercise

A critical sea change in management occurred within the last decade. Recognition that exercise

Table 12.2 Impact of Parkinson disease on communication and swallowing

Communication difficulties	Symptoms	Consequences
Voice	Quiet voice volume	Communication breakdown Communication avoidance Mood alteration Social isolation Participation limitation – employment Participation limitation – pastimes Participation limitation – social activities
	breathy, hoarse voice quality	
Speech	Monotone – flat sounding voice	
	Difficulties initiating phonation	
	Running out of breath when talking	
	Rushed speech rate	
	Imprecise articulation/slurred/unclear	
Facial expression and gesture	Lack of facial expression and small or no gestures/(flat affect)	
Communication	Needing time to understand the speaker	
	Losing train of thought during conversation	
	Word-finding difficulties due to changes in cognition	
Eating, drinking, swallowing	Difficulties managing saliva in mouth – drooling Difficulties chewing Difficulties moving/controlling food/drink in mouth Food/drink falling out the front of the mouth Food/drink sticking in the throat Coughing with food/drink/saliva Loss of appetite Loss of taste/smell	Weight loss Dehydration Aspiration pneumonia Choking Mealtime avoidance Medicine avoidance/alteration Mood alteration Social isolation

and exercise-based therapies were highly successful in PD occurred, and as a result a positive move for patients to be in control of some parts of their treatment was established [3]. Studies demonstrate changes in circulating levels of inflammatory mediators after exercise [37], suggesting that peripheral adjustment of cytokines such as TNF-α can translate to central benefits including improved sleep and mood [37, 38]. Physical training has demonstrated efficacy in voice [39], articulation [40, 41], cough [42], and now swallowing symptoms [28]. This is particularly important as these symptoms tend to be less responsive to pharmacotherapy or deep brain stimulation.

In clinical practice, speech-language pathologists often prescribe swallowing rehabilitation exercises to people with PD. These exercises, established and researched primarily in patients after stroke, focus on tongue, pharyngeal, and hyolaryngeal strengthening and function and include the Shaker head lift, effortful swallow, Masako and Mendelsohn maneuver [43]. Alternatives to these traditional exercises have been researched including skill training [44], expiratory muscle strength training (EMST) [42, 45], and neuromuscular electrical stimulation (NMES) [46].

Expiratory muscle strength training has been shown to improve voluntary cough and swallow function, specifically reducing aspiration scores, in people with PD [42, 45]. This respiratory exercise can be performed with speech-language pathologists or physiotherapists, and patients demonstrate significant maintenance of effect over 6 months following training [47].

Neuromuscular electrical stimulation (NMES) is a treatment that has been used in managing swallowing disorders in patients after stroke and following head and neck cancer treatments. A small study of 18 people with PD randomized to NMES or sham treatment in conjunction with swallow therapy identified an improvement in hyoid bone mobility, but this did not translate to better clinical pharyngeal function measures [46]. Less aspiration was identified in the treated group as measured on the penetration-aspiration scale [46]. Further work is required in this area to ascertain which muscular targets at what frequency is appropriate and whether application of

this treatment (as in other studies) entails increased aspiration risk by encouraging laryngeal descent [48].

The need to strengthen muscle groups, reinforce neuromuscular pathways, and retrain complex patterned behavior is a successful therapeutic strategy and has been applied specifically and effectively to otolaryngologic symptomatology [49]. Lee Silverman Voice Treatment LOUD (LSVT LOUD™) is a particularly popular speech therapy programme which has provided relief for many people internationally and is discussed further below.

Lee Silverman Voice Treatment LOUD (LSVT LOUD™)

First developed in 1987, Lee Silverman Voice Treatment LOUD (LSVT LOUD™) is a focused, high-intensity speech therapy program designed primarily to target loudness [39, 41, 50–53]. The developers have created a training package and structured, detailed treatment protocol available online for speech-language therapists (www.lsvtglobal.com). LSVT LOUD is a 16-session treatment over a four-week period. There are strict criteria for inclusion into the program including an otolaryngologist endoscopic assessment. Increasing complexity and high-effort vocal and speech exercises are completed with the certified therapist, and participants are expected to complete daily home practice. Key principles of the treatment are high intensity, high effort, and ongoing pitch and loudness instrumental feedback.

Over the last two decades, the developers of LSVT have published several studies demonstrating the benefits of LSVT for people with PD up to two years after treatment [39, 41, 50–53], and some of the general principles have also been applied to other neurologically impaired patient groups (Parkinsonian syndromes) [3, 54]. Treatment has been shown to not only lead to recalibration of loudness but also improved speech intelligibility, facial expression, breath support, and vocal quality [39]. The treatment has been applied successfully via telehealth methods increasing access to the intensive regimen [54].

High-effort pharyngeal and laryngeal musculature activities are the target of LSVT LOUD, and logically, recent work suggests that these improvements in muscle control for voicing have parallel benefits on pharyngoesophageal deglutition and involuntary cough efficiency [28, 33]. These spread effects may occur across more than one muscle system too, leading to corresponding improvements in voicing, swallowing, speech, breathing, and head posture. A noninvasive method of swallowing rehabilitation is appealing given the failure of medical therapies to date in addressing swallow symptoms, and as LSVT LOUD addresses both voice and swallowing problems, its applicability in therapy will likely expand. Transferring the identified benefits of exercise therapy to novel and engaging activities, such as singing, speech-making, and expiratory strength training programs, has opened up a wider range of choices for people with PD aimed at capitalizing on respiratory and aerodigestive benefits.

Toastmasters Gavel Clubs

Group therapy is known to provide benefits of social support and motivation in comparison with more traditional 1:1 therapy approaches and lends itself to therapy focused on social communication. Internationally, there is a trend toward group therapy for people with PD [55], and Toastmasters Gavel Clubs for people with neurological diseases are becoming more commonplace [56]. Toastmasters offer new social connections, emotional support, opportunity to practice and gain feedback on communicative abilities, and increased overall voice protection activity. Early work at The University of Auckland suggests significant improvements in communication confidence and lexical efficiency as well as improved voice-related quality of life in people regularly attending a Toastmasters group [57]. This may be an alternative treatment approach for people with PD, particularly those living alone at risk of social isolation and limited

communication opportunities, where secondary complications of depression and further deficits of disuse are likely.

Parkinson's Choir

In a similar vein, singing and choir participation have proven to offer similar benefits for people with neurological disease. Therapeutic choir singing has been shown to increase conversational intensity [58], maximum phonation time [58, 59], inspiratory and expiratory pressures [59, 60], prosody [60], vocal quality [61], electromyographic swallow activity [62], and voice-related quality of life [60, 63], as well as reduce feelings of social isolation [57] and loneliness [64]. A number of institutions have developed and published choral singing therapy protocols describing the role of a music therapist in these therapeutic groups [65]. These emerging alternatives offer promising and positive choices for people living with PD who are actively trying to "hold back" the effects of the disease in order to maintain independence and good quality of life.

Compensatory Swallowing Techniques

In addition to therapeutic treatment approaches, regular review by a speech-language pathologist and dietitian can mitigate some of the health and psychosocial consequences of living with swallowing difficulties. Common strategies include simple posture, volume, pace, or swallowing alterations. These must be recommended following a thorough swallow evaluation but may include a chin tuck posture, smaller volumes, smaller more frequent meals, taking more than one swallow to clear pharyngeal residue, a protective cough after drinking to clear residue, or an early airway closure technique.

Texture modification of food and/or drinks such as pureed meals or thickened fluids is often needed but should be avoided where possible as it can impact on mealtime pleasure and socialization. It is typical to find people with PD have self-modified their diets well before activating a swallow assessment, and it is therefore critical to initiate nutrition intervention for dietary advice. Meat is a typical food type to limit or eliminate in the early stages of swallowing difficulties in PD, and dietitians will often provide advice about alternative ways to maintain adequate protein intake.

Medical Therapy

Pathophysiologic changes first identified in people with PD were destruction of the substantia nigra dopaminergic pathways. A low dopamine (DA) environment ensues which creates many of the motor symptoms of PD. Replacement therapy was therefore advocated, and levodopa (LD) treatment became the mainstay of therapies for many years. Levodopa is given orally and is the precursor of dopamine with the ability to cross the blood-brain barrier (BBB) [66]. Unfortunately, LD is metabolized by peripheral enzymes, particularly catechol-O-methyltransferase (COMT) and aromatic amino acid decarboxylase (AAAD) [66], reducing effective doses. An estimated 1% of oral dose reaches the CNS [66]. New formulations including long-acting LD and intestinal gel forms have been created in attempts to "smooth" the LD effect over time [2].

Furthermore, over time, side effects of medication develop in combination with progression of the disease state resulting in dyskinesia and reduced clinical effect of LD. Recognition of the non-motor symptoms of PD (which are largely Dopa-refractive) has led to investigation and development of many new medicines which can help PD symptoms (Table 12.3). Some are directed at better symptom control and some at side effects. Amantadine is widely utilized for alleviating dyskinesia associated with long-term dopamine agonism. An extended-release form is now available [2, 67]. Dopamine agonists (bromocriptine, cabergoline, pergolide, pramipexole, ropinirole) and dopamine decarboxylase inhibitors (DDCIs; carbidopa, benserazide) are often

Table 12.3 Therapeutic drugs in current use for treatment of Parkinson disease

Drug	Mechanism of action	Currently available	Effect on eating/drinking or communication	Side effects
Levodopa	Replace lost DA	Y	Nausea/vomiting, taste disturbances, dry mouth	Dyskinesia, loss of effect
Opicapone (OPC), entacapone, tolcapone	COMT inhibitors (reduce peripheral DA metabolism)	Y	Nausea/vomiting, dry mouth. Constipation (OPC best effect, least side effects)	Insomnia, dyskinesia
Benserazide, carbidopa	AADC inhibitors, DDCIs (reduce peripheral DA metabolism)	Y	Not known	Rash and allergic reaction
Bromocriptine, cabergoline, pergolide, lisuride	DA agonists, antioxidants	Y		Syncope, obsessive-compulsive behavior, psychosis, fibrosis, increased sleep, valvular heart disease
Pramipexole	DA agonist, antioxidant, reduced depression	Y	Decreased appetite, nausea/vomiting	
Ropinirole	DA agonists, antioxidant	Y	Decreased appetite, nausea/vomiting	
Apomorphine	DA agonist	Y	Constipation	Hallucinations
Rotigotine	DA agonist, antioxidant	Y	Improvement in swallow	
Amantadine (and extended release version)	NMDA/glutamate antagonist (decrease dyskinesia)	Y	Nil	Hallucinations, confusion, gastrointestinal disturbances, dry mouth, edema, hypotension
Selegiline, rasagiline	MAO-B inhibitor, decrease DA degradation	Y	Minimal	Dry mouth, constipation
Safinamide	MAOB-I with glutamate release property	Y (phase III)	Unknown	Increased dyskinesia
Novel or experimental compounds				
PRX002	IgG MAB against α-synuclein	N	Unknown	Minimal

OPC opicapone, *AADC* aromatic amino acid decarboxylase, *CD* carbidopa, *COMT* catechol-O-methyltransferase, *LD* levodopa, *DA* Dopamine, *DDCIs* dopamine decarboxylase inhibitors, e.g., benserazide, CD, *IgG* immunoglobulin gamma, *MAB* monoclonal antibody, *Y* Yes, *N* No

given in combination with LD therapy or as L-dopa sparing monotherapy to forestall initiating dopamine treatment [68]. Although they act to achieve a steady state of dopamine availability peripherally, side effects are seen with all treatments, and the effect of medication is primarily directed at motor symptoms alone.

Rotigotine is a dopamine agonist enhancing dopamine levels. Application of this medicine has demonstrated benefit in motor symptoms of PD when administered both orally and transdermally [68–70]. This may assist in situations of poor gut absorption or inability to take enteral medication. It may also provide some benefit in swallow-related symptoms. Ropinirole is a dopamine agonist available in both short-acting and controlled-release formulations, with doses of 16–24 mg/day, demonstrating benefit for motor symptoms [71]. As patients become refractory to one combination, alternative drugs may be combined with core LD therapy to maintain ON effects. Combined therapy with rasagiline and

pramipexole (both DA enhancers via distinct pathways) demonstrated improvement in motor symptoms and quality of life in 136 people with PD with transient nausea and somnolence as the primary side effects [72].

Opicapone is a peripheral catechol-o-methyltransferase (COMT) inhibitor that reduces enzymatic degradation of levodopa administered to assist PD symptoms [66].

Other COMT inhibitors are tolcapone and entacapone. Opicapone has superior bioavailability peripherally and less side effects, particularly hepatotoxic effects, than its sister drugs [1]. In the same vein as COMT inhibitors, drugs designed to limit the action of aromatic amino acid decarboxylase (AADC) which disables LD peripherally are also available. These are known as dopamine decarboxylase inhibitors (DDCIs) and include carbidopa and benserazide. These drugs are now available in precombined formulations with levodopa to increase peripheral and central [active] drug concentrations [73].

Investigators are delving into novel substances including traditional medicines in search of active compounds. de Rus Jacquet et al. report activity of elderflower extract in reducing mitochondrial damage, improving antioxidant effect, and reducing neurotoxicity in PD models and in vitro cultures [74]. A number of traditional Japanese, Korean, and Chinese medicines have shown promise in PD and may contribute to the lower overall rates of PD traditionally seen in these populations.

Finally, a vaccination approach has been investigated with highly specific protein sequences of α-synuclein as the target. This may have the potential to eradicate aggregated α-synuclein from the brain or peripheral tissues. Benchtop work is promising, and clinical trials are about to begin [75].

Polypharmacy (taking of more than five medicines concomitantly) is a common finding in the elderly and more so in people with PD. In a New Zealand survey of PD individuals, the average number of medications taken by 71 respondents was 11 (range 2–25) [76]. In addition, 57% of this same cohort self-reported swallowing impairment. Many struggled to ingest medicines and used a variety of strategies to adapt; however some simply missed taking medicines [76]. This highlights a crucial area in patient care-medicine management [77, 78]. Reformulating medicines, using different types of vehicles to help passage, and reconciling medicines to the lowest number possible are all vital approaches to increase swallow safety and medicine compliance while limiting drug-drug interactions or side effects (particularly xerostomia and dyskinesia) [77, 78].

Surgical Approaches

In managing the symptoms and potential consequences of PD, surgical therapies may be employed in a targeted peripheral fashion for symptom control largely as airway protective or swallow-enhancing procedures or in a central manner through deep brain stimulation which targets the neurological control of PD.

Peripheral Procedures

Airway protection is the greatest risk factor for those with PD as it leads in many cases to their terminal illness – aspiration pneumonia. Commonly during the disease course, the glottis is affected by atrophy, weakness with poor contact pressures, in conjunction with loss of pharyngeal tone and swallow efficiency. This results in the combination of residue within the hypopharynx and an open airway (and often one that has a reduced ability to clear contaminant [weak cough]). Penetration episodes followed by aspiration occur and lead to pulmonary complications. Surgical therapy can be directed at the glottis to enhance airway closure and improve cough efficiency and subglottal pressure generation. Injection laryngoplasty may be performed in the operating room or, at times, in the physician's office depending on compliance of the subject. Avoiding general anesthesia is helpful for those with PD as anesthetic medication can result in marked postoperative fatigue. Injectates are temporary implants however and therefore provide only short-term relief (2–12 months

depending on the chosen product). An alternative is to use permanent nonabsorbable Gore-Tex® or silastic implants via an open external type I thyroplasty procedure. This may be accomplished under local anesthetic often with a small amount of sedative medication. In both types of procedures, the mass of the vocal folds is increased. This has effects on pitch modulation (either decreasing the pitch if not overfilled or increasing the pitch and producing a "squeaky tight" voice if overfilling occurs) and may create diplophonia if the vocal folds become markedly asymmetric in mass. In addition, increasing the vocal fold mass requires increased subglottal pressures and pulmonary airflow to produce phonation onset pressure (the energy needed to initiate vibration of the vocal folds entrained into the airstream). Patients may interpret this as effortful voicing. It is prudent not to over-medialize the glottis in those with PD or compromised respiratory systems. Often these surgical procedures are best combined with voice therapy both prior and following surgery.

Botulinum toxin treatment has been used in a variety of applications for people with PD. These include excessive salivation or difficulty in saliva control, tremor, dystonic reactions in cervical muscle groups (torticollis, blepharospasm), ineffective esophageal motility, gastroparesis, anal symptoms/constipation, hyperhidrosis, camptocormia (spinal flexion spasm), and detrusor spasms [79, 80]. Injection of the major salivary glands, particularly the submandibular glands, will reduce saliva volume. This occurs at the expense of the aqueous component of saliva, leaving a viscous and difficult-to-clear substance which may cause more difficulty than higher-volume regular saliva. Nevertheless, in some patients daytime control of oral escape is preferable to a moderately dry mouth. Risks include swallow deterioration if dispersion of toxin occurs and need for repeated injections over time. Ultrasound guidance improves precision of injections.

Individuals with PD may experience concomitant age-related changes such as development of a cricopharyngeal bar [81]. Coupled with pharyngeal weakness or mistiming of swallow, this may lead to increased pharyngeal residue and problematic aspiration. Balloon dilatation of the upper esophageal sphincter (UES) can be used to target an obstructive UES with or without a cricopharyngeal bar, as can cricopharyngeal myotomy in selected cases [81].

Central Procedures/Deep Brain Stimulation

Deep brain stimulation (DBS) is an established form of therapy for select people with PD which seems to provide relief for motor symptoms of bradykinesia, rigidity, and tremor. The primary centers targeted are the subthalamic nucleus (STN) and the globus pallidus interna (GPi). There has been variable reportage regarding DBS benefits for swallow-related impairments. Olchik and colleagues studied 10 males treated with DBS of the STN with pre- and posttreatment functional endoscopic evaluation of swallowing (FEES) exam [82]. They could not identify significant improvement in swallowing parameters after stimulation was in place [82]. Compulsive eating may occur after DBS treatment, even up to 3 years following stimulation [2]. Xie and colleagues studied DBS-STN effects on dysphagia, freezing of gait, and motor symptoms in a randomized crossover, double-blind study of 11 people with PD [83]. Using a 60Hz stimulation frequency achieved best results with reduced aspiration and less complaint of swallow difficulty as well as improvement in motor and bradykinetic symptoms [83]. Improvements in swallowing parameters did not persist, however, although motor benefits were sustained [83].

Summary

PD is the second most common neurological disease worldwide contributing to substantial morbidity and mortality, particularly through dysfunctional deglutition and laryngeal incompetence. Aspiration pneumonia remains the primary cause of death. The pathogenesis of the disease is being untangled, and insights into molecular

pathways may enable us in time to target specific abnormalities. Individualized patient care pathways will need to be developed considering each individual's own PD etiology and manifestations. Currently, as with other aspects of PD, exercise-based therapy has shown benefits in voice and swallow treatments. A select number of surgical procedures may also offer benefit to certain patient groups including those with swallow and voice impairments. These include glottic medialization and laryngoplasty techniques, balloon dilatations, and botulinum toxin injections.

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Parkinson-Plus Syndromes

13

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A summary comparison of typical clinical features of Parkinson disease (PD), progressive supranuclear palsy (PSP), and multiple system atrophy is shown in Table 13.1. These differences are elaborated in depth within this chapter.

Progressive Supranuclear Palsy

Clinical Features

PSP is characterized clinically by progressive parkinsonism, supranuclear ocular gaze palsy, bulbar symptoms, axial rigidity, early postural instability with frequent falls, and frontotemporal dementia [1]. Supranuclear gaze palsy refers to a condition in which voluntary ocular movements are impaired, but reflex movements are preserved. The typical ocular motor disorder of PSP includes prominent impairment of voluntary vertical saccadic and pursuit movements, particularly for downgaze, with preservation of oculocephalic reflexes (movements of the eyes when the patient fixes gaze on a distant object while the examiner rotates the patient's head up and down in a nodding motion). Axial rigidity occurs in association with hyperextension of the neck. Gait is stiff, hypokinetic, and disorganized, with significant lateral deviation, instability, and often prominent gait freezing. Loss of postural reflexes leads to frequent falls, often backward, which typically occurs early during the clinical course and may be the first symptom. Dementia often develops within the first few years of disease onset and is characterized by frontotemporal deficits such as apathy, poor planning, difficulty multitasking, and decreased verbal fluency. Other features include facial bradykinesia and dystonia, which produces a characteristic "startled" expression, eyelid opening apraxia, small rapid handwriting, and pseudobulbar affect (mood-incongruent crying or laughing) [2]. Prominent speech and swallowing deficits are a significant cause of morbidity and mortality in PSP and are described below.

Corticobasal degeneration (CBD) shares some clinical and pathologic overlap with PSP but is much less common. In addition to progressive asymmetric parkinsonism and early falls, CBD most frequently presents with dystonia, myoclonus, alien limb phenomena, and dementia. Cortical sensory deficits are frequently found, including inability to identify objects placed in

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Table 13.1 A comparison of the typical clinical features of Parkinson disease, progressive supranuclear palsy, and multiple system atrophy. The three diseases show extensive clinical overlap, especially early in disease course, and the clinical presentation of an individual disease can vary significantly between patients. Consequently, definite diagnosis depends on neuropathological evaluation at autopsy

	Parkinson's disease	Progressive supranuclear palsy	Multiple system atrophy
Shared motor features	Bradykinesia, akinesia, rigidity		
Distinguishing motor features	Unilateral onset; pill-rolling rest tremor	Symmetric onset; axial > appendicular rigidity; early backward falls	Symmetric onset; cerebellar ataxia; pyramidal signs or irregular postural kinetic tremor
L-DOPA response	Excellent, sustained	Usually poor or absent	Some patients respond but may require high doses
Autonomic	Early constipation; urinary/erectile dysfunction and orthostatic hypotension tend to occur late	Urinary incontinence common late in disease	Constipation, urinary/erectile dysfunction, and orthostatic hypotension may be severe and occur early
Cognitive/behavioral	Anxiety/depression frequently precede motor symptoms; dementia common in advanced disease and associated with visual hallucinations	Frontotemporal dementia nearly always present; may be presenting symptom and severe	Frontal dysexecutive syndrome may be present; severe dementia uncommon
Other typical features	REM sleep behavior disorder, anosmia	Supranuclear downgaze palsy	REM sleep behavior disorder, central sleep apnea (may be life-threatening)
Voice/swallow/airway	Hypophonia and hypokinetic dysarthria; severe swallowing difficulties uncommon	Mixed spastic/hypokinetic dysarthria; pseudobulbar palsy and progressive dysphagia	Spastic/hypokinetic or ataxic dysarthria; progressive dysphagia; dysphonia, nocturnal stridor, obstructive sleep apnea; bilateral vocal fold paralysis

REM Rapid eye movement

the hand (astereognosis) or figures drawn on the palm (agraphesthesia) with eyes closed, despite having apparently normal somatic sensation [2].

Epidemiology

PSP is the most common neurodegenerative cause of parkinsonism after Parkinson disease, comprising around 5% of all parkinsonian patients seen in a movement disorders clinic. The reported prevalence is 1.39–14.3/100,000 and incidence is 0.3–1.1/100,000/year [3]. Median onset is 63 and median survival from symptom onset is 6.9 years [4]. The sex ratio is unclear, with different studies reporting varying data [3].

Pathophysiology

The pathology of PSP is characterized by neuronal loss in the basal ganglia, midbrain, pons, dentate nucleus, and inferior olive, causing the characteristic movement, gait, and oculomotor abnormalities. Frontal cortical and adjacent subcortical white matter involvement occurs and is typically associated with prominent cognitive and behavioral changes [4]. Pseudobulbar palsy is caused by degeneration of corticobulbar fibers innervating relevant cranial nerve nuclei in the brainstem [5]. Inclusion body pathology in PSP includes neurofibrillary tangles and neuropil threads [6], tufted astrocytes, and coiled bodies within oligodendrocytes [7]. These pathological inclusions contain insoluble, hyperphosphorylated aggregates of the microtubule-associated protein tau, leading to PSP being classified as a tauopathy. CBD is also a tauopathy, although there is more prominent pathology in motor cortical areas and the putamen, and ballooned neurons in the cortex, and the inclusion body pathology differs, including corticobasal bodies in the brainstem and accumulations of tau in distal astrocytic processes called astrocytic

plaques [7]. The origin and role of the extensive tau pathology seen in PSP and CBD are currently unclear.

Genetics

Tau is encoded by the *MAPT* gene located on chromosome 17. Mutations in this gene have been associated with an autosomal dominant tauopathy that can overlap clinically and pathologically with PSP [8, 9]. However, most PSP cases have no family history and no *MAPT* gene mutation. Inversion of the genomic locus containing *MAPT* is present in 20% human chromosomes and appears protective against PSP. Genome-wide association studies have identified genetic variants that confer an increased risk of PSP, including non-coding variants adjacent to the *MAPT* gene and several other genes [10].

Voice-, Airway-, and Swallow-Specific Symptoms: Findings or Sequela

Voice Dysarthria is present universally early in the disease, although of variable severity. Speech is characterized by mixed spastic and extrapyramidal hypophonia and dysarthria, resulting in quiet, slow, strained, and sometimes nasal speech [11]. Spastic dysarthria and hypokinetic features usually predominate over ataxic features [12, 13].

Airway Airway obstruction is not an expected feature of PSP.

Dysphagia Dysphagia in PSP involves the oral phase of swallowing more than the pharyngeal phase, contrary to patients with PD [14]. The onset of dysphagia in PSP occurs with a mean latency after initial presentation of 42 months [15]. Only 18% of patients complained of dysphagia 2 years after symptom onset, but nearly 50% had dysphagia at 5 years [16]. Given the relatively rapid progression of PSP, it is imperative to begin dysphagia education, evaluation, and treatment prior to onset of symptomatic problems.

Oral Phase Oral phase complaints are common in PSP. Abnormalities include excessive pooling of saliva in the oral cavity, sialorrhea, difficulty with mastication and bolus formation, unintentional bolus loss, and residue throughout the oral cavity after swallow. Excessive saliva has been reported in 63% of PSP patients [17], while only 20% of patients were found to have pharyngeal pooling of secretions [18] on FEES exam, illustrating the importance of oral dysphagia in PSP. Interestingly, dysarthria severity did not correlate with dysphagia severity on endoscopic evaluation (FEES) [17]. Oral phase dysphagia in PSP is characterized by incomplete mastication, forceful lingual pressing of food against the hard palate, lingual pumping, uncoordinated lingual movements, reduced lingual strength, extra movements of the velum, non-cohesive bolus transfer, delayed or uncoordinated bolus transfer, piecemeal deglutition, and passive bolus transfer prior to swallow (which is worsened by retrocollis) [17, 19, 20]. On clinical swallowing evaluation, mastication is prolonged in the early stages of dysphagia; however, once the disease has progressed, oral preparation and mastication are essentially absent. Lingual movement also appears to diminish over time.

Pharyngeal Phase Common pharyngeal findings in patients with PSP include delayed swallow initiation and vallecular residue. Aspiration due to pharyngeal deficits is less common. Pharyngeal contraction, base of tongue retraction, and hyolaryngeal elevation and excursion are relatively preserved, especially in the early stages of the disease. FEES examination showed that laryngeal penetration/aspiration events occurred frequently prior to swallow initiation in patients in the early stages of PSP; this suggests that passive bolus transfer due to poor bolus formation, reduced posterior oral control, discoordination, and oral residue (oral dysphagia) contributes to laryngeal penetration/aspiration [18]. The link between poor bolus control and aspiration was

confirmed in another study [17]. Importantly, half of the episodes of penetration/aspiration were silent, greatly elevating the risk of aspiration pneumonia, which is a major cause of morbidity and mortality in PSP.

Pharmacology/Medical Management

Treatment of PSP is symptomatic and includes fall prevention, management of complications such as eyelid opening apraxia and sialorrhea with botulinum toxin injections, and management of pseudobulbar affect with dextromethorphan/quinidine. The movement disorder of PSP rarely responds to L-DOPA or amantadine.

Voice-, Airway-, and Swallow-Specific Procedures: Treatment Outcomes

Voice Early in the course of PSP, enhancing vocal intensity by increasing subglottic air pressure during phonation may help ameliorate hypokinetic dysarthric features, though to a lesser degree than with PD [21]. Long-term efficacy has yet to be proven. As dysarthria progresses and speech becomes unintelligible, computer-assisted technologies may be useful to maintain communication.

Dysphagia Progressive dysphagia may lead to poor oral intake, dehydration, and malnutrition. There is no research showing improvement or slower swallowing decline with swallowing therapy. Despite this, periodic swallowing evaluation via videofluoroscopy or endoscopic evaluation (FEES) may assist with developing a plan to reduce or prevent aspiration. Compensatory strategies including chin tuck, cough–swallow, breath hold, or head turn can be tried. The nature of the deficits should determine compensatory strategies. For example, cough–swallow is unlikely to be effective in a patient with severe hypophonia, and chin tuck is challenging in the presence of retrocollis. Simpler swallowing strategies may be needed as cognitive deficits worsen. Overall, a softer diet is often used as the disease progresses. High-risk foods for aspiration include nuts, dry meats, rice, and bread. "Mixed" consistencies (such as cereal with mild, chunky soups) can be challenging. If thin liquids become an issue due to poor posterior oral control or discoordination, nectar liquids can be used. However, nectar liquids increase the risk of dehydration due to poor fluid intake. In the presence of downgaze palsy, raising the level of a meal tray may improve the ability to self-feed, which in turn lowers aspiration risk [22, 23]. As the disease advances, enteral nutrition usually via percutaneous endoscopic gastrostomy (PEG) is frequently required, not only to ensure proper daily caloric intake but also for safety (aspiration, asphyxiation from food bolus). Patients and families, however, must be cautioned that PEG placement does not eliminate the risk of developing aspiration pneumonia, since the risks of aspirating secretions or tube feeds via gastroesophageal reflux remain.

Dysphagia complications may be mitigated by patient and family education regarding signs of dysphagia, aspiration, or pneumonia and the importance of oral care. Through dietary modification, use of compensatory swallowing strategies, and patient education guided by a speech–language pathologist, a plan can be developed to maximize swallowing safety, improve quality of life, and prevent aspiration pneumonia for as long as possible.

Management options for sialorrhoea can include off-label use of antimuscarinic medications such as 1% atropine ophthalmic solution applied sublingually and oral glycopyrrolate, although the use of these agents is derived from evidence for PD and they are often poorly tolerated [24]. Botulinum toxin injected into the parotid glands can be effective in treating sialorrhoea in parkinsonian disorders including PSP [25].

Frontiers

One major goal of recent research has been to identify disease-modifying therapies for PSP through development of agents that target tau pathology. Two recent double-blind placebo-controlled clinical trials of putative disease-modifying treatments did not show efficacy [26, 27]. However, these

studies demonstrated that large, multicenter, randomized trials are possible in PSP, despite it being a comparatively rare disease, and validated the PSP rating scale [28] as a replicable way to monitor clinical progression. Several other clinical trials are underway, or in planning stages, involving agents that may inhibit tau aggregation, stabilize neuronal microtubules, or prevent cell-to-cell transmission of aggregated tau [29]. Other approaches such as accelerating degradation of pathological forms of tau are also under preclinical development. This is a very active area of research that is likely to evolve rapidly in the next few years.

Multiple System Atrophy

Clinical Features

MSA is a neurodegenerative disorder characterized clinically by various combinations of parkinsonism, autonomic failure, and cerebellar ataxia, all caused by a common underlying pathology. Depending on the predominant movement disorder, MSA is categorized clinically as MSA-parkinsonism (MSA-P) or MSA-cerebellar (MSA-C) types. MSA-P is characterized by rapidly progressive parkinsonism with early postural instability and poor response to L-DOPA. MSA-C is characterized by progressive ataxia, including cerebellar oculomotor signs and gait ataxia [30]. Dysautonomia occurs in both types of MSA and can appear early during the course of the disease, causing urinary incontinence, male erectile dysfunction, orthostatic hypotension, and syncope. In addition, central sleep apnea, orofacial dystonia (especially following exposure to L-DOPA), axial dystonia, and hyperreflexia with extensor plantar responses are typical. Dementia may occur uncommonly, but is not usually a prominent feature [2]. Prominent deficits in speech and swallowing are typical in MSA and are discussed below.

Epidemiology

The reported prevalence of MSA is 3.4–4.9/100,000 and incidence is 0.1–2.4/100,000/year. Peak age of onset is in the early 50s, and the median survival from symptom onset is 6–10 years. MSA affects males and females equally. MSP-P is more common than MSA-C in most countries, although the converse is true in Japan [31].

Pathophysiology

Neuronal loss, astrogliosis, and microglial infiltration in MSA occurs in different topological patterns reflecting the clinical phenotype. In MSA-P, prominent neuronal loss is seen in the putamen and substantia nigra (striatonigral degeneration; SND). In MSA-C, neuronal degeneration is more obvious in the pons, inferior olives, and cerebellum (olivopontocerebellar atrophy; OPCA) [32]. Neuronal loss is usually also present in the autonomic nuclei of the hypothalamus and brainstem and in the intermediolateral columns and Onuf's nucleus of the spinal cord, resulting in autonomic symptoms [32]. Central sleep apnea is likely due to degeneration of respiratory centers in the brainstem [33]. Prominent inclusion body pathology in MSA occurs in CNS oligodendrocytes as perinuclear crescent-shaped structures called glial cytoplasmic inclusions (CGIs, also known as Papp–Lantos bodies) [34]. GCIs occur in CNS regions undergoing neurodegeneration in MSA and are found in both MSA-P and MSA-C. Interestingly, GCIs are composed of aggregates of the protein α-synuclein [35], which is also a major component of Lewy bodies, the neuronal cytoplasmic inclusion body of PD. The origin and consequences of oligodendroglial α-synuclein accumulation in MSA are controversial.

Genetics

MSA is a sporadic disease, and pathologically proven cases with clear monogenic Mendelian inheritance have not been described. A recent large unbiased GWAS study in samples from sporadic MSA cases of European ancestry found no significant associations after stringent correction for multiple comparisons [36].

Voice-, Airway-, and Swallow-Specific Symptoms: Findings or Sequela

Voice Ataxic and spastic vocal features predominate over hypokinetic features [13]. Ataxic dysarthria is characterized by fluctuations in pitch and intensity. With prolonged exposure, listeners are often able to understand ataxic speech better than hypokinetic speech, which may explain the perception of dysarthria in MSA being rated as less severe than in PSP, even though many markers of dysarthria are greater in MSA [37].

Airway Sleep-disordered breathing is common in MSA. Over half of patients have obstructive sleep apnea (OSA) or central sleep apnea (CSA), with OSA being more common. Of those with OSA, approximately 10% eventually develop CSA [38]. Most patients have REM sleep behavior disorder [31]. About one-third of patients have nocturnal stridor, which is a frequent cause of death in MSA if left untreated.

Dysphagia Dysphagia has been identified as an early symptom of MSA, which implies that it is either more common than in other neurological disorders or that awareness is greater than in other parkinsonian disorders [39]. Dysphagia symptoms begin around 3 years after onset of MSA symptoms, with no difference in latency between patients with MSA-C and MSA-P [38]. About 75% of patients eventually have dysphagia complaints [15]. The characteristics of swallowing deficits in patients with MSA may differ between clinical subtype.

Oral Phase Oral phase dysphagia is prominent in MSA. Prolonged oral preparation, incomplete mastication, oral holding, and lingual residue are typical findings on instrumental swallowing examinations. Delayed bolus transit is common 1–3 years following onset of MSA symptoms but becomes nearly universal by 7 years. Tongue pressures in both MSA-P and MSA-C cases are lower than normal controls. Patients with MSA-P demonstrated longer oropharyngeal transit times and more difficulty propelling the bolus posteriorly in the oral cavity than patients with MSA-C, correlating with more severe oral phase complaints, such as increased meal time, drooling, sensory changes in the oral cavity, and difficulty with mastication [38]. MSA-C patients demonstrated discoordinated oropharyngeal bolus transit but not obviously prolonged AP transfer within the oral cavity.

Pharyngeal Phase Two-thirds of patients have either laryngeal penetration or aspiration on videofluoroscopic study, with no difference noted between MSA subtypes [38]. Vallecular residue was the most common finding on videofluoroscopic study (90%). Vallecular residue is more severe in patients with MSA-P, likely due to reduced base of tongue retraction and poor ability to form and transfer a cohesive bolus. Upward movement of the laryngeal complex during swallow is also slowed, although hyolaryngeal elevation was not found to be reduced in either the superior or anterior planes. Patients with MSA-C had more frequent aspiration symptoms, such as coughing, throat clearing, etc., than patients with MSA-P, suggesting these instances of laryngeal penetration and aspiration were likely more related to oropharyngeal transit, discoordination, and delayed laryngeal elevation and closure.

Esophageal Phase Upper esophageal sphincter opening seems to remain stable throughout the course of MSA [40] and thus is not a factor in dysphagia.

Pharmacology/Medical Management

Management of MSA is symptomatic and includes fall prevention, treatment of complications such as sialorrhea, and cervical dystonia with botulinum toxin injections. Bradykinesia and rigidity in approximately 30% MSA-P patients show a significant response to L-DOPA, although high doses may be necessary, and this commonly precipitates unusual craniofacial dyskinesias. Orthostatic hypotension is managed by compression stockings, increased salt intake,

pyridostigmine, fludrocortisone, or midodrine. Urinary incontinence can be managed by antimuscarinic medications or catheterization depending the underlying mechanism.

Voice-, Airway-, and Swallow-Specific Procedures: Treatment Outcomes

Voice Vocal fold motion impairment is common with the progression of MSA [41]. The etiology is unclear, but a laryngeal examination is recommended for all patients with MSA. Decreased or absent bilateral vocal fold motion is likely a contributing factor to hypophonia, nocturnal stridor, and OSA. The presence of decreased or absent vocal fold motion is a relative contraindication for vocal fold augmentation (injection, laryngoplasty) due to the risk of further airway compromise.

Airway Previously, tracheotomy was the recommended treatment for nocturnal stridor. However, more recently, continuous positive airway pressure (CPAP) has been found useful in the nonsurgical management of stridor [42, 43]. Different variations of CPAP can help to address stridor, OSA, and to a less extent CSA [44], but CPAP is ineffective for central hypoventilation. A formal sleep evaluation and appropriate treatment is recommended in the care of MSA patients.

Dysphagia Dysphagia in MSA can cause significant difficulties with nutrition, hydration, and airway protection. There is no evidence showing swallowing therapy to be beneficial. Periodic swallowing evaluations (videofluoroscopy or FEES) are recommended to guide appropriate compensatory strategies, which often change as the disease progresses. Transition to a softer diet is often necessary as mastication and oral transfer deteriorate. Thickened liquids are recommended as posterior oral control and incoordination become challenging. Enteral nutrition is often needed as swallowing function deteriorates. Attention to oral hygiene is recommended. Coordinated care with a speech language pathologist can help the patient and their caregivers to understand the signs of aspiration. Compensatory swallowing strategies and diet modifications can maximize swallowing safety, thus reducing the risk of aspiration pneumonia.

Frontiers

A variety of therapeutic interventions directed at different aspects of MSA pathogenesis, and supported by preclinical studies, showed no evidence of efficacy. Evaluation of active immunization against α-synuclein is currently in progress after promising results in preclinical studies [45]. A recent phase 3 randomized clinical trial found that droxidopa, a norepinephrine precursor, significantly reduced orthostatic symptoms compared to placebo [46]. This drug is now FDA approved for treating neurogenic orthostatic hypotension in adult patients.

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Multiple Sclerosis

14

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Multiple Sclerosis

Multiple Sclerosis (MS) is a long-lasting neurogenic progressive disease that is characterized by a chronic inflammation of the central nervous system (CNS), mostly affecting the brain and the spinal cord [1]. Next to inflammation, MS causes demyelination to occur in the white matter of the central nervous system (CNS).

The pathophysiology of MS is a complex process in which the body's immune system attacks the myelin sheaths surrounding nerve fibers, resulting in scars (also known as "plaques" or "sclerae") which will cause impaired transmission of neural signals in the CNS. There is no known cause for MS [2]. Currently, there is no cure for MS. Treatments consist of medication to slow disease progression or target-specific symptom to improve quality of life. In recent years, there has been an emerging focus on healthy lifestyle (like the use of a Mediterranean diet) and regular aerobic exercise.

MS affects around 30 per 100.000 people globally, and the initial manifestations of the disease are evident during early adulthood, between the ages of 20 and 40. MS mostly affects females, with a female to male ratio of 3:1 [3]. The cause of MS is still unknown; however, specialists believe that MS is caused by several different factors including immunologic, environmental, and genetic factors that result in a permanent deterioration of the nerves. MS is known to be more common in Caucasians of Northern European decent compared to persons with other ethnical backgrounds. Possible factors that might play a role in the pathogenesis of MS are geographical, physical environment (including exposure to sunlight and vitamin D) and socioeconomic factors, although relationship to causality remains unclear [2]. In the last decennia, the incidence of MS has increased. The reason for this increase is not clear, with possible contributors including increased awareness of the disease, improved access to medical care, and enhanced diagnostic measures [4].

MS is diagnosed based on strict criteria (McDonald criteria), that are based on the number of episodes where a person shows signs of an "acute inflammatory demyelinating event" in combination with the existence of lesions (plagues) in MS-typical regions of the central nervous system (such as periventricular, juxtacortical, infratentorial, or spinal cord), as confirmed by MRI [2].

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There are four types of MS including relapsing remitting multiple sclerosis (RRMS), secondary progressive multiple sclerosis (SPMS), primary progressive multiple sclerosis (PPMS), and progressive relapsing multiple sclerosis (PRMS) [5, 6]. As the cause of MS is unknown, it is also unknown why these four different types of MS develop [2]. The most common variant is RRMS, which begins with a single attack and is then followed by relapses over time [5]. In SPMS, symptoms get more severe gradually over time, with or without the incidence of a relapses or remissions [6]. PPMS is not very common and occurs in 10% of people with MS [5]. It is characterized by slow aggravation of symptoms without relapses or remissions [5]. PRMS is the least common type of MS and only occurs in 5% of people with MS [5].

The symptoms of MS vary widely from one person to another depending on the location and size of the lesions in the brain and spinal cord [7]. However, MS is mainly characterized by loss of muscle strength in various muscle groups in the body [8]. MS is also characterized by fatigue, which is the sensation of tiredness, lack of energy, and exhaustion [9]. Other major symptoms of MS include general weakness, vision problems, mobility problems, cognitive problems, spasticity, numbness and tingling in the extremities, and bowel and bladder dysfunction [10].

The incidence of swallowing problems, voice problems, and communication problems in people with MS is high. In a recent study, 38% of people with MS report frequent coughing and choking while eating and drinking [11]. Another 43% of people with MS reported problems with controlling the loudness of their voice, specifically that other people find it difficult to hear their voice. Another 31% reported that their speech rate was slower than normal. Up to 68% reported word finding problems (i.e., productive language) and 36% reported "difficulty making sense out of what people say to me" (i.e., receptive language). These problems with speech, language, and swallowing did not correlate with the time since diagnosis of MS, suggesting that these impairments can occur at any stage of the disease [12]. Speech, language, and swallowing problems, however, are correlated with a negative effect on social activities and are associated with depressed feelings in people with MS [4].

Swallowing Problems in Multiple Sclerosis

Persons with MS often experience dysphagia [6, 13, 14]. Dysphagia is due to a combination of impairments in the CNS including the corticobulbar tracts, cerebellar, brainstem, and lower cranial nerves [13]. The location and degree of impairment in the CNS determine how dysphagia is manifested in adults with MS [15]. The definite frequency of dysphagia in MS is unknown; however, it is estimated to range from 30% to 40% [13].

Dysphagia may be chronic or intermittent in people with MS and differs from patient to patient [16]. It can appear in early stages of MS; however, it is more common in progressive stages of the disease [17]. It can also appear in people with MS with a mild impairment; however, it worsens in adults who have moderate to severe brainstem impairment [13, 18]. A study of seven adults with MS found that some of these adults had dysphagia before getting diagnosed with MS [16]. Other adults presented with dysphagia shortly after diagnosis [16]. One patient showed symptoms of dysphagia before getting diagnosed with MS, and after her first remission, those symptoms disappeared [16].

Symptoms of dysphagia in MS may be due to impairments in the oral and/or pharyngeal phases of swallowing [13]. Symptoms can range from mild discomfort in the oral cavity or pharynx when swallowing to an inability to masticate solid food or swallow safely, as aspiration is a frequent finding in people with MS [19]. The effects of dysphagia may be rather hazardous to the patient, both physically and socially [20]. Some of the most frequent physical symptoms reported by adults with MS include coughing while eating, feeling like food is going "down the wrong way," food sticking in the throat, difficulty managing saliva, difficulty initiating a swallow, and drooling. Upon examination, symptoms like jaw jerk and slow tongue

movement can be observed [14, 18]. Such problems may lead to insufficient oral intake, malnutrition, dehydration, and inability to take oral medications, resulting in partial or complete dependence on tube feeding, which in turn increases healthcare costs [13, 21]. More importantly, in later stages of MS, dysphagia can lead to morbidity and death from aspiration pneumonia [13, 22, 23]. Dysphagia can also affect patients' quality of life resulting in embarrassment and avoidance of social events that involve consuming food and/or drink [16, 20].

A more recent study showed numerous physical and psychological symptoms associated with swallowing problems in people with MS [11]. When comparing people with MS with swallowing disorders and people with MS without swallowing disorders, people with MS-related dysphagia had reduced scores across all domains of SWALQOL, a swallowing-related quality of life questionnaire [24]. Some of these physical symptoms include coughing, throat clearing, and choking on food and liquid, which may be harbingers of more serious consequences such as pneumonia and increased mortality. Other symptoms people with MS experience are sociopsychological and can include a reduced desire to eat and increased food avoidance. These symptoms may lead to social withdrawal and mealtime anxiety. Eating and drinking play an important role in the physical, psychological, and social aspects of life. It is thus necessary for healthcare professionals who work with people with MS to be aware about dysphagia, its symptoms, and its impact. Early assessment and intervention can delay and/or reduce serious complications (like aspiration pneumonia) in later stages of the disease [11].

Communication and Language Problems in Multiple Sclerosis

The body of literature primarily describes the impact of MS on basic language functions, but does not sufficiently characterize the impact on more complex language skills. Due to the focus on basic language functions, current evidence is inconclusive regarding the presence or absence of language deficits in people with MS. Research into the language capacity of people with MS has primarily come from studies investigating cognitive functions, which use neuropsychological assessments rather than tools developed specifically to evaluate language abilities. These tools only assess the basic functions of language such as verbal fluency and naming. Other studies have utilized aphasia assessment batteries, which are designed to assess the language skills of individuals following a cerebrovascular accident [25, 26]. These earlier studies identified that the performance of people with MS did not vary significantly from controls.

In 2013, a small study explored possible language deficits in 39 Dutch people with MS. In this pilot study, standardized language assessments used following cerebrovascular accidents were administered (including the Boston Naming Test and the Dutch Semantic Association Test). Scores on these tests showed that all people with MS in this cohort had deficits in semantic and phonemic word fluency. Of all participants, 73% had word finding difficulties, and 95% had difficulties with the interpretation of metaphors. Prior to assessment, only 15 participants reported they experienced language difficulties, indicating a possible limit insight in communication problems in persons with MS [27].

Again, these assessments only provide insight into basic language functions while failing to evaluate complex language skills. A recent systematic review identified that impaired word retrieval was the most common language symptom in people with MS [28]. The authors of this review were however unable to draw any general conclusions on high-level language skills in people with MS due to the limited number of high-level language tasks used in included studies [28]. More recent studies investigating the language skills of people with MS have used assessment tools that measure complex language skills. These studies demonstrated that people with MS have trouble with language tasks that require planning, abstract reasoning, problem solving, and decision-making [29].

Traditionally, language functions were felt to be controlled by cortical neurons that remain

unaffected in people with MS. In recent years, several models of language processing have described white matter tracts connecting subcortical structures, including the thalamus and basal ganglia, to cortical language areas [30]. The cortico–subcortico–cortical loop model proposes that language functions are controlled by a circuit of white matter pathways between subcortical and cortical structures. These pathways operate in an organized and synchronized fashion to allow for the comprehension and production of language [29]. As such, it is only recently that deficits in the area of language have been considered a potential clinical manifestation in people with MS.

Speech and Voice Problems in Multiple Sclerosis

Speech motor skill is another variable that may interact with the cognitive–linguistic abilities of people with MS. Dysarthria is a motor speech disorder prevalent in 40–50% of people with MS and is characterized by ataxic and/or spastic features [31]. Another recent systematic review described that articulation (slow articulation and imprecise consonants), voice (pitch and loudness instability), respiration (decreased phonatory time and expiratory pressure), and prosody (longer and frequent pauses, deficient loudness control) are affected in people with MS. This review also underlines the earlier described relationship of communication problems with cognition [32].

One study investigated the association between cognitive and speech motor skills in people with MS using rapid speech sound repetitions (dysdiadochokinesis when rapidly saying "pa-ta-ka") and neuropsychological tests that require verbal responses. Results showed that people with MS performed more slowly on cognitive tasks that require oral responses. The performance on these cognitive tasks were however similar to that of healthy controls when outcomes were statistically controlled for their poorer dysdiadochokinesis scores. Accordingly, the authors hypothesized that slower verbal responses were the consequence of motor speech deficits and not by cognitive deficits [33].

Regarding voice problems, a study with 143 people with MS from Australia ($N = 52$) and New Zealand ($N = 91$), 43% of respondents reported problems with controlling their voice [12]. A recent study compared the maximum expiratory times and maximum phonation times of MS patients with matched healthy controls and found that maximum expiratory times, maximum phonation times, and dysarthria scores were significantly altered compared with healthy controls [34]. This study also showed that with disease progression, the maximum expiratory time will decrease, possibly due to reduced breath support. This decrease in maximum expiratory time is associated with decreased phonation time and an increase in dysarthria scores [34]. These findings are supported by the findings of Fazeli et al. (2018), who describe the phonation and articulation subsystem changes in patients with multiple sclerosis compared to healthy individuals, in which a correlation between changes in an acoustic measure of dysarthric speech (Formant Centralization Ratio) and disease progression was found. Authors suggest that articulation subsystem changes might be useful signs for the progression of the disease [35]. Finally, the prevalence of spasmodic dysphonia in people with MS is higher than in the general population (2% vs. <0.001%) [36].

Although existing literature identifies voice and speech problems as a frequent finding in people with MS, showing a clear correlation between phonation and speech, the underlying aetiology of these (self-reported) voice and speech problems remains under-investigated.

Conclusion

In people with MS, the prevalence of swallowing, voice problems, and communication problems is high. Speech, voice, language, and swallowing problems all have a negative effect on the quality of life and are associated with depression in this population. Up to 38% of people with MS report

frequent coughing and choking. Around 43% of people with MS report voice problems, and over 30% report speech problems. Language and cognitive impairments are also common, with over 60% of MS patients reporting productive language problems and 36% reporting receptive language problems. Although MS is primarily associated with loss of muscle strength in various muscle groups, this chapter highlights the complex relationship between MS and cognitive/language function and associated communicative disorders.

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Alzheimer's Disease

15

Nicole Rogus-Pulia, Anne L. Foundas, and Kimberly D. Mueller

Introduction

With advancing age, there are expected changes in the brain structure and function. However, these expected age-related brain changes do not lead to disruptive changes in cognition, behavior, or function. By contrast, pathological age-related changes in the brain structure and function lead to cognitive decline that includes clinically significant memory loss. A cognitive decline with a change in functional independence can be an indicator of dementia. By definition, dementia is associated with cognitive decline, functional deficits, and behavioral problems. A number of factors underlie loss of memory and cognitive decline. Dementia is not a specific disease; rather, there are various subtypes of dementia.

Dementia Subtypes

Some causes of dementia are degenerative, which means that the pathological, physiological, cognitive, and behavioral changes are progressive. Other neurological conditions, such as stroke, traumatic brain injury, or multiple sclerosis, may predispose individuals to the onset of dementia. It is also well established that chronic alcohol abuse syndrome can result in dementia. A degenerative type of dementia, such as Alzheimer's disease (AD), has a slow and insidious onset. In contrast, poststroke or vascular dementia (VaD) is typically more abrupt in onset or may present with a stepwise decline. Finally, some dementia diagnoses can be due to a treatable condition, such as vitamin B12 deficiency or hypothyroidism. It is important that individuals experiencing cognitive impairment seek help as soon as possible for diagnosis and possible treatment. The major types of dementing disorders are summarized in Table 15.1. In this chapter, we will focus on AD, which is the most common degenerative dementia. Disorders of voice, swallowing, and

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Table 15.1 Dementia subtypes

Degenerative dementias	**Prevalence (%)**	**Subtypes**	**Symptoms**	**Pathology**
Alzheimer's disease	40	Early onset (before age 65) Late onset (after age 65)	Profound memory loss, cognitive decline	Amyloid (AB 42) plaques, neurofibrillary (tau) tangles
Frontal dementias (FTD)	10	Frontotemporal dementia (FTD) behavioral variant, pick disease, semantic dementia, primary progressive aphasia	Variable, less memory loss than AD	Heterogeneous, tau vs. non-tau types
Mixed dementia types	15	AD plus VaD, Lewy body disease, corticobasal degeneration	Variable	Heterogeneous
Vascular dementia	20		Variable	Vascular disease
Multi-infarct dementia (large-vessel stroke), small-vessel disease (chronic microvascular disease), mixed type (large and small vessel disease)			Variable	Vascular disease
Other dementia types	15	**Subtypes**	**Symptoms**	**Pathology**
Parkinson disease (PD) with dementia		Degenerative disease with about 30% of PD patients developing dementia; 60%–80% have depression	Variable, Greater executive function deficits	Lewy body, alpha synuclein
Traumatic brain injury (TBI)		Concussion, intracranial hemorrhage, hematomas—subdural, epidural		Heterogeneous
Toxic, metabolic, endocrine, deficiency		Alcoholic dementia; B12 deficiency; hypothyroidism		Deficiency states, endocrine
Infectious/inflammatory/ autoimmune		Creutzfeldt–Jacob disease (CJD), herpes simplex encephalitis, HIV dementia, multiple sclerosis/ demyelinating disorders		Heterogeneous
Chronic medical diseases		Chronic renal disease, hepatic disorders		Toxic/metabolic
Other disorders with cognitive decline		Multiple sclerosis, brain tumors, normal pressure hydrocephalus, Huntington's disease, chronic major psychiatric disorders, substance abuse syndromes		Heterogeneous

eating behaviors will be discussed in the context of AD, including treatment options and challenges with disease progression.

Epidemiology of Alzheimer's Disease

Major dementia subtypes are categorized by worldwide prevalence (percentages) as presented in Fig. 15.1. AD is the most common type of degenerative dementia with one in nine individuals over 65 years estimated to have an AD diagnosis in the United States (US). Recent US estimates reveal that 6.1 million individuals had clinical AD or mild cognitive impairment (MCI) in 2017, and this number is expected to grow to 15.0 million by 2060 [1]. Prevalence of AD increases with advancing age, with the highest prevalence (~35%) in those over 85 years of age. Also, AD prevalence is higher for women compared to men with approximately two-thirds of all individuals with AD being women [2]. AD also is more prevalent in African-American and Hispanic individuals compared to non-Hispanic white, American Indian and Alaska natives, and Asian and Pacific Islanders [2].

The consequences of AD are serious. AD is the sixth leading cause of death in the USA and the fifth leading cause of death among those over 65 years of age [2]. However, the number of deaths to which AD contributes is likely much higher than the number recorded on death certificates, given that AD results in a host of complications impacting survival. Pneumonia, due in many cases to dysphagia-related aspiration [3], is the most commonly cited complication leading to death in older individuals with AD [4, 5]. Other complications include ischemic heart disease, circulatory system diseases, and respiratory diseases. Additionally, persons with AD require regular care, most often from unpaid caregivers who provide an estimated 18.1 billion hours of care that is valued at more than $221 billion [2]. Average per-person Medicare payments for services to beneficiaries over 65 years of age are two and a half times greater for persons with AD compared to those without AD [2].

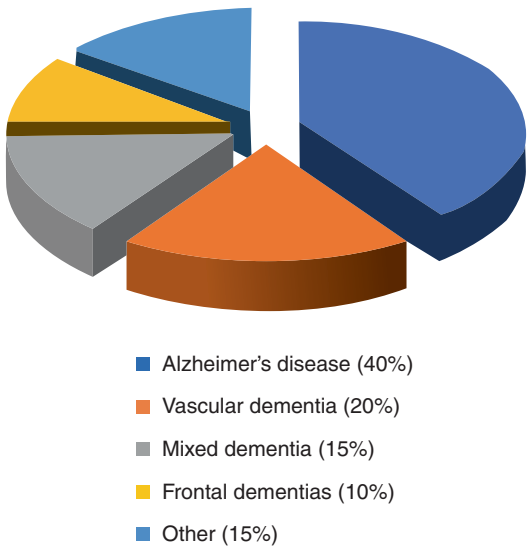

Fig. 15.1 Dementia subtypes: worldwide prevalence

Symptoms, Progression, Pathology, and Genetics of Alzheimer's Disease

Symptoms of AD are known to gradually worsen over a number of years. In its early stages, memory loss is mild, but with late-stage AD, individuals lose the ability to carry on a conversation, respond to their environment, and have difficulty eating and swallowing. Those with AD live an average of 8 years after diagnosis, but this time frame can vary from 3 to 20 years depending on age at time of diagnosis, gender, and other health conditions [12, 13]. Diagnosis can also be delayed with the average length of time between the onset of symptoms and the diagnosis of AD around 2.8 years [13].

The hallmark pathologies of AD disease are the progressive extracellular accumulation of the protein fragment beta-amyloid (plaques) and the intracellular accumulation of twisted strands of the protein tau (neurofibrillary tangles). These cellular changes are progressive and bilateral. Beta-amyloid clumps block cell-to-cell signaling at synapses and can activate immune system cells that trigger inflammation which destroys these disabled cells, causing further brain injury. Neurofibrillary tangles destroy a vital cell protein transport system. These changes lead to cell death and volume loss (atrophy) in discrete brain regions. Plaques and tangles spread through the brain in a predictable pattern as AD progresses.

Two regions of localized early pathological changes include bilateral cellular changes in the hippocampal formation within the mesial temporal cortex and the nucleus basalis of Meynert within the basal forebrain (acetylcholine is produced in this structure). Dysfunction within these discrete regions accounts for the profound difficulty with new learning and memory, which is the most severe and disabling cognitive deficit. Early localized cortical pathology is greatest within the inferior parietal lobe. Left parietal lobe involvement accounts for early changes in language, often beginning with word-finding difficulty; right parietal lobe involvement accounts for the early changes in disrupted spatial maps, which may lead to patients becoming lost while driving. Finally, the insular cortex develops bilateral pathological changes in AD [14], and age-related volume loss has been found in healthy older adults [15]. This matter is important, as the insula plays a critical role in swallowing physiology [16].

In advanced AD, most of the cortex is seriously damaged. The brain shrinks dramatically due to widespread cell death. Individuals lose their ability to communicate, to recognize family members and loved ones, and to care for themselves. Changes in eating and swallowing occur with disease progression, but the precise nature, pattern, and degree of changes are unclear, as there are very few well-controlled longitudinal studies [17].

A single gene does not cause AD. More than one gene mutation can cause AD; genes on multiple chromosomes are involved. The two basic types of AD are *familial (early onset)* and *sporadic (late onset*). *Early-onset or familial AD (FAD)* is a rare form, affecting less than 10% of all people with AD. FAD is caused by a mutation in one of three genes: *amyloid precursor protein (APP)* gene on chromosome 21, the *presenilin 1 (PS1)* gene on chromosome 21, and the *presenilin 2 (PS2)* gene on chromosome 14. Each of these genes is inherited in a dominant fashion. This means that it is only necessary to inherit one mutated copy of the gene in order to develop AD. Those who do inherit a mutated form of these genes tend to develop AD early in life (younger than age 65, commonly with symptom onset in the third decade) and have a strong family history of the disease.

The majority of AD cases are sporadic and late onset. Late-onset AD has no known cause and shows no obvious inheritance pattern. However, in some families, clusters of cases are seen. Although a specific gene has not been identified as the cause of late-onset AD, genetic factors do appear to play a role. Only one risk factor gene has been identified so far: the *apolipoprotein E (APOE)* gene on chromosome 19. *APOE* has functions throughout the body, including transporting cholesterol, regulating the immune system, aiding in nerve regeneration, and metabolism. There are four different forms of the *APOE* gene. Inheriting the *E4 allele* increases a person's risk of developing AD by threefold. Inheriting two *E4* copies of the gene increases the risk by 12–15 times. People with two copies of *E4* tend to develop AD earlier in life than the general population. The *E4* version of *APOE* is present in about 15% of Caucasian people and is even more common in people of African descent. However, not all of these people develop AD, and not all people who have AD have the *E4* version of *APOE*. This scenario means that other environmental or genetic factors are also required in order for a person to develop AD. Genetic testing for the *APOE* gene is not recommended for healthy people. However, it may be a useful confirmatory test in someone with dementia [18].

Communication and Swallowing Deficits in Patients with Alzheimer's Disease

Prevalence of Communication and Swallowing Issues

"Communication" can be defined as the act of receiving, sending, processing, and comprehending verbal and nonverbal symbols and concepts [6]. These skills require the recruitment of multiple cognitive and biologic processes and neural networks, including (1) *semantic and episodic memory*: memory for concepts, words, events; (2) *executive function*: selective word search and retrieval, processing of complex syntax; (3) *speech*: the accuracy, speed, and fluency of motor

articulation of speech sounds; (4) *voice:* ability to produce phonation by vibrating the vocal folds efficiently; and (5) *language*: the understanding and expression of meaningful content, grammatical rules, and social conventions. Voice disorders are also more common in adults over 65 years of age [7] and those with various types of neuropathology (e.g., Parkinson's disease, Huntington's disease, dementia) [8]. The exact prevalence of dysphonia in patients with AD is unknown but is likely to be higher than the general population. Thus, by definition of dementia, nearly, if not definitively, *all* individuals with AD will show impairments in one or more of the prerequisite abilities necessary for communication.

Persons with AD often experience various issues during the eating process, including impairments in self-feeding and dysphagia, or swallowing dysfunction. Self-feeding involves the process of transporting food or liquid from the table to the mouth. An estimated 50% of all persons with AD will lose the ability to feed themselves within 8 years of diagnosis [19]. Prevalence estimates for dysphagia in persons with AD vary from 32% to 84% [10, 11]. This variation is based on methods employed to determine prevalence, including the care setting (e.g., acute care, inpatient rehabilitation, nursing home), age, dementia subtype and stage progression, and methods used to identify dysphagia (e.g., clinical versus instrumental evaluation) [10, 11].

Communication Deficits

Some of the earliest and most common language-related issues reported by adults with AD and their caregivers are word-retrieval problems. Although difficulties with word retrieval are a known effect of typical aging (i.e., the "tip of the tongue" phenomenon), the deficits characteristic of dementia are severe and frequent enough to cause disruption in conversation early in the disease course. These problems are thought to result primarily from impaired semantic processing [20, 21], but lexical retrieval and degradation of semantic storage have also been suggested as early contributors. *Semantic paraphasias*—substitutions of semantically related words (e.g., drive instead of car)—occur in early and mid-stages of dementia and worsen with disease progression. In mid-stages of dementia, language is often characterized by an overabundance of pronouns and other nonspecific words, rendering vague and incoherent phrases often termed "*empty speech*" (e.g., "hmm, the only, the only thing I know, uh, of it is to get back, uh, get back and then up to another thing"). Although many of the grammatical rules (e.g., word endings such as plural or past-tense markers, word order) of syntax remain until later stages of dementia when syntax production is simplified and comprehension of complex syntax is severely impaired. Repetitive questioning and impaired comprehension of verbal and nonverbal cues can negatively impact communication with others and may cause social withdrawal. In the late stages of dementia, verbal communication is often limited or completely absent.

Articulation

The articulation of speech sounds remains intact in the early and mid-stages of AD dementia, although in later stages, *phonemic paraphasias (*sound substitutions such as "prip" for "trip") may occur. *Speech fluency*, or the rate, rhythm, and flow of speech, is often disrupted in early and mid-stages by filled ("um," "uh") and non-filled pauses, circumlocutions, and repetitions, likely compensatory behaviors for word retrieval, and/or executive function deficits.

Voice

Voice production is another important component of communication that can be affected in persons with AD and can greatly affect the quality of life. Dysphonia, or abnormal voicing, is more common with advancing age (termed presbyphonia) as is AD. Therefore, alterations in voice quality due to age-related laryngeal anatomical and physiologic changes, including reduced volume, increased breathiness, a change in pitch, decreased endurance, and reduced vocal range, may affect patients with AD [22] of advanced age. While voicing in patients with AD is understudied, one study did show that the speech of persons with AD consists of a higher number of periods of sound (one period = time

taken to complete one cycle). This higher number of periods implies that the voice vibrates at fewer cycles per second during connected speech, presenting as deeper voice, slower speech, and slower rate of speed or rhythm of glottal pulses [23]. Additionally, patients with AD were found to have a higher proportion and number of voice breaks or sudden changes in voice pitch, which allow tremors in the voice to appear [23]. Additionally, a recent study revealed that abnormal vocal behavior, specifically an impaired pitch reflex (vocal response to auditory feedback pitch perturbation), predicted executive and memory dysfunction in patients with AD [24].

Eating and Swallowing Impairments

There are a variety of adverse health consequences of eating and swallowing impairments in patients with AD. Dysphagia results in aspiration, or entry of foreign material into the airway, that frequently leads to the development of pneumonia. Pneumonia is the most common cause of mortality in patients with AD [5, 25, 26], with many cases due to dysphagia-related aspiration [3], and a leading cause of hospitalization and decreased quality of life [25, 27]. Patients with AD and dysphagia are also at increased risk for malnutrition, feeding tube placement, longer hospital length of stay, and discharge to a nursing home [27–29]. Additionally, eating and swallowing impairments substantially impact quality of life for patients with AD and their caregivers [30], especially when modified diets are recommended [31].

The eating process involves more than the act of swallowing. Successful eating requires cognitive awareness of the eating situation, ability to transport the correct amount of liquid or food to the mouth with appropriate timing, physiologic reaction to the smell and presence of food, and visual recognition of food all prior to swallowing [9, 32, 33]. AD patients receive more self-feeding cues or direct assistance from their eating partner than control participants, which can enable feeding dependency [34]. Feeding dependency is an independent predictor of increased pneumonia risk and mortality in patients with AD [35, 36] which is likely due to less control over the swallowing process affecting swallow safety [37]. Patients with AD who have difficulty beginning a meal, have more severe AD, and are dysphagic are at higher risk for feeding dependence [32].

In addition to issues with self-feeding, patients with AD experience difficulties with swallowing, as documented via videofluoroscopic assessment beyond expected aging-related changes (presbyphagia) [38–42]. Biomechanical changes in swallowing displayed in Table 15.2 begin in the mild stage of AD and worsen with disease progression, resulting in more frequent and severe occurrences of airway invasion in the moderate to late stages of AD [10, 38, 40–43]. These changes in swallowing

Table 15.2 Communication, eating, and swallowing impairments in persons with Alzheimer's disease

Deficit area	Types of impairments
Communication	Word-retrieval difficulties
	Semantic and phonemic paraphasias
	Simplified syntax production
	Decreased comprehension of complex syntax
	Repetitive questioning
	Impaired comprehension of verbal and nonverbal cues
	Disrupted speech fluency (filled and non-filled pauses, circumlocutions, repetitions)
	Dysphonia (reduced volume, increased breathiness, voice breaks, sudden changes in pitch)
Eating	Loss of independence with feeding
	Decreased amount of oral intake
Swallowing biomechanics	Inefficient mastication
	Delayed initiation of oral bolus transport
	Ineffective/discoordinated oral bolus transport (increased oral transit times)
	Delayed triggering of pharyngeal response
	Decreased hyolaryngeal displacement
	Incomplete airway closure (resulting in penetration or aspiration episodes)
	Decreased upper esophageal opening

function correlate with altered neural activation patterns during swallowing as measured by functional magnetic resonance imaging (fMRI). These studies with fMRI have shown decreased signal intensity, representing lower blood oxygenation levels, in the pre- and postcentral gyri, the Rolandic opercula, and the frontal opercula bilaterally [44]. These areas of the brain have previously been shown to play important roles in the neural control of swallowing [45–47]. While they are not typically atrophied in early AD, they all receive input from the insula [48], which is involved during preparation to swallow [49] and atrophies early in the AD process [50]. Additionally, more neural effort is thought to be required for patients with AD to inhibit swallowing, evidenced by increased signal intensity (blood oxygenation levels) in the frontal operculum and insula during an inhibitory task [51]. It is possible that this difficulty with inhibiting a swallow in patients with AD may result in discoordination or initiation of a swallow when the system is not prepared to protect the airway.

Beyond changes in swallowing-related neural activation, patients with AD may experience decreased force generation during swallowing as a result of sarcopenia, or age-related decreases in muscle mass, affecting muscles of the head and neck [52]. Patients with AD have also been found to produce less saliva than older healthy individuals, which can result in xerostomia [53], or the perception of dry mouth, as well as slower, more effortful swallowing. Issues with dentition can also affect the patient's ability to chew and swallow safely. Additionally, patients with AD have been shown to have poor olfactory function [54, 55], which can affect taste and may impact desire to eat and appetite [56, 57].

Treatment of Communication and Swallowing Impairments in Patients with Alzheimer's Disease

If there is clinical concern for dysphagia in patients with AD, then patients should be referred to a speech–language pathologist (SLP) for an instrumental assessment (e.g., videofluoroscopy, flexible endoscopic evaluation of swallowing [FEES]) to determine the biomechanical impairments underlying observed clinical signs. Given that changes in swallowing begin early in AD progression, it is ideal for the SLP to be incorporated as part of the interdisciplinary care team from the time of AD diagnosis to ensure adequate management throughout disease progression. Treatment approaches and associated outcome measures for communication and swallowing impairments in persons with AD are summarized in Table 15.3.

Pharmacology and Medical Management

There are no medications that have been shown to improve communication or swallowing in patients with AD. Medications commonly prescribed to enhance cognitive function for patients with AD, such as donepezil/memantine, have not been shown to affect speech, language, or swallowing function. However, the increased risk for depression associated with these medications may have a negative impact on the frequency and/or quality of communicative interactions. Medications with anticholinergic properties or diuretics may exacerbate xerostomia in patients with AD, which can lead to inefficient swallowing, changes in voice quality, diet alterations, and poor oral health [58]. Antipsychotic medications, often prescribed to patients with AD for management of agitation and psychotic symptoms, have been associated with worse swallow function [59, 60] and increased pneumonia risk [61].

Communication and Swallowing-Specific Procedures and Treatment Outcomes

Management of Communication Deficits

Evidence-based communication interventions for dementia include direct, cognitive stimulation approaches in individual and group settings, reminiscence group therapy, and targeted nam-

Table 15.3 Communication, eating, and swallowing treatments and outcomes for persons with Alzheimer's disease

Impairments	Treatment approach	Outcomes
Communication	Cognitive stimulation therapy	Quality of life scales, communication scales, depression and anxiety scores, ADAS-Cog scores
	Reminiscence group therapy	Verbal fluency, quality of life, nonverbal communication acts
	Montessori group therapy, "Breakfast club" group	Conversational turn-taking, functional independence scales, depression/anxiety scores
	Memory books/wallets	Decreased frequency of repetitive questioning and vocalizations
	Spaced retrieval training	Confrontation naming, recall of meaningful information (familiar names and compensatory strategies)
	Communication skills training for caregivers	Increased number of words by persons with dementia, words per topic, conversational turns
	Vocal exercise regimens	Voice Handicap Index, objective vocal parameters (e.g., maximum phonation time, S/Z ratio, jitter/shimmer)
Eating	Mealtime environmental modifications	Changes in meal intake, clinical signs of dysphagia, nutritional status (e.g., energy intake, weight, body composition, biochemical indices, MNA)
	Caregiver training in optimal feeding techniques	Aversive feeding behaviors, time spent providing feeding assistance, changes in meal intake
Swallowing	Diet modification (e.g., thickened liquid, pureed solids)	Swallowing biomechanical changes (MBSImP), swallow safety (PAS), swallow efficiency (oropharyngeal residue), patient-reported outcome measures for swallowing (e.g., EAT-10), level of oral intake (e.g., FOIS), nutritional status
	Postural adjustments (e.g., chin tuck, head turn)	
	Oropharyngeal strengthening regimens (e.g., effortful swallow, oral tongue strengthening, expiratory muscle strength training)	Swallowing biomechanical changes (MBSImP), swallow safety (PAS), swallow efficiency (oropharyngeal residue), patient-reported outcome measures for swallowing, level of oral intake, nutritional status, maximum isometric tongue pressures (measured with IOPI), maximum expiratory pressures, peak cough flow, respiratory phase patterning
	Swallowing coordination training (e.g., respiratory–swallow treatment)	

ADAS-Cog Alzheimer's Disease Assessment Scale-Cognitive Subscale test, *MNA* Mini Nutritional Assessment, *PAS* Penetration–Aspiration Scale, *EAT-10* Eating Assessment Tool, *FOIS* Functional Oral Intake Scale, *MBSImP* Modified Barium Swallow Impairment Profile, *IOPI* Iowa Oral Performance Instrument

ing therapy. Outcomes for these approaches include measures of conversation participation, production of novel phrases, or improved naming accuracy. Other evidence shows positive effects of spaced retrieval training on the recall of personal and relevant information [62]. Compensatory strategies, such as the training on and use of memory books consisting of pictures of meaningful people, places, and objects, have produced several positive outcomes, including the reduction of repetitive verbalizations or questions [63]. Finally, the effect of caregiver

communication training has been shown to increase engagement in conversation and topic maintenance in persons with dementia and to improve caregiver satisfaction [64]. While efficacy of voice therapy has not been determined in patients with AD, vocal exercise programs have shown positive results in older adults [22]. Therefore, voice therapy may be attempted for dysphonic patients with AD who are still able to participate cognitively. Education regarding vocal hygiene should also be provided to patients with AD and their caregivers. Vocal fold atrophy has been treated successfully with injection laryngoplasty in select geriatric patients [22], but these surgical approaches have not been studied in patients with AD.

Management of Eating and Swallowing Impairments

It is critical that a multifaceted approach is taken to the optimization of eating and swallowing in patients with AD. Physical environment has been shown to influence eating in individuals with AD, with more "homelike" environments that include music, décor, and table dressings resulting in increased oral intake. While social interaction during meals may also result in increased oral intake, minimization of distractions during mealtime, such as television, is important in optimizing swallowing safety [65]. Food presentation also plays an important role in the amount of food consumed, such as limiting items on plates to food items only and removing condiments or delaying presentation of dessert until the end of the meal. One study found that, when food was presented on plates of a high-contrast color (e.g., red or blue) as compared with white plates, patients with AD consumed more [66]. Additionally, adaptive plates, bowls, and eating utensils as well as presentation of finger foods support self-feeding for individuals with AD longer into disease progression [9]. When caregiver feeding is necessary, a hand-under-hand feeding approach (caregiver holds the utensil and supports the patient's hand engaging them in the eating process) has been shown to be efficacious for increasing the amount of food intake and decreasing negative mealtime behaviors in patients with AD [66]. A person-centered caregiver feeding approach will result in increased swallowing safety as compared with a task-centered approach [37].

Based on biomechanical impairments identified with instrumental assessment of swallowing, SLPs will often recommend compensatory approaches to management of dysphagia, such as diet modification (e.g., thickened liquids, pureed diets) or use of postural adjustments during swallowing. Sensory enhancement techniques, such as bolus alterations or olfactory enhancement, may enhance swallowing biomechanics, but these approaches require study in patients with AD [9]. A large clinical trial of 711 patients with AD and Parkinson's disease showed honey-thick liquids to be most effective in immediate elimination of thin liquid aspiration in patients with AD [67] as compared with nectar-thick liquids and chin tuck posture. However, aspiration of honey-thick liquids was most strongly associated with pneumonia onset in a subset of this same cohort [68]. Also, more patients in this cohort taking thickened liquids had dehydration, urinary tract infections, and fever as compared to those using the chin tuck posture. When recommending pureed diets to patients with AD, it is important to ensure that sensory appeal of these foods is maximized and that nutritional content is enhanced [69]. In some cases, tube feeding may be recommended; however, studies have shown that tube feeding does not decrease the risk of respiratory infection in individuals with AD [70, 71] or the risk of mortality [73].

Frontiers

With advances in technology and computing, including digital recording, automatic speech recognition, machine learning, and natural language processing, there is growing interest in using recorded speech as a digital biomarker for detecting and measuring cognitive change on the AD disease trajectory. Retrospective studies have shown that subtle changes to speech and language were evident years prior to a diagnosis of dementia [74], and a recent prospective study showed correlations between changes in speech and subtle cognitive decline in asymptomatic adults at

risk for AD [75]. As the identification of AD pathological biomarkers continues to advance, a digital and functional biomarker such as spontaneous speech may be an ideal disease monitoring tool for pharmacological and nonpharmacological clinical trials. Multimodal interventions that include cognitive stimulation, physical activity, diet, and medical management have emerged as promising preventions of cognitive decline [76]. Interest is also growing for internet-based speech–language interventions for individuals with early cognitive decline and dementia [77], which is a promising service delivery model for an aging population, both in terms of cost savings and logistical barriers (mobility and travel constraints).

Dysphagia management approaches for individuals with AD have been largely limited to compensatory approaches that may negatively affect quality of life and increase caregiver burden. Rehabilitative approaches to improve the underlying physiology of swallowing, such as exercise regimens targeting swallowing-related musculature, have not yet been studied in individuals with AD but are promising given their efficacy for older adults with dysphagia and patients with other neurodegenerative diseases [78, 79]. Several studies have supported the feasibility of exercise-based approaches for individuals with early-stage AD [80–82]. Neuromodulation through transcranial, neuromuscular electrical stimulation, electromyographic biofeedback, or functional magnetic stimulation has been found to have positive effects on swallowing in healthy cohorts and patients with poststroke dysphagia [83–86]. The potential of these approaches for improving swallowing function in individuals with AD has yet to be examined but is promising as well.

Conclusions

In summary, communication and swallowing deficits are common in patients with AD and require early identification and management by an interdisciplinary team to avoid negative health consequences and decreased quality of life. Treatment approaches should take into account the patient's values and goals of care. Caregiver training and education will be critically important in the implementation of any recommendations to improve communication and swallowing. Novel methods for improving diagnosis and treatment of communication and swallowing impairments in this population are promising and will ensure optimal care into the future.

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Laryngeal Dystonia

16

Justin M. Hintze, Christy L. Ludlow, and David G. Lott

Spasmodic dysphonia almost ended my career. After 6 years of doctors telling me it was 'all in my head,' two physicians … finally diagnosed spasmodic dysphonia. I was given my first injection of Botox that very day. Three weeks later I was back on the air.

Diane Rehm
Talk show host (now retired)
National Public Radio

Introduction

Spasmodic dysphonia (SD), a form of laryngeal dystonia, is a task-specific focal dystonia characterized by irregular and uncontrolled voice breaks that interrupt normal speech flow and effortful phonation [1–3]. There are, broadly speaking, two different types of SD based on the predominant spasms present: adductor SD (AdSD) and abductor SD (AbSD), with AdSD being more common than AbSD. The former is typified by adductor spasms causing choked, harsh voice breaks, especially on vowels and voiced phonemes, while the latter is characterized by hyperabduction of the vocal folds leading to prolonged voiceless consonants [3, 4] (Table 16.1). In some instances, both types of SD can occur in the same patient.

First accounts of SD hypothesized a psychosomatic cause for the pathogenesis of SD. This changed in 1960 when Robe et al. postulated a central nervous system (CNS) etiology [5]. Since then, environmental, genetic, and neurologic risk factors have been proposed.

Table 16.1 Differences between adductor and abductor spasmodic dysphonia

Adductor spasmodic dysphonia	Abductor spasmodic dysphonia
"Sentences loaded with voiced segments will worsen symptoms"	"Difficulty with voice onset following voiceless sounds"
Intermittent glottal stops (vowel breaks) in vowels on voiced sentences	Intermittent breathy breaks in voiceless consonants before vowels in sentences
Strain-strangled, effortful, tight voice quality	Symptoms most evident during connected speech
Patient report of speaking effort	Few symptoms on prolonged vowels
Symptoms reduced during whisper	Intermittent abductor spasm of the vocal folds or arytenoids during speech
Intermittent vocal fold or arytenoid hyperadduction	

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Epidemiology

SD is a rare clinical condition. Prevalence estimates vary between 1 in 100,000 and 2.9 per 1,000,000 persons [6, 7]. Roughly two-thirds of all patients affected are female, predominantly in their middle decades of life [1, 8]. Several case series have identified a range of female predominance between 62% and 80% [8–12] and a mean onset between 45 and 51 years of age [8, 10–12]. AdSD occurs more frequently than AbSD, with reported AdSD percentages ranging from 82% to 96.6% [8, 9, 12]. Vocal tremor can also coexist with SD and has been described as occurring in 29–55% of SD patients [8, 13] with a slightly higher incidence in females noted by one study [8].

Frequently described risk factors include a personal or family history of cervical dystonia or tremor [8, 13], previous sinus or throat infections, mumps or rubella infections [12], extensive voice use, and stress [14]. The link between viral illnesses and neurological sequelae is established in other diseases such as Ramsay Hunt syndrome, virus-induced vocal fold paralysis, and long-term neurological deficits following meningitis or encephalitis, but not as yet found in SD [12, 15]. Controlled epidemiological studies are needed to identify genetic and environmental risk factors for SD. Such findings might help to identify "at-risk" patient populations for SD and might eventually contribute to the diagnosis of SD.

Genetics

There has been significant growing interest in the possible association of genetic factors with the development of SD. This is in part due to accessible genetic testing and recent evidence that certain polymorphisms in generalized dystonia-causing genes can affect the risk of developing focal or segmental dystonias [16]. Four different genes have been found to be related to familial dystonias with varying degrees of dysphonic features: *TUBB4A, THAP1, TOR1A,* and *GNAL.*

The *TUBB4A* gene is responsible for tubulin beta-4a chain proteins, which are major components of microtubules. *TUBB4A* mutations can lead to atrophy in the basal ganglia and cerebellum. This gene has been shown to contribute to an autosomal-dominant dysphonia that has a "whispering" voice quality and is distinct from the sporadic forms of AdSD and AbSD [17].

The *THAP1* gene regulates endothelial cell proliferation. Its mutation can lead to a generalized form of dystonia, DYT6, that frequently has laryngeal features [16].

TOR1A mutations can lead to a different form of generalized dystonia that frequently manifests in childhood or early adulthood [16].

GNAL encodes Gαolf, a G protein (guanine nucleotide–binding protein) that mediates odorant signaling in the olfactory epithelium. Although the G protein subunit Gαs is the predominant stimulatory G protein subunit in the brain, Gαolf replaces Gαs in striatal medium spiny neurons and couples with dopamine type 1 receptors. Gαolf is also expressed in striatal cholinergic interneurons. Various *GNAL* mutations have been found in families with primary torsion dystonia, *DYT25* [18].

One study examined *TUBB4A*, *THAP1*, and *TOR1A* in 86 patients with SD and found that none had mutations in these three genes, although two patients (2.3%) had novel/rare variants of the *THAP1* gene [16]. Another study of 57 patients with SD examined *TUBB4A, THAP1, TOR1A,* and GNAL and found that one patient with SD but without *DYT25* was a *GNAL* mutation carrier, indicating that *GNAL* mutation may represent a rare genetic factor contributing to SD risk [19]. These studies suggest that further work is needed. As with other forms of dystonia, there may be sporadic and genetically determined types of SD. The genetic patterns may become more apparent with further genetic research.

Pathophysiology

Most recent evidence supports the idea that SD is a focal dystonia affecting primarily the laryngeal musculature and is task specific, i.e., only evident during certain types of speech [20]. Three differ-

ent neurological mechanisms have been proposed in the pathophysiology of SD: loss of cortical inhibition, sensory processing abnormalities, and neuroanatomical and neurophysiological differences from normal [1–3].

Loss of Cortical Inhibition

Research on other focal dystonias, such as cervical dystonia, focal hand dystonia, blepharospasms, and oromandibular dystonia, has demonstrated reduced cortical inhibition when transcranial magnetic stimulation is used to measure short-interval intracortical inhibition (SICI) and cortical silent periods (CSPs) [21]. Samargia et al. found reduced CSP in the masseter and first dorsal interosseous muscles in patients with AdSD when compared to controls [22]. As unaffected muscles also seem to demonstrate shorter CSPs in SD, this might suggest a GABA-ergic dysfunction. One case report indicated reduced voice symptoms in neuroleptic-induced dysphonia following administration of a GABA antagonist, clozapine [23]. A questionnaire study in an SD patient registry found reduced symptoms reported following the consumption of alcohol in 55.9% of patients [24].

Sensory Processing Abnormalities

Sensory processing disturbances have been found in patients with SD when compared to controls on visual temporal discrimination testing [25]. Patients with SD required longer intervals between two flashing lights to be able to discern the difference between the two. These were similar findings of impaired somatosensory temporal discrimination in SD to those previously found in cervical dystonia [26].

Studies of sensorimotor reflex inhibition for the laryngeal adductor response to electrical stimulation of laryngeal sensory nerves showed reduced central inhibition in AdSD [27] and AbSD [28]. Similar abnormalities in blink reflex conditioning were found in patients with SD [29].

Neuroanatomical and Neurophysiological Differences

Neuroimaging studies have found neuroanatomical and neurophysiological differences from healthy controls in patients with SD that pertain to the pathophysiology of SD. Functional magnetic resonance imaging studies have shown increased activation in the primary somatosensory cortex, insula, and superior temporal gyrus during symptomatic and asymptomatic tasks and decreased activation extent in the basal ganglia, thalamus, and cerebellum during asymptomatic tasks in AdSD and AbSD [30]. Increased activation intensity in SD patients was found only in the primary somatosensory cortex during symptomatic voice production, which correlated with AdSD symptom severity [30]. In another study, diffusion tensor imaging of white matter tracts in a group of AdSD patients and a neuropathological investigation in a single case found altered microstructural integrity along the right genu of the internal capsule of the corticobulbar tract [31]. Deficits along these tracts could interfere with neural control between cortical and subcortical brain regions that are essential for voluntary voice production (Fig. 16.1) [1, 31].

Diagnostic Considerations in SD

Diagnosis of SD can be difficult given the complex symptom presentations and lack of awareness among clinicians. Diagnostic difficulties can lead to significant delays in treatment, with one study reporting delays up to 4.5 years [32]. Since this disorder is not common in the general population, many clinicians, including otolaryngologists and speech-language pathologists (SLPs) not specializing in voice disorders, are unfamiliar with the disease. Therefore, diagnostic teams should ideally include a multidisciplinary team of otolaryngologists, SLPs, and neurologists [33]. While the inclusion of a neurologist in the multidisciplinary team is not universal, some advocate the addition of a neurologist with special interest in dystonias to help rule out other neurologic disorders since there is an increased incidence in this patient population.

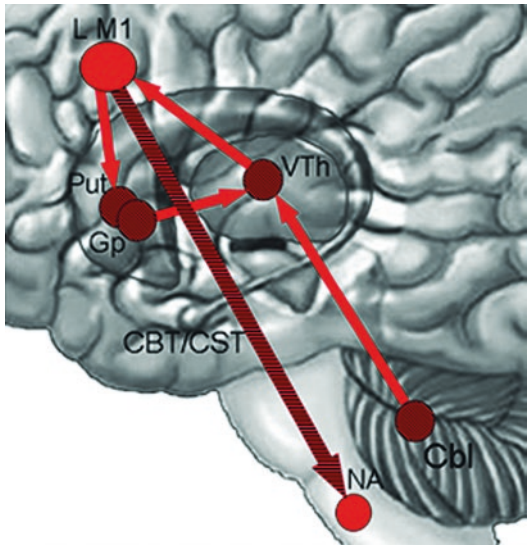

Fig. 16.1 Neural network of voluntary laryngeal control: LM1 (laryngeal motor cortex) to phonatory motor nuclei (nucleus ambiguus, NA), descending via the corticobulbar/corticospinal tract (CBT/CST). Cbl cerebellum, Gp globus pallidus, Put putamen, VTh ventral lateral thalamus. (Adapted from Simoyan et al. [31], with permission Oxford University Press)

Diagnosis of SD can still be quite difficult even when a multidisciplinary team is used. A recent multicenter study across four voice centers specializing in SD examined classification agreement for voice disorders including AdSD, AbSD, vocal tremor, and MTD based on reviewing voice and nasolaryngoscopy video recordings of 178 patients without standardized criteria [34]. There was poor agreement between specialists regardless of profession (otolaryngology, speech-language pathology, or neurology with special interest in voice) or whether specialists were from the same or different voice centers. As a result, a four-stage Delphi method was employed to determine group consensus on criteria for classifying the various voice disorders among 46 specialists in SD across the United States [34]. There was good agreement on the top features for AbSD, "intermittent breathy breaks" (97%) and "symptoms most evident in speech" (76%); however, there was relatively low agreement on features for AdSD, "intermittent glottal stops" (53%) and "patient report of speaking effort" (47%) [34]. Thus, there seems to be a better agreement on the features of AbSD than AdSD. Based on the results, a multidisciplinary group consisting of 12 specialists from four voice centers was able to develop a spasmodic dysphonia attribute inventory (SDAI), where a small number of attributes were selected to help identify each disorder [34]. The main attributes selected for AdSD and AbSD can be seen in Table 16.1 [34].

The primary technique for diagnosing SD includes a combination of speech examination and transnasal laryngoscopy. In 2008, Ludlow et al. recommended the addition of a screening questionnaire to help identify probable SD [3]. While the screening questionnaire is not considered standard of care, it is a tool that may help improve diagnostic accuracy and communication for both voice experts and nonexperts. This three-tiered approach (screening questionnaire, speech examination, and transnasal laryngoscopy) is described below.

Screening Questionnaire

Initial screening questions aim to determine the likelihood of an SD diagnosis and involve questions regarding the presence of effortful phonation, persistence or variability of symptoms, duration of symptoms (greater than 3 months), and if some tasks are less affected than speech (including shouting, crying, laughing, whispering, and singing) [34].

Speech Examination

The speech examination focuses on typical presentations of the SD variants and other possible confounding voice disorders, such as MTD or vocal tremor. Symptoms of SD are usually characterized by uncontrolled voice breaks due to laryngeal muscular spasms and complaints that phonation is effortful. The voice breaks are most prominent during connected speech. With both AdSD and AbSD, sentences performed in a shouted and/or whispered voice should elicit

fewer symptoms than in conversational speech at a normal volume [3].

In AdSD, voice breaks are evident during voiced vowel segments with a choked, strained characteristic, whereas in AbSD, breathy breaks occur following voiceless consonants preceding vowels [4] (see Table 16.1). During voice breaks in AdSD, quick glottic closures interrupt airflow and phonation, leading to breaks during vowels in speech. In AbSD on the other hand, prolonged vocal fold abduction during voiceless consonants interferes with the rapid onset of vowels resulting in breathy voice breaks during voiceless consonants (/h/, /s/, /f/, /p/, /t/, /k/). A rare form of SD is the mixed type, where patients display features of both AdSD and AbSD.

SD can be easily confused with muscle tension dysphonia (MTD). Additionally, MTD can sometimes be superimposed on SD. However, the vocal tasks in MTD do not alter between speech sounds (vowels or consonants) or among voice tasks such as shouting or singing. MTD patients tend to find all aspects of connected speech and vocalizations equally difficult. Such patients are usually responsive to voice therapy alone [35, 36]. In SD patients on the other hand, symptoms tend to be task-dependent, are most prominent during connected speech, and do not respond to voice therapy alone [37] (see Table 16.2).

Table 16.2 Differences between spasmodic dysphonia and muscle tension dysphonia

Characteristic	Spasmodic dysphonia	Muscle tension dysphonia
Glottal stops and vowels	Breaks on vowels	Equal symptoms on vowels and voiceless consonants
Shout/whisper	Less affected	Equally affected
Strained voice	Less strained at high frequency	Constant strain
Vocal fold tremor	May coexist	Not present
Laryngoscopy	Normal structure and symmetry at rest	Supraglottic compression obscuring vocal folds during voice production
Voice therapy	Poorly responsive	Responsive

Vocal tremor often coexists with SD, complicating diagnosis and management. It can be characterized by regular pitch and/or amplitude oscillation during a sustained vowel, visible laryngeal tremor on nasolaryngoscopy, tremor of the pharyngeal constrictor muscles, and possible additional bobbing of the laryngeal position during voicing [34]. This has been reported to occur in 29–54% of patients with SD [8, 13]. Large sex differences have also been reported by Patel et al., with 60% of females and 32.8% of males with AdSD having concurrent vocal tremor [8]. There is also some suggestion that botulinum neurotoxin (BoNT) injections are less effective in patients with concurrent vocal tremor [38].

Transnasal Laryngoscopy

Laryngoscopy is performed to rule out other structural/functional disorders that may be causing the patient's symptoms. Since SD is a disorder of connected speech, laryngoscopy should be performed transnasally to allow for visualization during connected speech. The vocal folds should appear normal during quiet breathing and have full range of motion during coughing and whistling [3, 39]. No masses or lesions should be evident. One study found that only 10% of video-only clips of patients with SD were correctly classified as SD, whereas 73% of audio-only clips were correctly identified, highlighting the importance of the clinical speech examination in the classification of SD.

Supportive Diagnostic Procedures

Occasionally, tremor or spasms may be difficult to visualize during adductor or abductor sentences. Either videokymography (Fig. 16.2) or high-speed videolaryngoscopy can help identify such movement [40]. These methods are not widely available in the clinical setting and currently mostly confined to research centers.

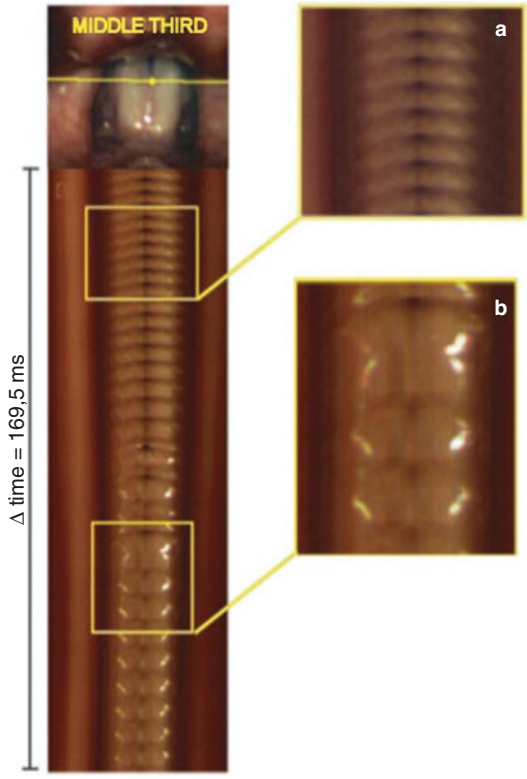

Fig. 16.2 High-speed videokymography of a patient with AdSD showing reduction in vibration amplitude and propagation of the mucosal wave, as well as longer duration of the closed phase compared to the total duration of the cycle, (**a**). Spasms can be observed in detail, (**b**). (From Tsuji et al. [40] with permission from Thieme)

Electromyographic (EMG) methods can be used to detect characteristic motor activation patterns in laryngeal muscles. Some suggest that the thyroarytenoid muscle is hyperactive in patients with SD [41]; however, others have found this to not be the case when compared to controls [42]. Increased muscle latencies have been found in patients with SD, as well as overactivity of the cricothyroid muscle in AbSD [43]. When combined, these EMG characteristics can be used to help identify the specific muscles contributing to SD and monitor treatment response [44]. However, EMG is invasive and can be time-consuming, and abnormal muscle activation is usually not restricted to a single muscle. A neurolaryngology study group in 2009 investigated the use of EMG in SD and concluded that there is insufficient evidence for EMG to be used as a diagnostic tool by itself [45].

Medical Management

Both medical and surgical treatments for SD have focused on denervation of one or more of the laryngeal muscles to reduce muscle force and the impact of muscle spasms on phonation. Such treatment approaches, however, may not alter the central neural control abnormalities causing muscle spasms but only reduce the impact of the CNS abnormalities on voice production.

Blitzer in 1985 reported early EMG results in patients with SD indicating an abnormality in the motor control system [46]. These findings were then followed by early attempts at reducing dystonic movements using BoNT injections into affected laryngeal musculature [47, 48]. BoNT inhibits release of acetylcholine from the presynaptic terminals into the neuromuscular junction, causing a temporary partial paralysis. These effects usually last between 3 and 4 months as reinnervation occurs and symptoms return [49]. BoNT remains the most commonly used treatment for SD today.

Several studies have shown improvement in acoustic, aerodynamic, and perceptual characteristics of voice after BoNT injection [50]. Table 16.3, adapted from Murry [2], outlines some of the acoustic and physiological changes that occur after BoNT injections. A study by Rojas et al. used acoustic voice analysis and found significant reductions in changes in the intensity contour and breaks in the fundamental frequency (fo) contour and reduced rhythmic variations in intensity and fo on a sustained vowel /a/. The patients reduced their Voice Handicap Index (VHI) scores at 30 days post-injection, but not 120 days post-injection [51]. Airflow rates also increase after BoNT injection, but these plateau after a few weeks [50].

Although the primary basis for improvement of AdSD symptoms after BoNT injection is due to reduction in local vocal fold muscle activation [52], there may also be some central effects

Table 16.3 Acoustic differences after botulinum neurotoxin (BoNT) injection

Parameter	Findings
Prolonged vowels	
Fo	Unchanged
Jitter	Lower post BoNT
Shimmer	Lower post BoNT
Harmonic/noise ratio	Improved post BoNT
Subglottic pressure	Lower post BoNT
Airflow rate	Higher post BoNT (normalized by ~2 weeks)
Voice breaks	Fewer post BoNT
Tremor	Reduced post BoNT in some cases
Speech sentences	
Mean *Fo*	Unchanged
Speech rate	Increased speech rate post BoNT
Airflow rate	Higher post BoNT
Voice breaks	Fewer post BoNT

Adapted from Murry [2], with permission

on the origin of muscle spasms after BoNT injection [53]. Following a unilateral thyroarytenoid muscle injection, spasms in contralateral, non-injected vocal fold muscles are reduced [54]. This potentially highlights the more complex neural network that is involved in the pathophysiology of SD. Previous basic research has shown that BoNT can be transported from the site of muscle injection centrally to motor neurons in the brain stem altering muscle spasms [55–57], although it is not known if this occurs in the human.

BoNT injections can either be unilateral or bilateral and are usually guided by EMG or nasolaryngoscopy [58]. Doses for BoNT injection may vary from 0.1 to 7.5 units per side [58], with median starting doses per side ranging from 0.25 to 1.5 units [59]. As reinnervation usually occurs in 3–4 months resulting in return of symptoms, repeat injections are required over time. A recent systematic review found that the duration of effect ranged between 14.66 and 18.03 weeks [58]. However, laryngeal EMG demonstrated that effects on motor unit physiology can still be present one year later. Based on a series of 900 patients with SD reported by Blitzer et al. [49], no clinical impressions indicated that there was a need to increase BoNT doses over time to achieve the same clinical benefit. While generally considered safe, a histopathological study of the effects on eye muscles after repeated injection for blepharospasm found muscular atrophy, scarring, and fibrosis in orbicularis oculi muscles [60]. For patients with AbSD, most laryngologists in the United States (79% in one study) advocate unilateral BoNT injections into one posterior cricoarytenoid muscle first. The reported mean starting dose was higher in AbSD patients at 5 units per side and ranged from 1 to 15 units. Most laryngologists (92%) prefer to target the posterior cricoarytenoid muscle alone [59].

In 2007 speech benefits of supraglottic injection were found in four AdSD patients with sphincteric supraglottic contraction of the ventricular fold obscuring the view of the vocal folds during phonation [61]. Using EMG control and a thyrohyoid approach, a traditional injection in the upper portion of the adductor muscles (the thyroarytenoid and lateral cricoarytenoid muscles) with BoNT did not result in significant voice benefit. In contrast when the oblique portion of the lateral cricoarytenoid muscles was injected with BoNT, all four patients demonstrated improved voice quality post-injection into the supraglottic region. More recently, ratings of voice function and patient completion of VHI scales were administered to evaluate the outcome of 198 supraglottic injections of BoNT injection into the false vocal folds, also termed supraglottic injection in AdSD patients [62]. The intended benefits are a reduced incidence of breathy voice after injection and the preservation of fo control during singing. Slightly higher doses were used for these injections (mean dose 6.94 units per side), with an average interval between injections of 15.6 weeks [62]. Most patients (74%) reported no post-injection voice decline that can sometimes accompany BoNT injections. However, given the wide variation in the extent of muscle fibers in the ventricular fold and the supraglottic region in the human larynx [63], the diffusion pattern of injection into muscle fibers in the supraglottic region is unknown.

Surgical Management

The first reported procedure for reducing vocal spasticity, reported in 1976 by Dedo, involved sectioning of the recurrent laryngeal nerve [64]. However, recurrence of symptoms was found 3 years later in a high proportion of patients [65] due to reinnervation of the thyroarytenoid muscle by the recurrent laryngeal nerve [66]. Since then, other surgical alternatives have been described, including thyroarytenoid myotomy, type 2 laryngoplasty, selective laryngeal adductor denervation-reinnervation, laryngeal nerve crush [58], and extensive avulsion of the recurrent laryngeal nerve on resection [67, 68].

Tsuji et al. investigated using endoscopic neurectomy of the thyroarytenoid branch of the recurrent laryngeal nerve, combined with partial myectomy of the thyroarytenoid muscle using CO2 laser for patients with AdSD [69]. Neurectomy was performed by directing an electrocautery tip between the perichondrium of the thyroid cartilage and the fasciae of the lateral cricoarytenoid and thyroarytenoid muscles [69]. A significant improvement in the Voice Handicap Index (VHI) was found postoperatively (mean preoperatively, 99; mean postoperatively, 24) in a cohort of 15 patients. Similar results were reported by Gandhi et al. in 2014, with an improvement of VHI noted from 70 to <25 [70].

Type 2 laryngoplasty has also been described. A midline thyrotomy is performed and the edges are separated between 2 and 5 mm, either with a titanium bridge [71] or with a T-shaped Silastic shim [72]. In a study by Sanuki et al. in 2017 of 47 patients with AdSD, 69% of patients reported a reduction in glottal tightness, strangulated voice, and phonation difficulties [71]. VHI-10 scores improved from 26.8 to 9.4 and these changes were maintained up to 36 months [71]. Nomoto et al. in 2014 compared thyroarytenoid muscle myectomy with type 2 laryngoplasty and found no overall significant difference postoperatively, but scores for strangulation, interruption, and tremor were lower in the myectomy group [73]. Importantly, postoperative complications were significantly increased in the myectomy group, in particular breathiness, and these changes were irreversible [73]. Although laryngoplasty is considered reversible, extensive scar tissue can interfere with surgery.

In 1999, Berke et al. described a selective laryngeal adductor denervation-reinnervation (SLAD) surgery, whereby the thyroarytenoid branch of the recurrent laryngeal nerve is divided before insertion into the muscle and the sternohyoid or sternothyroid branch of the ansa cervicalis is used for thyroarytenoid reinnervation. It is believed that by reinnervating the muscle with a different nerve, the ansa cervicalis, spontaneous RLN reinnervation is less likely and spasms are less likely to recur in the majority of patients. Follow-up of 136 patients who underwent this type of surgery found that VHI-10 scores improved from a mean of 36.6 preoperatively to 14.27 postoperatively. Moderate to severe postoperative breathiness occurred in 20% of patients and appeared to be related to lateral cricoarytenoid myotomy [74]. In one case however, described by deConde et al. in 2011, SD symptoms recurred 9 years after SLAD surgery. This might have been due to progression of the focal laryngeal dystonia to a more regional dystonia involving motor neurons to the ansa cervicalis [75].

To date there have been no studies comparing the voice outcomes of BoNT with voice characteristics following various surgical interventions and it is not clear if surgery should be considered as an adjunct to BoNT or as an alternative. It is important to note that to date most surgical interventions have not been demonstrated to have permanent long-term benefits on voice in SD.

Frontiers

Pathogenesis

The pathogenesis of SD is still poorly understood and is likely multifactorial in nature. It can be viewed as a multiple-hit mechanism with some endogenous predispositions and environmental triggers combined to produce the SD phenotype.

Genetic screening for mutations known to produce various familial dystonias in SD patients

have only found mutation of *GNAL* in one patient with SD and some variants of *THAP1* in a couple of SD patients. In general, familial cases with SD are rare and most cases seem to be sporadic in nature. Further advances in identifying genetic factors in other types of dystonia may shed some light on additional genetic influences in SD.

Pathophysiology

Neuroanatomical and neurophysiological research has highlighted the complex neurophysiological nature of SD. SD is likely a complex neural network disorder involving basal ganglia, cerebellum, and cortical mechanisms, rather than one single neuroanatomical defect (see Fig. 16.1).

Experimental neurophysiological techniques using EMG of laryngeal muscles and transcortical magnetic stimulation to quantify the CSP have found that the period is shortened in patients with SD [76], and the CSP in hand muscles differentiates between SD and MTD [22]. The CSP could potentially be used as diagnostic adjunct and also to monitor central changes following BoNT therapy [77].

Previous evidence of dopaminergic dysfunction comes from case reports of the effects of antipsychotics such as haloperidol and dopamine antagonists causing acute laryngeal dystonic reactions [78]. A recent neuroimaging study using positron emission tomography quantified raclopride (RAC) uptake to examine striatal dopaminergic neurotransmission at rest, while producing sentences, and during finger tapping in SD patients. Compared to healthy controls, the patients had bilaterally decreased RAC binding to striatal dopamine receptors by 29.2% while speaking, but increased RAC in the bilateral striatum during asymptomatic tapping. Patients with more severe voice symptoms had greater RAC differences, and those with longer SD duration had a decrease in task-induced RAC. Decreased dopaminergic transmission during speech may be pathophysiological in SD, whereas increased dopaminergic function during unaffected task performance may be compensatory. These differences may represent neurochemical alterations in this disorder. Other results have highlighted the role of the thalamus and cerebellum in the pathophysiological processes of SD [53]. Any dysfunction along the laryngeal neural network could contribute to the occurrence of SD symptoms (see Fig. 16.1).

As previously highlighted, there may be underlying reduced cortical inhibition and GABA-ergic dysfunction in SD, evidenced by the benefit experienced by some patients taking clozapine or consuming alcohol [23, 24]. These pathways may offer potential treatment targets in the future.

Diagnosis

In cases where there still is not a definitive diagnosis following speech examination using SD sentences and nasolaryngoscopy, additional procedures may be available in the future. This is especially important, given the difficulty in diagnosing SD and the lack of objective testing. Automated acoustic analysis tools such as the cepstral spectral index of dysphonia (CSID) developed by Awan and colleagues can now be performed on connected speech which is most affected in SD [79, 80]. Such measures can be used to determine the severity of voice disorders. However, the automated tool was only able to achieve sensitivity of 67% and specificity of 64% in differentiating SD from MTD, indicating that it is a measure of dysphonia but not specific to SD [37]. Previous research by Rees et al. has demonstrated the value in using spectrographic features in SD. SLPs were able to correctly distinguish AdSD from MTD in 96% of cases using spectrograms [81].

Another approach used for the differentiation of SD from other voice disorders was the use of a telephone-screening interview. Experienced clinicians from the same voice center were able to correctly identify patients as having SD or voice tremor with 90% sensitivity and 95% specificity [82]. Further validation across multiple voice centers is required to determine if this approach could be used to screen patients for possibly having SD before scheduling them for clinical evaluation.

Treatment

Currently, the main treatment modality for SD involves BoNT injection and less frequently surgery. While patients with AdSD have an average benefit of 90%, AbSD patients only experience a 66% benefit [9]. Large-scale multicenter comparisons of quantitative and qualitative measures of immediate and long-term voice outcomes in SD patients following BoNT (as a gold standard) and each of the different surgical techniques is urgently needed for patients and clinicians to make informed treatment decisions.

Deep Brain Stimulation for Voice Tremor and Spasmodic Dysphonia

Deep brain stimulation (DBS) involves the surgical implantation of stimulating electrodes into specific brain regions such as the basal ganglia and thalamus. The electrodes stimulate in one region to alter the brain network dysfunction and improve symptoms. An example is bilateral stimulation of the subthalamic nucleus (STN) used for the treatment of dyskinesia in Parkinson disease. The stimulation does not alter the disease; it only alters the abnormalities in brain function to reduce symptoms. DBS in the globus pallidus internus (GPi) is now used in generalized dystonia but speech and voice difficulties may not benefit as much as walking. However, one study reported that a patient with adductor SD had a marked benefit [83].

Control of arm tremor can be benefitted by stimulating the ventral intermediate (Vim) nucleus of the thalamus bilaterally, and it was found to benefit voice tremor in two patients with both arm and voice tremor [84–86]. A similar approach was used in a patient with essential tremor and coincident AdSD undergoing deep brain stimulation (DBS) and investigated the effects on vocal function. The target of the DBS was the left thalamic ventral intermediate nucleus and ventral oralis anterior nucleus. They found significant improvements in the SD symptoms, both qualitatively and quantitatively, in the form of the voice-related quality of life and the Unified Spasmodic Dysphonia Rating Scale [87]. Interestingly, they did not find any benefit when the ventral oralis anterior nucleus was stimulated alone (palladial outflow), whereas the best clinical effects occurred when the ventral intermediate nucleus (cerebellar outflow) was stimulated. These are only single cases but suggest that this may be helpful in a few persons with voice tremor and SD by stimulating one part of the brain to reset abnormalities in the brain networks (see Fig. 16.1). However, great care must be taken as surgical implantation of electrodes in these small brain regions may injure the brain causing significant side effects such as slurred speech (dysarthria). Very refined stimulation techniques are needed to reduce side effects [88].

Summary

SD is a focal dystonia characterized by irregular and uncontrollable voice breaks. There are two types of SD, abductor and adductor SD, typified by different muscle spasms, leading to different voice symptoms.

SD is a rare clinical condition, with an estimated prevalence as high as 1 in 100,000. It predominantly occurs in females in their middle decades of life. Limited case series have indicated possible risk factors associated with the occurrence of SD, including a personal or family history of other types of movement disorders, previous viral illnesses, extensive voice use, and stress. While genetic testing has identified polymorphisms in other focal dystonias, only a *GNAL* mutation has been found in one patient with SD and variants in *THAP1* in a couple of cases. In general, most cases of SD appear to be sporadic. Only a few are familial and may be genetically determined. Other pathophysiological mechanisms have been identified, including sensory processing disturbances, reduced cortical inhibition, and neurophysiological increases in excitability in the primary somatosensory cortex. Few neuroanatomical abnormalities have been found, including white matter reduction in the right genu of the internal capsule. Overall, SD is likely a complex neural network disorder, rather than one single neuroanatomical defect.

Diagnosis of SD is frequently delayed and should involve a multidisciplinary team. Diagnosis involves speech examination, a diagnostic nasolaryngoscopy, and occasionally a screening questionnaire. However, there can still be poor agreement between voice specialists. This has led to the development of a score sheet to aid in the identification of SD and other voice disorders based on certain attributes, and validation and generalizability is still under investigation.

The mainstay of treatment of SD is BoNT injections into the affected muscle(s), which need to be repeated every 3–4 months to control symptoms. Surgical options include manipulation of the larynx, either by neurectomy/denervation, myectomy of the thyroarytenoid muscle, or thyroplasty. Experimental methods for future exploration include DBS and GABA antagonists.

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Essential Tremor

17

Julie M. Barkmeier-Kraemer, Elan D. Louis, and Marshall E. Smith

Introduction

Essential tremor (ET) is a chronic, progressive, and highly prevalent neurologic disease [1]. It is the most common abnormal form of tremor and among the more prevalent neurological diseases. Patients with this disease receive treatment from a wide variety of health professionals including general practitioners, internists, geriatricians, neurologists, neurosurgeons, speech-language pathologists, and otolaryngologists. As discussed below, the hallmark clinical feature of ET is a 4 to 12 Hz kinetic tremor (i.e., a tremor occurring during voluntary movements such as eating or writing), which occurs in the arms and hands and may spread over the lifespan to involve cranial structures (e.g., the neck, jaw, tongue, lips, soft palate, pharyngeal constrictors, and larynx).

Historically, humans have written about their tremors for several millennia, with general references to tremor found in the Edwin Smith Surgical Papyrus (c. 1600 BC). However, the term *essential tremor* was not used until 1874 when Burresi described an 18-year-old man who presented with severe, isolated action tremor [2]. In the early twentieth century, the term *essential tremor* appeared with increasing frequency within medical literature, and by mid-century, the core motor feature of ET, action tremor in the arms, and its familial distribution were well documented by treating physicians [2].

Clinical Presentation and Natural History

The onset of clinical disease in ET may occur at any age, although the majority of cases have an onset in their 60s, 70s, and 80s [1]. This being said, the disease is not restricted to advanced age as childhood-onset cases have also been described in the literature, with many of these having a familial form of ET [3].

As noted above, the central clinical feature in ET patients is kinetic tremor of the arms. This tremor may be apparent during a variety of common daily activities, including eating,

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drinking, and writing (Fig. 17.1) with functional consequences. Patients also often exhibit a postural tremor; this is elicited by asking them to hold their arms outstretched in front of their body. In general, the amplitude of the kinetic tremor is greater than that of the postural tremor [4]. The kinetic tremor has an intentional component in nearly two-thirds of patients. For example, during the finger-nose-finger maneuver of the neurological examination, the tremor may worsen when the patient approaches the target [5]. Some patients with ET also develop tremor at rest in the absence of other features of parkinsonism. Thus, while the sine qua non of ET is the kinetic tremor of the hands and arms, tremor phenomenology can be quite varied and complex. As such, kinetic tremor generally worsens with time with recent estimates indicating a median annual increase in tremor severity of approximately 2.0% [6]. Further, patients often experience progression of tremors over time occurring under different conditions (e.g., with intention, at rest) and in different regions of the body (e.g., neck, jaw, voice).

The most commonly represented form of ET is arm tremor, whereas the most common form of cranial tremor is head (i.e., neck) tremor with a varied prevalence range across studies of 15–55% [7]. Head tremor is more often a side-to-side, or "no-no," type, but sometimes is a "yes-yes" tremor. It can also acquire a mixed phenotype (e.g., multidirectional and/or rotatory) as the disease progresses. The other interesting feature of neck tremor is that it is strongly associated with female gender; that is, women with ET are severalfold more likely to develop neck tremor than are men [8–10]. Clinically, neck tremor of ET is a postural tremor and is observed while the patient is seated or standing and resolves when the patient's neck is at rest (i.e., while the patient lies down). Jaw tremor may also occur in patients with ET with a prevalence estimated to range from 7.5% to 18.0% [11]. Jaw tremor is predominantly a postural tremor (i.e., occurring while the mouth is held slightly open or during sustained phonation) or a kinetic tremor (i.e., occurring during speech). Voice tremor is also exceedingly common in patients with ET and must be distinguished from that of dystonic tremor [12]. Voice tremor may range in severity from mild and barely detectable to marked, with distortion of sound. Tremors affecting axial structures (i.e., neck, jaw, voice) are more common among patients with gait and balance issues [13].

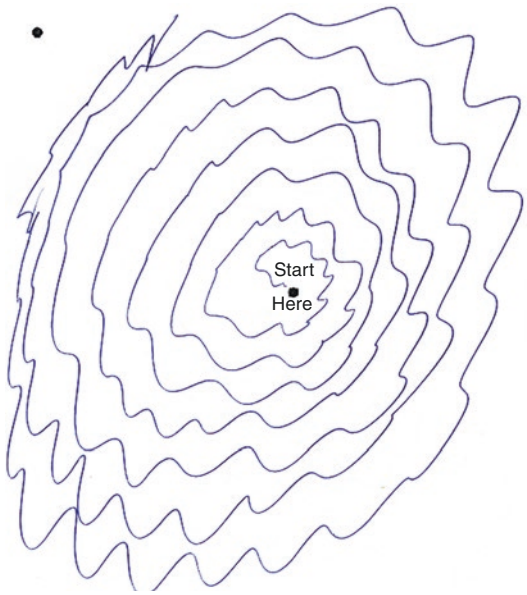

Fig. 17.1 Tremor on spiral drawing. An essential tremor patient's attempt to draw a spiral with their right arm. Tremor of moderate severity is present

In some instances, mild tremor of ET can be associated with significant functional disability. Thus, more than 90% of patients who come to medical attention report disability [14], and severely affected patients may be unable to feed or dress themselves [15].

While classically described as a tremor disorder, motor features aside from tremor have been described in ET patients. In numerous studies [16], postural instability and mild to moderate ataxic gait, beyond that seen in normal aging, have been demonstrated in patients with ET. In addition, subtle saccadic eye movement abnormalities have been observed in patients with ET [17]. These features support the notion that the cerebellum is centrally involved in disease pathophysiology.

The presence of a variety of nonmotor features in ET is also gaining wider recognition [18]. Numerous studies substantiate the presence of a range of such features occurring in excess in ET cases compared to age-matched controls.

These comprise cognitive features (including a full spectrum from mild cognitive difficulty to frank dementia), psychiatric features (including depression, apathy, anxiety, and personality characteristics), sensory features (hearing and possibly olfactory abnormalities), and other nonmotor features (e.g., sleep dysregulation) [18].

The diagnosis of ET is made by history and physical examination as there is no diagnostic biomarker, either serological or imaging. When arriving at a diagnosis, it is important to distinguish patients with ET from those with enhanced physiological tremor, drug-induced tremor, Parkinson's disease, and dystonic tremor. Studies indicate that 30–50% of "ET" cases have one or more of these other disorders, thereby underscoring the challenges in arriving at the correct diagnosis [19].

Epidemiology

The disease incidence has been estimated in one population-based study. Based upon cases ascertained from central Spain, the adjusted incidence among persons age 65 and older was 619 per 100,000 person-years [20]. That is, if one were to follow an ET-free cohort of 1000 persons aged 65 and older for 1 year, 6 would be expected to develop ET.

Establishing a precise prevalence has been challenging due to differences across studies in methods of case ascertainment and case definition. In a recent meta-analysis, the pooled prevalence was 0.4–0.9% (all ages), and the prevalence among persons age 65 and older was 4.6–6.3% [1]. The prevalence rises with age and reaches values in excess of 20% among those in their 90s. Through epidemiological studies, several risk factors for ET have been identified. Most reproducible among these are older age [1] and a family history of ET [21].

Etiology: Genetic and Environmental Risk Factors

On an etiological level, ET is generally considered to be a highly genetic disorder, as evidenced by the presence of numerous kindred with multiple affected members. A familial aggregation study demonstrated that first-degree relatives of ET cases are 4.7 times more likely than first-degree relatives of controls to develop ET [21]. Yet identifying underlying genes for ET has been a challenging task for a variety of reasons [22]. Recent discoveries linking Leucine Rich Repeat And Ig Domain Containing 1 (LINGO1), Fused in Sarcoma (FUS), and Teneurin transmembrane protein 4 (TENM4) to ET have met with some optimism, and large-scale efforts are currently underway to shed additional light on this area [23].

Environmental factors likely contribute to the etiology of ET as well. Twin studies show that concordance for ET in monozygotic twins was far lower than 100%; in one study it was 60% and in another it was 63% [24]. In terms of environmental factors, recent epidemiological studies have implicated several specific toxicants in ET such as β-carboline alkaloids (e.g., harmane, a highly tremorogenic dietary chemical) and lead [24]. As with studies of the genetics of ET, additional work is needed.

Pathophysiology

The pathophysiology of ET remains far from clear. For many years, ET was thought to result from abnormal brain pacemaking activity that originates in the inferior olivary nucleus of the medulla. This notion has little empirical support and is falling out of favor [25]. More recent studies have been able to identify a set of structural changes in the ET brain, most of which are centered on the Purkinje cells and connected neuronal populations within the cerebellar cortex (Fig. 17.2) [26]. This shift of attention to the cerebellum fits with data from a wide variety of neuroimaging studies indicating the presence of functional and metabolic abnormalities in the ET cerebellum as well as structural abnormalities in both the cerebellar gray and white matter [27]. The presence of cerebellar features on neurological examination in many patients (e.g., intention tremor, mild gait ataxia, saccadic eye movement abnormalities) lends further credence to these findings. Based on the nature of postmortem findings, including evidence of

Fig. 17.2 Pathology of essential tremor. A Bielschowsky-stained section of the cerebellar cortex (20×) of an essential tremor (ET) case reveals the presence of two abnormal swellings ("torpedoes") of the same Purkinje cell axon. Torpedoes are one of a myriad of structural changes observed in the ET cerebellum

Purkinje cell loss, it appears likely that this progressive, age-associated disease is degenerative in nature [26].

Voice, Speech, and Deglutition Signs and Symptoms

ET affecting axial structures can potentially impact speech and deglutition, depending upon the severity of involvement. To date, few studies have reported on the kinematic patterns of respiratory and speech structures in the same manner as limb tremor patterns have been studied in those with ET. Although feeding problems due to limb tremor are well documented, only one study in the literature directly addressed the underlying pathophysiology of symptoms of dysphagia in those with ET. The latter study used video fluoroscopic evaluation of deglutition to compare dysphagia findings between individuals with ET and typically aging adults [28]. The sole difference identified in those with ET was a slightly impaired esophageal bolus transit [28]. Despite the paucity of literature on the topic of ET and dysphagia, it is possible that individuals with severe involvement of the upper airway structures could experience difficulty with mastication and swallowing. Further investigation of dysphagia in those with ET is needed.

The association of ET with voice and speech problems has been predominantly reported in studies utilizing standard clinical methodology including patient self-report, auditory-perceptual ratings, endoscopic imaging, and acoustic measures of voice and speech. Individuals with ET affecting axial structures may report experiencing increased effort to produce intelligible speech [29, 30], or a shaky voice [31–34]. Approximately 30–40% of individuals with ET exhibit voice tremor resulting from involuntary oscillation of speech (e.g., respiratory, phonatory, and articulatory) structures [33–36]. Individuals diagnosed with isolated vocal tremor in the absence of tremor affecting the hands or head are referred to as having *essential voice tremor*, or EVT [33, 34, 37]. Of those diagnosed with vocal tremor associated with ET or classified as EVT, 90% are female [34, 38]. Individuals with ET and severe voice tremor have been shown to report significantly impaired voice function on the Voice Handicap Index (VHI) compared to individuals with Parkinson's disease or ET with mild voice tremor [12]. Thus, careful evaluation for determining optimal and effective treatment approaches for those with EVT or ET with vocal tremor can improve their ability to participate in activities of daily living. From this point forward, both forms of voice tremor (i.e., EVT and ET + vocal tremor) will be referred to as *ETVT*.

Voice and Speech Assessment

Auditory-perceptual characteristics of those with ETVT are described as a nearly rhythmic modulation of pitch and loudness that is optimally identified during sustained phonation of a vowel [35, 39, 40]. The perception of a shaky voice quality, or voice tremor during conversation may vary, depending upon the severity level of the ETVT [40]. That is, those with mild ETVT may sound normal during conversation or reading tasks. In contrast, those with moderate ETVT may exhibit perceptible voice tremor during production of some sentences or phrases where voicing is more consistent (e.g., "we mow our lawn all day") compared to sentences or phrases where voicing is interrupted (e.g., "Peter will keep at the peak"). Those with severe ETVT exhibit noticeable voice tremor across all speech tasks [40] and also have difficulty purposefully shortening voicing duration during staccato-like production of speech sounds or phrases [41]. Individuals with ETVT may also speak at a slower rate than typical for their age (e.g., 3 syllables per second compared to 5 syllables per second) [42]. Thus, clinicians should systematically evaluate voice and speech patterns across sustained phonation and connected speaking tasks and test whether individuals are capable of shortening voicing duration to determine contexts when voice tremor is improved versus worsened [31, 43].

Endoscopy is used to identify visible pharyngeal and laryngeal structures exhibiting tremor during quiet breathing and speech tasks. Determining the specific structures affected by ETVT is useful for linking audible voice and speech patterns and to determine optimal medical or behavioral treatment recommendations [44, 45]. For example, prior work showed that standard botulinum toxin (BTX) injections to intrinsic laryngeal muscles did not benefit individuals to the same degree when multiple structures of the upper airway exhibited tremor compared to those with tremor isolated to the larynx [44, 45]. Finally, individuals with mild ETVT capable of purposefully reducing voicing duration may benefit from behavioral treatment intervention alone, or supplemental to laryngeal BTX injection [31, 33, 46, 47].

Acoustic measurement of ETVT is useful for characterizing the rate and extent of pitch and loudness modulation and speaking rate and for comparing pre- and posttreatment outcomes (Fig. 17.3) [29, 31, 36, 42]. The rate of modulation of fundamental frequency (fo) and intensity (sound pressure level, or SPL) reported in individuals with ETVT ranges between 3 and 8 Hz [29, 31, 35, 36, 48]. The extent of modulation varies from 19 to 61% for SPL and between 3 and 17% for fo [29, 31]. An unpublished study also demonstrated measurable acoustic modulations of F1 and F2 in those with vertical laryngeal tremor or tongue, pharyngeal wall, and/or soft palate tremor [49].

Electromyography (EMG) can be used to identify the source of tremor within laryngeal musculature in those with ETVT [32, 45]. Laryngeal EMG is important for the diagnosis of ETVT as well as identification of the primary laryngeal musculature to target for treatment of voice tremor using BTX injection. Optimally, laryngeal EMG should be completed using multichannel hooked-wire electrode recordings from laryngeal muscles to compare and contrast their participation in voice tremor across pitch and loudness levels (Fig. 17.4).

Pharmacology and Medical Management

Patients may elect medical management approaches to improve their voice when voice tremor is severe enough to impair functional communication. The main medical management options at this time include medications and BTX injection [50]. Medications for voice tremor are the same as for ET and include propranolol and primidone [51]. Methazolamide was also studied in the 1990s for its effect on voice tremor. Though an early study had promising results [52], a placebo-controlled study that tracked patient-based and acoustic measures did not [53].

Propranolol has been used for many years to treat ET. Overall, the effect of propranolol on axially based tremors (head, neck, voice) tends not

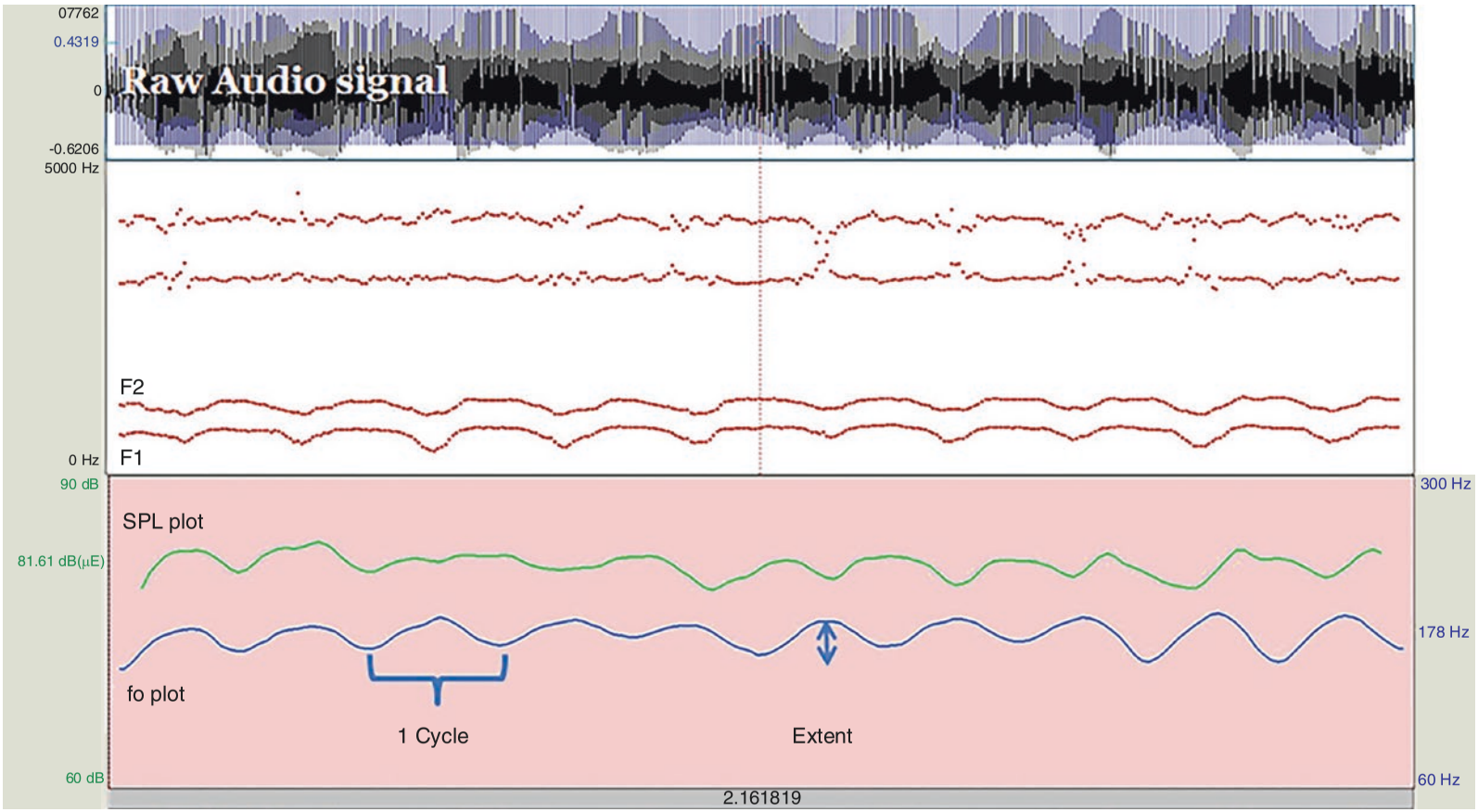

Fig. 17.3 Acoustic measures of essential tremor and vocal tremor (ETVT). Raw audio signal from a 2.1-second segment of a recording from an individual with ETVT. The *middle window* displays a plot of the first 4 formants with formants 1 and 2 (F1 and F2) *shown at the bottom* with a regularly recurring modulation associated with observed movements of the base of tongue and posterior pharyngeal wall. The sound pressure level (SPL) and fo plots also show a rhythmic modulation that begins in phase and eventually transitions to being out of phase. The rate can be measured from the valley to valley or peak to peak of each cycle plotted. Extent is measured from the maximum to minimum range of modulation for each cycle (maximum – minimum/maximum + minimum × 100 = %). SPL values are converted into pascals to transform the logarithmic values into a more linear unit before calculating extent

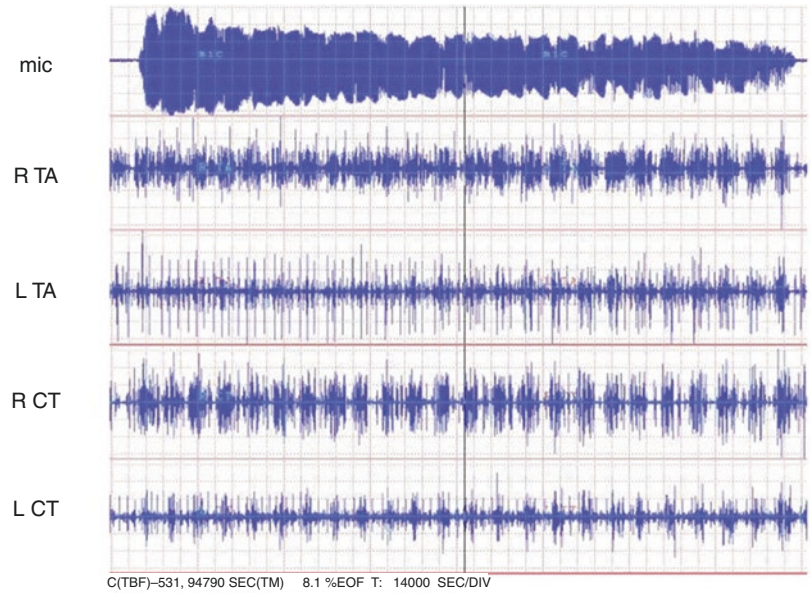

Fig. 17.4 Multichannel hooked-wire electrode electromyography (EMG). This figure provides an example of a multi*channel hooked-wire electrode EMG recording* from 4 intrinsic laryngeal muscles. Note the association between expansion and compression of the raw audio signal and associated increased and decreased modulations of intrinsic laryngeal muscle EMG patterns. Mic microphone signal, or raw audio display, RTA right thyroarytenoid, LTA left thyroarytenoid, RCT right cricothyroid, and LCT left cricothyroid muscles)

to be as beneficial as for limb tremor. Two recent studies compared propranolol and laryngeal BTX injection treatment outcomes in patients with ETVT. One study used a crossover design to evaluate the response of 18 patients with ETVT to both propranolol and BTX injection [54]. The average improvement in voice-related quality of life (VRQOL) measures was 9.3 with propranolol; one-third of participants scored greater than 10. In contrast, the average improvement in VRQOL score after BTX injection was 22.0. A second study compared five participants with ETVT to ten individuals with dystonic tremor as per clinician auditory-perceptual assessment [55]. Participants completed a randomized crossover design with propranolol and BTX injection. Those with dystonic tremor responded favorably to BTX injection but not propranolol. Those with ETVT did not have a significant response to either treatment, although the authors acknowledged the low sample size of ETVT participants as a potential factor.

Primidone for ETVT was recently studied in a retrospective review [56]. Fourteen of 26 individuals with ETVT (54%) reported voice improvement with primidone. Drug side effects were experienced by nearly three-fourths of the participants, causing discontinuation of therapy in 52%. Despite the side effect profile, the authors advocated primidone as an alternative to BTX injection. The study outcomes have limited generalization as 30% of participants had another coexisting voice disorder.

BTX injections for ETVT have been used for several years to reduce voice symptoms. In one study, voice symptoms in an individual with ETVT reportedly improved after 16 weeks of bilateral administration of 2.5 units of botulinum toxin into the TA muscles [57]. In the same year, these authors published a prospective study comparing unilateral and bilateral BTX injections in individuals diagnosed with ETVT. In that study, only 3 of the 10 patients receiving bilateral injections and 2 of 9 patients receiving unilateral injections experienced improvements in the acoustic measurements of ETVT. The authors also reported that 8 of the 10 patients requested a reinjection of the BTX because of vocal effort;

however, the authors emphasized the need for further studies to clarify the subgroups likely to benefit from this treatment [58]. The beneficial effects of laryngeal BTX injection have been documented by others [59]. A recent study suggested further improvement in laryngeal BTX outcomes in those exhibiting vertical laryngeal, horizontal laryngeal (i.e., abduction/adduction vocal fold tremor), or a combination of both forms of tremor [60]. Individuals with vertical laryngeal tremor demonstrated improved outcomes with BTX injection to the laryngeal strap muscles. Injection of the interarytenoid muscle in those with horizontal tremor also exhibited improved outcomes [61]. The differences in voice response to vocal fold BTX injection between spasmodic dysphonia (SD) and ETVT has also been studied [62, 63]. Those with ETVT respond to a lower dose of BTX than those with SD. Also, the magnitude of self-reported voice improvement after injection is not as pronounced for ETVT as for those with SD.

Frontiers in ETVT

Future directions in clinical evaluation and treatment of ET would greatly benefit from improved measurement and profile-based comparison of the kinematics and associated neural pathways associated with ETVT compared to those with ET only. Such information would enable insights regarding potential differences in ET manifestations that affect axial structures compared to the larger representation of those with involvement primarily affecting the limbs. It is also possible that research linking structural kinematic patterns and corresponding acoustic output patterns would lead to noninvasive acoustic recording methods for diagnosing midline cranial structural contributions to ETVT.

Future treatments for ET and ETVT on the horizon reflect advancements in technology as well as pharmaceuticals. Advancements in the use of deep brain stimulation (DBS) show promise for addressing voice problems in individuals with ETVT through unilateral versus bilateral electrode placement into the ventral intermediate nucleus (V_{im}) [64, 65] and the caudal zona incerta of the posterior subthalamic region to reduce voice tremor symptoms [66]. At present, those currently treated using DBS placement with ETVT exhibit severe limb tremor. However, future research in this area may lead to advanced forms of DBS technology to warrant use with individuals with a range of ETVT severity.

Recent research addressing pharmacological approaches are on the horizon that may also prove helpful in treating ET and associated impact on communication problems that result [67, 68]. Although currently implemented with individuals diagnosed with dystonia and tremor, insights gained from neural imaging and pharmaceutical outcomes may lead to new directions in developing systemic medications that better manage tremor affecting speech structures [69].

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Cerebrovascular Accident

18

G. Todd Schneider and Sheryl A. N. Maier

Introduction

Strokes cause significant post-event morbidity including impaired mobility, intellectual deficits, impairment in communication, and dysphagia. These effects have both functional and social implications for patients and their families. A multidisciplinary team is generally employed to manage these complex issues including neurologists, physical therapists, occupational therapists, physical medicine and rehabilitation physicians, otolaryngologists, and speech-language pathologists. In this chapter, we will discuss the accurate assessment and efficient management of communication and swallow deficits in these patients.

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Epidemiology

Stroke

In the United States, approximately 795,000 strokes occur per year with 77% representing first time strokes. Stroke is now the fifth leading cause of death in America, accounting for 140,000 total deaths per year. Due to improvements in post-stroke care and management of modifiable risk factors, death rates of stroke have declined 38% since 2000 but with diminishing returns in the most recent years [1]. The cost of stroke in the United States is estimated at $34 billion dollars per year including medical costs and lost productivity, making stroke the leading cause of long-term disability [2]. Second to hemiparesis, communication and swallow disorders are most common in persistent deficits in stroke patients [3].

Dysphagia

Dysphagia affects an estimated 37–78% of stroke patients depending on the timing and extent of testing [4]. However, on average, the incidence approaches 50% [5]. While 50% of post-stroke dysphagia spontaneously resolves within 2 weeks [6], 15% will have dysphagia which persists beyond 1 month [7]. When post-stroke dysphagia is present, it becomes a potent predictor of both overall clinic outcome and

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need for posthospital institutionalization [8]. Patients with post-stroke dysphagia are at three times the risk of developing pneumonia and up to 11 times the risk of pneumonia with evidence of aspiration on objective swallow testing [9]. Post-stroke pneumonia occurs in 10–40% of patients and is associated with death or significant disability [10].

Aphasia, Dysarthria, and Dysphonia

Communication disorders occur in roughly 33% of stroke patients, who in turn have a higher incidence of depression and social isolation, can perform fewer activities of daily living, and have poorer overall long-term outcomes [11–14]. Dysarthria affects 24–42% of all patients with stroke and is strongly correlated with physical weakness at the onset of stroke [3, 5]. Aphasia is present in 30% of all stroke patients and seen most commonly with advanced age, female gender, more severe stroke, atrial fibrillation, and cardioembolic etiology [15–18]. In a 5-year review of a large stroke registry, the coincidence of post-stroke dysphagia, aphasia, and dysarthria was found to be 10%, and the most significant coincidence was between dysphagia and dysarthria at 28% [5]. Finally, dysphonia post-stroke is usually secondary to a vocal fold paralysis due to a lesion in the lateral medulla which only accounts for 7% of all ischemic strokes [19].

Pathophysiology

Stroke Etiology

Stroke refers to central neurologic damage from a vascular cause with evidence of end-organ damage on imaging, symptoms which persist beyond 24 hours, and typically considered irreversible. The area of the brain affected by the vessel occlusion has an "ischemic core" which will suffer irreversible rapid damage if perfusion drops to <10 ml/100 g/min. Surrounding the ischemic area, the "penumbra" contains hypoxic and functionally inactive neurons, which may recover function if vascular flow improves via collateral vessels or antithrombotic therapies (Fig. 18.1). Strokes can be classified as ischemic (80%) or hemorrhagic (20%). Hemorrhagic causes of stroke include either rupture of intracerebral of arterioles or aneurysms leading to a subarachnoid hemorrhage. Ischemia is the most common cause of stroke and can either be thrombotic, cardioembolic, or due to systemic hypoperfusion secondary to cardiac failure or massive blood loss. Thrombotic strokes can be classified as either "large vessel," due to atherothrombosis of the cerebral, vertebral, or carotid arteries, or "small vessel/lacunar," due to lipid-hyaline buildup in penetrating vessels secondary to hypertension.

Dysphagia

The neural control of swallow is complex and may be due to lesions in the supratentorial or infratentorial regions of the brain (Fig. 18.2). Supratentorial control of swallow is most commonly associated with the corticobulbar tracts which project from the parietal and temporal lobes to the brainstem. Parietal lobe lesions have been correlated with pharyngeal residue, diminished cough response, and aspiration [20], whereas temporal lobe damage has been associated with oropharyngeal residue and impaired swallow response from impaired temporal sequencing of swallow [21]. The role of the subcortical structures, thalamus and basal ganglia, in post-stroke dysphagia remains unclear but have been correlated with prolonged oropharyngeal transit, delayed onset of laryngeal closure, and increased aspiration risk compared to cortical strokes [22–24]. While the corticobulbar tracts descend from both sides of the cortex, right hemisphere lesions have been associated with more severe dysphagia, pharyngeal dysfunction, and aspiration, whereas oral phase dysphagia results from damage to the left cerebral hemisphere [25, 26]. Despite these findings, the laterality of the control of swallow can change during recovery from a hemispheric stroke likely due to cortical neuroplasticity [27].

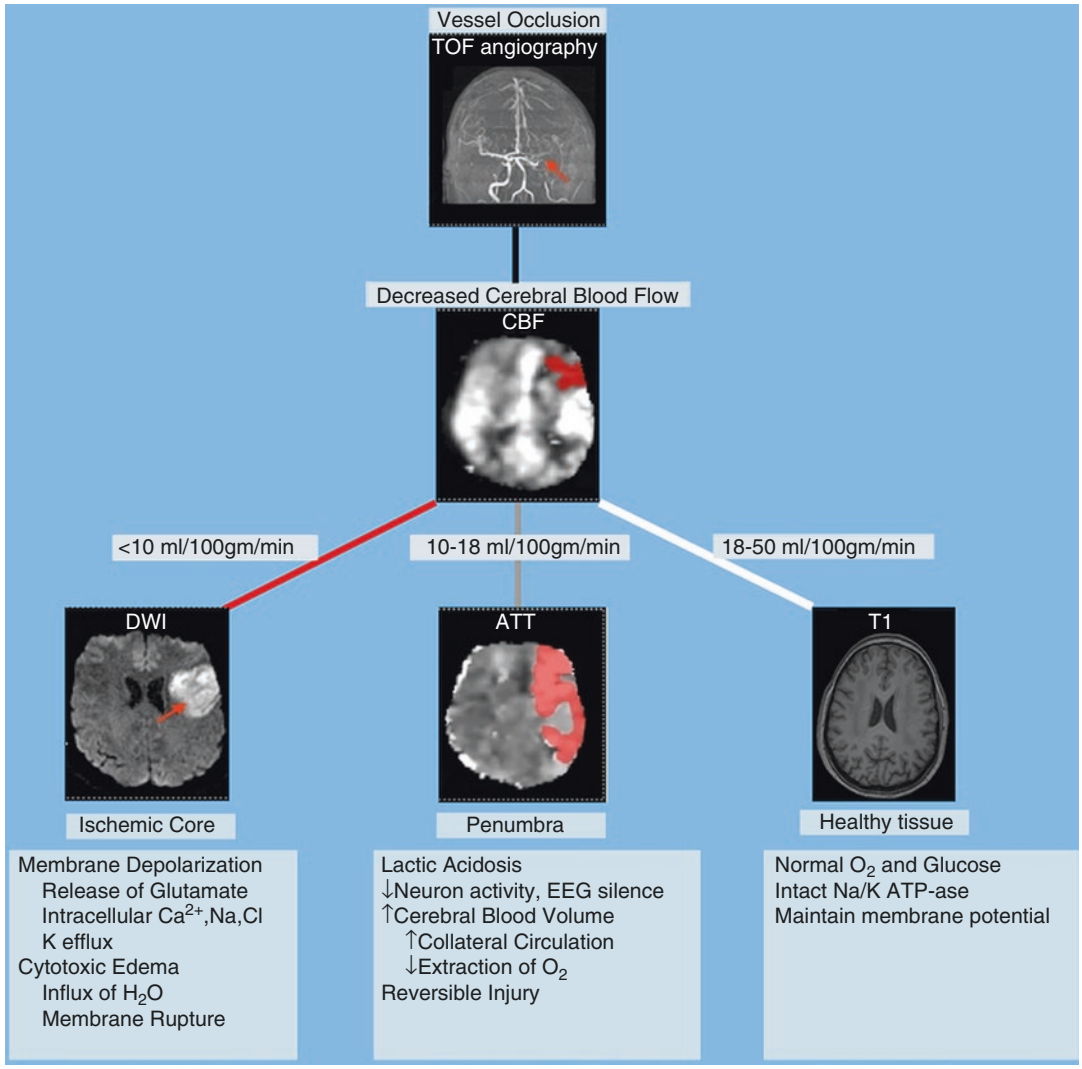

Fig. 18.1 Ischemic core and penumbra. During an ischemic stroke, a vessel is occluded as seen by the *red arrow* on angiography of middle cerebral artery infarction. Cerebral blood flow is measured in this setting on the image labeled CBF with impaired flow *highlighted in red* in this image. This leads to three tissue types: ischemic core, penumbra, or the healthy tissue. When blood flow is <10 ml/100 g/min, the tissue becomes ischemic as seen on the diffusion-weighted image (DWI) on MRI as marked by the *red arrow*. Neurons in this area are irreversibly damaged during stroke secondary to hypoxia-induced cytotoxic edema and necrosis. The penumbra represents the area of tissue with reversible ischemia with a blood flow between 10 and 18 ml/100 g/min. This area is represented by the red area on the arterial transit time (ATT) on perfusion-weighted MRI. Mismatch between the DWI and perfusion-weighted MRI defines this area. During ischemia, neurons in the penumbra have decreased metabolic activity and may survive, depending on the severity of the stroke. Normally perfused brain tissue has a blood flow rate of 18–50 ml/100gm/min as seen on this T1-weighted MRI of the same patient ("ischemic core and penumbra" is a derivative of "fneur-04-00060-g002" by Macintosh, BJ. Used under CC BY 3.0)

The infratentorial region includes the medulla, pons, midbrain, and cerebellum. These areas are perfused by the posterior circulation from the vertebral, cerebellar, and basilar arteries. The most common posterior circulation stroke involves occlusion of the posterior inferior cerebellar artery (PICA), historically known as Wallenberg syndrome. Dysfunction of the

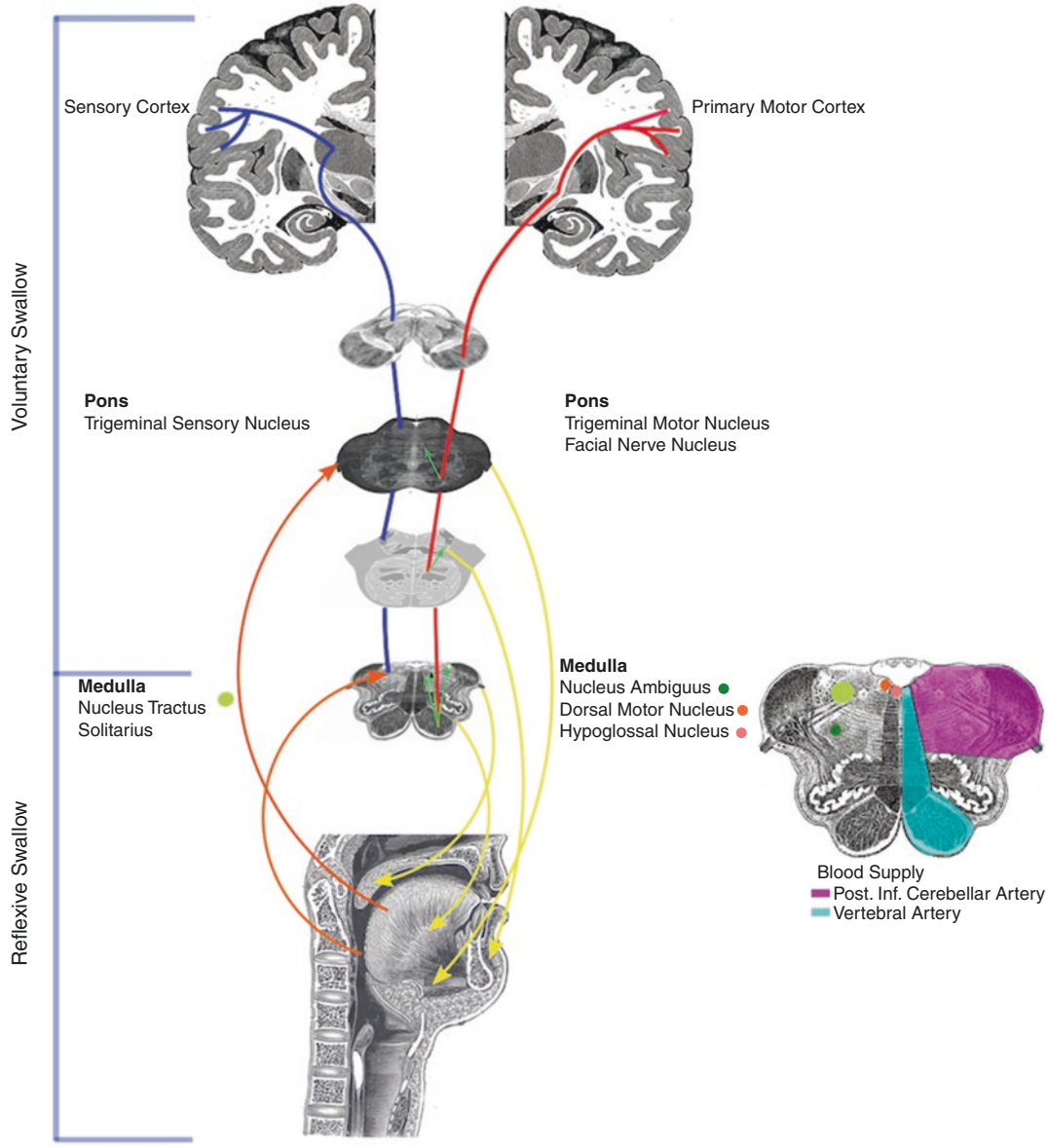

Fig. 18.2 Neuroanatomy of swallow. Swallow function is represented bilaterally but is only represented unilaterally for clarity in this figure. Voluntary swallow function begins with neurons in the primary motor cortex at the facial and oral distribution of the homunculus near the lateral fissure. These fibers descend via the corona radiata and genu of the internal capsule and into the midbrain via the cerebral peduncles as the corticobulbar tract (*red*). These descending fibers to the brainstem allow for voluntary cortical control of swallow. In the pons, fibers terminate on both the trigeminal motor and facial nerve nuclei (*green arrows*). In the medulla, fibers of the tract synapse on the nucleus ambiguus, dorsal motor nucleus of the vagus, and hypoglossal nucleus (*green arrows*). The brainstem nuclei then project lower motor neurons to muscles of mastication, facial expression, oral cavity, oropharynx, and larynx (*yellow arrows*). Sensory information is then fed back to the brain stem via the glossopharyngeal, vagus nerves to the nucleus tractus solitarius in the medulla, and the trigeminal sensory nucleus in the pons (*orange arrows).* A reflexive swallow loop exists between the nucleus tractus solitarius and the nucleus ambiguus, allowing for involuntary swallow. The brainstem sensory information ascends via the reticular formation to the ventral posterior medial nucleus of the thalamus and then to the primary sensory cortex. Lesions along this course can cause dysphagia; however, the lateral medulla is the most common brainstem area correlated with dysphagia due to the numerous brainstem nuclei in the distribution of the posterior inferior cerebellar artery ("neuroanatomy of swallow" image is a derivative of *Gray's Anatomy* plates 695, 701, 711, 717, and 994 by user Arcadian under Public Domain and is a derivative of "Lower Pons Horizontal KB.svg," by user mcstrother under CC BY 3.0)

lateral medulla causes contralateral truncal and extremity sensory deficits, as well as ipsilateral Horner's syndrome and cerebellar ataxia. Cranial nerve deficits from this syndrome cause vertigo and facial numbness. Dysphagia occurs due to damage to the nucleus ambiguus and dorsal motor nucleus which carry pharyngeal, laryngeal, and palate motor and sensory information important for voice and swallow function (see Fig. 18.2). In a meta-analysis of 656 infratentorial ischemic strokes, dysphagia was correlated with damage to the medulla and pons, but not to the cerebellum or midbrain. The relative risk of dysphagia, using the cerebellum and midbrain data as control, was highest in the lateral medulla, followed by the medial medulla, and pons [28]. These areas contain the corticobulbar tracts and lower brainstem nuclei responsible for both voluntary and reflexive swallow [29]. While cerebellar activation has been seen on fMRI studies of swallow, damage to this region has not been significantly correlated with post-stroke dysphagia symptoms.

Aphasia

Aphasia is a group of disorders of speech comprehension and formulation most commonly caused by stroke affecting the cerebral cortex. The Broca doctrine (1865) asserted that right-handed patients had a left cerebral hemisphere dominance for language and that the reverse was true for left-handed patients. However, there have been 180 reported cases in the modern literature of exceptions to this rule [30]. The language deficits seen in aphasia correlate to the region of the cortex damaged by a stroke (Fig. 18.3). The subtypes of aphasia include expressive, receptive, global, and conductive. However, controversy exists on how these subtypes are organized and assessed; therefore, accurate incidence of each is currently unclear. Location-based categorization of the aphasia subtypes relies on the function and connections between the Broca area (BA) and the Wernicke area (WA). Expressive aphasia is caused by damage to BA, the inferior frontal gyrus and inferior frontal operculum, due

Fluent		Language Comprehension	Repetition of words	Vessel Territory	Lesion Location	
1	Conduction Aphasia	Intact	Impaired	Inferior division of Left MCA	Inferior Parietal	
2	Anomic Aphasia	Intact	Intact	Small vessel disease	Peri-Sylvian Fissure	
3	Receptive Aphasia	Impaired	Impaired	Posterior Branch of MCA	Wernicke's Area	
4	Transcortical Sensory Aphasia	Impaired	Intact	Left Carotid Artery	Inferior to Sylvian Fissure	
Non-Fluent						
1	Expressive Aphasia	Intact	Impaired	Anterior Branch of MCA	Broca's Area	
2	Transcortical Motor Aphasia	Intact	Intact	Anterior Cerebral Artery	Left Frontal + Prefrontal Areas	
3	Global Aphasia	Impaired	Impaired	Trunk of MCA	Broca + Wernicke's Areas	

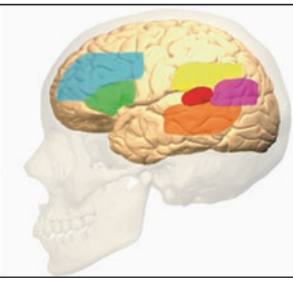

Fig. 18.3 Classification of aphasia. Aphasia can be classified in either fluent or nonfluent types. Fluent aphasias include conduction, anomic, receptive, and transcortical sensory. With conduction aphasia the repetition of words is impaired. It is typically secondary to an inferior parietal lesion from occlusion of the inferior division of the left middle cerebral artery (MCA). Anomic aphasia is mild with intact fluency, language comprehension, and repetition of words, but difficulty with word finding. The location of lesions causing anomic aphasia is poorly defined, but most functional studies localize this aphasia to the peri-Sylvian fissure region. Receptive aphasia has both impaired language comprehension and repetition of words. It is due to damage at WA secondary to a posterior branch of the left MCA stroke. Transcortical sensory aphasia has impaired language comprehension from injury to tissue inferior to the Sylvian fissure due to a left carotid artery occlusion. Nonfluent aphasias include expressive, transcortical motor, and global. Expressive aphasia is nonfluent with impaired repetition of words, usually secondary to a lesion in the Broca area (BA) due to occlusion of the anterior branch of the left MCA. Transcortical motor aphasia occurs due to anterior cerebral artery occlusion affecting the left frontal and prefrontal cortex. In global aphasia both language comprehension and repetition of words are impaired. Both the BA and the Wernicke area are damaged usually due to occlusion of the trunk of the left MCA. Clinically, many of these aphasias may overlap ("classification of aphasia" image is a derivative of "Broca area – lateral view" created by the Database for Life Sciences, used under CC-BY-SA-2.1-jp)

to occlusion of the anterior branch of the middle cerebral artery (MCA). Patients with expressive aphasia have impaired production of language and fluency but intact comprehension of speech. With receptive aphasia, patients have difficulty understanding language, but have intact fluency. The WA, the posterior-superior temporal gyrus, is commonly damaged from either a cardioembolic occlusion of the posterior branch of the MCA or a hemorrhagic stroke. Global aphasia occurs when both WA and BA are affected by stroke, commonly from a cardioembolic thrombus occlusion of the main trunk of the MCA [31].

Transcortical aphasias occur when tissue surrounding BA and WA are damaged. In many cases, motor or sensory transcortical aphasias are noted in the recovery period after expressive or receptive aphasias, respectively. Transcortical motor aphasia occurs due to damage to the left frontal and prefrontal regions as a result of a watershed infarct or occlusion of the anterior cerebral artery (ACA). Transcortical sensory aphasia occurs after a watershed infarct in the parietal and temporal lobes posterior to the Sylvian fissure [32]. Conductive aphasia etiology has been controversial but currently is thought to be due to lesions in the inferior parietal cortex, which is important for verbal working memory [33]. These patients have intact fluency and language comprehension but have difficulty with sentence repetition. They also commonly make paraphasic errors of semantic and phonemic substitution. Finally, anomic aphasia results in difficulty in word recall; otherwise the patient's language function remains intact. The anatomic site for this subtype remains unclear but likely arises from lesions along the Sylvian fissure secondary to small vessel ischemic strokes [31, 34].

Dysarthria

Dysarthria is the dysfunction in initiation, coordination, and control of articulatory structures involved in speech. The pathway for speech articulation was initially thought to be the corticobulbar tracts; however, extrapyramidal inputs from the cerebellum and basal ganglia have been found to play significant roles in articulation [35]. Lacunar infarcts to the deep cortex and brainstem are the most common causes of post-stroke dysarthria, with roughly equivalent incidence of 46% and 54%, respectively [36]. Supratentorial lesions in the distribution of the left MCA lead to upper motor neuron damage causing increased tone in the muscles of speech leading to spastic dysarthria. Weakness of the face or tongue, hemiparesis, hyperreflexia, spasticity, hemianopia, and the Babinski sign typically accompany the dysarthria symptoms. Infratentorial infarcts of the lower motor neurons in the pontine base lead to flaccid dysarthria. Basilar artery and PICA infarctions may involve the nucleus ambiguus as well as the facial and hypoglossal nuclei leading to coincidence of face, tongue, or palatal weakness, dysphonia, and dysphagia with dysarthria.

The extrapyramidal system controls automatic movements by modulating the lower motor neurons of the pyramidal tract with multisynaptic and indirect connections. Due to the complex nature of the connections between these centers, there is controversy regarding the precise regions involved in post-stroke dysarthria [36–38]. The basal ganglia receive cortical input to the caudate and putamen which in turn project to the globus pallidus which sends signals to the motor thalamus in order to regulate the motor cortex via either excitatory or inhibitory signals. Lesions of the basal ganglia arise from obstruction of the deep penetrating arteries of the MCA and ACA. Hyper- or hypokinetic dysarthria can result from these strokes due to impaired neuroregulation of cortical motor signals. Hyperkinetic dysarthria is caused by irregular, inaccurate, and spastic movement in the form of chorea or dystonia. Hypokinetic dysarthria is marked by reduced amplitude and range of movements, which can be seen in Parkinson disease. Lesions in the cerebellum cause inaccurate direction and rhythm of movement, slowed movement, and flaccidity. The resulting ataxic dysarthria is characterized by poor coordination of speech and respiration as well as a "scanning" quality due to unnatural separation of syllables. Dysdiadokokinesia, dysmetria, nystagmus, and truncal ataxia are commonly seen in these patients due to collateral damage to the cerebellum.

Apraxia of Speech

Apraxia of speech (AOS) is an acquired speech impairment that is caused by a disruption to central motor planning resulting in deficits in positioning and sequencing of the muscles required to produce speech. AOS following stroke is typically accompanied by aphasia as both typically arise from an MCA stroke. Pure AOS in stroke is rare but most likely arises from lesions in the premotor cortex [39]. Characteristics of AOS include a reduced rate and rhythm and intonation of speech and phoneme distortion or substitution [40].

Genetics

Determining the heritability of stroke is difficult because it does not represent a uniform clinical entity but rather a spectrum of disorders of various subtypes and severity that contribute to the stroke event. Most of the genetic data regarding stroke risk comes from genome-wide association studies (GWASs), which search for single nucleotide polymorphisms (SNPs) to associate with various diseases in large populations [41]. The largest GWAS for stroke demonstrated three candidate SNPs, two of which were associated with a 20–40% increased risk of cardioembolic stroke and a third associated with a 40% increased risk in large vessel ischemic stroke [42]. However, these findings are merely associative and have yet to be proven in animal models as causative.

Post-Stroke Patient Assessment and Associated Outcomes

Bedside Screening for Dysphagia

Although formal bedside swallow evaluations are performed by speech-language pathologists for all stroke patients, swallow screens are often administered after an acute stroke by medical personnel such as nurses, emergency room doctors, or neurologists. The purpose in administering a swallow screen is to have a quick, informal, noninvasive, nontechnical, accurate, and reliable way to determine if a patient can safely take food or medications by mouth, or whether swallow abilities should be evaluated more in depth prior to the initiation of peroral intake. This screening should take place in less than 4 hours of arrival to the hospital [43]. A systematic review looked at numerous bedside screening tools but was unable to demonstrate superiority of any testing method [44]. Unfortunately, false-positive screens were identified in 23–46%, causing inappropriate NPO orders or placement of feeding tubes [45]. Therefore, a thorough clinical assessment should be performed by a speech-language pathologist or an ear, nose, and throat provider (otolaryngologist) following a positive screen.

Clinical Assessment of Dysphagia

Beyond bedside screening, the clinician must be able to further assess the swallow and communication in each post-stroke patient. Although each clinician will develop their own method and sequence of a thorough head and neck exam, there are several specific tests that are meaningful in predicting the severity of dysphagia and communication disorders. Ability to cough may be impaired in post-stroke patients which increases the risk for aspiration pneumonia. Testing of cough is complicated given that there are many types of cough including voluntary cough, reflexive cough, and laryngeal expiration reflex. Deficits in each cough type have been correlated with aspiration pneumonia, but this literature is complicated by lack of objective cough assessment and inconsistencies in methodology [46]. It is important to remember that cough reflex may return quickly in the acute phase of stroke likely due to recovery from "brainstem shock" [47]. Following a stroke, the gag reflex may be absent ipsilateral to the lesion. Absent gag reflex was previously considered a good predictor of dysphagia following a stroke, but more recent research has not supported this theory. Healthy individuals without a gag reflex have demonstrated normal palatal function during phonation

indicating a physiological difference between these two functions [48]. Clinical Guidelines for Stroke Management published by the Stroke Foundation have specifically indicated that gag reflex testing is not a valid screening tool for dysphagia.

Instrumental Assessment of Swallow

In order to objectively assess the swallow mechanisms post-stroke, modified barium swallow study (MBSS) or functional endoscopic evaluation of swallowing (FEES) can be used. Delays in laryngeal ascent and closure against the epiglottis, slowed pharyngeal transit and swallow response time, and short duration of laryngeal closure in post-stroke patients on MBSS have been correlated with more severe dysphagia and increased aspiration risk [49–51]. Evaluation of the upper esophageal sphincter (UES) is especially important on post-stroke MBSS, as UES dysfunction can result after a stroke and can increase the risk of pyriform sinus pooling and aspiration. The UES dysfunction is more commonly associated with infratentorial lesions especially involving the lateral medulla due to injury to the nucleus ambiguus and nucleus tractus solitarius of the vagus nerve [4, 52]. Early recognition of UES dysfunction not only influences the treatment of post-stroke dysphagia but may influence long-term function of the inferior pharyngeal constrictors [52].

FEES testing is also commonly used in assessment of the post-stroke patient. Despite its limitations in assessing the oral and esophageal phases of swallow, FEES testing has been shown to be as sensitive and specific in diagnosing aspiration as MBSS [53]. The portability and ease of a bedside FEES exam has been shown in post-stroke inpatients to decrease the time to instrumental swallow study compared to those assessed with MBSS alone. The group that had FEES studies also had a lower rate of pneumonia which was thought to be due to earlier objective testing as well as better staff understanding of dietary restrictions for the patient [54].

Laryngeal Sensation Testing

Sensation testing can be done in combination with the FEES exam either via palpation with the end of the flexible scope or with graded pulses of air to the mucosa. In patients with either supra- or infratentorial strokes, the sensory threshold was significantly elevated compared to controls only on the affected side in unilateral strokes [55]. More recently, in patients with supratentorial strokes, decreased laryngeal sensation was significantly correlated with aspiration and penetration on FEES regardless of consistency of the bolus [51]. The addition of sensory testing allows for more accurate bedside diagnostic testing of dysphagia in the post-stroke patient population.

Communication Evaluation

Assessment of dysarthria involves a thorough oro-motor examination assessing the resting posture, sensation, and motion of the face, lips, jaw, tongue, palate. Diadochokinetic tasks, such as sequential (pa-pa-pa) and alternating motion rates (pa-ta-ka) can provide information on the rate, rhythm, and precision of speech. Assessment of vocal quality provides information regarding the integrity of the larynx, through tasks examining sustained phonation, pitch range, and cough. Aspects of respiration and phonation must also be assessed to look at respiratory drive and coordination to support voicing and speech [56].

Aphasia assessment should include receptive language tasks such as answering yes/no questions, pointing to named pictures, and following auditory or written commands, as well as expressive language tasks such as naming pictures, answering questions, describing picture scenes, and naming items in a category. AOS assessment involves an oro-motor examination to examine the strength, range of motion, coordination, and agility of the articulators to identify motor planning problems separate from language deficits. During assessment, individuals are required to produce phonemes, syllables, words, and sen-

tences of increasing linguistic complexity in order to identify any breakdowns in the motor speech system. Diadochokinetic rates may be used to assess the speed and regularity of the movement of the articulators as well as articulatory precision when moving quickly from one sound to another.

Patients with extensive MCA strokes typically have dysphonia characterized by roughness, breathiness, slowed speech, imprecise articulation, hypernasality, and instability during sustained vowel sounds [57]. Depending on the exact location of the stroke, laryngeal findings may include delayed laryngeal elevation and closure, vocal fold paresis/paralysis, tremor, dystonia, rigidity, and/or atrophy. Vocal fold paralysis/paresis tends to be contralateral for cortical and subcortical strokes and ipsilateral for medullary or brainstem strokes [58].

Post-stroke Therapy

Dysphagia Therapy

Treatment for oropharyngeal dysphagia post-stroke may involve both alterations to diet/liquid consistency and behavioral interventions to improve the efficiency and strength of swallow function. Changing diet or liquid consistency can compensate for deficits in the timing of the swallow or control of the bolus, thus reducing aspiration in the short term, but does not improve the physiology of the swallow [53, 59]. Small studies of post-stroke patients have been performed on specific dysphagia therapies including chin tuck against resistance, effortful swallow, lingual strengthening, and the Shaker and Masako maneuvers demonstrating improvement in swallow function [60–62]. Interpreting these trials individually is difficult given the small sample size and heterogeneity of outcome measures. Meta-analyses lumping these techniques together as "dysphagia therapy" have demonstrated improved swallow function and decreased risk of aspiration pneumonia but did not have an effect on overall mortality [63, 64].

Neuromuscular Electrical Stimulation

Neuromuscular electrical stimulation (NMES) has been studied in post-stroke dysphagia either alone or in combination with traditional dysphagia therapy. In most recent studies, early intervention with a combination of these techniques resulted in improved swallow function [65–68]. Unfortunately, interpretation of this conclusion is limited given that exact electrode placement and use of the sensory vs. motor thresholds continue to be debated and studied [68, 69]. The effectiveness and safety of NMES for post-stroke patients remains controversial within the field of speech-language pathology, with current clinical practice guidelines suggesting use only by "experienced clinicians."

Aphasia, Dysarthria, Apraxia of Speech Therapy

For the treatment of aphasia, there are numerous therapies that have demonstrated efficacy for each area of impairment: receptive language, expressive language, reading, and writing. A systematic review analyzing the results of various aphasia therapy techniques compared to no treatment revealed that functional communication, reading, writing, and expressive language improved with therapy [70]. Individual therapies demonstrating efficacy in treatment of aphasia include computer-based treatments, augmentative and alternate communication (AAC), semantic feature analysis, and communication partner training. Computer-based treatments have shown promise in aphasia treatment, but controversy exists if they are as effective when self-administered [71, 72]. A review of AAC demonstrated improved communication for individuals with chronic aphasia, but no one system has been identified as superior [73]. Semantic feature analysis has been shown to improve confrontational naming for fluent aphasias; however, generalization to untrained items or conversational speech has been limited and requires more research [74]. Communication partner training

has shown to improve patient participation, but not language outcomes [75].

Treatments for AOS most supported by research include articulatory-kinematic and rate-rhythm approaches. Articulatory-kinematic approaches have been developed from the principles of motor programming and involve the use of external sensory information to achieve accurate speech movements using an intensive practice regimen. Rate-rhythm approaches focus on using prosody and intonation patterns to improve speech as length of utterance is increased over time [40, 76].

Compared to other post-stroke interventions, therapy for dysarthria is significantly heterogeneous as it is typically based on the specific deficits and needs of the patient. Techniques for treatment may include oral musculature exercises, strategies to decrease rate and/or overarticulate speech, and increasing volume using biofeedback or personal amplifier. Unfortunately, due to few current studies and variability in treatment methods, systematic reviews of therapy for dysarthria have shown no effect on the impairment, activity, or participation levels in post-stroke patients [77]. Dysarthria treatment remains a part of clinical practice guidelines for speech-language pathologists; however, further research is needed to provide evidence and guidance for appropriate use of specific therapy techniques for dysarthria [78].

Post-stroke Surgical Interventions

Many of the acute motor and sensory symptoms of stroke resolve with time. In general, motor recovery occurs at 63% at 3 months and 78% at 6 months [79, 80]. Additionally, the risk of major cardiac events 30 days postoperatively following a noncardiac elective surgery was significantly increased until 9 months post-stroke [81]. Therefore, surgical intervention should be a last resort treatment for immediate post-stroke deficits.

To date, there are no recommendations regarding timing of vocal fold injection post-stroke. Vocal fold immobility post-stroke tends to follow generalized motor recovery, which is somewhat less than the 86% predicted recovery at 6 months in idiopathic unilateral vocal fold paralysis [82]. In general, early injection at <3 months with a temporary agent is associated with more favorable position of the paralyzed vocal fold and decreased need for permanent medialization [83]. To minimize perioperative risk, this procedure should be performed under local anesthesia when possible. In addition to improvement in voice, medialization of a paralyzed vocal fold may also improve pulmonary toilet by improving cough and decreasing risk of aspiration [84, 85].

Surgical intervention for post-stroke dysphagia includes esophageal dilation, cricopharyngeal botulinum toxin injection, or cricopharyngeal myotomy. These techniques are generally used in conjunction with swallow therapy and when ample time has been given for spontaneous recovery. A modified balloon dilation technique using transnasal catheters to perform serial dilations on awake patients has led to long-term improvement in post-stroke dysphagia symptoms as well as measures of UES opening and hyoid displacement on MBSS [86]. No studies have been performed comparing more traditional methods of esophageal dilation in the post-stroke population. In addition to dilation, botulinum toxin injection into the cricopharyngeus has demonstrated a roughly 80% response rate for both cortical and brainstem strokes with 79% of these patients having improvement in dysphagia for over 4 months [87]. However, there is risk of spread of the toxin to neighboring muscles or creating fibrosis at the site of the injection. Post-stroke patients were shown to have the most significant functional outcome scores compared to other etiologies of dysphagia after CO2 laser endoscopic myotomy [88]. No set protocol for the surgical management of post-stroke CP dysfunction exists; therefore, the otolaryngologist should consider each of these options along with the severity and duration of the patient's symptoms.

Frontiers

Noninvasive Brain Stimulation

Transcranial stimulation of the brain is currently being studied for both post-stroke dysphagia and aphasia. The goal of these stimulation techniques is to modulate the activity of regions of the brain associated with post-stroke functional deficits. The methods employed are transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS). While both of these techniques cause immediate effects during therapy, posttreatment effects lasting hours to weeks have been recorded and may be due to changes in NMDA receptor activation [89, 90]. For the treatment of dysphagia, there have been small randomized controlled trials of both tDCS and TMS. In two meta-analyses, a positive immediate posttreatment effect was seen on swallow function but long-term results are still conflicting [91, 92]. In a meta-analysis of tDCS for aphasia, there was no significant benefit of tDCS over traditional therapy, specifically in naming accuracy [93]. Many issues remain regarding the type and laterality of stimulation, duration of treatment, and long-term safety prior to clinical use. With further clinical trials, these techniques may become part of our post-stroke treatment protocols in the future.

Pharyngeal Electrical Stimulation

Pharyngeal electrical stimulation (PES) is a newer rehabilitation modality for the treatment of dysphagia. For PES, intraluminal catheters are passed transnasally and positioned to stimulate the pharynx directly during swallow. Initial clinical trials have shown improvements in initiation of swallow and airway protection, reduced aspiration, and accelerated recovery of swallow function in stroke patients. PES may be a promising treatment modality for post-stroke dysphagia; however, limitations such as the exact location of the stimulation catheters still require further research [94].

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Iatrogenic Injury

19

Randal C. Paniello

Introduction

The motor and sensory nerves of the larynx and pharynx are supplied by the vagus (X) and glossopharyngeal (IX) nerves, and injuries to these nerves may occur anywhere along their paths from their origins at the brainstem to their end organs. The most common injuries are iatrogenic, from open surgical procedures involving the thyroid gland, the larynx and pharynx, the cervical spine, the carotid arteries, and the aortic arch.

Etiology

The etiologies of recurrent laryngeal nerve (RLN) injuries as reported by the three largest published series are shown in Table 19.1 [1–3] for unilateral vocal fold paralysis (UVFP) and in Table 19.2 [1, 4, 5] for bilateral vocal fold paralysis (BVFP). It can be seen that the proportion of cases that are iatrogenic (caused by surgery, trauma, or intubation) ranges from 42.3% to 61.8% for UVFP and from 50.0% to 57.7% for BVFP. Despite advances in intraoperative laryngeal nerve monitoring, thyroid surgery remains the most common cause of both unilateral and bilateral paralysis.

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The true incidence of RLN injuries is likely higher than reported because many surgeons do not wish to admit that they might have caused an injury, and therefore they do not check for one routinely. If a patient wakes up from surgery with a hoarse voice, the surgeon may suggest that the hoarseness is related to intubation, and sometimes it is, but other times there is neuropraxic or more severe injury that is not acknowledged. Also, swelling of the vocal fold caused by intubation may position an immobile vocal fold near midline, resulting in fairly normal phonation, and such patients may not become hoarse until the edema resolves several days later.

Additionally, some patients with UVFP have good compensation and are asymptomatic despite the paralysis. Such patients have been identified on preoperative laryngeal nerve screening exams by flexible laryngoscopy [6–8]. Randolph and Kamani found that 10 of 15 invasive thyroid cancer patients with vocal fold paralysis on preoperative laryngoscopy reported no voice changes [9]. In a series of thyroidectomy patients for benign and malignant disease, Steurer et al. reported 6 patients with preoperative UVFP and 11 patients with postoperative UVFP who were completely asymptomatic [10]. Similarly, Farrag et al. reported that 7 of 22 patients found to have UVFP on preoperative laryngeal nerve screening were asymptomatic [7]. In another series, Caroline et al. found 10 of 17 patients with

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Table 19.1 Etiology of unilateral vocal fold paralysis in three large series

Etiology	Rosenthal et al. [1] ($n = 643$) (%)	Takano et al. [2] ($n = 797$) (%)	Spataro et al. [3] ($n = 938$) (%)
Surgery, total	36.5	51.1	55.6
Thyroid/parathyroid	12.4	14.1	16.8
Nonthyroid	24.1	37.1	38.8
Intubation	5.8	7.3	6.2
Malignancy	18.4	9.9	17.8
Idiopathic	18.5	16.8	13.2
Left side	60.9[a]	64.0	66.2

Adapted from Spataro et al. [3], with permissio)
[a]Data reported for only 56.4% of patients in study

Table 19.2 Etiology of bilateral vocal fold paralysis in three large series

Etiology	Rosenthal et al. [1] ($n = 189$) (%)	Hillel et al. [4] ($n = 92$) (%)	Bauer and Paniello [5] ($n = 237$) (%)
Surgery	37.0		32.1
Thyroid surgery	26.9	17.4	25.7
Nonthyroid	7.4	20.7	6.3
Trauma	7.4		5.5
Malignancy	14.3	18.5	11.0
Intubation	13.2	12.0	16.8
Idiopathic	11.1	15.2	9.3
CNS/ neuropathy	10.6	13.0	–
RA/ inflammatory	2.6	3.3	–
Autoimmune	–	–	6.3
Radiation therapy	1.6	–	5.1
Other/multiple	2.1	–	10.1
Iatrogenic[a]	57.7	50.1	54.4[b]

[a]Iatrogenic = surgery + trauma + intubation
[b]Does not include cases with multiple causes

preoperative vocal fold paralysis had no vocal symptoms [11].

Data on the etiology of injuries to the external branch of the superior laryngeal nerve (eSLN), the pharyngeal plexus, and the innervation of the cricopharyngeus muscle is much more limited in the literature. While the risk to the eSLN from thyroid surgery is well established [12], other causes are rarely reported. Injury to the pharyngeal plexus is often iatrogenic, such as during anterior cervical spine procedures, resulting in dysphagia [13]. The cricopharyngeus muscle receives innervation from both the RLN and the pharyngeal plexus, bilaterally [14], and injuries to any of these four nerve inputs may result in cricopharyngeal achalasia [15].

Types of Injuries

Iatrogenic injuries generally traumatize nerves by one or more of the following mechanisms: crush, partial or complete transection, cautery/thermal injuries, stretch injuries, or placement of surgical clips. The severity of injury can be categorized using the Sunderland classification (Fig. 19.1) [16]. Most crush injuries will be grade I (neuropraxia) or II (axonotmesis) and have a high chance of recovery. Stretch injuries are usually grade III or IV; their recovery is determined by the number of axons involved, which correlates with degree of stretch. Partial transection injuries are usually grade IV in addition to some grade I or II injury to the non-transected portions of the nerve. Complete transections are, by definition, grade V (neurotmesis), with the lowest chance of recovery. Surgical clips most likely resemble partial or complete transection injuries, but with no potential for recovery of the crimped portion.

Cautery injuries can be any grade but, in addition to the Sunderland class, have the potential for coagulation necrosis of endoneurial tubes and destruction of perineurium at the injury site (the direct result of the cautery) [17]. Newer energy-delivery devices such as the Harmonic scalpel or

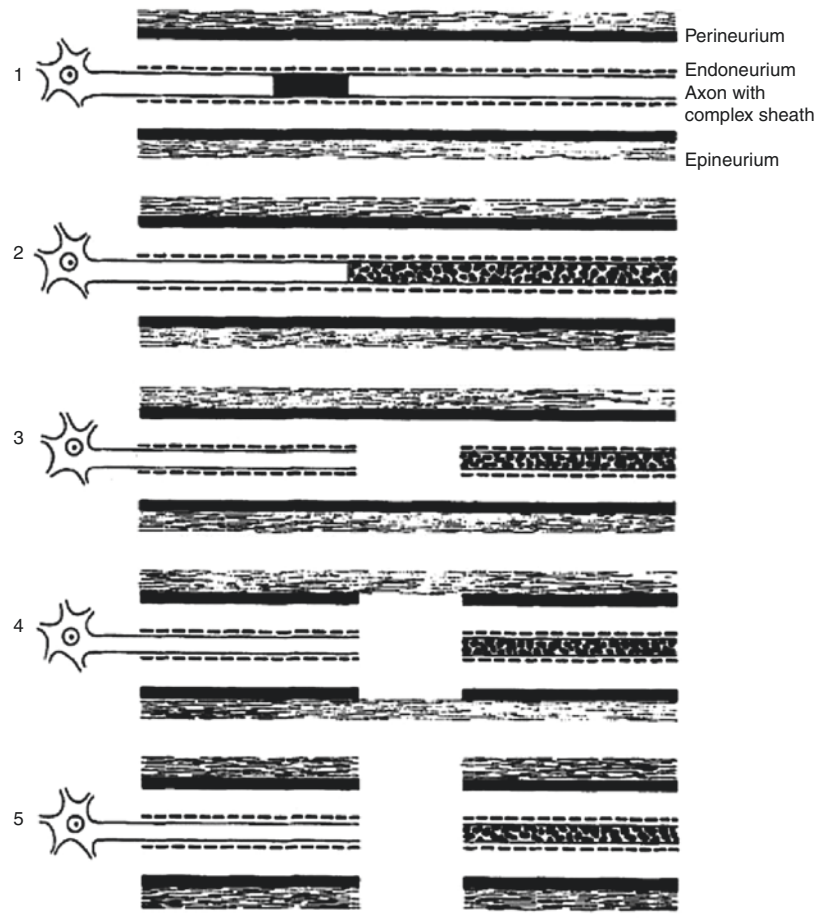

Fig. 19.1 Sunderland classifications of peripheral nerve injuries. (From Sunderland [16] with permission)

LigaSure in thyroidectomies were found to have a higher rate of RLN injury than the clamp-and-tie method in a large meta-analysis published in 2013 [18]. This difference was not found in some more recent studies [19–21], suggesting increased experience with these technologies has increased their safety. The risk of injury is related to the proximity to the nerve that the device is applied, with a zone of "relative safety" at 3 mm and "absolute safety" at 5 mm according to one study [17].

For mixed injuries (more than one of these mechanisms involved), such as stretch with partial transection (avulsion), the final recovery potential will be dictated by the grade of the most severe injury, as well as the total number of injury sites and the length of nerve involved [22], since a fraction of axons are lost at each injury site.

Most iatrogenic injuries are not recognized intraoperatively and are identified postoperatively only when patients are symptomatic.

Injuries to motor nerves of the larynx and pharynx tend to be the most clinically obvious, but sensory nerve injuries may occur as well. The RLN carries the sensory innervation of the ipsilateral glottis and subglottis, while the internal branch of the SLN (iSLN) provides sensation to the supraglottis. Injuries to either of these nerves may cause anesthesia of this region, which can contribute to aspiration. Sensation in the pharyngeal walls comes from the pharyngeal plexus, with contributions from both the vagus and glossopharyngeal nerves. Injury to the pharyngeal plexus may cause loss of sensation to portions of the pharynx, which may manifest clinically as globus sensation as well as dysphagia.

Physiology of Nerve Injury and Recovery

The nerves of the larynx and pharynx behave like other peripheral nerves following injury; a nice summary is provided by Caillaud et al. [23]. Acute axonal degeneration, in which the two cut ends of the axon pull away from one another, typically occurs within 30 minutes of injury [24], and then the endings are sealed [25]; these processes are calcium-dependent. Schwann cells (SCs) and endoneurial fibroblasts near the injury die by apoptosis, creating axonal and myelin debris [23]. Wallerian degeneration, in which the axons distal to the injury degenerate, begins within 24–36 hours; the distal nerve typically remains stimulable for about 72 hours [26], beyond which distal axons are fully degenerated, although the endoneurial conduits remain intact. The axolemma (membrane surrounding the axon) swells and then degenerates. Within 7 days, SCs begin to release monocyte chemoattractant protein-1, which recruits macrophages to phagocytose axonal and myelin debris. SCs also release neurotrophic factors (NFs) including nerve growth factor (NGF), ciliary NF, brain-derived NF, and glial-derived NF. SCs attract axonal sprouts from the proximal stump, and axons begin to grow back across the injury site from proximal to distal following "Büngner bands" (channels formed from basement membrane by SCs). SCs also attract macrophages, which help remove debris from the injury site. The regeneration and reorganization of blood vessels accompany the growth of axons and deliver oxygen, which is required for nerve regrowth [23].

Axonal regrowth across the injury gap is often incomplete, due to fibrin, collagen, and other debris that block the distal target. In our animal experiments involving nerve anastomoses, the rate of axons successfully crossing an injury gap is 50–85% (unpublished). In addition, there is no process that guides regenerating axons into the correct muscle. The RLN, for example, contains nerve fibers leading to three adductor muscles (thyroarytenoid, TA; lateral cricoarytenoid, LCA; and interarytenoid, IA) and one abductor muscle (posterior cricoarytenoid, PCA), as well as sensory fibers to the ipsilateral glottis and subglottis (about 10% of the axons). Gacek et al. showed, in cats, that these fibers are not organized into bundles or fascicles within the RLN until they coalesce at their distal branch points [27]; prior to that they are randomly distributed. Thus, a regenerating TA axon could potentially find its way into any of these muscles. Flint et al. also showed that there is no topographic orientation of adductor vs. abductor representation in the nucleus ambiguus; using a double-retrograde labeling technique in rats, the origins of these antagonistic nerves almost completely overlap [28].

Synkinesis

The process whereby muscles become reinnervated by the wrong nerve is called *synkinesis*. The RLN is fairly unique as a peripheral nerve that carries fibers for antagonistic functions within the same nerve bundle; the oculomotor nerve and the facial nerve are two others. The matching up of regenerating axon into recipient endoneurial tubule appears to be a random process. In a canine study, we compared the functional results of a complete transection injury with immediate reanastomosis [29, 30]. In one study group, the two nerves were aligned as precisely as possible to their original orientation; in another group, one side was rotated 180° to create maximum misalignment. At 6 months, there was no difference in the functional results of these two groups (Fig. 19.2).

The result of the random alignment of fibers during reinnervation also depends on the number of axons that originally innervated each muscle. It is generally accepted that the adductor fibers outnumber the abductor fibers in a ratio of about 3:1, based on retrograde labeling studies [27]. This suggests that both adductor and abductor muscles are approximately three times more likely to be reinnervated by adductor axons, but also that some abductor axons are likely to reinnervate both muscle groups [31]. When activated, the co-contractions of these antagonistic muscle fibers cancel each other out to some extent. The net adduction or abduction of the vocal fold thus depends on how

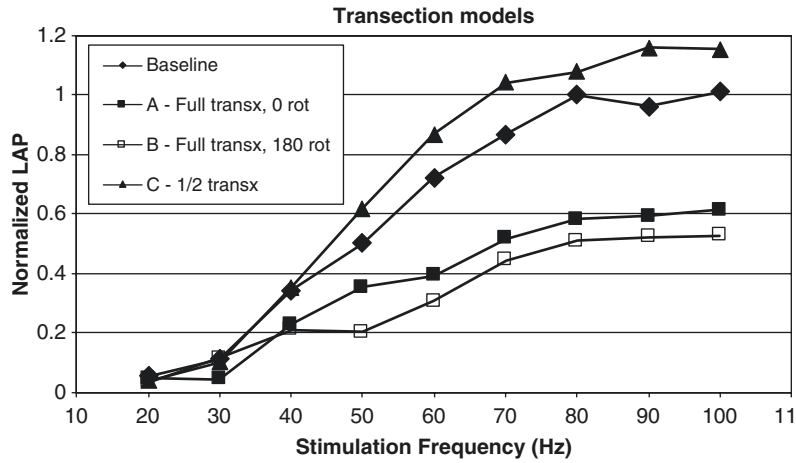

Fig. 19.2 Functional results at 6 months in canine RLN transection models. There was no difference between complete transection groups with precise realignment (group A) and maximum misalignment with 180° rotation (group B). LAP laryngeal adduction pressure. (Data from Paniello et al. [30])

many fibers actually regenerated, as well as how many of these reinnervated the correct muscle. Clinically, the result is often a vocal fold that does not appear to move at all, and the resting vocal fold position is dictated by the balance of "tone" of the partially reinnervated muscles.

The concept of adductor-to-adductor synkinesis also follows from this construct (e.g., TA axons innervating LCA muscle fibers), but this has received no attention in the literature. The most likely result would be some gross adductor function that is less coordinated than it was originally.

Rate of Axon Growth

Axon growth in regenerating peripheral nerves has been thought to proceed at a rate of about 1 mm/day, since the early work of Ramon y Cajal [32, 33]. Some more recent work has called this belief into question. For example, we performed monthly electromyographic exams on a series of canines with various RLN injury models [34]. Two of the study groups had a crush injury or a complete transection with reanastomosis at a site 5 cm inferior to the cricothyroid joint; two additional groups had these same injuries 10 cm from the joint. At the rate of 1 mm/day, we would expect the more inferior injuries to take about 50 days longer to show signs of recovery. Instead, we found the time course of EMG findings (appearance or disappearance of fibrillations potentials, polyphasic action potentials, and mature motor unit potentials) was the same for the 5-cm and 10-cm groups for each injury type. This suggests that some additional, unidentified factors are involved in determining the rate of axon regrowth.

Muscle Fiber Types

Voluntary muscle fibers are subdivided into type I, "slow twitch," and type II, "fast twitch," based on their speed of contraction. These phenotypes correspond to differences found in the composition of their myosin heavy chains, for which subtypes I, IIa, IIb, and IIx (and a few others) have been identified. Type I muscles tend to be weaker and slower to contract but may maintain contraction for a longer period without fatigue. Type II muscle fibers are faster and stronger but cannot sustain contraction for very long. Most muscles consist of a mixture of myosin isoforms, with the predominant subtype teleologically matched to their function. Thus, it would be expected that muscles with respiratory function should be predominantly slower and non-fatiguable type I, while muscles involved with reflexes such as glottic closure should be mainly faster type II fibers.

In general, this is what has been found in mammalian laryngeal muscles, with species-specific variations [35, 36] (Fig. 19.3). The findings among various species were summarized

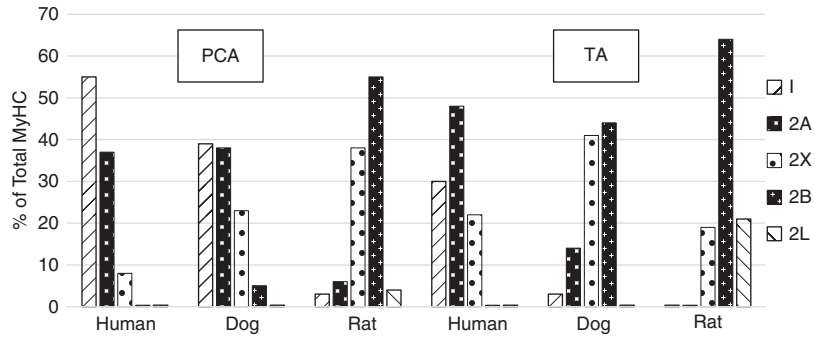

Fig. 19.3 Muscle fiber types for laryngeal muscles, species comparisons. Left three groups are PCA muscles and right three groups are TA muscles. For each species, TA muscles are faster than PCA muscles. (Data from Wu et al. [35])

nicely by Hoh [37]. In humans, most investigators have found that the PCA is predominantly type I. Li et al. reported the PCA has 65% type I fibers [38], while Qiu et al. found 78.9% type I in PCA [39]. However, others have found that all laryngeal muscles were predominantly type II isoforms, although PCA had more type I than the other muscles [40, 41]. Further studies have found that myosin ratios differ even among different subunits of the same muscle, likely corresponding to differences in the functions of these subunits [42–44].

Muscle fiber type is determined by its innervation. In a classic study, Buller et al. exchanged nerves between fast and slow muscles in cat hindlimbs and found that the slow muscle became faster and the fast muscle became slower [45]. This effect has been observed in experimental laryngeal studies as well [46, 47]. For example, Kingham et al. used the slow phrenic nerve to reinnervate the larynx of a minipig and found all of the laryngeal muscles transformed to a slower myosin heavy chain profile [48]. In another study, we used the fast hypoglossal nerve to nonselectively reinnervate the larynx and found an increase in fast type II myosin isoforms in all laryngeal muscles [49].

Laryngeal muscles have also been found to change phenotype when denervated without reinnervation. Shiotani and Flint found a decrease in type IIB (the fastest) in favor of an increase of types IIA and IIX with little change in type I, following denervation in a rat model [50]. Delguadio and Sciote (also in a rat model) found type I nearly disappeared following reinnervation [51]. Qiu et al. examined a series of human PCA samples obtained during arytenoidectomy and compared myosin isoform composition as a function of duration of denervation. They found a gradual loss of type I fibers that peaked at around 2 years after denervation [39]. This suggests that fast type II fibers are the "default" type for laryngeal muscles, and slow type I fibers are the ones that require maintenance innervation.

Effects of Denervation

Most muscles undergo rapid, irreversible atrophy following denervation. The laryngeal muscles seem to resist this tendency, often maintaining their bulk for a prolonged period. Kano et al. found that denervated canine PCA muscles are unchanged in size for at least a year [52]. Miyamaru et al. reported the same findings for rat TA muscles [53]. Johns et al. measured isometric contractile force in cat TA muscles 6 months after denervation and found no change from normal controls [54]. The RLN has the potential for spontaneous reinnervation across a gap; even a few axons that successfully reach the target muscle may be enough to serve a "babysitter" function and prevent atrophy while the muscle patiently awaits the arrival of additional nerve fibers. Shindo et al. removed a 2.5-cm segment of canine RLN and followed their function and EMG results monthly. They found gradual return of neural activity beginning at 3 months post-injury [55]. Some degree of babysitter function may explain the successful ansa-RLN reinnervation results reported by Olson et al. up to 6 years after RLN injury [56]. The tendency for laryngeal

muscles to atrophy slowly and remain receptive to new nerve input has led some investigators to propose that reinnervation procedures can be performed routinely with good results up to 2 years after RLN injury [57].

Effects of Neurotrophic Factors

Investigators have tried to positively influence axon growth and recovery after injury by adding neurotrophic factors to the milieu. Wang et al. [58], Vega-Cordova et al. [59], and Halum et al. [60] all found differences in expression of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and glial cell-line derived neurotrophic factor (GDNF) between TA and PCA in denervated rat larynges. Hernandez-Morato et al. found increases in NGF, BDNF, and netrin-1 during denervation and reinnervation, with levels returning to normal after reinnervation was complete [61]. This suggests that administration of exogenous growth factors could influence laryngeal nerve recovery. Accordingly, Halum found that adding genes expressing ciliary neurotrophic factor (CNTF) to muscle stem cells prior to implantation resulted in increased neuronal sprouting [62]. Ongoing work will further explore the potential of this therapeutic approach.

Diagnosis

Videolaryngoscopy

The gold standard of diagnosis of RLN injuries is flexible laryngoscopy. Video recording of the exams allows review and archive for future comparisons. The key finding is rotation of the arytenoid cartilage, with the vocal process moving medially. Confounding the exam is the interarytenoid muscle, which is innervated by both RLNs. It translates the arytenoid body medially but does not rotate it. The cricothyroid muscle, innervated by the eSLN, also produces mild vocal fold adduction along with elongation. Its effect can be ascertained by asking the patient to attempt to phonate at both low and high pitch. Also, if the RLN has been injured for a few weeks or longer, the patient may have started squeezing the false vocal folds (plica ventricularis) as a compensatory mechanism, which may partially block the view of the arytenoid and vocal fold motion. The specific vocal task requested affects the degree of adduction [63] and timing of the exam is important [64]. Further, some degree of asymmetry of vocal fold motion is probably normal; in a study by Woo et al., only 9 of 25 patients with vocal fold motion asymmetry were found to have paresis by EMG criteria [65]. Some data suggest that even experienced laryngologists can have difficulty diagnosing paresis [66, 67], although another study found good diagnostic agreement among specialists [68].

Electromyography

Laryngeal electromyography (LEMG) can be used to determine the innervation status of laryngeal muscles, which can be used prognostically to help make treatment decisions. A needle electrode is typically inserted percutaneously into the target laryngeal muscle, and characteristic waveforms are obtained with the muscle at rest and activated. A nice summary was provided by Munin et al. [69] who found that recruitment of active voluntary motor unit potentials or the presence of polyphasic action potentials within 6 months of nerve injury predicted recovery. They also reviewed studies that provided information on whether LEMG changed clinical management and found that it did so in 48% of cases. They concluded LEMG should be performed between 4 weeks and 6 months post-injury if prognostic information is needed.

LEMG does have limitations. First, patients frequently complain of discomfort with the procedure. Refinements of surface electrode techniques may ameliorate patient discomfort [70]. Second, special equipment is needed. It requires experience to gain confidence that the electrode is placed within the desired muscle, but this is rarely certain. Bipolar electrodes (used by 27% of laryngologists) [71] minimize electrical

interference from other muscles, but sample only a small portion of the muscle. Monopolar (57%) and hook-wire (17%) electrodes sample a wider area but may have more contamination by non-laryngeal electrical activity. LEMG is generally considered a qualitative procedure, although some reports using "turns analysis" have attempted to make it more quantitative [72].

Treatment Principles

Unilateral Vocal Fold Paralysis

Patients who emerge from anesthesia with a unilateral RLN injury most commonly notice a weak, breathy voice, along with aspiration of thin liquids and sometimes shortness of breath with talking or exercise. Often they are told these changes were caused by intubation and will improve in a couple of days, and their surgeon may prefer to assume this rather than admit that there may have been an RLN injury. Some patients rapidly compensate for a paretic or paralyzed vocal fold and do indeed improve within a few days. Such patients are unlikely to undergo early flexible laryngoscopy, so the true rate of postoperative vocal fold paresis or paralysis is probably underreported. Other patients may wake up with a fairly normal voice but develop breathy dysphonia several days later and are found to have vocal fold immobility. These patients most likely had significant vocal fold edema from their intubation that served to medialize the edge and temporarily mask their paresis. When the edema subsides, the glottal gap no longer closes completely and symptoms emerge. Other frequently reported symptoms of UVFP include persistent throat congestion, weakened cough, globus, and dysfunctional Valsalva [73].

Patients with neuropraxic injuries may regain normal-appearing laryngeal function, with purposeful adduction and abduction, over a period of weeks or months, depending on severity. Other patients will develop good compensation from the non-paralyzed side and will be satisfied with their voice quality and swallow without aspirating. Together, these recovery groups comprise about 40–50% of patients with iatrogenic vocal fold paresis or paralysis.

Because the RLN may take many months to complete its natural recovery, most surgeons recommend waiting 6–9 months from the time of injury before undertaking any permanent surgical correction. At our institution, 71% of patients present for treatment of UVFP within 3 months of onset [3]. To help patients with symptoms while waiting, most surgeons today offer injection laryngoplasty for temporary improvement in laryngeal function. Vocal fold injections can be done in the office or at the bedside with local anesthesia, using a percutaneous or channel-laryngoscope technique [74]. Currently available injectables, including carboxymethylcellulose (CMC) (Prolaryn™ gel, Merz, Raleigh NC, USA; Renú® gel, InHealth Technologies, Carpinteria CA, USA), CMC with calcium hydroxyapatite (Prolaryn Plus™), micronized human acellular dermis (Cymetra®, Life Cell Corp., Branchburg, NJ, USA), and cross-linked hyaluronic acid (Restylane®, Galderma, Fort Worth TX, USA; Juvéderm®, Allergan, Irvine CA, USA), as well as autologous fat, are all resorbable, all lasting between 3 and 12 months [75].

Some surgeons have noticed that a subgroup of patients who underwent injection laryngoplasty did not subsequently proceed to a permanent procedure, even though they did not recover any purposeful motion of the paralyzed vocal fold. We did a systematic review and meta-analysis of these reports and found that patients who underwent an "early" (first 3 months from injury) vocal fold injection were only one-fourth as likely to later have a permanent correction as those who had a later injection or no injection [76]. We speculate that the injected material serves as a sort of "internal physical therapy" for the opposite, normal vocal fold. Untreated, the glottal gap is too wide for compensation, hence the symptoms, but after injection, the gap is closed, and the gradual resorption of the material allows the good vocal fold to strengthen and increase its compensation in small increments. Thus, injection does not increase the likelihood of nerve recovery, but it may increase the

effectiveness of the compensatory behavior so that some patients do not need a permanent correction.

The most common procedure performed today for permanent correction of UVFP is a type I thyroplasty, as defined by Isshiki [77], in which the vocal fold is medialized by placing an implant in the paraglottic space. Implant materials in current use include silastic, expanded-polytetrafluoroethylene (Gore-tex®, W. L. Gore & Associates, Newark DE, USA), and titanium. The procedure is usually done with the patient under conscious sedation anesthesia, to avoid intubation and to permit the patient to phonate during the operation so that the implant can be adjusted by observing glottal closure via flexible laryngoscopy and listening to the voice product. In rare cases where the patient cannot tolerate the conscious sedation approach, this author has used general anesthesia with a laryngeal mask airway (LMA), through which the flexible laryngoscope can be passed while still avoiding intubation. Although thyroplasty is a straightforward concept, it is deceptively complex with nuances that must be learned with experience. Even in experienced hands, revision rates of 10–15% are typical [78]. The most challenging aspect is learning how much to overcorrect to account for intraoperative edema which will subsequently resolve; if this is not taken into account, there will be undercorrection and a persistent glottal gap.

A related procedure, also introduced by Isshiki, is arytenoid adduction (AA), in which the muscular process of the arytenoid is sutured anteriorly, simulating the action of the LCA muscle, causing the vocal process to rotate medially [79]. This procedure generally does a better job than thyroplasty at closing a wide posterior glottal gap and has the advantage of avoiding any implant, which may lead to better voice quality. However, it may require general anesthesia (with LMA) and is technically more difficult than thyroplasty. Often AA is combined with thyroplasty in order to close a very large anterior and posterior glottal gap [80].

Another approach to treating UVFP is laryngeal reinnervation, largely popularized by Crumley [81]. The goal of this method is to reestablish neural input to the laryngeal muscles, thereby preventing atrophy and establishing good muscle tone. Several potential donor nerves have been reported, but the ansa cervicalis is used most often due to easy dissection, good caliber with adequate axons, and no significant donor site morbidity. Although adductor activity during phonation and deglutition would be ideal, arytenoid movement is rarely seen in these cases. Because the vocal fold remains surgically untouched, it usually vibrates quite naturally once adductor tone is established. In a small, multicenter, randomized clinical trial, ansa cervicalis-to-RLN reinnervation was found to have results superior to type I thyroplasty for voice quality ratings (untrained listeners and trained GRBAS ratings) and voice-related quality of life [82]. Patients typically begin to have voice improvement 4–6 months following the procedure. A vocal fold injection is usually performed at time of the reinnervation operation to provide benefit during this waiting period. Results are better if patients are not over age 60 and are not more than 2 years out from the onset of paralysis [57, 82]. Although reinnervation is gaining in popularity, it takes longer and is technically more difficult than thyroplasty and is therefore eschewed by some surgeons.

Sometimes the recommended 6- to 9-month waiting period can be waived and an "early" permanent correction can be performed. One concern about early permanent correction is that the vocal fold muscles may continue to atrophy. Correcting the position of the vocal folds before they are in their final position may increase the likelihood of needing to perform revision surgery to further medialize the vocal fold to make up for the lost muscle mass. If the RLN is sacrificed due to its involvement in tumor, it will not recover so there is no point in waiting. Patients with a poor overall prognosis and UVFP, such as some with advanced lung cancer, might prefer to undergo an early thyroplasty to maximize their voice-related quality of life for their remaining days. In a recent study of patients who underwent aortic arch surgery, early thyroplasty gave satisfactory long-term voice results with an acceptable revision rate [83].

Table 19.3 Comparison of type I thyroplasty, arytenoid adduction, and ansa-RLN reinnervation options for treatment of UVFP (author's opinions—see text)

Attribute	Type I thyroplasty	Arytenoid adduction	Ansa-RLN reinnervation
Implant?	Yes	No	No
Operative time (min)	45–60	60–90	90–120
Technical difficulty[a]	6	7	8
Anesthesia	Sedation	Choice	General
Time to benefit	0–14 days	0–7 days	4–6 months
Age	Any	Any	≤ 60
Post-glottal gap closure[a]	5	8	6
Voice quality result[a]	6–8	7–8	8–10

RLN recurrent laryngeal nerve, *UVFP* unilateral vocal fold paralysis
[a]Scale of 1–10, with 10 as the highest rating

Type I thyroplasty, arytenoid adduction, and ansa-RLN reinnervation are compared in Table 19.3. The surgical details of these procedures are described in Chap. 30, Laryngeal Reinnervation.

Bilateral Vocal Fold Paralysis

Patients with injuries to both RLNs are unable to abduct the vocal folds, potentially leading to airway obstruction, depending on their resting position. When such patients awaken from anesthesia, some will have an airway problem immediately upon extubation, while others will be OK initially but then develop progressive stridor as the vocal folds drift into a resting medial position over the next few days. Some patients will have vocal folds that rest in a paramedian position that provides an adequate airway at rest, but an inadequate airway for activity. In our experience, more than half of these patients will require a tracheotomy at some point in their management.

The ideal treatment for BVFP would restore dynamic vocal fold abduction for respiration while allowing adduction for phonation and deglutition, but such techniques have been elusive. Most approaches are static in nature, hoping to achieve a compromise vocal fold position that provides just enough breathing space but still adequate voice and swallowing protection.

Acutely, vocal fold suture lateralization can be performed, such as the procedure described by Ejnell et al. [84]. This approach avoids a tracheotomy, which is especially desirable when a patient has undergone a central compartment dissection for thyroid cancer and has exposure of the innominate artery. It can also be reversed if one or both vocal folds recover abductor function, but it is usually performed on the side that is considered less likely to recover.

The most common static approaches seek to create some breathing space posteriorly by removing a portion of one arytenoid and/or posterior vocal fold while maintaining the anterior vocal fold for phonation. Posterior cordotomy [85] or partial arytenoidectomy [86] can be performed endoscopically, often with a CO2 laser, and may provide enough airway to allow decannulation. Granulation or scar may require repeat procedures, and there is often a negative impact on voice despite the preservation of the anterior vocal fold. The procedure must be performed conservatively in order to prevent aspiration. Nevertheless, these approaches are the most commonly performed procedures for BVFP today.

Two approaches to dynamic rehabilitation of BVFP are currently being tried. "Laryngeal pacing" attempts to provide direct electrical stimulation to the PCA muscles. A series of patients underwent implantation of a pacemaker with tripolar leads implanted into one PCA [87]. Voice and airway results were superior to those from a series of cordotomy patients [88]. The pacing device delivered stimuli at a constant rate that did not change with demand; this will be incorporated in a future version of the device.

Reinnervation of the PCA has also been described. The most logical donor nerve for this is the phrenic, so that vocal fold abduction can occur that is phasic with respiration; however, surgeons have been generally unwilling to sacrifice the innervation of the diaphragm for this purpose. A significant advance in this realm came from Marie, who found that one phrenic root (C3 or C5) can be used for the PCA and the diaphragm will still have function [89]. This procedure is technically much more challenging than the static procedures but offers the potential for complete return to normal laryngeal function. A more complete review of treatment for BVFP was provided by Li et al. [90].

Frontiers

Many researchers continue to investigate new ideas for treating vocal fold paralysis.

Nimodipine is a calcium channel-blocking agent that has been found to be neuroprotective by reducing cellular apoptosis after neuronal injury and promoting axonal sprouting at the nodes of Ranvier, perhaps accelerating nerve growth. It was first reported by Mattson et al. in a case report of RLN repair [91]. Subsequent studies in rat laryngeal nerve injury models appeared to support its use [92, 93]. Rosen et al. carried out an open-label prospective trial in which 28 patients who presented with acute vocal fold paralysis were given nimodipine for 3 months [94]. They found 60% of the patients recovered purposeful movement, compared with an estimated 20% without nimodipine based on historical controls. Mattson et al. reported results for 19 patients with complete RLN transection injuries (more severe than the Rosen group) who were treated by primary microneural repair and postoperative nimodipine for 2–3 months [95]. All had good voice recovery, with 8/19 (42%) having some purposeful movement on videolaryngoscopy and one having completely normal function. Neither study reported any adverse side effects. A randomized clinical trial comparing nimodipine to placebo is the next step.

The use of stem cells to restore laryngeal function was first reported by Halum et al. [96]. She was able to demonstrate that autologous muscle progenitor (stem) cells could be isolated from skeletal muscle, cultured to a suitable mass, and implanted into a denervated vocal fold. Subsequent analysis shows the stem cells become incorporated into the recipient vocal muscle, and reinnervation of the muscle is enhanced. In a canine study using a complete transection-repair model, we were able to also demonstrate that the strength of adduction was increased by implanting autologous muscle stem cells into the TA muscle, to as much as 128% of baseline [97]. We have also found this approach reduced glottal resistance in canines with bilateral RLN transection and repair when stem cells were implanted into the PCA muscle (*manuscript under review*). The role of stem cells for rehabilitation of vocal fold paralysis is still in evolution but shows great promise [98].

Another approach under investigation by this author is to reduce synkinetic reinnervation of the PCA muscle by blocking it with an injectable microtubule inhibitor such as vincristine [99, 100]. In a canine model of complete RLN transection with repair, blocking PCA reinnervation with a single injection results in recovery of adductor strength to 80% or more, compared with 60% for control animals without the blocking agent. But the blocking agent does not work if given after reinnervation has already taken place, which is typically in the range of 4–6 months after the model nerve injury. Thus, a window of opportunity exists to use this approach. We compared results in our model in which vincristine was given at various time points after the initial injury and found that 3 months gave the same benefit as giving the drug at time 0, 5 months did not offer any benefit, and 4 months gave an intermediate result [101]. Intramuscular vincristine injection did not cause any adverse tissue reactions [102]. A human trial is planned.

Basic fibroblast growth factor (bFGF) has been found to promote both nerve and muscle regeneration and has been applied to laryngeal injury models. Kaneko et al. reported a series of rats that underwent RLN transection followed by four weekly injections of bFGF or saline starting

4 weeks from the date of injury [103]. Four weeks after the last injection, the bFGF group had greater TA muscle cross-sectional area and an increase in the numbers of neuromuscular junctions and satellite (stem) cells. Goto et al. found the same positive results using a single high-dose injection [104]. Further work will help define the role of this adjunct therapy in patients with vocal fold paralysis, as well as vocal fold atrophy from other causes.

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Congenital Neurologic Disease

20

Kästley M. Marvin and Matthew T. Brigger

Introduction

Congenital anomalies of the larynx encompass a broad range of disorders, of which neurologic disease makes up a sizeable percentage. Congenital neurologic disease that affects the larynx manifest in unique ways in children compared to adults. Instead of patients presenting with dysphonia, infants will typically have airway and/or swallowing difficulties, which may progress to voice complaints in childhood. As such, congenital neurologic disorders of the larynx must remain in the differential for any child with stridor, dysphagia, or dysphonia. Congenital disorders with a neurologic basis that affect the neonatal larynx include vocal fold paralysis, laryngomalacia, cerebral palsy, and laryngeal discoordination.

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Epidemiology

Given the variety of congenital disorders that can affect the neonatal larynx, it is difficult to define the incidence and epidemiology. When examining causes of neonatal stridor, the two most frequent causes, which comprise up to 85% of cases, are laryngomalacia (60–75%) and vocal fold paralysis (10%) [1].

Pathophysiology

Laryngomalacia

Laryngomalacia is the most common cause of stridor in infants. The typical presentation is inspiratory stridor that begins in the first weeks of life, increasing over the initial several months, peaking around 6 months of age, and then resolving between 12 and 24 months. The hallmarks are short aryepiglottic folds, a curled or omega-shaped epiglottis, and prolapse of the arytenoid mucosa with collapse of supraglottic structures during inspiration (Fig. 20.1). Most infants with laryngomalacia do not require intervention; however, a subset of patients, up to 22%, with severe disease marked by airway obstruction, cyanosis, or failure to thrive do require surgical intervention [2].

The neurologic component of laryngomalacia arises from abnormal laryngeal tone and

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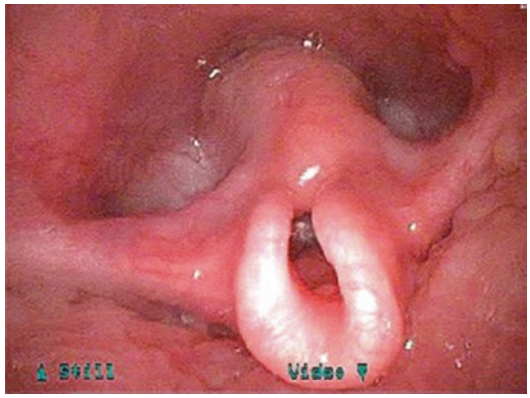

Fig. 20.1 Laryngomalacia with curled, omega-shaped epiglottis, short aryepiglottic folds, and collapse of supraglottic structures

impaired sensorimotor integrative function of the larynx [2]. Disease severity tends to correlate with degree of neurologic impairment, as more severely affected infants have greater mucosal sensory deficits. Interestingly, the observed higher laryngopharyngeal sensory thresholds tend to normalize all patients around 9 months of age, which corresponds with their improved symptomatology [2]. Developmental immaturity may play a role in the etiology of laryngomalacia.

A comorbid neurologic disorder is observed in up to 20% of infants with laryngomalacia, with a higher incidence in those with severe laryngomalacia compared to infants with mild or moderate disease [2]. Approximately 50% of patients with syndromic craniosynostosis have airway disorders, including laryngomalacia. These patients are more likely to have severe laryngomalacia and additional secondary airway disorders than patients with isolated laryngomalacia [3]. Infants with laryngomalacia that require surgical intervention who also have a concomitant neurological comorbidity more often fail to improve with supraglottoplasty alone and require tracheostomy [4]. Surgeons must bear this in mind when a patient with laryngomalacia continues to be symptomatic after supraglottoplasty.

Discoordinate pharyngolaryngomalacia (DPLM) is another entity that can be responsible for failure to improve after supraglottoplasty. These patients have severe laryngomalacia with excessive supraglottic collapse on exam, but often without the classic foreshortened aryepiglottic folds and redundant mucosa. In one series, almost 33% of affected infants with severe laryngomalacia failed to improve after supraglottoplasty and were subsequently discovered to have DPLM [5]. This is frequently associated with severe swallowing issues. These children require investigation to identify additional sites of obstruction and may ultimately require tracheostomy to secure a safe airway.

Vocal Fold Paralysis

Vocal fold paralysis (VFP) is the second most common cause of stridor in infants. The term paralysis applied here may be slightly misleading; more appropriate is a description of impaired mobility as some adductor movement may be observed despite impairment of abductor motion. This dysfunctional innervation is thought to be responsible for the range of motion impairment and symptoms observed [6].

The most common presenting symptoms for vocal fold paralysis in children are dysphonia in 61.4%, respiratory symptoms in 54%, and dysphagia in 49.5% of patients [7]. In cases of unilateral paralysis, infants usually have a weak, breathy cry and feeding difficulties including aspiration (Fig. 20.2). Bilateral paralysis typically presents with stridor, a preserved strong cry, and signs of respiratory distress. Bilateral VFP is more common than unilateral in neonates, but this reverses in older children [6]. Unilateral VFP is frequently, but not exclusively, due to iatrogenic causes, while bilateral VFP is more likely to be congenital with a neurologic or idiopathic etiology [8]. In unilateral VFP, the left vocal fold is more likely to be affected than the right owing to its longer course into the chest [7]. Table 20.1 outlines the causes of VFP in children [6].

In neonates, neurologic causes of unilateral VFP include central nervous system (CNS) abnormalities, iatrogenic surgical or intubation trauma, cardiovascular anomalies, and birth trauma [9].

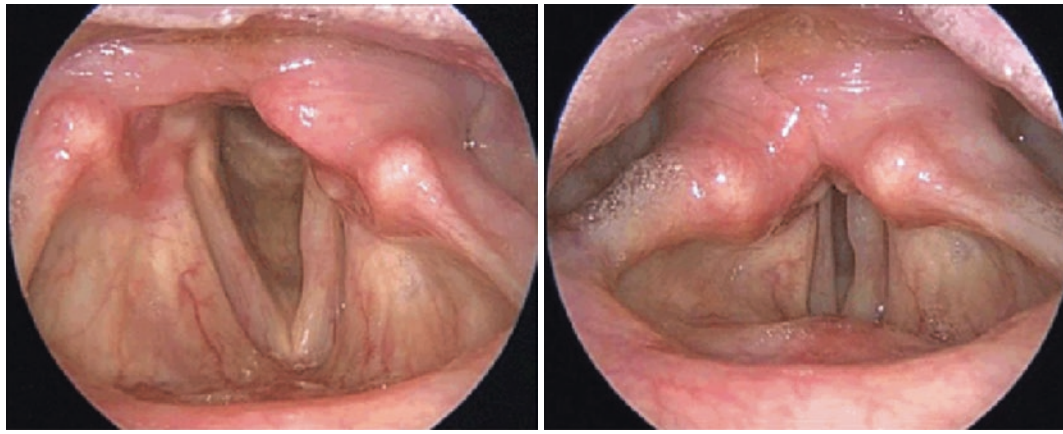

Fig. 20.2 Unilateral left vocal fold paralysis

Table 20.1 Causes of vocal fold paralysis in children [6]

Congenital	Cerebral agenesis
	Hydrocephalus
	Encephalocele, meningomyelocele, meningocele
	Arnold-Chiari malformation
	Nucleus ambiguous dysgenesis
	Congenital myasthenia gravis
	Skull base platybasia
	Cardiovascular anomalies
	Bronchogenic cyst
	Esophageal cyst, duplication, atresia
	Cricopharyngeal stenosis
Inherited	Autosomal dominant
	Autosomal recessive
	X-linked
	Charcot-Marie-Tooth disease
Acquired	Trauma
	Birth injury
	Iatrogenic surgical (cardiovascular or esophageal)
	Foreign body ingestion
	Pertussis encephalitis
	Polio encephalitis
	Diphtheria
	Rabies
	Syphilis
	Tetanus
	Botulism
	Tuberculosis
	Guillain-Barre syndrome
	Vincristine neurotoxicity

Almost 80% of cases of unilateral paralysis are the result of cardiac surgery [7]. Compared with idiopathic VFP, paralysis associated with birth trauma is more likely to be unilateral, though the most common cause of traumatic bilateral VFP is birth-related trauma, and that associated with birth trauma has a higher rate of resolution [10, 11]. Bilateral VFP is most commonly idiopathic, accounting for almost half of cases, with iatrogenic surgical injury (31%), neurologic causes (19%), and other etiologies including trauma (3%) comprising the remainder [7].

CNS abnormalities implicated in both bilateral and unilateral VFP include Arnold-Chiari malformations, hydrocephalus, encephalocele, cerebral dysgenesis, hemorrhage, and leukodystrophy [9, 10, 12, 13]. Magnetic resonance imaging is necessary to rule out these CNS abnormalities, including Arnold-Chiari malformation, which accounts for one-third of neurologic causes [10]. Given that approximately 50% of cases of VFP will have no other identified abnormality and the relatively high rate of spontaneous resolution, one suggested theory of idiopathic VFP is delayed maturation of the vagal nuclei [14]. A family history of VFP should alert the provider to the possibility of familial or hereditary VFP, especially in cases of bilateral paralysis. Autosomal dominant, autosomal recessive, and X-linked etiologies have been

reported [15]. In all presumed idiopathic cases, the possibility of an unrecognized chromosomal abnormality or neuromuscular disorder should be considered [13, 16].

Additional neurologic causes of VFP include congenital myasthenic syndrome and Charcot-Marie-Tooth disease (CMT). Laryngeal manifestations of congenital myasthenic syndrome include stridor and feeding difficulties; thus, clinicians should be suspicious of this diagnosis in patients with stridor from bilateral VFP and concurrent feeding issues [17, 18]. These are a heterogenous group of disorders that cause fatigable muscle weakness, similar to myasthenia gravis, and early treatment with acetylcholinesterase inhibitors can improve weakness including that which contributes to respiratory distress and feeding difficulties [17, 18]. Charcot-Marie-Tooth disease is a hereditary peripheral sensory and motor neuropathy disorder that can manifest anywhere but occasionally affects the larynx. CMT comprises several types with type 2 being the most commonly associated with VFP. Most of these cases manifest in adulthood, but there are cases of presentation of VFP in childhood [19].

The timing and choices for management of VFP depend on the cause and natural history of the paralysis. In cases of VFP due to a medical cause, such as infection, the underlying primary disease process should be treated appropriately. If VFP is the result of intracranial hemorrhage or hydrocephalus, the paralysis can be expected to improve after appropriate management such as decompression/shunt or resolution of the hemorrhage. As such, tracheostomy can often be avoided in lieu of intubation or CPAP until airway improvement. Recovery of function in idiopathic VFP occurs in most cases. Rates of spontaneous recovery reported in the literature for idiopathic paralysis are approximately 40–65% for bilateral VFP and approximately 75% for unilateral VFP [7, 11, 20, 21]. In a meta-analysis of patients with idiopathic bilateral VFP, 74% of patients without additional comorbidities have been observed to regain movement, whereas only 38% of those with major comorbidities experienced recovery [21]. Most recover in the first year of life, though there are reports of recovery in children up to 11 years of age [1]. Given these rates of spontaneous recovery in children with idiopathic bilateral VFP, some suggest waiting until 2 years of age before performing any permanent surgical procedure [20]. Tracheostomy or another temporary adjunctive airway procedure, such as suture lateralization, may be required in the neonatal period to ensure an adequate airway [22]. In one series of children with congenital idiopathic bilateral VFP, 73% required intubation at birth for a mean duration of 60 days. About three-fourths of these patients subsequently failed extubation and underwent tracheostomy. Ultimately, 85% of these patients were able to be decannulated at a mean age of 36 months [20].

Cerebral Palsy

Cerebral palsy is a group of disorders of motor development due to nonprogressive brain damage. Dysphagia has been reported in 19–99% of these patients [23]. The dyscoordination of breathing and swallowing leads to higher rates of post-swallow inhalation. This pattern places patients at higher risk of penetration and aspiration events [23]. Impaired voluntary cough function in children with CP adds to this risk of aspiration and poor airway clearance.

Laryngeal Dyscoordination

Dysphagia and aspiration in infancy is a frequent complaint, owing to the complexity of effective swallowing and airway protection. During the pharyngeal phase of swallowing, the airway must be closed and the cricopharyngeus muscle must relax to allow food to enter the esophagus. Airway protection requires intact sensory stimulation from tactile receptors in the pharynx and an intact sequence of cessation of respiration, closure of the glottis, compression of the supraglottic structures, movement of the epiglottis, and elevation of the larynx. Then, just as important, the larynx must relax again and respiration resumes. If this so-called laryngeal adductor

response is compromised, penetration and/or aspiration can result [24].

Frequently a cause for an infant's dysphagia can be found, such as with a unilateral VFP, laryngomalacia, or neuromuscular disease. However, in a certain subset of patients there is no obvious underlying cause identified. Indeed, almost 60% of patients referred for swallowing evaluation due to persistent respiratory symptoms were found to have signs of aspiration on video fluoroscopic swallow study in the absence of additional risk factors for dysphagia [25]. The impairment in these patients is unclear. Most display cricopharyngeal dysfunction and/or impaired laryngeal elevation [26]. An element of immaturity has also been proposed, especially in premature infants [24]. Interestingly, neurobehavioral examination of preterm neonates has been shown to be associated with feeding outcomes at 1 year of age [27]. In a series of long-term follow-up of these patients, most experienced resolution of their symptoms by 3 years of age, though several persisted into the school-age years [25].

Infants with feeding difficulties with signs of aspiration on swallow study may require feeding modifications including positioning, consistency alterations, or even alternate methods of feeding to ensure safety until resolution of their symptoms.

Management

Initial evaluation of any child with an airway or swallowing disorder should begin with a thorough history, including the timing of onset of symptoms, and physical exam. This exam should include flexible laryngoscopy to assess the configuration of the larynx and vocal cord mobility. In many cases, direct laryngoscopy and bronchoscopy are also indicated to assess for synchronous airway lesions and to palpate the laryngeal structures to assess for cricoarytenoid joint mobility in cases of vocal fold immobility and to assess for a laryngeal cleft in cases of suspected aspiration. For patients with signs or symptoms of aspiration, a swallowing evaluation should be included in the initial workup. This may include a clinical evaluation, video fluoroscopic swallow study (VFSS), and/or functional endoscopic evaluation of swallowing (FEES). In children, clinical evaluations and FEES are important and are often preferred to minimize potential radiation risks associated with VFSS. Imaging should be considered in cases of VFI. Intracranial imaging is warranted for those with bilateral VFP. In cases of unilateral VFP, imaging should include the entire course of the recurrent laryngeal nerve from the brainstem to mediastinum [1].

For unilateral VFP, injection medialization or laryngeal reinnervation can be considered. Injection medialization has shown good outcomes with respect to both voice and swallowing in children [9]. It is a popular choice for children due to the temporary nature of most injectable materials and it is an endoscopic procedure with a relatively short anesthetic time. Type 1 thyroplasty is typically avoided in children due to continued growth of the framework. For bilateral VFP, treatment options include tracheostomy, vocal fold lateralization procedures, partial cordotomy, arytenoidectomy, and anterior or posterior cricoid expansion [1, 4]. Supraglottoplasty for severe laryngomalacia has a 53–100% success rate reported in the literature with 8% complication rate [2]. The rate of success decreases to 67% in patients with neurologic or syndromic comorbidities [28].

The ultimate priority, especially with bilateral VFP, is to establish a safe airway, and tracheostomy may be necessary to secure the airway thereby bypassing the site of obstruction in selected cases. Tracheostomy is more likely to be required in patients with comorbid conditions in addition to their airway anomaly [1, 3, 28]. In one meta-analysis, 59% of patients with congenital BVFP required tracheostomy with mean age of 2.54 months, 17% of these patients underwent a secondary airway surgery, and overall decannulation was achievable in 44% of cases after a mean of 14.31 months [21].

In infants with laryngeal discoordination, or aspiration of an unclear etiology, a direct laryngoscopy and bronchoscopy should be performed to rule out a laryngeal cleft or other airway anomaly. If a deep interarytenoid groove is dis-

covered, a type 1a laryngeal cleft repair or temporary augmentation can be considered to improve swallowing and reduce aspiration.

Frontiers

Laryngeal Electromyography

The use of laryngeal electromyography (LEMG) in pediatrics was first described in 1987 but is still not widely reported [29]. Unlike LEMG in adults, which is ideally done with the patient awake to record voluntary muscle action potentials with the patient speaking, LEMG in children is typically performed under general anesthesia. Needles are placed under direct visualization and/or with the use of a rigid telescope into the thyroarytenoid muscles. Spontaneous respiration allows recording of action potentials during the respiratory cycle. For this reason, communication with the anesthesiologist to maintain the correct plane of anesthesia is vital for accurate recording. A rate of 83% concordance of LEMG with endoscopic findings has been reported [29]. The optimal timing of LEMG is debated, though proposed timelines are at the time of diagnosis for bilateral VFP with a suspected central etiology and 3–6 months postoperatively in cases of iatrogenic surgical injury [8].

The utility of LEMG is also variable in the literature. In one series of patients with congenital bilateral VFP, the findings on LEMG did not impact treatment decisions in any patient [29]. However, in another small series, findings correlated with subsequent recovery of function and impacted treatment decisions in at least 1 of the 3 patients [8]. Children with bilateral VFP due to Arnold-Chiari malformation who were treated with a shunt were found to have normal LEMG postoperatively and all had recovered normal vocal fold mobility at subsequent follow-up [8]. For patients with evidence of other laryngeal abnormalities in addition to VFP, LEMG data affected treatment decisions in 25% [29]. It has more conclusively been shown that in unilateral VFP due to iatrogenic surgical injury, abnormal muscle unit action potentials are a poor prognostic indicator for spontaneous recovery [8].

It seems reasonable to conclude that routine application may not be especially useful. Rather, LEMG appears most useful to evaluate patients with non-idiopathic vocal fold motion abnormalities.

Neuromuscular Treatment Options for VFP

Laryngeal pacing provides direct stimulation to one posterior cricoarytenoid (PCA) muscle during the inspiratory phase of the respiratory cycle [30, 31]. There has been some preliminary success in outcomes for both airway and voice in adults with bilateral VFP; patients had improved post-op ventilation parameters and superior voice outcomes compared to posterior cordotomy [30]. The use in children has not been investigated.

Laryngeal reinnervation has been described for adults with bilateral VFP due to nerve injury in which a foreign nerve, typically branches of phrenic, is connected to the denervated PCA to trigger vocal fold abduction during the respiratory cycle [32]. Use in children has not been investigated. This approach contrasts with reinnervation for unilateral VFP, which is established in pediatric patients. The goal of unilateral reinnervation is to restore muscle bulk and tone and improve synkinesis rather than restore functional motion to the vocal fold. There are a variety of techniques; however, nonselective ansa cervicalis-recurrent laryngeal nerve reinnervation has had the most favorable results [33]. Reinnervation for unilateral VFP has demonstrated superior voice outcomes compared to injection laryngoplasty and has shown to improve liquid dysphagia [33]. Another benefit is that reinnervation avoids injecting a foreign material into these children's larynges. However, there are risks that include the potential need for revision procedures, alteration of the laryngeal framework, and longer anesthetic time. Thus, it is advisable to wait to ensure that there will be no spontaneous recovery of RLN function. However, a negative correlation is reported between the

elapsed time since initial injury and reinnervation outcomes [33].

In adults, the use of Botox for bilateral VFP is predicated on paralysis being related to synkinetic reinnervation of the laryngeal musculature after injury [34]. Selective injection into the thyroarytenoid and lateral cricoarytenoid muscles allows unopposed activation of PCA abduction during the respiratory cycle [34]. Botox has been used in children with avoidance of tracheostomy in 6 of 7 children in a small case series who underwent injection into the external laryngeal musculature including cricothyroid, sternothyroid, and sternohyoid muscles. The theory behind injection into the external laryngeal musculature in these cases is that selective paralysis of the external laryngeal muscles relaxes the position of the larynx to increase the glottic aperture and thus create an adequate airway [35].

Multidisciplinary Aerodigestive Teams

Care of patients with complex congenital or acquired disorders that affect breathing and/or swallowing including conditions that affect the airway, lungs, gastrointestinal tract, and growth requires a team of multiple specialists. The first multidisciplinary aerodigestive program was developed at Cincinnati Children's Medical Center in 1999 and since then additional 50 programs in 32 states have been created. The appropriateness of a child for evaluation by these multidisciplinary team is defined as: "a child with a combination of multiple and interrelated congenital and/or acquired conditions affecting airway, breathing, feeding, swallowing, or growth that require a coordinated interdisciplinary diagnostic and therapeutic approach to achieve optimal outcomes" [36].

The core specialties involved in the care of aerodigestive patients include otolaryngology, pulmonology, gastroenterology, and speech-language pathology and/or occupational therapy with feeding/swallowing therapy experience. Additional members of the team should include nursing and a care coordinator. One key component of the aerodigestive team is triple endoscopy and coordination of anesthetic episodes with laryngoscopy and bronchoscopy, flexible bronchoscopy, and esophagogastroduodenoscopy. These teams have been shown to decrease costs of care and reduce the number of anesthetic episodes by 41% [37].

Conclusion

Congenital neurologic disorders that affect the larynx are varied, but nearly all present early in life with airway and/or swallowing dysfunction. Laryngomalacia and vocal fold paralysis are the most common causes of stridor in the neonate. In all infants with laryngeal pathology, optimizing the airway should be the first priority. Secondarily, investigation into the underlying cause of the pathology and full evaluation to evaluate for secondary airway lesions can be carried out. These patients should ideally be treated in coordination with a multidisciplinary aerodigestive team and often require long-term follow-up.

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Neurogenic Cough

21

Alissa M. Collins

Introduction

Cough is a natural defense mechanism that clears the larynx, trachea, and bronchi of mucus, foreign bodies, and pathogens. It can also be a warning sign of disease such as malignancy, asthma, or an infectious process. It is a common symptom which leads patients to seek evaluation by primary care physicians and specialists. Viral infection is the most common cause of acute cough and typically abates within 3 weeks. When cough persists beyond 8 weeks, it is deemed chronic and can have a significant impact on the quality of life. Neurogenic cough (also known as postviral vagal neuropathy and idiopathic neurogenic cough) by definition is a chronic cough and is typically the result of a laryngeal sensory neuropathy following a viral illness [1]. While sensory neuropathies typically manifest as a decreased responsiveness of the nerve to stimuli, in the case of neurogenic cough, the larynx is in a hypersensitive state.

Neurogenic cough is a diagnosis of exclusion, and other causes of cough such as gastroesophageal reflux (GER), allergies, postnasal drip, pulmonary disease (asthma, chronic obstructive pulmonary disease, malignancy, etc.), and sinonasal infection must be investigated. Patients often have been seen by their primary physicians and specialists such as pulmonologists and gastroenterologists prior to being referred to an otolaryngologist. Patients may have been treated for allergies, postnasal drip, GER, and reactive pulmonary disease with steroids, antibiotics, nasal sprays, antireflux medications, and inhalers, without significant improvement in the cough. Many will have undergone extensive testing including pulmonary function tests, methacholine challenge, esophagogastroduodenoscopy, manometry, pH probe testing, and radiologic studies. Patients often endorse specific triggers for the cough [2] and potentially other complaints relatable to the hypersensitive or irritable larynx such as laryngeal spasm, globus, throat irritation, throat clearing, throat pain, dysphonia, odynophonia, and/or dysphagia [3].

The normal cough reflex is complex and involves both central and peripheral pathways. Upregulation of cough receptors in the larynx and brainstem sensitization have been implicated in neurogenic cough. Behavioral modification, voice therapy, medications, vocal fold injection augmentation, laryngeal Botox injections, and peripheral nerve blocks have been reported for the treatment of neurogenic cough with varying degrees of success.

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Epidemiology

Chronic cough in adults is estimated to have a global prevalence of 9.6% [4]. Neurogenic cough specifically has been reported in 12–42% of patients in specialty cough clinics [5, 6]. Multiple studies report more women than men have neurogenic cough, but it is unclear if this is a true gender predilection or a function of the study group being a treatment-seeking population. Those with neurogenic cough tend to be in their sixth and seventh decade, though all ages can be affected [6–11]. There have been no studies to suggest an ethnic or racial predilection for neurogenic cough. Those with neurogenic cough were more likely to report a history of URI (48%) [6] or surgery preceding the onset of the cough, but no other risk factors have been reported in the literature. Anecdotal evidence suggests patients with a history of resolved neurogenic cough are more susceptible to recurrence.

Pathophysiology

Neurogenic cough is a laryngeal sensory neuropathy which is thought to be the result of hyperexcitability of the nerves that respond to cough stimuli. In the normal functioning cough reflex, sensory receptors in the epithelium of the larynx such as transient receptor/ion channel potential vanilloid 1 (TRPV1), transient receptor potential ankyrin (TRPA1), rapidly adapting receptors (RARs), slow adapting receptors (SARs), and C-fiber receptors are stimulated by their specific threshold stimuli (e.g., capsaicin, stretch, acid). Release of neuropeptides such as neurokinins and substance P mediate the afferent response to the brainstem vagal nuclei at the nucleus solitarius where central coordination of efferent signals takes place. The cerebral cortex is also involved in the cough reflex as the urge to cough can be voluntarily controlled. Motor signals for the efferent limb of the cough reflex arise in the cortex, cerebellum, and nucleus ambiguous [12] and the reflex terminates with production of the cough.

While the mechanism is poorly understood, injury to the laryngeal sensory nerves from either viral illness, mechanical trauma, or surgery is thought to alter laryngeal sensory signaling [13]. Other well-studied manifestations of isolated neuropathy affecting cranial nerves include glossopharyngeal neuralgia, Bell's palsy, sudden sensorineural hearing loss, olfactory dysfunction, and trigeminal neuralgia. Indirect injury to the nerve via disruption of the blood supply and/or direct injury to the nerve has been shown in other cases of viral-induced neuropathies [14]. Parallels have also been drawn between the sensory dysfunction in neurogenic cough and chronic pain. The abnormal pain sensation in neuralgias can manifest as allodynia (nonpainful stimulus causing pain) and hyperalgesia (a below threshold painful stimulus triggers pain) which is similar to neurogenic cough with allotussia (non-tussive stimulus triggers cough) and hypertussia (a below threshold cough stimulus triggers cough) [15]. Additionally, paresthesias are present in both pain neuralgias and manifest in neurogenic cough as a "tickle" or a feeling of laryngeal dryness or irritation [2].

Central to the idea of hyperexcitability in neurogenic cough is the elevated response to cough stimuli through peripheral sensitization via upregulation of receptors and decreased cough reflex threshold via excitation of the vagus nerve afferents. Increased expression of TRPV1 receptors [16, 17] and lowered threshold for the cough reflex when exposed to capsaicin [18] have been demonstrated in patients with chronic cough. Neuropeptide release has also been implicated in the pathophysiology of neurogenic cough. It is thought that neuropeptide production and release can increase following viral injury leading to local neurogenic inflammation with smooth muscle spasm, edema, and mucus secretion which can further exacerbate the cough [19]. Chu et al. propose that the harsh glottic closure and vocal fold trauma with each cough further perpetuate neuropeptide release and cough [10].

One way in which central sensitization in chronic pain has been explained is by repeated exposure to noxious stimuli which leads to alterations in the dorsal horn spinal cord due to neural

plasticity whereby nociceptive neurons are responsive to nociceptive and non-nociceptive pain [20]. Again, this is similar to neurogenic cough where non-tussive stimuli trigger cough. Theories of central sensitization are further supported by improvement in cough with medications such as GABA analogues [1, 15] and tramadol [21], which are known to work at central mechanisms.

Neurogenic cough is described as a sensory neuropathy, but some authors [9, 10] have proposed the coexistence of motor neuropathy given the proximity of the sensory and motor fibers of the vagus nerve. It has been suggested that the neuroplastic changes leading to sensory hyperexcitability can also to lead to an increased laryngeal tone causing the larynx to sit in a "ready state" for cough [10]. Crawley et al. propose motor neuropathy manifesting as vocal fold paresis increases glottal closure forces, causing laryngeal trauma and perpetuating the neurogenic cough [9].

Voice-, Airway-, and Swallow-Specific Symptoms, Findings, or Sequela

Neurogenic cough is a diagnosis of exclusion, and while no specific symptom or exam finding confirms the diagnosis, there are aspects of the patient history and exam that can be helpful in guiding the clinician to the diagnosis. Patients may report the onset of the dry cough following a viral illness or surgery [1, 6]. Laryngeal hypersensitivity is the hallmark of neurogenic cough, and thus specific triggers for cough may be elicited such as strong smells; mechanical stimuli such as laughing, talking, or singing; or extreme temperatures of the air, food, or liquids [2, 7] (Table 21.1). Talking is a common trigger for cough and it has been hypothesized that vocalization triggers laryngeal pressure receptors and cough [2].

Symptoms of neurogenic cough can occur in conjunction with other laryngeal symptoms such as globus sensation, dysphagia, dysphonia, odynophonia, throat clearing, and laryngeal pain suggesting there is overlap in the presentation of neurogenic cough with other laryngeal disorders

Table 21.1 Triggers for neurogenic cough

Paresthesia	Throat irritation/dryness/itch Mucus sensation

Tussive	Inhalation
	  Cleaning chemicals (bleach, ammonia, aerosols)
	  Perfume/cologne
	  Smoke
	Dust/pollen
	Shortness of breath

Non-tussive	Mechanical
	  Talking
	  Laughing
	  Singing
	  Swallowing
	  Change in body position
	  Forceful inhalation (exercise)
	  Laryngeal manipulation
	Thermal
	  Air temperature
	  Food or liquid temperature
	Humidity
	Fan/air-conditioning
	Stress/anxiety

such as irritable larynx syndrome [2, 14]. Altman et al. offer that "our current limited understanding of the pathophysiology underlying these disorders, combined with variation in clinical phenomenology, prevents drawing clear boundaries between them" [14].

The coexistence of cough with motor and/or sensory deficits in the vagus, recurrent (RLN), or superior laryngeal nerve (SLN) can suggest peripheral nerve injury. Examination of the upper aerodigestive tract with a flexible laryngoscope allows visual assessment of function and often appears normal in the resting state [22]. Velopharyngeal closure can be assessed with the patient saying "ka-ka-ka" or "kitty cat." Symmetry of pharyngeal contraction can be assessed with the patient saying a high pitched "eee." Deficits in either of these maneuvers as well as pooling of secretions in the vallecula or hypopharynx can suggest central or vagal nerve deficit [14]. Pooling of secretions in the hypopharynx suggests cricopharyngeal hypertonicity, which is seen in RLN injury [14]. Vocal fold motion is best assessed with stroboscopy. Vocal fold paresis/paralysis, glottic insufficiency, vibratory asymmetry, vocal fold atrophy, vocal fold height differences, unilateral hyperfunction contralateral to the affected side,

and decreased tone can all suggest RLN injury. The SLN has both motor and sensory functions in the larynx via its external and internal branches, respectively. In patients with suspected neurogenic cough, it is important to assess the ability to lengthen the vocal fold via pitch glide as a deficit in this task could suggest concomitant SLN sensory neuropathy [14].

Assessment of motor paresis on stroboscopic examination can be challenging as there are no universally agreed upon findings that make the diagnosis. Laryngeal electromyography (LEMG) has been used in assessment of laryngeal motor abnormalities to prognosticate about the potential for recovery of function. A 2005 study by Lee and Woo used LEMG assessment of laryngeal motor function to predict the response to gabapentin in patients suspected of having laryngeal sensory neuropathy [8]. A more recent study by Bock et al. used surface-evoked laryngeal sensory action potential (SELSAP) technique to assess for sensory neuropathy in patients with chronic cough. They found the peak amplitude of SELSAP waveform was lower in patients with chronic cough compared to a control group. They argue SELSAP should be used to assess for laryngeal sensory in patients with chronic cough but admit that confirmation of the neurogenic cough diagnosis is made with response to medication [13]. Altman et al. point out that little is known about the utility of LEMG in the assessment of paresis and chronic cough. They recommend when the physician is considering LEMG in this patient population they ask "how the LEMG findings are going to change their treatment plans" [14].

Currently, there are no laboratory tests or imaging studies for diagnosing neurogenic cough. Since it is a diagnosis of exclusion, most patients will have undergone chest X-ray to rule out structural pulmonary causes of cough and no further diagnostic imaging is indicated.

Pharmacology/Medical Management

Neurogenic cough can coexist with other common causes of chronic cough such as GER, allergic rhinitis, postnasal drip, asthma, and COPD. It is imperative to treat these underlying conditions while simultaneously addressing the neurogenic component of the chronic cough. Neurogenic cough frequently presents in the setting of irritable larynx syndrome and patients often complain of concomitant throat irritation and globus. Often, the response to this sensation is throat clearing which then causes further laryngeal irritation. Patients should be discouraged from throat clearing and should be taught alternative responses to this sensation such as taking a sip of water, pursed-lip breathing, or dry swallowing to attempt to relieve the sensation and minimize further laryngeal irritation. Ensuring adequate hydration while minimizing caffeine and alcohol intake is important as the urge to cough has been shown to be higher in those with poor vocal hygiene [2]. Consideration should be given to discontinuation or dose reduction of medications that can be drying. Patients should be encouraged to avoid laryngeal irritants such as throat lozenges with mint, menthol, or eucalyptus as well as specific triggers for cough. Referring the patient to a speech-language pathologist (SLP) for cough therapy can be useful.

Vertigan et al. published the only randomized placebo-controlled trial comparing the efficacy of speech pathology treatment and placebo in the management of chronic cough. Both groups had four 30-minute visits with an SLP over a 2-month period. Participants in the treatment group were provided cough reduction strategies, education, counseling, and behavioral modification techniques to reduce laryngeal irritation, while those in the placebo group received healthy lifestyle education with no specific education given about cough management. Subjective symptom scores were documented pre- and posttreatment for both groups using an author-designed survey assessing severity of cough, breathing, voice, upper airway symptoms, and limitation. Both groups had improvement but the treatment group had greater improvements than placebo for all symptoms assessed. More patients in the treatment group felt to have a successful outcome as determined by the treating SLP when compared to the placebo group, but this finding is subject to bias as it was not possible to blind the SLP to the intervention type [23]. Those unable to participate in

therapy due to time constraints, proximity to a trained SLP, cost, or cognitive abilities or who do not achieve meaningful improvement with therapy may benefit from medications.

The pharmacologic therapies investigated for the treatment of neurogenic cough have been successfully used for the management of neuropathic pain which is not surprising given the parallels in their pathophysiology. Drugs for neurogenic cough (Table 21.2) [1, 7, 9, 10, 15, 21, 24–27] can be divided into two groups: neuromodulators or those working at the central nervous system (CNS) and those working at the receptor antagonist. Most of the drugs working at the receptor antagonist are investigative (not commercially available) and will not be discussed here. However, there are two commercially available receptor antagonists, ketamine and Orvepitant (GlaxoSmithKline, Philadelphia, PA, USA), which have been evaluated in the treatment of chronic cough. Ketamine is commonly used for analgesia in acute and chronic pain. N-methyl-D-aspartate (NMDA) receptors are present in both central and peripheral tissues and are involved in acid-evoked reflexes such as the cough reflex via TRPV1 and acid-sensing ion channels (ASICs). A recent study investigating the use of ketamine in chronic cough showed no improvement compared to controls with regard to capsaicin cough reflex sensitivity or cough frequency [28]. Orvepitant is a neurokinin-1 receptor (NK_1R) antagonist, which is currently in a phase 2 trial evaluating its use in chronic refractory cough. Preliminary data suggest it is safe, is well tolerated, and offers durable improvement in cough frequency at four weeks posttreatment [29].

Tramadol is a weak opioid analgesic which functions centrally at mu receptors and peripherally by inhibiting serotonin and norepinephrine reuptake. It is typically dosed 50 mg every 8 hours as needed with a maximum daily dose of

Table 21.2 Treatment options for neurogenic cough

Drug	Dosing	Maximum safe dose	Study
Tramadol	50 mg every 8 hours as needed, taper off	400 mg/day	Dion et al. [21]
Amitriptyline[a]	10 mg daily (bedtime) 10 mg at bedtime, titrate up every 7 days by 10 mg to max dose of 100 mg, taper off	200–300 mg/day	Bastian et al. [24], Jeyakumar et al. [25] Ryan and Cohen [26]
Gabapentin	300 mg daily, titrate up by 300 mg daily to max dose of 1800 mg, taper off	1800 mg/day	Ryan et al. [15]
Pregabalin	75 mg twice per day, titrate up to 150 mg twice per day over 4 weeks, taper off	600 mg/day divided every 12 hours	Halum et al. [1]
Baclofen	10 mg daily	80 mg divided four times per day	Dicpinigaitis and Rauf [27]
Botulinum toxin type A	Average 4 units (range 1–10 units) total to thyroarytenoid muscles	n/a	Chu et al. [10]
Equal parts triamcinolone acetonide or methylprednisolone *and* 1% lidocaine with 1:100,000 epinephrine or 0.5% bupivacaine	2 mL injected at insertion of SLN into thyrohyoid membrane	n/a	Simpson et al. [7]
Carboxymethylcellulose/calcium hydroxyapatite[b]	Vocal fold injection augmentation	n/a	Crawley et al. [9]

SLN superior laryngeal nerve
[a]Nortriptyline can be dosed like amitriptyline but the maximum safe dose is lower, 160 mg/day
[b]Hyaluronic acid is another alternative

400 mg [30]. There are no RCTs investigating the use of tramadol in neurogenic cough. Sindrup evaluated the use of tramadol for polyneuropathy and found statistically significant improvements in scores for both pain and allodynia [31]. However, a 2017 Cochrane Review of tramadol use in neuropathic pain concluded there are few, low-quality studies that fail to support its use [32]. A recent study investigating the use of tramadol 50 mg every 8 hours as needed for neurogenic cough showed improvement in cough with average Cough Severity Index (CSI) scores decreasing 9 points (23–14, $P = 0.003$). Likewise, average Leicester Cough Questionnaire (LCQ) scores improved 29 points (74–103, $P = 0.005$) [21]. Potential side effects of tramadol include constipation, nausea, vertigo, and somnolence. There is a risk of serotonin syndrome when tramadol is taken with other serotoninergic medications making it important to query patients about whether they are taking a SSRI or SNRIs [33]. Tramadol is a controlled substance with potential for abuse and addiction. Dependence has been reported at doses as low as 50 mg per day [34].

Tricyclic antidepressants (TCAs) such as amitriptyline and nortriptyline inhibit serotonin reuptake and have been used in the management of neurogenic cough. Jeyakumar investigated the use of amitriptyline 10 mg vs codeine-guaifenesin in patients with postviral vagal neuropathy. The Cough QOL questionnaire was completed prior to commencing treatment and after 10 days of treatment. Patients self-reported their response to treatment as complete (75–100% improvement), partial (25–50% improvement), or no response (0% improvement) [25]. Eighty-seven percent of those treated with amitriptyline had a >50% improvement in their cough compared to 8% in the codeine-guaifenesin group [14]. Similar improvements in cough with amitriptyline were also found in studies by Bastian and Norris [24, 35]. Ryan and Cohen reported on the long-term follow-up of patients with laryngeal hypersensitivity and neurogenic cough treated with amitriptyline. Thirty percent of the study group was found to still be taking the 10 mg dose of amitriptyline prescribed at the initial visit and 80% reported greater than 50% improvement in their cough. Almost half of the patients no longer taking amitriptyline at the time of the long-term follow-up noted side effects as the reason for discontinuation of the medication [26]. Reports of side effects with amitriptyline include sedation, xerostomia, and dizziness and are reported in up to 45% of patients [26, 36]. Nortriptyline has also been used in the treatment of neurogenic cough and is felt to have a more favorable side effect profile.

Gabapentin is a structural analogue of gamma-aminobutyric acid (GABA) and works by blocking centrally located voltage-gated calcium channels. In a randomized placebo-controlled trial evaluating the effectiveness of gabapentin (300 mg titrated to a max of 1800 mg) versus placebo in neurogenic cough, patients treated with gabapentin had improvement in LCQ with a mean change from baseline of 2.5 (SD 3.1) points for gabapentin and 1.4 (SD 4.1) for placebo ($P = 0.004$). However, after tapering off the gabapentin at 12 weeks, the improvements were not sustained. In the same study, Ryan also evaluated central sensitization via cough reflex sensitivity to capsaicin and the presence of specific cough triggers; cough reflex sensitivity did not change while on gabapentin suggesting its effect was not via peripheral sensitization [15]. Lee and Woo have reported the co-occurrence of motor and sensory vagal neuropathy [8]. A 2017 retrospective study indicates an improved response to gabapentin (100 mg titrated up to 1800 mg daily) in patients with neurogenic cough found to have vocal fold paresis on stroboscopy compared to those with neurogenic cough without paresis. No EMG was performed to confirm the stroboscopic findings and no durability of benefit was evaluated [37]. Side effects of gabapentin include somnolence, fatigue, and drowsiness and are reported in up to 31% of patients [15].

Pregabalin is structurally similar to gabapentin and works via the same mechanism. A retrospective review by Halum et al. investigated the use of pregabalin 75 mg twice per day titrated to 150 mg twice per day over 4 weeks in patients with laryngeal hypersensitivity. Ten of the 12 patients in their study had subjective improvement in their symptoms with pregabalin [1]. In 2016, Vertigan published an RCT comparing

speech pathology treatment with placebo medication for chronic cough vs speech pathology treatment combined with pregabalin. The change in LCQ between pre- and posttreatment was 6.6 (SD 4.5) for the speech pathology and pregabalin groups and 3.3 (SD 2.3) for the speech pathology and placebo groups ($P = 0.024$). This improvement was sustained in both groups 4 weeks after discontinuing interventions with no significant change in LCQ scores ($P = 0.702$). Seventy-five percent of participants from each group reported side effects including dizziness, weight gain, and changes in vision and cognition though no participant withdrew from the study secondary to these effects [38]. Pregabalin is a controlled substance with abuse and addiction potential. Pregabalin is more expensive than some of the other neuromodulators. It may not be covered by the patient's insurance or may require preauthorization.

Similar to gabapentin and pregabalin, baclofen is a GABA agonist. A double-blind crossover trial of 10 mg baclofen daily showed improvement in cough sensitivity as well as reduced cough severity and frequency. The improvement persisted for two weeks after medication cessation [27].

Considerations prior to commencement of pharmacologic therapy include medication cost, potential for side effects, risk of abuse/addiction potential, and interactions with other medications. There is a high rate of sedation with the neuromodulators making evening or bedtime dosing preferred. For this reason, a "trigger reduction" approach to treatment has been proposed prior to the initiation of systemic therapy for neurogenic cough. The regimen includes regular use of nasal irrigation, nasal steroid, and nasal antihistamine along with a Mediterranean diet with alkaline water and reflux precautions. Twenty-nine patients with chronic cough were prescribed the regimen and found to have 10- and 11-point reductions in their RSI and CSI scores at 6 weeks, respectively [11].

Antibiotics and steroids are often prescribed empirically in cases of chronic cough. However, for neurogenic cough these medications have not been studied and would be unlikely to provide benefit given the mechanisms of neurogenic cough as we currently understand them.

Procedures and Treatment Outcomes

Neuromodulators with or without cough therapy are the mainstay of treatment in neurogenic cough. However, some procedures (see Table 21.2) show promise in the management of neurogenic cough. Chu et al. report significant improvement in chronic cough in four patients with botulinum toxin type A injections to the thyroarytenoid muscles. Patients underwent a minimum of four injections with an average dose of 4.0 units per injection. The mean duration of therapy prior to symptom resolution was 25.7 months. Symptom resolution was attributed to the reduction in laryngeal hypertonicity secondary to postviral vagal motor neuropathy and Botox-induced vocal fold paresis with reduction in laryngeal trauma during cough [10].

Vocal fold injection augmentation has been proposed as a treatment option for neurogenic cough patients presenting with vocal fold paresis on stroboscopic examination. In their small study, five of six patients reported improvement in cough following injection augmentation of the paretic vocal fold with methylcellulose or calcium hydroxyapatite. They attributed the improvement in the cough to the reduction in glottal closure forces leading to changes in neuropeptide release and alterations in sensory signaling [9].

Simpson et al. report 83% of patients had improvement in their chronic cough with the injection of a 50:50 solution of long-acting particulate steroid and a local anesthetic at the insertion point of the internal branch of the superior laryngeal nerve at the thyrohyoid membrane. They hypothesized the nerve block alters the aberrant sensory pathways involved in the cough reflex [7].

Frontiers

Neurogenic cough continues to be a challenging problem to treat despite the advances in our understanding of the parallels in the pathophysiology of neuropathic pain. The diagnosis is often made based on the history and in many cases a normal laryngeal examination. Readily available

diagnostic testing to reliably confirm laryngeal sensory neuropathy is lacking. Current available treatment options are limited to cough therapy and medications targeting on the central portions of the cough reflex pathway. Unfortunately, not all patients with neurogenic cough respond to medications and many abandon treatment due to undesirable side effects. Randomized controlled trials comparing neuromodulators are lacking and could aid in better understanding of dosing, titration, and duration of therapy. The variable response to medication also suggests heterogeneity in the etiology of the cough despite a common presentation and underscores the need for a better understanding of pathophysiology of neurogenic cough. Further understanding of the specific cough mechanisms as they relate to the peripheral sensitization, central sensitization, and inhibitory pathways could guide the development of more useful disease state animal models and ultimately the development of novel therapies. New insights into neurogenic inflammation as it relates to neurogenic cough may provide additional therapeutic targets.

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Inducible Laryngeal Obstruction/ Paradoxical Vocal Fold Motion

22

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Introduction

Paradoxical vocal cord motion or laryngeal dyspnea has classically been described as the inappropriate (or paradoxical) adduction of the vocal folds during respiration resulting in intermittent airway obstruction, stridor, and dyspnea. Recent data suggests that symptoms of laryngeal dyspnea with stridor can occur in the absence of airflow restriction with an open glottic configuration [1] which suggests this disease process is more heterogeneous than initially thought. Many different terms exist to describe this disease and prior nomenclature reflects historical beliefs about its etiology including hysterical croup and Munchausen's stridor. The most common terms utilized today are vocal cord dysfunction (VCD), paradoxical vocal fold motion (PVFM), and most recently inducible laryngeal obstruction (ILO). A clinician's training (otolaryngologist, speech-language pathologist, respiratory therapist, allergist, or pulmonologist) tends to determine their preference of terminology. In 2013, an international task force of 13 multispecialty experts from 9 countries supported by the European Respiratory Society, European Laryngological Society, and American College of Chest Physicians was assembled with the goal of better defining this disorder and unifying terminology. After reviewing the literature, they created a consensus term of "inducible laryngeal obstruction causing breathing problems," with the umbrella acronym of ILO [2]. For the purpose of this chapter, ILO will be used to describe these symptoms of dyspnea at the level of the larynx. Although there is a consensus regarding terminology, strict diagnostic criteria for this disorder have been elusive. As a result, it can be challenging to differentiate this disorder from others that cause dyspnea including, but not limited to, cough, muscle tension dysphonia, and anxiety disorders, as well as lung and neurologic disease. See Table 22.1 for a list of common diagnoses that can present with similar symptoms as ILO or in overlap.

Table 22.1 Common diagnoses with similar presentations to inducible laryngeal obstruction

Bilateral vocal fold immobility
Glottic insufficiency
Muscle tension dysphonia
Obstructing benign growth (e.g., papilloma, cyst, granuloma)
Obstructing malignant growth (e.g., glottic cancer)
Subglottic/tracheal stenosis
Intrinsic lung disease
Neurogenic (e.g., multiple system atrophy)
Dysrhythmic breathing
Cardiovascular disease

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Epidemiology

True incidence and prevalence of ILO in the general population has not been well defined due to lack of uniformity in diagnostic criteria and an inability to reliably measure outcomes, heterogeneity in terminology, and limited awareness in the general medical community. In patients presenting to the emergency room with dyspnea or asthma exacerbations, the prevalence is thought to be as high as 22% [3].

Amongst the adolescent population, the average age of diagnosis is 14.5 years [4], and the incidence of ILO is estimated to be 5.7% [5]. It is thought that symptoms are exacerbated by general anxiety and performance anxiety. Liao et al. found that in a group of adolescents aged 12–17 years presenting for respiratory retraining therapy, there was a female predominance (79%), 23% had asthma, and 5.1% reported a history of anxiety [6]. Forty-six percent of the study population were "straight-A" students, and one-third of subjects participated in competitive extracurricular activities. Interestingly, Maturo et al. [7] identified an incidence of comorbid psychiatric diagnosis in 30% of adolescent subjects with ILO, and symptoms improved with psychiatric treatment after failing a trial of behavioral intervention with speech therapy.

The adolescent population is also more likely to develop symptoms of exercise-induced ILO as a result of redundant supraglottic tissues (i.e., laryngomalacia), and in this population, some success has been seen with surgical management in the form of supraglottoplasty [8–10].

In adults, the average age of diagnosis is 33 years [4, 11], and there is a female predominance of 2:1 [12]. Episodes of ILO in adults are more commonly triggered by non-psychogenic causes including odors, voicing, cough, and cold air, though psychiatric contributions are common. Clinically, there appears to be significant overlap with ILO and laryngeal hypersensitivity-related complaints including hoarseness, throat clearing, cough, and globus sensation.

While data on epidemiology of ILO in the general public is lacking, certain cohorts, including military personnel, athletes, and adult asthmatics, have been a focus of investigation. In a retrospective review of military patients who presented with exertional dyspnea, the incidence of ILO was 12% [13]. Hanks et al. reported that in a cohort of 148 athletes referred for asthma evaluation due to exertional dyspnea, 70% had ILO, and a diagnosis of ILO was more common in female and adolescent athletes [14]. Thirty-one percent of the study population was found to have exercise-induced bronchoconstriction in addition to ILO. Newman et al. investigated the incidence of PVFM in a subset of patients with refractory asthma, and 30% were found to have ILO in addition to asthma [15]. These studies suggest that there is significant overlap between ILO and other disorders of the respiratory tract.

Pathophysiology

The pathogenesis of ILO is poorly understood as this is a heterogeneous group of entities. In order to better differentiate etiology, we will discuss ILO and exercise-induced ILO (EILO) separately. ILO is thought to be more likely induced by irritants and emotional stress, while EILO results during strenuous physical activity.

As the larynx is the gateway to the respiratory tract, it enacts many complex muscular and centrally mediated neural mechanisms that result in coordination of breathing, phonation, swallowing, and coughing [16] (Figs. 22.1 and 22.2). The laryngeal and hypopharyngeal mucosa is innervated by the internal branch of the superior laryngeal nerve, and stimulation of this mucosa results in an involuntary, brief closure of the vocal folds, or the laryngeal adductor reflex [17, 18]. Many theories exist regarding the etiology of ILO, including reflux-induced laryngeal hypersensitivity or chemical hypersensitivity leading to the development of overactive protective reflex via inappropriate glottic adduction, or mechanical/chemical stimulation of supraglottic mucosa resulting in activation of laryngeal adductor reflex [19]. Cough and ILO are thought to be part of the same spectrum of laryngeal hypersensitivity with cough possibly being an adaptive mechanism to maintain glottic opening during an ILO episode [20].

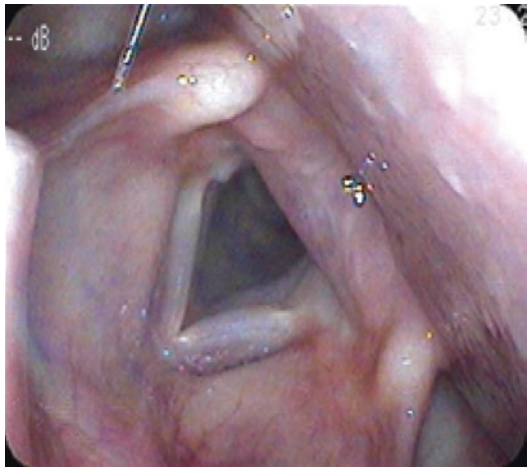

Fig. 22.1 Normal vocal cord abduction during inspiration. (Courtesy of Matthew S. Clary, MD, University of Colorado Hospital)

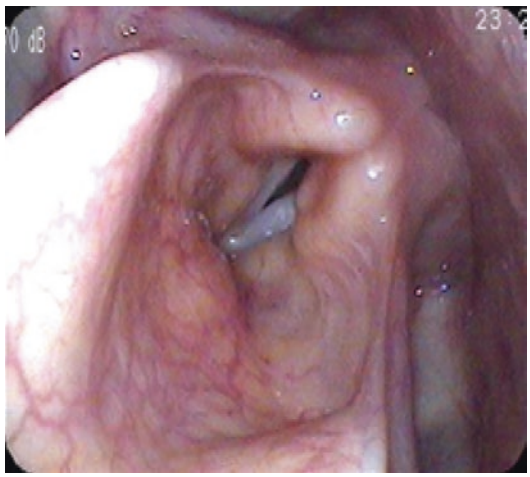

Fig. 22.2 Normal vocal cord adduction during exhalation. (Courtesy of Matthew S. Clary, MD, University of Colorado Hospital)

Behavioral predisposition is also considered an important, though poorly understood, contributor. In a case series with 171 patients, only 7% did not have a psychiatric diagnosis [21]. Diagnoses were varied and included conversion reactions, histrionic personality disorder, depression, anxiety, and psychosomatic, factitious, and somatization disorders. In this series, most common presentations included wheezing and dyspnea (43.3%), stridor (28.7%), bronchospasm (13.5%), and laryngospasm (2.9%); however, the relationship between symptom onset and psychiatric comorbidity is unclear. Based on anxiety symptoms preceding respiratory symptoms in a subset of adolescents with ILO and overlap of this phenomenon with panic disorder, Gavin et al. hypothesized a possible hyperresponsiveness of the brainstem leading to ILO [22]. It has also been postulated that ILO is one manifestation of conversion disorder. In a subset of patients newly diagnosed with ILO, compared to the normative population, patients had highly elevated scores on hypochondriasis and hysteria scales consistent with conversion disorder [23].

The causal mechanism of irritant ILO is unknown, and it is unclear whether irritant ILO is a direct response to the irritant stimulus through mucosal inflammatory reactions or related to altered reflex sensitivity. Inhalation of spasmogens however has been shown to induce bronchial hyperresponsiveness or narrowing of the intrathoracic airways which is characteristic of asthma. It is thought that the extrathoracic airways can similarly be narrowed via glottic spasm as a result to certain irritants. Reported irritants include odors, cold air, and environmental and occupational exposures [24–27].

A proposed etiology of EILO is mechanical insufficiency of the supraglottis. Laxity of muscles, ligaments, or the laryngeal cartilages can lead to reduced glottal opening via the Bernoulli principle resulting in more turbulent airflow dynamics [28]. This can occur at a supraglottic level due to medial movement of the aryepiglottic folds, retroflexion of the epiglottis, or anteromedial rotation of the cuneiform cartilages. At the glottic level, this is due to vocal fold adduction [10]. In an attempt to maintain normal measured airflow, it is hypothesized that patients compensate by increasing inspiratory pressure via increased negative intrathoracic pressure [1] (Fig. 22.3).

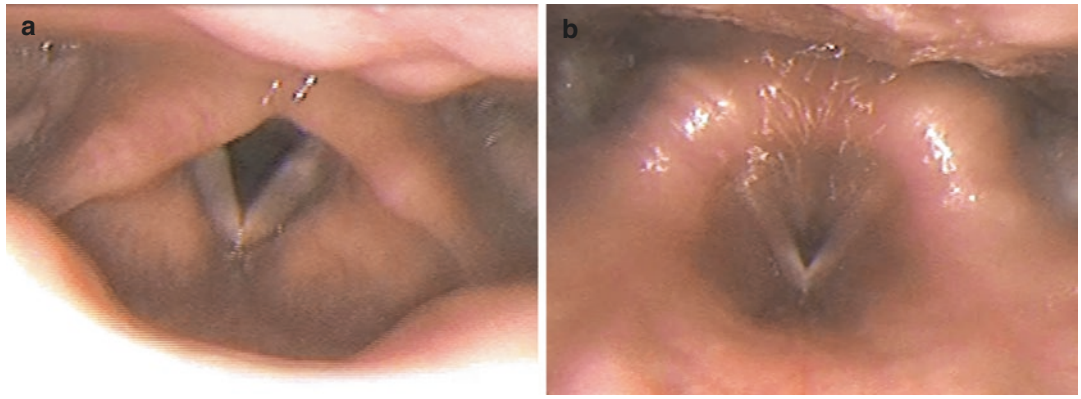

Fig. 22.3 (**a**) Vocal cord abduction with patent supraglottic airway. (**b**) Supraglottic collapse due to arytenoid redundancy. (Courtesy of Matthew S. Clary, MD, University of Colorado Hospital)

Voice, Airway, and Swallowing Symptoms: Findings or Sequela

The most common presenting symptom is dyspnea (73%), followed by wheezing (36%), stridor (28%), cough (25%), chest tightness (25%), throat tightness (22%), and changes in voice (12%) [29]. Other symptoms include pallor, lightheadedness, and paresthesias due to hyperventilation. While there is some overlap of the presentation of ILO with panic attacks, panic attacks are classically associated with intense fear, sweating, nausea, derealization, and depersonalization [30]. During ILO episodes, patients do not generally experience hypoxia. Inspiratory stridor occurs in 42% of patients and inspiratory and expiratory in 25%, and 33% of patients do not have any audible stridor [31]. With asthma, airway obstruction is typically peripheral, and wheezing is attributed to a fluttering of the peripheral airways resulting in a polyphonic sound. Inspiratory stridor is a monophonic sound due to narrowing of the extrathoracic airway at the laryngeal level. While expiratory stridor has typically been attributed to intrathoracic or fixed obstruction, acoustic analysis has suggested that expiratory stridor may be observed due to a transient fixed obstruction at the laryngeal level.

When exercise is a trigger, timing of symptom onset is important. EILO tends to occur during strenuous exercise and subsides rapidly after cessation of activity, in contrast to exercise-induced bronchoconstriction, in which symptoms can peak up to 20 minutes after cessation of physical activity. Again, many patients experience dyspnea, cough, chest tightness, and stridor. Patients are often unable to specify which phase of the breathing cycle is problematic, and self-reported symptoms have been shown to be poor predictors of EILO [32]. The use of inhalers can confound the clinical picture. In patients with EILO, focused breathing during medication administration can serve as a placebo or help break the aberrant respiratory cycle, while in asthma inhalers are useful for bronchodilation and subsequent symptom relief.

Diagnosis

Diagnosis of ILO can range from straightforward to extremely challenging. Classic cases of ILO can be diagnosed by a typical history with observed vocal fold adduction during inspiration on indirect laryngoscopy. However, this is seldom observed in patients presenting in the tertiary care setting. Diagnosis is most commonly made by applying a methodical diagnostic algorithm that is then confirmed by response to treatment and then revised according to response. The algorithm can be determined by the treating multidisciplinary team but should include history, physical exam with laryngoscopy, adjunct diagnostic testing, and treatment.

History

Diagnosis of ILO begins with a standard medical history. While physical exam and adjuvant testing (see below) can help in diagnosis or to rule out other potential diagnoses, most often a patient's description of symptoms is the primary basis for diagnosis of ILO. Patients will generally describe a sensation of tightness with restriction in the ability to move air. This is in contrast to a sensation of air hunger with inadequate oxygenation that accompanies most lung diseases. Location of the symptoms is a key differentiator. Restriction is generally described at the level of the larynx but can extend down towards the upper chest. Symptoms felt in the lower lungs are much less likely to be attributed to ILO. Concurrent inspiratory wheezing or stridor may or may not be described. Duration of restriction can vary from a few minutes to hours.

Triggers for the patient's episodes as well as the consistency of trigger are important to elicit. For classic ILO, these include strong odors (e.g., household cleansers, perfumes), smoke, cold air, talking, laughing, and/or coughing. There is generally considerable overlap with cough and throat clearing triggers. As a result, complete assessment of voice changes and voice demand is warranted. For EILO, it is generally exertion related but can be limited to only specific forms of exertion and even during specific situations (e.g., cycling during competitions). Treatments or behavior that abates symptoms can be helpful not only in making the diagnosis but helping tailor treatment plans. EILO generally has rapid resolution of symptoms upon discontinuance of exertion in contrast to exercise-induced asthma.

Assessment of comorbidities such as cardiopulmonary, neurologic, and psychiatric diseases is extremely important. These diseases can cause dyspnea themselves but can also predispose patients to the development of ILO. It is common to see patients with underlying lung disease that also have symptoms from ILO. Decreased pulmonary function can lead to inefficient phonation with laryngeal hypersensitivity and subsequently ILO.

Lastly, differentiation of ILO from occult diagnoses that mimic ILO such as bilateral vocal fold paralysis, laryngotracheal stenosis, tracheobronchomalacia, and neurodegenerative diseases such as multiple system atrophy is paramount. Patient history should be scrutinized for neck and chest surgeries, prolonged intubation, progressive worsening of symptoms, and dysphagia. Close collaboration between the physician(s), primarily otolaryngologists and pulmonologists, and speech-language pathologist (SLP) is crucial in treatment.

Physical Exam with Laryngoscopy

Physical exam should provide complementary information to the history. In general, physical exam is largely unremarkable in ILO. Exam findings that are consistent with ILO include: increased muscular tension of the strap muscles overlying the larynx and tongue base, rough or strained voice, and in some cases inspiratory stridor if symptomatic. There are no known EILO-specific exam findings. Cranial nerve deficits or anterior neck scars should prompt further investigation.

The standard of care in evaluation of ILO requires indirect laryngoscopy to potentially confirm diagnosis, as well as to rule out any anatomic abnormalities that could be contributing to symptoms. Unless laryngoscopy is performed during an episode, paradoxical vocal fold adduction should not be expected to be observed. Despite being considered the "gold standard," observed near-complete adduction during laryngoscopy while symptomatic is seldom seen. In addition, what constitutes a "positive" test is qualitative and can vary from minimal adduction to complete apposition of the vocal folds. Additionally, the discomfort or associated anxiety of laryngoscopy itself can induce guarding resulting in a false-positive exam. The results of flexible laryngoscopy should be interpreted with caution and in the context of the patient's overall clinical picture. The greatest value of laryngoscopy is generally ruling out other causes of airway obstruction. Laryngoscopy with stroboscopy can provide

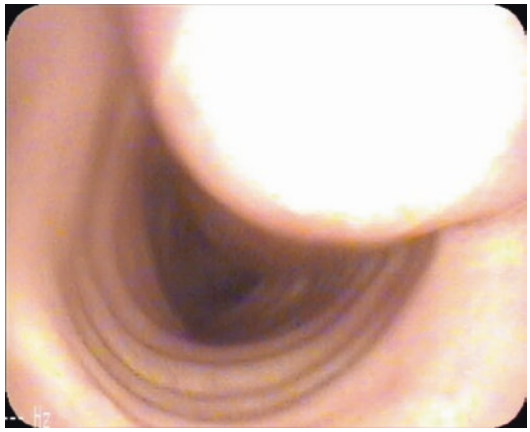

Fig. 22.4 Tracheal collapse noted during bronchoscopy during evaluation for inducible laryngeal obstruction. (Courtesy of Matthew S. Clary, MD, University of Colorado Hospital)

additional insights in patients with dysphonia believed to correlate with the patient dyspneic symptoms.

Because there is overlap in the presentation of ILO, exercise-induced asthma, laryngomalacia/tracheomalacia, and some neurogenic laryngeal movement disorders, correctly diagnosing ILO can be challenging (Fig. 22.4). Indirect laryngoscopy (+/− awake bronchoscopy) before, during, and after the trigger of symptoms is being employed more frequently to elucidate the true source of symptoms in more complex patients. This can include flexible laryngoscopy during an irritant-triggered episode or continuous laryngoscopy during exercise (CLE) for EILO. Physicians can witness an episode in real time and gather information relating to the nature of the episodes. This can help to guide treatment or as behavioral biofeedback training.

As mentioned previously, there is no standardized system by which to score glottic and supraglottic narrowing. In normal breathing, the glottic opening increases, especially during deep inspiration, and slightly adducts during expiration. It requires clinical judgement as to what qualifies as pathologic. Proposed methods include measuring laryngeal anterior-posterior diameter, measuring anterior glottis angle, or using computational measures of glottic aperture [3, 33, 34]. Most commonly, the diagnosis of ILO on laryngoscopy requires at least 50% glottic closure [29]. However, Olin et al. reported that a subset of patients undergoing continuous laryngoscopy during exercise were found to have an open glottic configuration with audible stridor and without evidence of inspiratory limitation on flow-volume loops [1]. These dyspneic symptoms are thought to be created by uncoordinated breathing patterns which may cause turbulence in the upper airway rather than a physical obstruction. The turbulence initiates a sensory feedback loop that creates a sensation of difficulty with breathing and moving air.

For patients with exercise-induced laryngeal obstruction, laboratory provocation studies with real-time laryngoscopy attempt to simulate real-life scenarios and often involve an indoor treadmill or stationary exercise bike. Exercise protocols vary but all aim to sequentially increase degree of physical exertion until an episode is induced. Often other biometric data including heart rate and oxygen saturation are also collected during these tasks (Fig. 22.5). Maximum obstruction severity is more likely to be seen at peak work capacity and can quickly diminish following cessation of activity. In a cohort of patients with EILO examined continuously during exercise, Olin et al. found that 67–84% of subjects had recovery of laryngeal narrowing within 60 seconds [35]. Given the rapid resolution of symptoms following cessation of activity, endoscopy following exertion can lead to falsely negative results.

Adjunct Diagnostic Testing

Pulmonary function testing with spirometry is often used to aid in the diagnosis of ILO (Figs. 22.6, 22.7, and 22.8), and if performed during an episode, the flow-volume loop will demonstrate flattening of the inspiratory limb consistent with fixed or variable upper airway obstruction [36]. This is due to the fact that there is variable extrathoracic obstruction due to increased resistance at the glottis from presumed vocal fold adduction. The flow-volume loop in patients with ILO has a normal expiratory phase; however, some data suggests that patients with

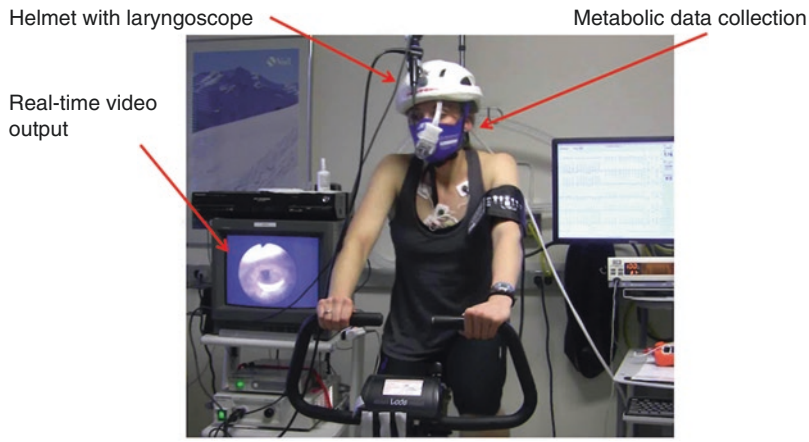

Fig. 22.5 Continuous laryngoscopy during exercise (CLE) setup. With laryngoscope in place and real-time video output, patients increase exercise intensity until peak work capacity or symptom onset. Additional metabolic data can be collected to correlate with symptoms and flexible laryngoscopy. (Courtesy of J. Tod Olin, MD, MSCS, National Jewish Health, Denver, Colorado)

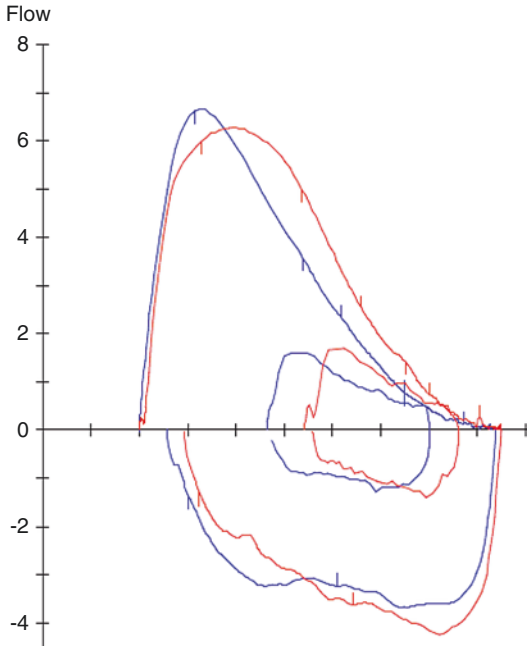

Fig. 22.6 Normal adult flow-volume loop. Flow-volume loop plots inspiratory and expiratory airflow (*y*-axis) against volume (*x*-axis). Positive *y*-axis values represent exhalation and negative values represent inhalation. These values are obtained during maximum forced inspiratory or expiratory maneuvers. The normal expiratory curve is characterized by a rapid rise to the peak followed by a nearly linear fall. The inspiratory curve is relatively symmetrical, a saddle-shaped curve. (Courtesy of Matthew S. Clary, MD, University of Colorado Hospital)

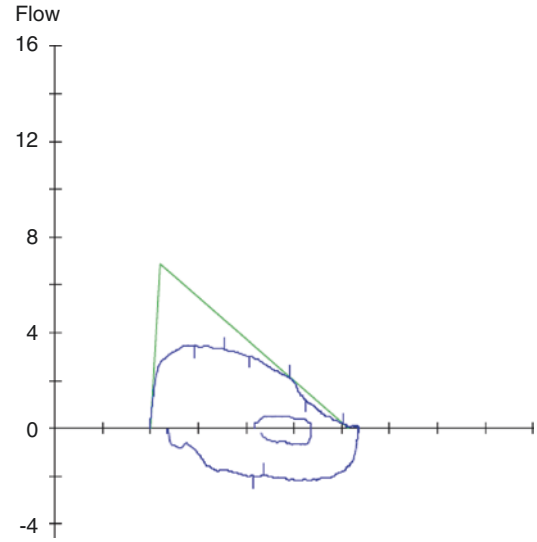

Fig. 22.7 Adult flow-volume loop with fixed obstruction. There is flattening of both the inspiratory and expiratory loops consistent with a fixed obstruction such as tracheal stenosis. (Courtesy of Matthew S. Clary, MD, University of Colorado Hospital)

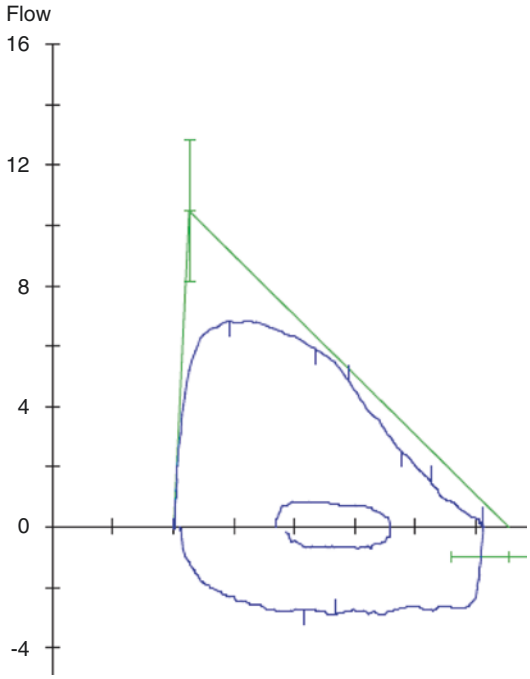

Fig. 22.8 Adult flow-volume loop with variable obstruction. There is flattening of the inspiratory loop which is consistent with upper airway obstruction. In inducible laryngeal obstruction, this is due to extrathoracic obstruction due to increased resistance at the glottis from presumed vocal cord adduction. (Courtesy of Matthew S. Clary, MD, University of Colorado Hospital)

ILO have significantly decreased forced vital capacity (FVC%) [37] relative to normal controls. Unlike the inspiratory limb truncation seen in patients with ILO, asthmatic patients have a normal inspiratory limb with attenuation seen in the expiratory phase [38]. Spirometry can also be useful to help differentiate ILO from asthma, as patients with ILO will not generally respond to methacholine. However, as there is a subset of patients with both ILO and asthma [15, 39], response to methacholine does not exclude the diagnosis of ILO.

The classic feature of ILO on spirometry is a truncated inspiratory limb of the flow-volume loop; however, this can be inconsistent and even normal at times. In addition, this feature can be affected by patient effort and even by the coaching of technician performing the test. From a practical standpoint, spirometry is probably best used to rule out lung disease and fixed airway obstruction. There are no prospective data describing the sensitivity and specificity of spirometry in the diagnosis of ILO. In a retrospective review of patients undergoing pulmonary function testing, nearly 50% were found to have an abnormal inspiratory curve in one of three test repetitions which was attributed to poor inspiratory effort as opposed to variable extrathoracic obstruction. In the remainder of patients with two or more abnormal inspiratory loops, of those who underwent further workup, only 36% were found to have vocal cord dysfunction [40]. Interpretation of spirometry results in conjunction with patient symptoms is essential.

For patients with irritant-induced laryngeal obstruction, surrogate methods have been used to precipitate ILO. Methacholine [41], mannitol [42], and histamine [43] have been used as laryngeal provocation agents in the setting of spirometry. Methacholine challenge testing is a common bronchoprovocation test and is a smooth muscle irritant. It was previously thought that patients with ILO would not respond to methacholine though asthmatics would, and the difference in response would be seen in alterations of the flow-volume loop. However, since there is a subset of patients with both ILO and asthma [15, 39], response to methacholine, as seen by changes in the flow-volume loop, does not necessarily exclude the diagnosis of ILO. Interestingly, new data suggests that methacholine provocation can illicit ILO as demonstrated by flattening of the inspiratory flow-volume loop on spirometry [41]. It is widely believed that methacholine laryngoscopy is similarly useful in establishing an episode of ILO; however, there is scant data to support its use, and technique can dramatically alter the results.

There is no role for routine imaging or blood work (including arterial or venous blood gas) in the workup of ILO. In patients with unclear diagnosis, imaging (computed tomography [CT] of the neck and chest with inspiratory and expiratory phases) can be useful to rule out dynamic collapse of the airways mimicking symptoms of ILO such as with tracheobronchomalacia.

Response to Treatment

While somewhat counterintuitive, the ability to differentiate ILO from confounding diagnoses can sometimes be performed through a diagnostic trial of respiratory retraining therapy. Patients whose history is suggestive of an ILO spectrum disorder but do not respond as expected to therapy should prompt further investigation including awake bronchoscopy and potentially imaging with CT (see above).

ILO can overlap with a spectrum of "dysfunctional" breathing disorders which includes hyperventilation syndrome, periodic deep sighing, thoracic dominant breathing, forced abdominal expiration, and thoracoabdominal asynchrony [44]. These patients do have symptoms of dyspnea (though not laryngeal in nature) and often have a respiratory alkalosis with normocapnia or hypocapnia. These alternate diagnoses can be distinguished by the basis of Nijmegen questionnaire, a validated questionnaire which assesses certain respiratory, ventilation, and central nervous system symptom, and plethysmography [45]. Treatment of these disorders is centered around respiratory retraining though exercises differ from those employed in the treatment of ILO.

Voice, Airway, and Swallowing Treatment

Management of ILO is often multidisciplinary in nature involving providers that could include speech-language pathologists (SLP), otolaryngologists, pulmonologists, gastroenterologists, allergists, and psychologists/psychiatrist. The speech-language pathologist typically plays the primary role in the assessment and treatment of ILO [46].

Behavioral Treatment

Respiratory retraining therapy is considered a primary treatment for ILO without other structural or physiological abnormalities and is typically done with an SLP [37, 39, 47, 48]. The SLP uses both direct and indirect approaches to treatment which can include patient education and reassurance, laryngeal hygiene, laryngeal massage, respiratory re-coordination/retraining, and possibly voice therapy to help reduce laryngeal tension and hypersensitivity. Traditionally, respiratory retraining is a direct approach to treatment which focuses on maintaining an open or adequate airway while coordinating the respiratory cycles to control symptoms. New techniques are emerging which focus on creating contrasting inspiratory resistance through a biphasic inspiratory phase during breathing where a high level of resistance is created in the oral cavity with the lips, teeth, or tongue, and then this resistance is suddenly released as the second phase of inspiration [49]. Biofeedback with laryngeal endoscopy (either exercise or non-exercise endoscopy) or desensitization with controlled exposure to triggers can also be used during therapy with an SLP to help the patient learn to control breathing during acute episodes.

There are research limitations regarding efficacy of behavioral therapy with this population. Overall, published research indicates that behavioral SLP treatment is beneficial for most patients, but a lack of consistent treatment approaches and common outcome measures limit the generalization of these data. Also, patients who present with ILO are heterogeneous in categories of age, triggers, and comorbidities [50]. There are no published studies that examine treatment outcomes based on patient-reported triggers with the exception of exertion/exercise. Sullivan et al. [51] reported 95% of patients with ILO symptoms triggered by exercise were able to control their symptoms after one session of behavioral therapy with an SLP.

Pharmacology/Medical Management

A number of treatment strategies exist which are aimed at trigger avoidance and symptom coping. Desensitization or laryngeal control therapy for irritant-induced ILO is a treatment strategy in

which exposure to an irritant is sequentially increased, and the patient employs breathing techniques with each exposure to develop tolerance [24]. Anxiolytics have some utility in managing symptoms of distress during an acute episode though standards do not exist for specific medication selection or dosing. Psychotherapy has also been shown to have some success in patients with comorbid psychiatric diagnoses, particularly conversion disorder [39], with additional benefit in conjunction with speech therapy [51]. As ILO is believed to be an entity that is along the spectrum of laryngeal hypersensitivity, medical treatment with amitriptyline or gabapentin is emerging as a potential medical modality in ILO [52].

Additionally, breathing treatments have been used in the treatment of ILO, particularly in the acute setting. Heliox, a mixture of helium and oxygen with no bronchodilating effects, has been used as a treatment for ILO given different properties in laminar flow relative to oxygen which can be useful in reducing turbulent airflow [53]. There are no guidelines for its use, though heliox can be attempted to provide symptomatic relief in patients who are unresponsive to bedside retraining exercises. Additionally, due to ability to blunt the laryngeal adductor reflex, nebulized lidocaine has been proposed as a treatment in the acute setting [16]. Given frequent misdiagnosis of ILO as asthma, many patients ultimately undergo treatment with racemic epinephrine and oral/inhaled corticosteroids. For patients with isolated ILO, these treatments are inappropriate and have no role in clinical management.

Surgical Treatment

Injection of the thyroarytenoid muscle (unilaterally vs. bilaterally) with Botox has been employed when more conservative measures are unable to control symptoms [54]. While dosing parameters vary, Altman et al. proposed a series of in-office injections starting with a unilateral thyroarytenoid injection of 2.5 units followed by bilateral injections ranging from 1.25 to 5 units depending on clinical response. In severe cases of refractory ILO, tracheotomy has been performed to bypass the obstruction.

As laryngeal hypersensitivity is thought to be a contributor to ILO, and laryngeal hypersensitivity can develop as a result of glottic insufficiency, one can extrapolate that ILO can result from glottic insufficiency. As such, surgical management with vocal fold augmentation, which has demonstrated improvement in globus and cough [55, 56], as well as superior laryngeal nerve block [57], holds significant potential in ILO. Though currently implemented clinically at multiple institutions, no data is available at this time. This however is a promising area for future research.

Frontiers

ILO represents a heterogeneous population that is slowly becoming better understood, but many unanswered questions remain. Due to the lack of specific diagnostic criteria and the wide array of symptoms and triggers, this patient population is difficult to study. Future research should look toward identifying the pathophysiology of these symptoms and possibly identifying subtypes of symptom presentation to better direct treatment. While behavioral management is often very effective, continued research in the field of laryngeal hypersensitivity may provide insight for treatment of recalcitrant symptoms using other surgical or medical interventions.

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Part III

Intervention

A Person-Centered Approach to Breaking Bad News

23

Lauren J. Breen and Samar M. Aoun

Introduction

Neurodegenerative diseases are associated with increasing disability, shortened life expectancy, and a host of physical, emotional, and existential problems coupled with unmet care needs starting from the time they receive the bad news of their diagnosis [1–5]. The term "breaking bad news" encompasses the communication of any information that seriously and adversely affects the receiver's expectations of the future, quality of life, and availability of choices. Examples include the communication of a serious diagnosis and/or prognosis such as life-limiting illnesses (e.g., cancer), chronic illnesses (e.g., diabetes), neurodegenerative illnesses (e.g., amyotrophic lateral sclerosis/motor neuron disease), and genetic conditions (e.g., Down syndrome).

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The delivery of bad news is one of the more stressful experiences of health professionals. Several studies have shown that medical and health professionals report the delivery of bad news to be a taxing experience [6, 7], yet it is a relatively new addition to their training [8, 9]. However, the delivery of bad news, such as communicating a serious neurological diagnosis to patients and their families, is not an optional part of clinical practice; instead, it is imperative that health professionals are prepared to deliver bad news. It is encouraging to know that this skill can be improved, via explicit instruction and practice of evidence-based protocols, to enhance the patient's satisfaction with care, promote their adjustment to the diagnosis and disease, and optimize their health outcomes [9–12].

The receipt of bad news is often experienced as being without respect or compassion, leaving patients and their family caregivers feeling shocked, confused, hopeless, angry, and devastated [13–16]. The rate of dissatisfaction was reported to be 56% in a survey of patients and caregivers in the United States [17] and data from Australia showed that 33% of caregivers [18] and 36% of patients were dissatisfied with the delivery of the diagnosis [19]. Some complaints about the process of receiving bad news are exemplified in Fig. 23.1, in which the presented scenario does not follow recommended practice standards [20] in the following aspects: the person should

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Fig. 23.1 Illustration of poor communication of a serious neurological diagnosis

Jim has been experiencing an increasing range of unusual symptoms for several months. Earlier today, Jim attended an appointment with his neurologist, on his own. The neurologist told Jim, "the diagnosis is Amyotrophic Lateral Sclerosis," and continued to use an array of medical terms. The consultation took less than twenty minutes.

Jim didn't really understand what the doctor said and was confused by the medical terms she used. He was also confused because, although the doctor seemed to say really serious things, she also smiled and said that things would be okay. Jim tried to ask questions but the doctor's phone rang—twice—and she made it clear that she still needed to see several more patients before the end of the day and stood up to indicate that the consultation was over.

Jim was now in a state of shock. He left the hospital and was all alone. He stood in the parking lot for what felt like a long time and has no memory of the 90-minute drive home. He became increasingly distressed and had so many questions running through his mind but it was Friday night—he wouldn't be able to contact the doctor, the hospital, or anyone else for assistance until Monday.

not be seen alone, and the consultation time was much shorter than the recommended 45–60 minutes. The delivery was not empathetic, the medical terms were not explained, no opportunity was given to respond to the patient's emotions, and it offered a false sense of hope. This bad news was delivered at the end of the week on a Friday in a locale where there were no support services operating on the weekend. Additionally, no referral was made to an appropriate disease-based support association for information and follow-up assistance.

SPIKES: A Protocol for Communicating Bad News

The SPIKES protocol was developed to provide a method for communicating a cancer diagnosis to patients. It is an acronym that outlines the six components of the protocol—Setting (creating the right setting), Perception (determining what the patient/family knows), Invitation (exploring what patient/family are expecting or hoping for), Knowledge (sharing information and suggesting realistic goals), Emotion (responding emphatically to the feelings of patient/family), and Strategy (making a plan and follow-through) (Table 23.1). Not only does the protocol facilitate the receipt of a diagnosis, it also assists the health professional by providing a structured way of communicating this news [10].

Utility of the SPIKES Protocol for Communicating a Neurological Diagnosis

The communication of a specific neurological diagnosis has been comprehensively investigated from the points of view of neurologists, people with motor neuron disease (MND), and their family caregivers [18, 19, 21–23], and this chapter's focus is to illustrate the challenges of breaking bad news associated with MND. Patients' and their families' confrontation with the diagnosis of MND has been understandably described as an "existential shock" (Brown [24], p. 210) and the catalyst for "constant loss" (Aoun et al. [15], p. 845). The majority of neurologists describe the communication of the diagnosis as stressful [25]. Despite this, however, very few neurologists report having received adequate training in the effective communication of a diagnosis of MND [25].

A series of studies investigated how neurologists communicate the news of a diagnosis of MND. Questionnaires were posted to neurologists, to people living with MND, and to their family caregivers and facilitated by all MND associations in Australia. Only 6% of the neurologists surveyed ($n = 73$) reported feeling no stress when communicating the diagnosis; the remainder reported slight (29%), moderate (53%), or high (12%) stress [21]. Similarly, only 7% described the delivery of diagnosis as "not difficult," with

Table 23.1 The six steps of the SPIKES protocol for breaking bad news (Baile et al. [10])

Steps	Guidelines	Examples
1. Setting	Setting up the interview might involve mental rehearsal of the planned conversation It also involves attention to the physical setting of the interaction: Arranging privacy Involving the patient's family and friends Being seated Making a connection with the patient (i.e., rapport and microskills of listening) Managing time and limiting interruptions	Try to deliver the news in a private room; if this is not an option, draw curtains around the patient's bed Use eye contact Sit down to show you will take the necessary time Let the patient know how much time you have and ensure that phones/pagers are on silent mode
2. Perception	Determine what the patient already knows/suspects, which allows you to correct any misunderstandings and to tailor the delivery of the information to the patient's level of understanding	Use open-ended questions, e.g., "why do you think we did the test?" or "what do you know about your symptoms so far?"
3. Invitation	Obtain the patient's invitation about how much information they would like to receive	Use questions like "would you like to have all the information about your test results?" Offer to provide further information in the future
4. Knowledge	Foreshadow the receipt of bad news Tailor the communication to the patient's vocabulary and comprehension use nontechnical words and avoid being blunt. Check to make sure the patient has understood the information being communicated	Use phrases like "unfortunately, I've some bad news to share with you"
5. Emotions	Recognize the patient's emotions and empathize with and validate them	Example phrases include "I can see this is upsetting to you" and "I can tell this news was not what you expected"
6. Strategy	Outline a plan for the future and provide a summary of the discussion	Ask, "would you like to discuss the next steps in terms of treatment?" Outline options and promote shared decision-making

the rest describing it as a "little difficult" (24%), "somewhat difficult" (32%), "difficult" (28%), and "very difficult" (9%). Nearly half (44%) reported having received no training in how to respond to patients' emotions, and importantly, 74% expressed interest in receiving such further training. The neurologists described being challenged by the need to be honest, yet not to take away hope, by the lack of an effective treatment, by fear of causing distress, by dealing with the patient's emotions, by spending the right amount of time, and by fear of not having all the answers.

For example, one neurologist wrote:

> Having had a migraine after each MND clinic, feeling stressed and anxious about having so little to offer, I have gradually accepted the limitations of my skills, and some confidence that assisting the patients honestly and empathetically, and not 'abandoning' them is of value to most patients. [21, p., 370]

A survey of 248 MND patients highlighted that 36% were dissatisfied with the way the diagnosis was communicated [19]. Further, in examining the six SPIKES domains, those neurologists whose skills and abilities were "above average" were significantly more likely to explore the domains of Invitation, Knowledge, Emotions, and Strategy than those who were "average or below." The largest difference related to the neurologists' abilities and skills in responding empathically to the feelings of patient/family (Fig. 23.2). The survey of 190 family caregivers told a similar story, in that 33% were dissatisfied with the delivery of the diagnosis, and there was the same pattern concerning differences in the SPIKES domains between neurologists they rated as "above average" and "average or below" [18].

These quantitative findings are complemented by an analysis of the responses to the open-ended

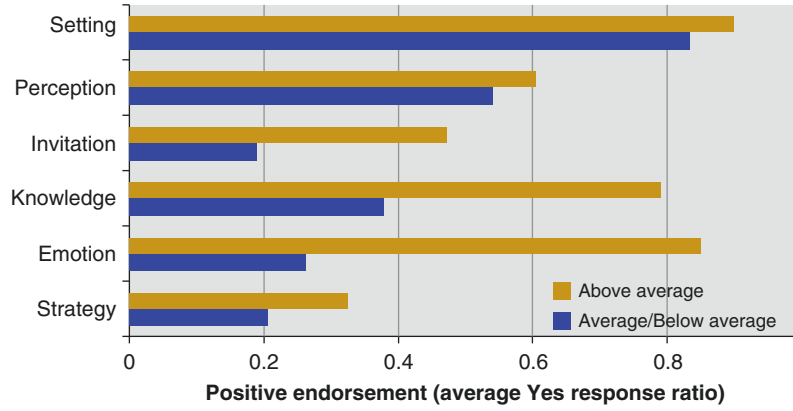

Fig. 23.2 Motor neuron disease patients' ratings of their neurologists' abilities/skills across the six SPIKES domains (Aoun et al. [19] reprinted by permission of Taylor & Francis)

-Difficulties in receiving the correct diagnosis:
"My husband attended a GP for 3 years with symptoms and was never diagnosed, he told my husband to exercise more to strengthen his muscles!!" (MND family cargiver)

-Shock and distress of being diagnosed:
"I was relieved to find out what was happening to me, but devastated there was no treatment." (MND patient)

"The shock of the diagnosis didn't really sink in until we left the neurologist's surgery. Lots of tears followed as the whole family tried to come to terms with it." (MND patient)

"Nothing can prepare you for the road ahead as a family carer—our life has changed forever." (MND family caregiver)

-Neurologist's manner and skills in delivering the diagnosis:
"The neurologist spoke clearly, calmly and answered my questions in 'layman's language." (MND patient)

"He watched our shocked reactions, but gave us time to digest his information. He came around the table and offered support." (MND patient)

"The neurologist was very sympathetic to both of us; he treated us with dignity and compassion." (MND family caregiver)

"I was not impressed by the number of interruptions during my neurologist consultations; i.e. phone calls, missing reports and copies of reports being brought in as no preparation was made prior." (MND patient)

-Being linked to further information and ongoing support:
"Planning and follow-up is vital to feel like care is considered, especially with rapid progression of MND – emphasis on getting the clinic to start a program needs to be priority, so as not to feel like left on my own! Can be very disheartening." (MND patient)

Fig. 23.3 The perspectives of motor neuron disease patients [22] and family caregivers [23] upon receiving the diagnosis

questions in the questionnaire. The patients and family caregivers described difficulties and time delays in receiving the correct diagnosis, the shock and distress of being diagnosed, the importance of the neurologist's manner and skills in delivering the diagnosis, and the importance of being linked to further information and ongoing support [22, 23] (Fig. 23.3).

Person-Centered Care in Communicating a Neurological Diagnosis

Person-centered care is an increasingly common philosophical approach to service delivery whereby the patient (and increasingly, their family caregivers being family members, friends, or

other informal caregivers) is respected, valued, and positioned to work in partnership with healthcare professionals in determining the healthcare plan. This approach to care is typically experienced positively by patients and their family caregivers [26] and tends to show reductions in symptomatology, pain, and hospitalization [27]. This approach is holistic and means that the diagnosis is delivered in a way that acknowledges the individual's emotional, psychosocial, and spiritual needs as well as addressing their medical and practical needs.

How is person-centered care achieved when delivering bad news? The challenge of holistic care is that it requires more of the clinician's time. Importantly for practice, studies show that the time the neurologist took to deliver the diagnosis was associated with higher patient ratings of the neurologist's abilities and skills (Fig. 23.4) and with satisfaction with the delivery of the diagnosis (Fig. 23.5) [19, 21]. Those who were satisfied had consultation times over 40 minutes confirming why best practice standards [20] set this time at 45–60 minutes. A two-stage approach to the consultation is best practice and has been confirmed in the Australian survey, where this approach was used by 68% of the neurologists [21], and also by a study in the Netherlands that showed that the organization of two appointments 10–14 days apart helped patients and their families cope better with receiving the diagnosis [4]. Given that 95% of patients reported receiving their diagnosis from a neurologist [19], and that guidelines specify that the diagnosis should be given by a consultant neurologist with experience and up-to-date knowledge of MND and its treatment and care [28], neurologists are a key group that must be encouraged to commit more time to communicate the diagnosis thoroughly, with the focus being on the needs of the patients and family caregivers. Neurologists would benefit from skills enhancing communication [23], managing distress, and being honest without removing hope [21] so that they experience less stress and discomfort in delivering the diagnosis. However, in a busy neurology clinic, adhering to such best practices may be challenging. In such circumstances, neurologists could be encouraged to adopt the two-stage approach to delivering the diagnosis. It is also worth noting that Australian neurologists working in dedicated multidisciplinary clinics were more able to provide longer consultation as per best practice standards compared to those whose practice was not in

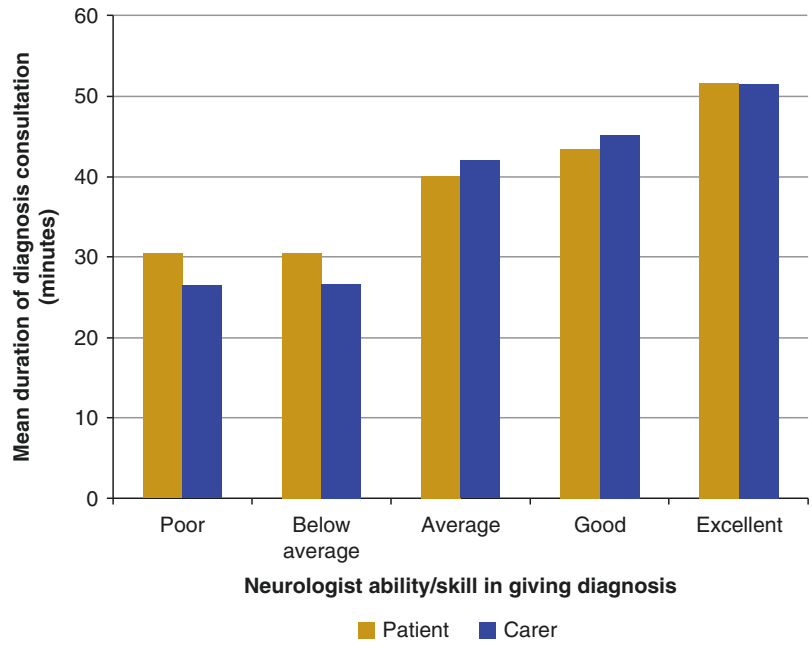

Fig. 23.4 Patients' and caregivers' ratings of neurologists' ability/skills and consultation duration (From Aoun et al. [18], with permission)

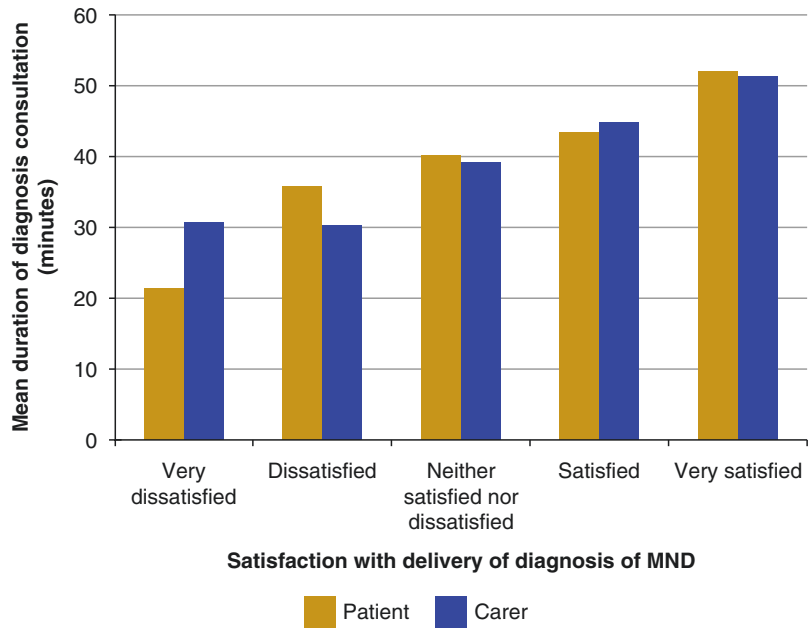

Fig. 23.5 Patients' and caregivers' ratings of satisfaction with the delivery of the diagnosis and consultation duration (From Aoun et al. [18], with permission)

multidisciplinary clinics, and in fact, the consultation time was twice as long (45 minutes compared to 23 minutes, respectively) [21].

It is imperative that health professionals are prepared to deliver bad news. There is growing evidence that these skills can be taught explicitly, both at university [29] and during residency [30, 31], in the context of cancer. Based on studies yielding comprehensive evidence from the perspective of both the givers and receivers of bad news, the need for education programs as well as the development of practice standards and protocols must be emphasized. The emphasis must be on a more person-centered approach to care for MND and other neurodegenerative conditions at this critical first step in an illness journey that may be traumatic and where there is currently no cure [22].

Conclusion

The challenges of delivering a serious diagnosis are common to a number of life-limiting illnesses, particularly those neurodegenerative diagnoses that are progressive, disabling, and lacking in curative options. Receiving a neurological diagnosis is typically an extraordinarily difficult time for patients and their families and has been described as a type of existential shock. For health professionals, communicating the news of a serious diagnosis is a frequent yet stressful part of their work. The method and content of imparting a terminal diagnosis can significantly impact people with the disease and their families and has implications for the way they move from this traumatic news to the actions required for support throughout the illness trajectory. The way forward for best practice is to implement a more person-centered approach to caring for terminally ill people, starting from the diagnosis stage. The SPIKES protocol is an evidence-based resource for communicating bad news and has been shown to be applicable to discussing difficult neurological diagnoses with patients and their families. Communicating the diagnosis in an evidence-based and person-centered manner is necessary in order to promote optimal outcomes for patients and their families, such as reductions in symptomatology, pain, and hospitalization and satisfaction with the delivery of the diagnosis. Doing so also has the added benefit of mitigating against the stress experienced by health professionals when delivering bad news.

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Treatment of the Velum

24

William S. Tierney and Paul C. Bryson

The Velum

Anatomy and Function

Anatomy The velum is the muscular portion of the palate and is commonly called the soft palate. This structure is attached anteriorly to the hard palate and laterally to the pharyngeal walls. It functions to dynamically separate the oropharynx from the nasopharynx by tightening during speech and swallowing to create a seal against the posterior pharyngeal wall. It relaxes to allow passage of air between these two spaces for nasal breathing. The velum is formed by five bilateral muscle groups that come together at the midline to form the arch of the palate (Fig. 24.1). The palatoglossus extends within the anterior tonsillar pillar from the tongue base to the palate. The palatopharyngeus follows a similar course within the posterior tonsillar pillar. The levator veli palatini extends from the skull base and lateral cartilaginous Eustachian tubes. The tensor veli palatini extends from the medial pterygoid plate and spina angularis of the sphenoid bone and the lateral cartilage of the Eustachian tube to the soft palate. Finally, the musculus uvulae, which modulates uvular shape and central palate tone, is entirely intrinsic to the palate. The vagus nerve supplies motor innervation to four of these muscles via the pharyngeal plexus, while the mandibular branches of the trigeminal nerve supplies motor innervation to the tensor veli palatine muscles. Behind the velum itself, the superior pharyngeal constrictor extends from the midline pharyngeal raphe to the pterygomandibular raphe and provides mechanism for circumferentially narrowing the pharyngeal lumen. Also innervated by the vagus nerve via the pharyngeal plexus, dysfunction of the superior constrictor muscles may also impair velopharyngeal function.

Function The most basic function of the velum can be understood as the swinging of a trap-door. At rest, the palate falls with gravity in an inferiorly sloping position approximately paralleling the curvature of the tongue as it slopes into the pharynx. During speech and swallowing, the velum is pulled in a posteriosuperior direction to meet the posterior pharyngeal wall and prevent reflux of food or air into the nasopharynx. The levator veli palatini is considered to be the primary muscle of palatal elevation [1, 2], while the palatopharyngeus and palatoglossus are engaged to inferiorly displace the palate. Beyond this simplified model of palatal function, there is a large body of literature describing the highly nuanced and complex interplay of these muscles to vary the shape of the upper aerodigestive tract during swallowing and the production of speech [3, 4]. The role of the velum in speech and swallowing

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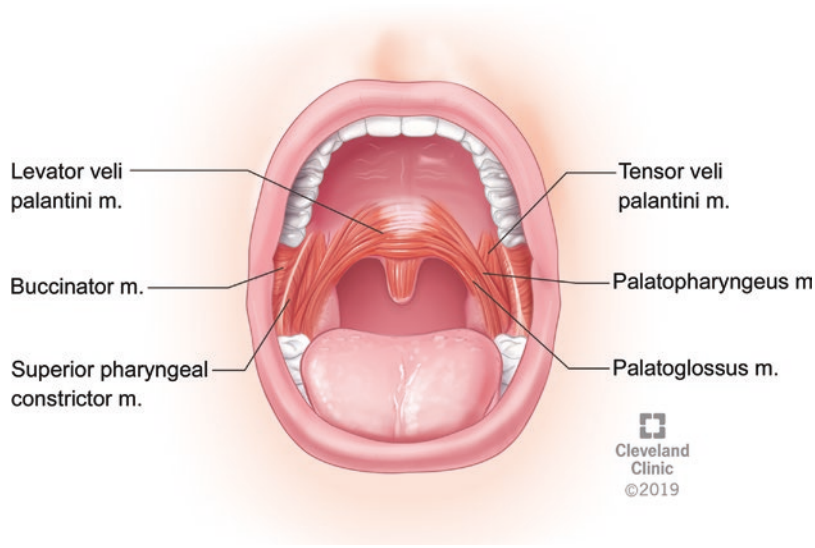

Fig. 24.1 Anatomy of the velum. (Courtesy Cleveland Clinic; © Cleveland Clinic 2019)

means that small derangements in its structure or neurologic coordination can manifest as grossly symptomatic dysfunction. In addition, the palatal musculature is responsible for opening the Eustachian tube to equilibrate pressure within the middle ear during swallowing [5]. As such, pathology affecting the palate may also impact middle ear health and lead to Eustachian tube dysfunction.

Velar Pathologies

Given the complex nature of velar anatomy, with multiple muscles acting to modulate soft tissue position and form, a wide range of pathologies exist which can affect this structure. Anatomic pathologies are well characterized by the study of cleft palate but include primary congenital clefts, palatal injuries, iatrogenic injury, and palatal neoplasms. Changes in velar soft tissue biomechanical properties from scaring related to surgical intervention or radiation therapy may not deform the gross structure of the soft palate but can lead to reduced mucosal pliability and palate dysfunction. Finally, neuromuscular disease can lead to discoordination or paralysis of the palate that can result in symptomatic and functional velopharyngeal insufficiency. Neuromuscular pathology of the palate is diverse and can be generally viewed as hyperfunctional disorders including spastic dyskinesias, tremors, and spasms and hypofunctional disorders including myopathies, neuropathies, paralysis, and paresis. While an in-depth discussion of each of these categories is beyond the scope of this chapter, the categorization into anatomic, biomechanical, and hyperfunctional (e.g., palatal myoclonus) or hypofunctional neuromuscular disorders is useful to the clinician endeavoring to treat patients suffering from velar pathology.

Evaluation of the Velum

History

Within the diverse causes of velar pathology, there are unifying signs and symptoms of velopharyngeal dysfunction that will aid the clinician in determining appropriate treatment. A well-established medical history is a useful tool in identifying a palate disorder. Specific lines of questioning should focus on dysphagia and dysphonia. Velopharyngeal insufficiency is marked by hypernasal speech, nasopharyngeal reflux of food and drink into the nasopharynx, and possibly chronic rhinosinusitis from gross or subtle nasopharyngeal reflux [6]. Symptoms of Eustachian tube dysfunction, odynophagia, otalgia, ear-clicking caused by palatal

myoclonus affecting the Eustachian tube, vertigo, tinnitus, and vocal tremor should also be discussed in addition to a complete characterization of speech, swallow, and head and neck pathology. Personal history of traumatic injury to the head and neck, radiation to the region, and inhaled or insufflated substance use should be obtained in addition to standard medical and surgical history. Standardized questionnaires assessing voice and speech and swallowing function, such as the EAT-10, VHI, and VRQOL batteries, should be included to evaluate these general functions. The Pittsburgh Weighted Speech Scale may be used to specifically evaluate for velopharyngeal incompetence [7]. Family history should be assessed with specific attention to neuromuscular disease and head and neck pathology.

Physical Examination

Physical examination of the velum should include direct visualization of the palate to inspect for anatomic or motor dysfunction. Palpation offers additional insight into submucosal structural formation of the soft and hard palates as well as oral and pharyngeal structures. Many palatal tremors, clefts, and muscle atrophy can be diagnosed primarily with physical examination alone. However, patient anatomy and gag reflex may limit physical examination in some cases. A complete head and neck examination should also be conducted; specific causes of palatal dysfunction may cause ocular symptoms of oscillopsia or amblyopia, while Eustachian tube involvement may be perceivable on otoscopic examination as fluctuations in middle ear pressure or as objective tinnitus on auscultation of the ear canals. Careful otomicroscopy is required in the specific instance of ear clicking as tensor tympani and stepedial muscle hyperfunction can present with similar symptoms to some palatal hyperfunction.

Endoscopy

If a velopharyngeal pathology is suspected, there are multiple diagnostic tools at the clinician's disposal. Perhaps the most widely used and effective tool in evaluation of the palate is transnasal flexible endoscopy. This tool allows indirect visualization of the palate from the nasopharyx and can be used to assess function during speech, swallowing, and at rest [8]. Furthermore, it is the preferred modality to evaluate for pharyngeal masses that can share symptomology with velar pathology and should therefore always be considered in patients with suspected palatal disease. Endoscopic evaluation of velopharyngeal closure can be used to direct therapy in cases of velopharyngeal insufficiency [9], and it is a critical tool in evaluation of neuromuscular disorders of the palate [10]. Inspection of both sides of the palate at rest, during swallow, and during speech will reveal even subtle unilateral or bilateral motion disorders. Interestingly, it has been reported that some palatal movement disorders are modulated by mouth opening with resolution of tremor during open-mouthed examination [10], and we recommend endoscopic evaluation whenever there is reasonable suspicion of velar pathology. A thorough endoscopic examination should evaluate the bilateral nasal airway focusing on the palate and nasopharynx. We recommend observation of the palate at rest, during speech, and during swallowing from the nasopharynx. Transition into laryngoscopic evaluation is recommended in most patients as speech, swallow, and neuromuscular disorders involving the velum can also involve pharyngeal and laryngeal structures. Videoendoscopy recordings can be especially useful in following velopharyngeal examinations over time or in frame-by-frame analysis of motion disorders to better characterize exact pathology. Functional endoscopic evaluation of swallowing, during which the patient eats and drinks under endoscopic visualization, may aid in characterizing velopharyngeal insufficiency. Occasionally, velopharyngeal insufficiency can be task specific, such as in brass and woodwind musicians. Having the patient play their instrument during the endoscopic exam while inspecting for posterior velopharyngeal gap-incompetence allows the astute clinician to capture the phenomenon [11]. Similarly, some velopharyngeal disorders that manifest with

fatigue and repetitive speech, swallowing, or other specific task-based incompetence may reveal pathology not immediately apparent on examination.

Imaging

Imaging studies to characterize velopharyngeal function can also be employed to better understand functional defects without instrumenting the nose or mouth. Lateral cephalogram x-rays can be used to characterize palate elevation during sustained oral exhalation or phonation [12]. Videofluoroscopic evaluation of velopharyngeal function can be used to characterize nasopharyngeal reflux [13] and provides information both on the degree of reflux as well as the consistencies of foods and their relative degree of reflux. For example, a large volume reflux may be observed with thin liquid intake with decreased volume with progressively thickened consistencies. This information should be shared with the speech-language pathologist so that he or she can assess for this during modified barium swallow examination.

Other Testing

While physical examination, endoscopic evaluation, and imaging studies are sufficient to clinically characterize most velopharyngeal disorders, there are a variety of additional evaluation techniques that may be useful in specific patients or in the research setting. Nasopharyngeal and oropharyngeal manometry may aid in the evaluation of swallowing disorders including velopharyngeal insufficiency [14]. Nasal airflow and nasal air pressure measurements may provide quantitative characterization of velopharyngeal insufficiency [15]. MRI can be used to dynamically assess swallowing function. Electromyographic measurements have been used to characterize specific muscles involved in hyperfunction or characterizing neuromuscular function during hypofunction [16].

Evaluation of Newly Diagnosed Velopharyngeal Neuromuscular Pathology

In addition to the many tools available to evaluate neuromuscular dysfunction of the velum, we recommend evaluation of each of these patients by a multidisciplinary team whenever doubt over etiology exists. While isolated palatal tremor may be a primary disorder, it might also be the first manifestation of a systemic tremor disorder such as Parkinson disease, a symptom of an isolated basal ganglia micro-infarct. It is therefore good practice to involve a multidisciplinary team including otolaryngology, neurology, and speech-language pathology early and maintain close communication between team members to maximize efficiency and efficacy of workup and treatment. A typical initial workup likely includes visits with the above providers as well as neuroimaging to rule out cerebrovascular or neurologic pathologies such as stroke or multiple sclerosis with the potential to progress during the sometimes-lengthy evaluation and treatment of the velopharyngeal pathology. Even when symptoms are limited to the palate, this collaborative evaluation can be informative. One example of this is the differentiation between symptomatic and essential palatal myoclonus. Symptomatic palatal myoclonus is related to an identifiable brainstem lesion and is characterized by hypertrophy of the olivary nucleus and may be accompanied by other symptoms while essential palatal myoclonus is not related to an identifiable neurologic lesion and usually presents with the primary complaint of ear clicking [17]. In our practice, the involvement of multiple practitioners leads to more effective diagnosis and treatment of neuromuscular pathology and is pursued in the majority of cases.

Interventions on the Velum

When considering treatment of the velum, it is most useful to characterize treatments into two functional categories: velopharyngeal insufficiency and spastic motor disorders of the velum.

Treatments of Velopharyngeal Insufficiency

Velopharyngeal insufficiency is characterized by failure of the velum to create an effective seal separating the nasopharynx from the oropharynx during swallowing and speech. Symptomatically this leads to hypernasal speech and nasopharyngeal reflux. A broad spectrum of disorders cause velopharyngeal insufficiency including cleft palate, palatal fistula, congenital or iatrogenic short palate, velar defect after resection, as well as neurodegenerative and neurologic conditions that lead to muscle wasting or hypotonia and include stroke, intracranial lesions, cranial nerve injury/lesion, and progressive neurologic diseases such as amyotrophic lateral sclerosis, cerebral palsy, myasthenia gravis, oculopharyngeal or myotonic muscular dystrophies, systemic lupus, and Moebius syndrome. The foundation for many therapeutic interventions to treat velopharyngeal insufficiency is derived from experience treating cleft palate and palatal defects following oncologic resection. The principles established during research on these conditions can be applied to any cause of velopharyngeal insufficiency with appropriate clinical insight, but it is critical to recognize this discrepancy between the narrow evidence base for velopharyngeal insufficiency and the wide patient population affected. These treatments focus on reestablishing a functional seal between the nasopharynx and oropharynx that is ideally dynamic with the respiratory, phonatory, and deglutatory functions of the pharynx.

Noninvasive Treatment Because of the involvement in voice, speech, and swallowing, we prefer to address the palate alongside a speech-language pathologist who can offer the patient strategies to adapt to modifications in velopharyngeal function. The most conservative therapeutic option for mild velopharyngeal insufficiency or in individuals expected to improve spontaneously is therapy alone. Speech-language pathologists can offer advice to minimize reflux and to maximize swallowing function in order to manage symptoms while patients recover or prepare for definitive treatment. Therapeutic interventions vary widely but may include palate-strengthening exercises, swallowing technique training, and compensatory speech strategies to minimize the effect of dysfunction on communication. Another minimally invasive measure is the use of a nasopharyngeal obturator/prosthesis. These devices are most often used after resection of the palate and have been shown to provide excellent phonatory results in select patients [18]. However, these prostheses are difficult to fit, require the availability of a subspecialized prosthodontist, and lack the permanence many patients desire from their velopharyngeal treatment.

Posterior Pharyngeal Augmentation A relatively new method for the treatment of velopharyngeal incompetence is augmentation of posterior pharyngeal tissues to improve nasopharyngeal separation with or without intervention on the velum itself. This method is limited because it is difficult to overcome large deficits in velopharyngeal closure; however in the appropriately selected patient, these techniques provide a minimally invasive option for treatment that avoids scaring and muscular rearrangement which impact palatal biomechanics. Minimally invasive techniques exist for the injection of collagen, temporary fillers such as hyaluronic acid, or long-term fillers such as calcium hydroxyapatite [19]. In patients with small velopharyngeal gaps, the clinician can consider injection of fillers in the office under local anesthesia with injectable and topical lidocaine to avoid general anesthetic administration. However, most patients require general anesthesia to suppress the gag reflex and to achieve sufficient augmentation. In any injection pharyngoplasty careful preoperative evaluation for medialized carotid arteries must be completed to avoid the catastrophic complication of intracarotid injection. Usually this evaluation can be completed with palpation and close inspection, but use of ultrasound or radiographic imaging is justified if physical examination alone leaves question of carotid anatomy. Transoral injection using a straight injection cannula can achieve functional improvement immediately post-injection. Injection should be targeted along Passavant's mucosal ridge that can be identified pre-procedure using flexible endoscopy

and should be visualized when elevating the palate during sustained "ahh" phonation or with gentle lift of the palate with instrumentation. Transpalatal and transnasal approaches are also options but less well described. We do recommend holding anticoagulation prior to injection to reduce the risk of hematoma. The choice of filler should be determined based on patient characteristics with absorbable fillers being selected in those patients who may recover function or as a temporary trial of this therapy in patients with complex velopharyngeal pathology. Operative posterior pharyngeal augmentation can also be conducted with autologous fat, which provides lasting benefit but reduces by approximately 50% volume over time and should therefore be used to initially overcorrect. This autograft offers the benefit of good tissue pliability and deformability. For patients with large defects or modified velopharyngeal anatomy, several techniques have been described to place implants using silicone or gortex blocks and provide structured and lasting anterior displacement of the pharyngeal mucosa with good results [20].

Surgical Interventions Surgical repair of velopharyngeal incompetence is well described and is the standard of care for cleft palate patients as it offers lasting results and good functional outcomes. While surgical intervention for velopharyngeal incompetence is extensively described in subspecialty textbooks relating to this topic, we will include only an overview of common surgical techniques here. It is important to note that surgical correction of neurogenic velopharyngeal insufficiency has not been widely studied, and as such, these operations are presented for clinical consideration but do not represent standard treatment for neurogenic or neuromuscular disease.

The Furlow double-opposing z-plasty (Fig. 24.2 [21, 22]) was first described in 1986 and is one of the most commonly instituted surgical interventions for velopharyngeal insufficiency secondary to cleft palate [23]. This technique begins with the elevation of a left-sided myomucosal flap and right-sided mucosal flap. The underlying left nasopharyngeal mucosal flap and right myomucosal flap are then freed from the palate. The right nasopharyngeal myomucosal flap is sutured posteriorly to the posterior aspect of the palate with the left mucosal flap sutured to its anterior surface. The left oral myomucosal flap is then sutured over the right nasal myomucosal flap with the right oral mucosal flap sutured anterior to the myomucosal flap. The net result is to posteriorly transpose and horizontally orient the levator veli palatini while elongating and narrowing the soft palate. This technique therefore increases palate tissue while tightening the nasopalatal aperture. Principles of this surgery may have applications in hypotonic neuromuscular palatal disease, but double z-plasty has never been widely studied for this population.

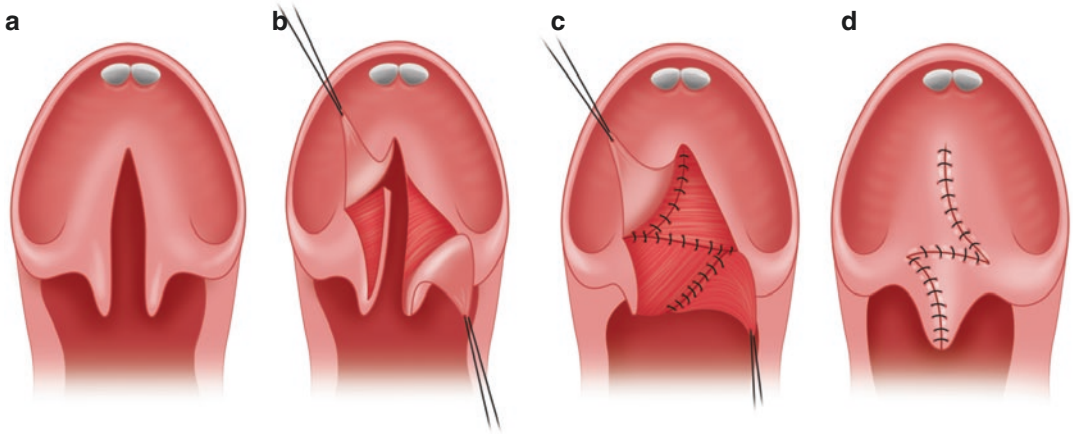

Fig. 24.2 The Furlow double-opposing z-plasty as originally described to repair cleft palate. This technique can also be applied to non-cleft patients to tighten the palate and treat velar hypofunction. (**a**) A central defect is isolated. (**b**) Mucosal and myomucosal flaps are raised. (**c**) The nasopharyngeal layer is repaired to reestablish velar function when neuromuscular function is intact. (**d**) The oraopharyngeal layer is closed to complete palate repair

Pharyngeal flaps are another technique commonly used for cleft palate repair that may be encountered in the treatment of neurogenic palate deficiency. This category of operations utilizes a superiorly based segment of posterior pharyngeal wall myomucosal tissue sutured to the nasopharyngeal aspect of the soft palate to create two lateral nasopharyngeal channels while posteriorly displacing the palate. Disadvantages to this method include reduction in nasal airway and impairment of pharyngeal swallowing, but it has proved effective in improving speech in cleft palate patients [24]. Again, this technique is described here to complete the discussion of surgical intervention for the velum but has not been evaluated for neuromuscular disorders of the palate.

Sphincter pharyngoplasty has been investigated in small case series as a treatment for congenital neurogenic velopharyngeal insufficiency with positive results [25]. This surgical technique was first described by Ortichochea in 1968 [26] and has since undergone countless modifications on the technique. The basis for the surgery is that the palatopharyngeus muscles and overlying posterior tonsillar pillar mucosa are bilaterally mobilized inferiorly and elevated to a mucosal incision in the posterior pharyngeal wall where they are sutured in place to augment the posterior pharynx while providing circumferential musculature to augment the ability of the palate to seal the nasopharynx. This technique is often coupled with a double z-plasty for cleft palate patients with large nasopharyngeal gaps. It strengthens the velopharyngeal closure at the risk of scaring and contracture of this region after healing.

Treatment of Velar Hyperfunction

Velar hyperfunction is most often caused by neuromuscular disorders leading to spastic contraction of the palate. Pharmacologic and toxic interactions should also be considered, but upon identification of palatal spasm, tremor, or dyskinesia, the initial evaluation usually focuses on neurologic etiology unless the history is strongly suggestive of another cause. While palatal hyperfunction exists as a spectrum of disorders with different frequencies, neurologic etiologies, and presentations [27, 28], the focus of this chapter is treatment of the velum itself, and we will therefore focus on the principles of management which can be broadly applied. We do recommend co-management of patients with palate hyperfunction by an otolaryngologist and neuromuscular neurologist whenever possible to evaluate for systemic disorders as well as those confined to the head and neck. Identification of the specific muscles involved in hyperfunction is important for targeted treatment although the anatomic properties of the palate can make this difficult in some patients with complex hyperfunction. The character of rhythmic tremor versus discoordinated spasms, frequency of movements (especially in rhythmic tremor), and timing of hyperfunction allow the astute clinician to identify action versus intention tremor versus task specific pathology based on history and physical exam alone. For example, palatal myoclonus commonly occurs in isolation and features rhythmic spasms at 1–4 Hz, follows a characterized movement pattern, and is often accompanied by symptomatic audible clicking of the Eustachian tube [29]. It is also important to evaluate for the involvement of any extrapalatal sites including the larynx, pharynx, perioccular muscles, muscles of mastication and facial expression, and muscles of the neck to correctly identify and treat syndromes affecting other sites.

Trials of Systemic Therapy Initial therapeutic intervention may include trials of oral medications. These therapeutic interventions are often based on treatment of systemic tremor disorders and have variable effects in the treatment of palatal hyperfunction (e.g., propranolol, benzodiazepines, anticholinergics, dopaminergics, primidone, gabapentin) [30]. Patients with these conditions and concurrent palatal tremors may benefit from these therapies, but pharmacologic treatments may be trialed in patients even with isolated palate disorders under supervision of a neurologist. Additionally, psychogenic palatal movements must be considered, and some patients may benefit from psychotherapy and psychopharmacologic interventions [31]. However, inconsistent clinical improvement and pharmacologic side effects have

resulted in botulinum toxin as the first-line therapy in many clinicians' arsenals [29].

Botulinum Toxin Injection Botulinum toxin is a protein neurotoxin produced by *Clostridium botulinum* bacteria and which blocks the presynaptic motor neuron release of acetylcholine at the neuromuscular junction. Its effect on the neuromuscular junction makes it an effective treatment for many hyperfunctional motor disorders, including tremor as well as temporary and clonic spasm, when delivered in appropriate dosages to the correct anatomic location (Fig. 24.3). When addressing palatal hyperfunction, both dosage and injection location can be challenging depending on patient presentation. Injection of botulinum toxin has been established as a relatively safe [29] and effective therapeutic option [31]. Large studies of this treatment have not been conducted, but positive clinical experiences and a mounting body of literature reporting symptomatic control support the use of botulinum toxin in patients with symptomatic palatal hyperfunction. Injection techniques vary between clinicians but may target specific muscles or generally target the palate.

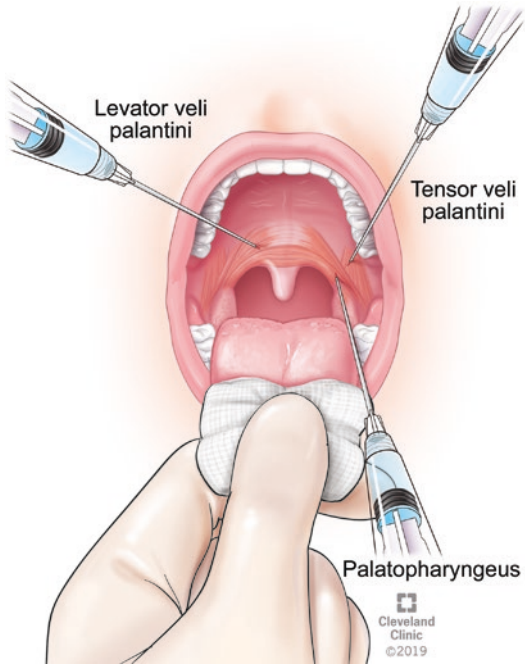

Fig. 24.3 Botulinum toxin injection sites for velar hyperfunction. 1–2.5 units of botulinum toxin are injected into involved muscle groups using surface landmarks and electromyographic feedback. (Courtesy Cleveland Clinic; © Cleveland Clinic 2019)

We recommend the use of an electromyographic (EMG) guidance with a fine-gauge EMG needle. Transoral injection is preferred although transnasal injection might be considered in specific cases. One technique to identify sites of hyperfunction is direct visualization of the region of maximal spasm followed by needle insertion into this site with EMG monitoring [31]. EMG evaluation should be directed by both physical examination, with evaluation of tremor appreciated on endoscopic or direct visual examination, and history. For example, the tensor veli palatini muscle should be evaluated in those patients with ear-clicking after workup to rule out middle ear myoclonus and supportive of palatal etiology. EMG can be relied upon to register increased feedback during contraction that is then compared to clinically apparent hyperfunction. Concurrent EMG reading with palate contraction indicates the muscle group involved in hyperfunction is at the tip of the needle and indicates appropriate site for injection. Localization of specific muscle groups is recommended, and EMG injection needles are nearly always used to confirm injection site in our practice. Injection can be targeted just lateral to the pterygoid hamulus when injection into the tensor veli palatine is desired. Paramedial palate injection primarily targets the levator veli palatini. Unilateral or bilateral injections can be conducted depending on the patient's presentation. An algorithmic approach to the treatment of palatal tremor has been proposed [32] and is useful when determining injection locations and addressing patients first presenting with uncomplicated palatal myoclonus. Injection of 1–2.5 units of botulinum toxin into muscle groups involved in the tremor or spasm is a reasonable starting dose. Dosage should be titrated to patient response over multiple injections, but it is recommended to begin with lower doses and escalate during subsequent sessions to avoid causing temporary iatrogenic velopharyngeal insufficiency and dysphagia.

Interventions for Eustachian Tube Dysfunction In the subgroup of patients who experience ear-clicking, objective tinnitus, aural fullness, or symptoms of patulous Eustachian tubes attributable to palatal dysfunction, middle ear and Eustachian tube interventions may be considered. As previously mentioned, the stapedius and tensor tympani muscles of the middle ear may also develop neuromuscular disorders, and it is of paramount importance to correctly diagnose palatal pathology to ensure appropriate treatment. While a detailed discussion of middle ear myoclonus is outside the scope of this chapter, interventions for middle ear myoclonus include pharmacologic therapies, surgical middle ear myotomy, and topical botulinum application [33]. In patients with Eustachian tube dysfunction correctly attributed to palatal pathology, tympanostomy tube placement may improve symptoms but comes with a risk of persistent perforation or cholesteatoma formation. Eustachian tube dilation has recently gained popularity and may also be considered in the patient with middle ear effusions or symptomatic Eustachian tube obstruction related to palate dysfunction or weakening of the tensor veli palatini due to botulinum toxin injection to treat velopharyngeal pathology. However, these interventions have not been rigorously studied specifically among patients with hyperfunction of the palatal musculature, and we recommend treating Eustachian tube dysfunction as needed and based on the judgment of the otolaryngologist involved in treatment of the patient.

Deep Brain Stimulation While botulinum toxin injection is effective in treating the majority of patients with palatal tremor, some patients are refractory even to this therapy. With its efficacy in the treatment of Parkinsonian dyskinesia, deep brain stimulator neuromodulation has been applied to severe cases of head and neck dyskinetic disorders. Meige syndrome, a rare condition with blepharospasm and associated craniofacial and neck muscular spasms – sometimes including palatal and laryngeal hyperfunction – has been treated with globus pallidus internus deep brain stimulation to great effect [34]. However, treatment of oculopalatal tremor via red nucleus deep brain stimulation was ineffective in resolving tremor [35]. In patients with severe motor disorders or who fail to adequately respond to botulinum toxin treatment, neurosurgical consultation may be warranted. This therapeutic option offers the possibility of future therapies but currently is only considered in the most severe cases of head and neck dyskinesias.

Conclusions

Even subspecialized otolaryngologists, neurologists, and speech-language pathologists uncommonly encounter velopharyngeal pathology. Careful history and visualization of the palatal and nasopharyngeal/oropharyngeal junction during specific tasks is critical in establishing a diagnosis and treatment plan. Multidisciplinary collaboration with speech-language pathology and neurology may be beneficial. Treatment of velar pathology can be grossly categorized into hypofunctional and hyperfunctional subgroups. General treatment patterns for these two subgroups should be modified to meet specific patient needs.

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Laryngeal and Extralaryngeal Botulinum Toxin Injections

25

William Z. Gao and Michael M. Johns III

Introduction to Botulinum Toxin

History

Botox, as botulinum toxin is colloquially known—and the term that will be used for convenience in this chapter (Botox®; Allergan)—is borne from the clinical disease of botulism. The historical roots of botulism span back to ancient times ever since mankind first tried to preserve and store food. However, it was not until the early nineteenth century that a German poet and medical officer named Justinus Kerner first described botulism in detail [1]. He noticed that the clinical phenomenon arose from ingestion of spoiled sausages. *Wurstgift* is what he called the substance he believed to be responsible, which is German for "sausage poison." At that time, the term botulism had not yet existed and was only later coined by the German physician Muller in 1870 after the Latin word "botulus," meaning sausage [2].

Belgian physician and professor of microbiology Émile van Ermengem then isolated the bacterium *Clostridium botulinum* in 1895 as the source of the toxin responsible for botulism [3]. Further work was done in the early twentieth century to purify botulinum toxin type A (BoNT-A] and elucidate its mechanism of action. The first therapeutic use of BoNT-A in humans came in the 1970s, with ophthalmologist Alan B. Scott reporting its clinical utility for strabismus in 1980 [4]. In 1989, BoNT-A was approved by the US Food and Drug Administration (FDA) for treatment of strabismus, blepharospasm, and hemifacial spasm. Since then, we have witnessed the steady growth of botulinum toxin formulations and treatment indications [5], a number of which are for voice and swallowing disorders.

Mechanism of Action

In most clinical applications, the key goal of Botox is in preventing transmission at the neuromuscular junction, which leads to paralysis of the target muscle. Normal nerve signaling to muscle is facilitated by the release of acetylcholine from motor neurons into the synaptic cleft. Acetylcholine diffuses across to the motor end plate, where it binds receptors on muscle cells that lead to muscle activation. Botox exerts its

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Table 25.1 Different commercial preparations of botulinum toxin available in the United States (strength is denoted relative to Botox)

Commercial name	Generic name	Company	Type	Strength
Botox®	OnabotulinumtoxinA	Allergan, Madison, NJ	A	1:1
Dysport®	AbobotulinumtoxinA	Medicis, Bridgewater, NJ	A	1:2–4
Xeomin®	IncobotulinumtoxinA	Merz, Raleigh, NC	A	1:1
Myobloc®	RimabotulinumtoxinB	Solstice, Louisville, KY	B	1:50–55

effect by cleaving SNARE proteins that are responsible for releasing acetylcholine-laden vesicles. This family of proteins includes SNAP-25, synaptobrevin, and syntaxin. Different serotypes of botulinum toxin affect different SNARE proteins, with the two clinically used serotypes A and B acting on SNAP-25 and synaptobrevin, respectively. Ultimately, this action inhibits nerve transmission to muscle, causing paralysis.

Return of muscle activity after Botox treatment occurs in two stages. Early recovery occurs from axonal sprouting in response to growth factors secreted from denervated muscle cells. Later, there is actual recapitulation of vesicular acetylcholine release at the original neuromuscular junctions resulting from new SNARE protein synthesis [6]. Complete recovery after botulinum toxin type A injection typically occurs after 3–4 months and occurs after even shorter duration after type B toxin injection [5, 7].

In addition to the primary effect of Botox on motor neurons via inhibition of acetylcholine release, regulation of C-fiber nociceptive neurons has also been seen [5]. Glutamate and substance P release from these neurons cause vasodilation and promotion of pro-inflammatory factors. Since Botox appears to also block this pathway, it provides a basis for potential use in chronic pain disorders such as migraine headaches and neuralgias. However, detailed discussion of these treatments lies outside the scope of this chapter.

Types of Botulinum Toxin

There are seven serotypes of botulinum toxin: A–G. Types A and B are currently used clinically, with three different commercial preparations of type A and one of type B toxin. They are detailed in Table 25.1 [5]. Of note, Botox is the primary product used in the larynx and serves as the focus for further discussion within this chapter. A national survey study [8] did indicate some laryngologists have tried using Dysport® and Xeomin® for adductor spasmodic dysphonia, but they are still not in wide use. Dysport® has been reported to have a greater diffusion effect once administered in tissue [5]. Xeomin® is fairly similar to Botox in terms of dosing but is stripped of all complexing proteins. This theoretically would lend to decreased risk of sensitization/antibody formation but has yet to be demonstrated clinically [9]. Lastly, Myobloc® is the only formulation of type B toxin available in the United States. It appears to have a quicker onset of action (2 as opposed to 3 days) and a shorter duration of effect than type A toxins [7]. MyoBloc® can be useful in select patients who have developed tolerance to type A preparations over time.

Indications/Contraindications for Botulinum Toxin Treatment

As previously mentioned, the clinical indications for Botox treatment have expanded dramatically beyond its initial introduction into medicine for strabismus. Within this chapter, we will delve into use of laryngeal and extralaryngeal Botox injections to treat various neurologic disorders affecting the larynx.

Indications for Botox injections include:

- Adductor spasmodic dysphonia (ADSD)
- Abductor spasmodic dysphonia (ABSD)
- Essential voice tremor (EVT)
- Bilateral vocal fold paresis/paralysis
- Respiratory dystonia

- Paradoxical vocal fold motion
- Neurogenic cough
- Cricopharyngeal dysfunction

Contraindications and precautions for Botox injections include [10]:

- Known hypersensitivity/allergy to botulinum toxin or components in toxin preparations
- Active infection at intended injection site(s)
- Pregnancy or breastfeeding (relative contraindication)
  - Botox is labeled as Pregnancy Category C
- Neuromuscular disease (use with caution)
  - Patients with peripheral motor neuropathic disease, amyotrophic lateral sclerosis, or neuromuscular junction disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) are at higher risk of adverse side effects and should be monitored closely if treated with Botox
- Active aminoglycoside treatment (use with caution)
  - Effect of botulinum toxin may be potentiated

Within the context of these more common clinical problems, we will discuss relevant Botox injection technique, dosing strategies, complications, and expected outcomes. As for details and nuances of diagnosis, we direct the reader to reference Chaps. 15, 16, 20, 21, and 22, as well as other texts.

It is important to remember that many of these conditions do not occur in isolation and can exist concurrently with others, like adductor spasmodic dysphonia and comorbid essential voice tremor. Additionally, there is an abundance of neuropathology not specifically addressed within this chapter or book that present with laryngeal manifestations. Synthesizing a treatment plan that incorporates targeted Botox chemodenervation in these scenarios should stem from thoughtful analysis of clinical phenomenology at play. The basic concepts from this chapter will empower you to tackle those challenges.

Botulinum Toxin Treatment of Neurologic Laryngeal Disorders

The driving principle behind using Botox injections to treat the variety of laryngeal conditions mentioned relies on targeting muscles responsible for symptomology. These targets are primarily limited to the thyroarytenoid-lateral cricoarytenoid (TA-LCA) complex, posterior cricoarytenoid (PCA), the false vocal folds, and the cricopharyngeus (CP). Other less commonly treated sites include the interarytenoid and cricothyroid muscles. In the first part of this section, we will address our preferred approaches to injecting each of the major end organ targets as well as potential complications. For review of relevant procedural anatomy, refer to Chap. 1. Then we will review Botox injection targets, dosing strategies, and treatment outcomes for different indications.

Procedural Technique for Laryngeal Botulinum Toxin Injections

Preparation The first step in preparation involves Botox reconstitution. Botox comes as a vacuum-dried concentrated powder in either 50- or 100-unit vials. Of note, there is considerable variation among practitioners regarding toxin dilution protocol, volumes administered, etc. [8]. We prefer to use sterile, preservative-free normal saline to reconstitute to 2.5 U/0.1 mL initially, with further dilution as needed for smaller doses. The preferred injection volume is 0.1–0.2 mL per site treated, but most commonly is 0.1 mL when treating ADSD. It is our preference to use 1 mL Luer lock syringes, with separate syringes for each side to be injected (except when performing supraglottic injections via percutaneous thyrohyoid approach). For the first syringe, we include an extra 0.05 mL of injectate in order to prime the needle. When the volume of dosed Botox is less than 0.1 mL, we make up the total volume to 0.15 mL with sterile normal saline for the first syringe (or 0.1 mL for the second syringe). In that scenario, the dose of Botox drawn up in the

first syringe will contain an appropriate extra amount to account for dilution. In the process of drawing up the reconstituted Botox, it is critical to avoid any trapped air bubbles within the syringe as that alters the dose of Botox injected, which can be significantly affected with small volumes.

These syringes are then connected to a monopolar, 26- or 27-gauge, 1.5-inch-long needle electrode to allow for electromyography (EMG) guidance in most of our percutaneous injections. The needle is primed so that the exact intended dose is retained in the syringe. When using an EMG-guided percutaneous approach, the EMG machine must also be set up and calibrated properly along with placement of ground and reference electrodes on the patient. It is helpful to have an assistant control the volume of audio feedback from the EMG machine, with it turned up only after the needle electrode has entered soft tissue to avoid loud static signal during the preparatory phase.

Next, we ensure proper patient positioning. There is a dichotomy in terms of positioning, with the majority of laryngologists surveyed preferring a seated position and the remainder using a supine position [8]. It is our preference to have the patient sitting comfortably upright in the examination chair with hands in the lap, to avoid any white-knuckled gripping of the armrests. The neck is slightly extended or neutral. Local anesthesia is achieved using 1% lidocaine with 1:100,000 epinephrine administered via a 30-gauge needle in a superficial bleb spanning the site(s) of intended needle entry. Strap muscle activation and tension in the neck can compress the cricothyroid and thyrohyoid spaces, which makes needle advancement more difficult. So prior to starting, we encourage patients to take a deep breath in followed by a slow exhalation out to allow complete relaxation of the neck, shoulders, and remainder of the body. Additionally, parting the lips can help open up the cricothyroid/thyrohyoid space.

Laryngeal Injection Targets and Approaches

Thyroarytenoid-Lateral Cricoarytenoid (TA-LCA) Complex While the TA and LCA are distinct muscles, Alonso et al. [11] showed that diffusion from TA injections includes the LCA 94% of the time, and so we treat them as a singular unit. There are multiple approaches that can be utilized to accomplish the same therapeutic goal of TA/LCA muscle complex denervation, but our preferred injection approach is via EMG-guided percutaneous injection through the cricothyroid membrane. This modality offers the greatest patient comfort coupled with accurate and consistent needle placement. However, it requires access to and comfort with use of an EMG machine. Other injection methods include transoral and percutaneous approaches, with endoscopic guidance or based solely on landmarks. However, it is our opinion that the latter technique is less precise, especially for those without extensive experience.

Technical considerations for EMG-guided injection of the TA/LCA complex through the cricothyroid membrane are as follows (Fig. 25.1) [12]:

- The needle is introduced into the skin overlying the cricothyroid membrane at 5 mm offset from midline on the side to be injected.
- The trajectory of the needle is directed approximately 10° laterally and 30° superiorly. The needle will traverse the cricothyroid membrane and should be kept in a submucosal plane.
- Prior studies have demonstrated that both the TA [13] and LCA [14] exhibit the highest concentration of motor end plates in the middle portion of their muscle bellies. Based on clinical experience, needle advancement along the aforementioned trajectory facilitates muscle entry near this region and is aided by auditory response from the EMG, with increasing

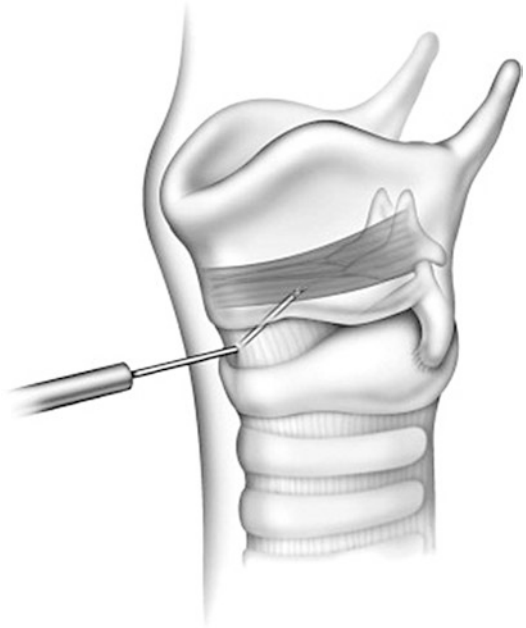

Fig. 25.1 Electromyographically guided injection approach of the thyroarytenoid-lateral cricoarytenoid (TA-LCA) complex through the cricothyroid membrane. (From Shah and Johns [12], with permission)

frequency of a "popping" signal serving as positive feedback.

- Alternatively, topical laryngotracheal anesthetic can be injected into the airway first for a trans-tracheal approach. The needle is placed in a similar location as above but advanced initially into the airway (indicated by the loud EMG static signal from contact with air) prior to directing laterally in order to enter the TA muscle.
- Upon entering the muscle, there usually will be a visible and audible insertion potential on the EMG. Asking the patient to phonate should elicit robust recruitment that can be heard and observed from the EMG, which confirms needle tip position.
- The prescribed aliquot of Botox is injected at this point and the needle withdrawn. This is then repeated on the contralateral side in similar fashion with the second syringe of Botox when performing bilateral injections.

Posterior Cricoarytenoid (PCA) There are two approaches to percutaneous injection of the PCA: the posterolateral (retrolaryngeal) or the transcricoid (translaryngeal) approach. EMG guidance is used for both of these techniques but the latter can also be aided by endoscopic visualization. We prefer the posterolateral approach when anatomically feasible in patients, again for reasons of patient comfort and technical efficacy. However, this may not be possible in a patient with a thick neck or very immobile larynx, in which case we use the transcricoid approach.

Technical considerations for EMG-guided injection of the PCA through the posterolateral approach are as follows (Fig. 25.2) [12]:

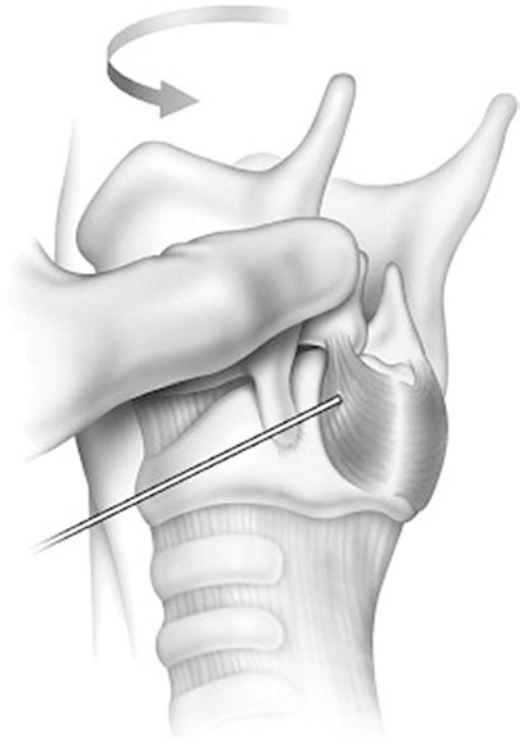

Fig. 25.2 Electromyographically guided injection of the posterior cricoarytenoid (PCA) muscle through the posterolateral approach. (From Shah and Johns [12], with permission)

- The needle is introduced into the skin medial to the anterior border of the sternocleidomastoid muscle and just superior to the inferior border of the cricoid cartilage. A common pitfall to avoid is setting the vertical level of needle insertion too high, since the bulk of the PCA is located along the posterior cricoid lamina below the thyroid cartilage inferior border.
- Slight rotation of the larynx can help expose the posterior aspect of the cricoid cartilage but oftentimes simple counter pressure against the contralateral side of the larynx is all that is needed.
- With the needle directed medially, the tip will first contact the lateral aspect of the cricoid and then can slowly be marched to the posterior aspect.
- It may pass through the cricopharyngeus muscle during this process, which can be identified by the tone of basal resting action potentials that ceases with swallowing. Adjust the needle so that it abuts the posterior cricoid lamina and with slight withdrawal it should be in the muscle belly of the PCA. This can be confirmed via brisk recruitment from a short and then long sniff.
- The toxin is then injected and needle withdrawn. The above can be repeated on the contralateral side in similar manner if performing bilateral injections.

Technical considerations for EMG-guided injection of the PCA through the transcricoid approach are as follows (Fig. 25.3) [12]:

- Laryngotracheal anesthesia with 4% topical lidocaine is additionally administered given necessary needle entrance through the endolaryngeal mucosa.
- Flexible laryngoscopy can optionally be performed by an assistant to help visualize needle trajectory.
- The needle is passed at the midline through the cricothyroid membrane until it enters the airway. It is then angled 15°–20° superiorly and 30° laterally towards the side to be injected, making contact with the posterior cricoid lamina. This trajectory can be more easily navigated under direct visualization.
- A controlled push or boring action of the needle will help traverse the cartilage, at which point the tip should be in the PCA. Asking the patient to perform a short and long sniff will confirm this with brisk recruitment observed on EMG. The injection is then performed and the needle can immediately be redirected to the contralateral side if needed.
- When injecting, significant force may be required in the presence of a cartilage plug. Hence, it is safest to only have the intended unilateral dose in the syringe when performing bilateral injections. In elderly patients, this approach may not be feasible if there is prohibitive cartilage calcification.

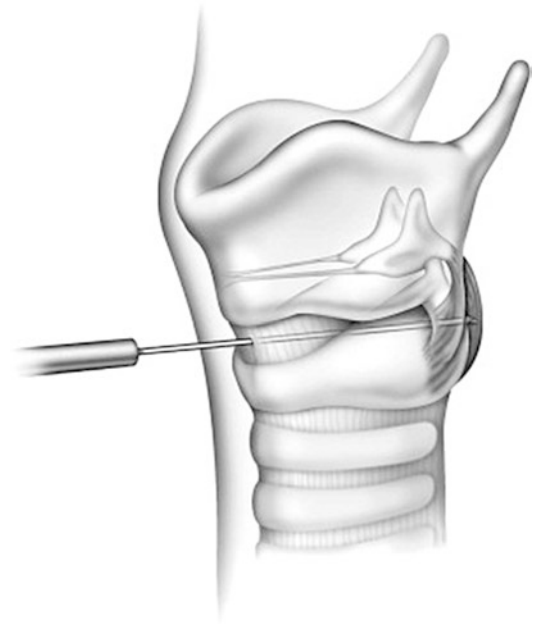

Fig. 25.3 Electromyographically guided injection of the posterior cricoarytenoid (PCA) muscle through the transcricoid approach. (From Shah and Johns [12], with permission)

False Vocal Folds Injections into the false vocal folds can be accomplished in one of two ways. The preferred technique is with percutaneous injection through the thyrohyoid membrane. The needle is not angled as inferiorly as it is when using this approach for injection aug-

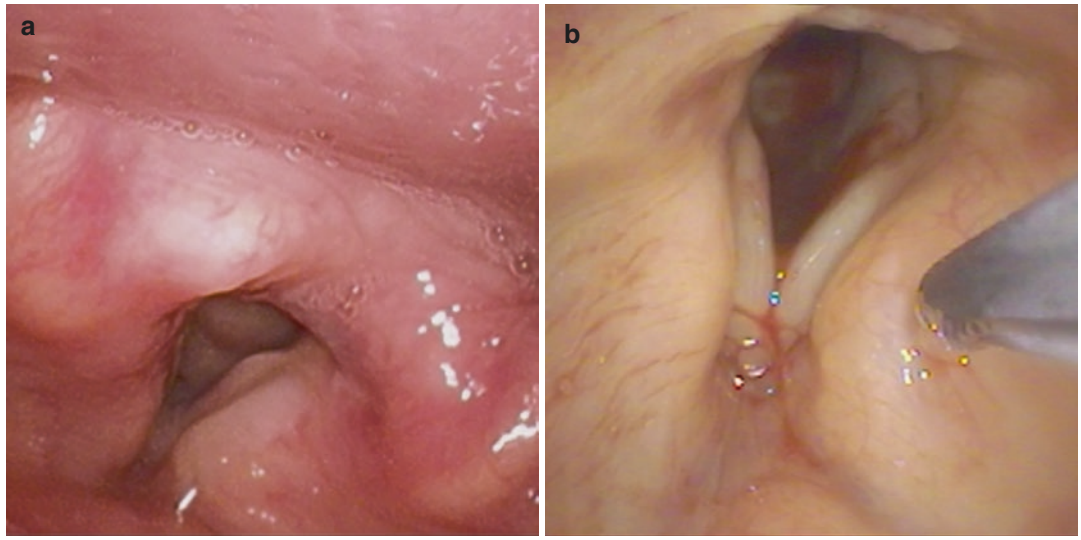

Fig. 25.4 (**a**) Endoscopically guided injection of the false vocal folds: (**a**) through the thyrohyoid approach and (**b**) via a therapeutic laryngoscope

mentation. Topical anesthesia of the larynx is required with the needle entering the endolarynx. The toxin is deposited in the submucosal space with the needle tip just deep to the mucosa of the false vocal fold so there is a more diffuse bleb/infiltration (Fig. 25.4a). The contralateral injection can be executed by redirecting the needle after withdrawing to the petiole. It can also be done via a channeled endoscope with a sclerotherapy needle directed through the working channel (Fig. 25.4b) but requires more waste of Botox. This method is usually only selected if percutaneous injection is anatomically impractical.

Cricopharyngeus (CP) The cricopharyngeus can also be injected in the office setting with a similar approach as the EMG-guided injection of the PCA previously mentioned but with a more lateral and posterior position of the needle tip. Basal resting action potentials should be heard with the needle in the CP, which ablate with swallowing. These should not change with sniffing, which is checked to avoid accidental PCA injection. There is still risk of toxin diffusion resulting in PCA paralysis, which is the reason only unilateral injections are done with this approach so as to avoid potential airway compromise.

Our preferred approach is in the operating room under suspension laryngoscopy. A bivalved laryngoscope can be used to gain exposure of the cricopharyngeal bar as if preparing for an endoscopic cricopharyngeal myotomy. The toxin can then be injected in the muscle at the 5 o'clock and 7 o'clock positions to ensure adequate distance from the PCA. If concurrent dilation is performed in this setting, Botox injections should be performed after dilation to avoid dispersion.

Complications Laryngeal botulinum toxin injections in the office are generally well tolerated, with a very low incidence of complications. Known side effects can be anticipated and minimized with consistent technique paired with judicious dosing.

Vasovagal Episode/Syncope It is very uncommon for a vasovagal episode or syncope to occur secondary to pain or anxiety from the injection, especially in return patients. However, these reactions tend to be self-limited when they do happen and can be mitigated by laying the patient

supine. Very rarely are procedures aborted due to pain or discomfort.

Prolonged Dysphonia An anticipated side effect of TA-LCA Botox injections is an initial period of breathiness, with the goal of dosing to keep that period to 1–2 weeks. However, there is the risk of prolonged breathiness if administering too high a dose relative to the patient's needs. Appropriate counseling can help prepare a patient for this possibility and should guide dose down-titration when it does occur.

Dysphagia/Aspiration With weakening of the bilateral TA-LCA muscle complex, mild dysphagia and/or aspiration can occur. Diffusion of toxin to the inferior constrictor and cricopharyngeus muscles may also contribute to dysphagia risk. That risk peaks in the first 1–2 weeks following injection, as that is the period of maximal toxin effect. Significant aspiration can be avoided with appropriate dosing and symptoms can be managed with a modified diet as needed.

Dyspnea/Stridor Dyspnea from narrowing of the glottic airway can occur from excessive weakening of bilateral PCA muscles and is less likely with staged unilateral PCA injections. However, the overall safety profile of simultaneous bilateral PCA injections is favorable with total bilateral doses under 5 U [15] and is commonly performed in our practice. Abductor paralysis has also been reported with injections to the TCA-LCA complex, likely from inadvertent diffusion of toxin around the muscular process of the arytenoid to the PCA [16]. When it does occur, conservative management with rescue breathing techniques and activity restriction is usually all that is necessary.

Dosing and Outcomes for Laryngeal Conditions

Spasmodic Dysphonia (Adductor) The most common indication for Botox injections in the larynx is for laryngeal dystonia, specifically adductor-type spasmodic dysphonia (ADSD). Its use was first described by Blitzer et al. in 1986 [17] and has since become the standard of treatment. The TA and LCA adductor laryngeal muscles are the main end organ perpetrators in this disorder. Consequently, the TA-LCA muscle complex is the primary target of Botox injections for symptomatic improvement. False vocal fold injections can be an effective alternative in some patients with ADSD who are more sensitive to breathiness or wish to preserve singing voice/pitch control [18]. They can also be used as an adjunct treatment for residual compensatory supraglottic hyperfunction [19].

Dosing While there is no standard dose for ADSD, typical doses range from 0.625 to 2.5 U per side for bilateral TA-LCA injections. Our starting dose is usually 1.25 U to the bilateral TA-LCA for a newly diagnosed patient. A comparison of 1.25 U to 2.5 U starting dose showed that using 1.25 U decreased the period of breathiness without significantly compromising good voice outcomes or duration of effect [20]. It is also the most commonly surveyed starting dosage [8]. A higher dosing is usually required for false vocal fold injections used as primary treatment of ADSD (2.5–10 U). In the art of managing expectations, we find it better to titrate up to optimal results than overcoming discouraging side effects. The dose should be evaluated and adjusted at each repeat injection in the context of individualized patient goals, with the general aim of minimizing the period of breathiness/other side effects and maximizing duration of serviceable voice. Unilateral injections (starting with 1.25 U) can be useful in managing those sensitive to breathiness [21]. Although Lerner et al. [22] have shown gender differences in type A toxin dosing with women requiring approximately twice as much as men, the majority of providers do not report using different dosages [8].

Outcomes Overall voice outcomes are excellent for patients with ADSD treated with TA-LCA Botox injections, with an estimated 90–95% success rate [8, 23]. In select patients with refractory

symptoms and limited benefit from TA-LCA directed injections, interarytenoid muscle chemodenervation has been reported to be helpful [24]. These are performed similarly to the translaryngeal PCA injection described except with needle insertion into the interarytenoid region.

Spasmodic Dysphonia (Abductor) After the introduction of laryngeal Botox injections for treatment of adductor spasmodic dysphonia in the late 1980s, it naturally followed that its use would expand to encompass abductor spasmodic dysphonia. Blitzer et al. [25] were the first to describe EMG-guided percutaneous retrolaryngeal Botox injections directed to the PCA muscles in 1991 for treatment of ABSD. That same year, Rontal et al. [26] described the alternative endoscopic-guided transcricoid approach to injecting the PCA, which remains a valuable technique. In recent survey of practitioners, the preferred PCA injection approach is the EMG-guided translaryngeal method used by half of responders, while one-third preferred the EMG-guided retrolaryngeal approach [8].

Dosing Classically, unilateral PCA injections were performed with a typical starting dose of 3.75–5 U and interval follow-up in 2 weeks for potential contralateral PCA injection. This methodology was adopted to avoid precipitating airway embarrassment from bilateral PCA paralysis. While this remains the popular practice (~80%) [8], we prefer to perform simultaneous bilateral PCA injections with starting dose of 2.5 U per side. Prior studies have demonstrated that simultaneous bilateral PCA chemodenervation is both safe and effective for ABSD [14, 27]. When patients return in 2 weeks, assessment of vocal improvement and dyspnea along with flexible laryngoscopy findings guide the decision to perform an additional unilateral injection. If needed and not limited by dyspnea, this is usually performed on the more mobile side with an extra 2.5–5 U depending on clinical situation, airway caliber, and initial response. If one side is completely immobile, we either defer the booster injection or use a smaller dose of 1.25 U.

Outcomes In contrast to the outcomes with ADSD, patients with ABSD do not experience as consistent benefit from Botox injections. Generally, the success rate approximates 66–75% in previously reported series [8, 23, 25]. However, the cohort of simultaneous bilateral PCA injections performed by Klein et al. [27] demonstrated benefit approaching 90%. In spite of this, there are key factors that temper the ability to achieve comparable results as with ADSD patients. Firstly, PCA injections are technically more challenging and have a higher chance of missing. When surveyed, laryngologists estimate that 1 in 8 PCA injections end up in a miss vs. 1 in 20 for TA-LCA injections [8]. Secondly, treatment is dose limited by consequent dyspnea and airway narrowing. And lastly, it is difficult to compensate vocally with abductor voice breaks.

Essential Voice Tremor The impetus to utilize Botox to treat essential voice tremor was an extension of its use for disabling head and hand tremor [28]. Ludlow and Koda [29] conducted an EMG study on laryngeal muscle activation in voice tremor and found the thyroarytenoid to be highly involved, which suggested targeted botulinum toxin injections may be a potentially beneficial treatment for EVT. As treatment paradigms for EVT have evolved, we find it helpful to distinguish between those that exhibit horizontal vs. vertical laryngeal tremor [30].

With horizontal laryngeal tremor, our first-line target for Botox is the TA-LCA complex injected in bilateral fashion similar to that for ADSD with a dose of 1.25 U per side. In poor responders, we will attempt false vocal fold injections as a second-line option. Combining TA-LCA and interarytenoid injections has also been suggested as another option [31]. If there is vertical laryngeal tremor present, injections to the strap muscles (sternohyoid and sternothyroid) may be helpful. Since the "horn" of our vocal tract also can be affected by significant cervical/head tremor, more extensive treatment of the cervical musculature may be warranted to reduce oscillations in the voice.

Perceptual analysis of the voice can also inform decision-making. Patients that suffer from significant glottal stops in their voice secondary to tremor tend to do better with laryngeal Botox injections. Those that demonstrate more predominant glottal insufficiency or simple tremulousness may be better addressed with other treatments such as injection augmentation or medical therapy, respectively. Overall, outcomes in EVT from Botox treatment appear mixed, likely related to heterogeneity of phenomenology present within the EVT population [30, 32–34].

Bilateral Vocal Fold Paresis/Paralysis Airway difficulties arise from bilateral vocal fold paresis/paralysis partially secondary to synkinetic reinnervation (see Chap. 19). Selective adductor chemodenervation with Botox theoretically allows greater unopposed abduction during respiration. The concept of using botulinum toxin to lateralize the vocal fold and improve the airway in bilateral vocal fold paralysis was first introduced in a dog model in 1987 [35]; the first case report of its use in humans occurred much later in 2001 [36]. From subsequent published series, we do see it has value as an intermediate intervention that can both help avoid a surgical tracheostomy and facilitate decannulation [37–39]. Acuity and degree of respiratory distress in each individual case dictate whether Botox injection is a valid option as it takes at least 3 days to have appreciable clinical effect. We typically start with 3.75 U delivered to bilateral TA-LCA complexes. Injection of the cricothyroid muscles has also been reported [40, 41].

Paradoxical Vocal Fold Motion Paradoxical vocal fold motion disorder remains poorly understood in terms of etiology but is frequently treated successfully with a combination of medical management, laryngeal control/respiratory retraining, and biofeedback therapy with speech language pathology (see Chap. 22). In the small number of severe refractory cases, targeted Botox can be helpful [42] but must be accompanied by adequate counseling. Since the underlying pathophysiology involves inappropriate vocal fold adduction, the TA-LCA complex can be weakened for therapeutic effect. Dosing typically starts at 2.5–3.75 U bilaterally and can be titrated to breathiness.

Neurogenic Cough Medical treatment is the main cornerstone of treatment of neurogenic cough, which is expounded in Chap. 21. However, for refractory patients that have exhausted all other options, serial Botox injections to bilateral TA-LCAs exist as a final treatment modality. We use doses of 2.5–3.75 U bilaterally to achieve breathiness. Based on our experience and published data [43, 44], multiple injections are usually required to see significant improvement/resolution of the cough. Hence, patients need to be counseled appropriately regarding expected side effects and treatment course.

Cricopharyngeal Dysfunction Botox injections to treat cricopharyngeal muscle dysfunction was first described in the literature in 1994 [45]. While feasible to perform in the office under local anesthesia, we prefer to perform the injections in the operating room under general anesthesia with the cricopharyngeus muscle exposed via suspension laryngoscopy as previously detailed. Our standard starting dose is 25 U distributed in two injections along the cricopharyngeal bar. Most dosages reported in the literature span from 5 to 50 U, and even as high as 100 U [46]. Success rates are variable, ranging from 43 to 100% based on a recent systematic review [46]. Some use Botox injections alone, some in conjunction with dilation, and others as a trial treatment prior to surgical myotomy. Refer to Chap. 31, for a more detailed treatise on this subject.

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Saliva Management

26

Charley Coffey

Overview

Aspiration of saliva and respiratory secretions can be a particular risk for patients with neuromuscular or neurodegenerative disease. Inability to adequately clear saliva can also result in problematic drooling, throat clearing, and cough, with significant quality of life implications. This chapter will review the management of sialorrhea and drooling in patients with neurologic disorders.

Anatomy and Physiology

Saliva plays an important role in a number of critical functions pertaining to diet, speech, social interactions, and general quality of life. Saliva softens and lubricates the food bolus to permit swallowing and promotes mobility of the tongue and oral soft tissues critical for speech and articulation. Sense of taste is dependent upon saliva to dissolve and distribute tastants around the mouth, and sense of smell is to a lesser degree dependent upon similar actions within the nasopharynx. Salivary enzymes initiate the digestion of carbohydrates and fats, while salivary glycoproteins, enzymes, and antibodies play roles in both local and systemic immune protection. The buffering capacity of saliva protects the mouth, pharynx, and esophagus from fluctuations in pH due to gastric or ingested fluids. Finally, the mechanical and chemical protections provided by normal saliva are critical to dental health [1, 2]. Although the various roles of saliva may be difficult to fully appreciate when functional status is normal, alterations in salivary production or clearance can have significant functional consequences and resulting impacts on quality of life.

Saliva is the product of six major salivary glands, including paired parotid, submandibular, and sublingual glands, as well as minor salivary glands located throughout the mucosa of the oral cavity and pharynx. The majority of resting or unstimulated salivary volume is produced by the submandibular glands (SMGs), while the parotid glands contribute the majority of stimulated salivary flow during food consumption. The thin, serous saliva produced by parotid glands aids in softening the food bolus, while minor gland production is primarily mucinous, with higher viscosity contributing to lubrication of the mucosal surfaces with a viscoelastic film. The saliva produced by submandibular and sublingual glands is mixed serous and mucinous. Normal total salivary production ranges from 0.5 to 1.5 L per day, with significant fluctuations in rate based upon mechanical or gustatory stimuli, hydration, and circadian rhythms [3, 4].

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Saliva is cleared from the mouth via a combination of evaporation, absorption through the oral mucosa, and swallowing. A single functional swallow allows clearance of about 0.3 ml of saliva [5]. Under normal circumstances, it is possible to maintain a balance of residual fluid within the mouth by varying the frequency of swallowing to equilibrate the rates of salivary production and loss. Disorders of swallowing which affect ability to clear saliva can result in pooling of the excess fluid and spillage out of the oral cavity. This excess can either drain posteriorly into the pharynx and larynx, potentially resulting in aspiration, or spill anteriorly via the lips to result in drooling. It is important to distinguish drooling, which most commonly results from impairment of salivary clearance, from ptyalism or hypersalivation, which more accurately refer to overproduction of saliva [6].

Neuromuscular and neurodegenerative diseases are frequently characterized by significant swallowing dysfunction, which in turn can be associated with disorders of salivary clearance. Drooling is one of the prominent non-motor symptoms of Parkinson's disease (PD) and is also commonly seen in patients with amyotrophic lateral sclerosis (ALS), myasthenia gravis, oculopharyngeal muscular dystrophy, multisystem atrophy, progressive supranuclear palsy, and cerebrovascular disease, among others [6–8]. Objective swallowing evaluation has demonstrated direct correlation between severity of dysphagia and severity of drooling in PD patients [8], and it is believed that inability to adequately clear oral saliva is similarly the biggest contributor to drooling in other common neurologic disorders. Head-down posture, hypomimia (masked facies), and reduced oral motor control can also contribute [9, 10]. Autonomic impairment directly resulting from neurologic disease may also contribute to salivary dysfunction, though this is likely a minor component. Indeed, quantitative evaluations have demonstrated that salivary production in PD patients who drool is actually lower than normal controls [11–13] and that ALS patients have rates of stimulated and unstimulated salivary flow which are either normal or reduced compared to normal controls [14–16].

Estimates of the prevalence of drooling in neurologic diseases range widely, in part due to lack of standards of definition, diagnostic criteria, and assessment tools. The prevalence of drooling in PD has been reported to range from 10% to 84% [7, 9, 13, 17] and in 25% to 50% of patients with motor neuron diseases [18, 19]. The negative impact of salivary dysfunction on quality of life can be significant, including disruption of eating and speaking, psychosocial distress and isolation, halitosis, perioral dermatitis, and hardship for caregivers [20]. Buildup of thick, tenacious mucoid saliva can contribute to sensations of choking or panic, can interfere with sleep, and in severe cases can also contribute to aspiration, with potentially fatal consequences [21, 22]. Despite this, it is speculated that salivary dysfunction in patients with neurologic diseases is frequently underrecognized and undertreated [9]. This chapter will discuss medical and surgical management of drooling in affected patients with neuromuscular or neurodegenerative disorders, with a focus on the role and use of botulinum toxin.

Age-Related Changes

It is frequently observed that salivary symptoms increase with aging, though there is a lack of consensus regarding the nature, degree, and underlying pathophysiology of these changes. Subjective reports of xerostomia are much higher in older populations than young people, and there is some evidence that rates of stimulated and unstimulated salivary flow decrease with age [23]. However, it has also been suggested that age-related decrease in the number of salivary acini is offset by increased efficiency of the remaining tissue, such that salivary volume and protein production may be relatively preserved with aging [24]. It can be very difficult to distinguish the primary effects of aging from a range of other factors which are frequently associated with aging and which can have secondary effects on salivary function. Namely, dehydration and decreases in both taste sensitivity and bite forces are all common with aging and can all independently decrease salivary

flow. Most notably, a wide range of medications can effect salivary production, and it can thus be difficult to discern the primary effects of aging on salivary symptoms from the effects of the polypharmacy common in aging populations [25]. In the assessment of older patients with neurologic disorders and swallowing dysfunction, it is important to keep in mind the potential role that age or age-related factors may play in contributing to salivary complaints.

Management

Techniques which prove successful in management of salivary dysfunction for patients with neurologic disorders may vary significantly across patients and may require changing strategies based upon disease progression. A variety of behavioral, medical, and surgical techniques may be employed, dependent upon the severity of symptoms, tolerability of side effects, preference of the patient and clinician, and availability of techniques.

Behavioral

Efforts to improve swallowing function are fundamental in the management of patients with neuromuscular and neurodegenerative disease and may contribute significantly to the management of sialorrhea and drooling in addition to the dietary benefits. While pharmacologic or surgical treatments aim to decrease salivary production, behavioral measures seek to improve salivary clearance. These measures are largely focused on improvements in swallowing function, which is addressed in detail in Chap. 33. In addition to general efforts to improve swallowing, several techniques specifically target management of saliva. Use of a timed auditory cue to promote conscious swallowing efforts on a regular basis may prove successful for motivated patients [10]. Some of the same techniques taught by speech-language pathologists to address oropharyngeal dysphagia may also be employed to improve salivary clearance and reduce spillage or aspiration. Such techniques may include postural changes (e.g., chin tuck, head turn) as well as specific maneuvers to increase the duration of upper esophageal sphincter opening (e.g., Mendelsohn maneuver) or improve airway protection (e.g., supraglottic swallow) [26]. Oral motor training and biofeedback techniques have also been successfully employed to assist salivary clearance, though reports are limited to use for children with cerebral palsy [27–29]. Efforts to implement behavioral techniques should be guided by speech-language pathologists, physical or occupational therapists, or clinicians similarly experienced in management of neurologic disorders and sequelae.

Pharmacologic

Pharmacologic measures to manage drooling and sialorrhea primarily target the autonomic mechanisms which regulate salivary function. Salivary glands receive sympathetic and parasympathetic innervation, and stimulation via either component of the autonomic system will increase salivary flow, albeit not equally. Either parasympathetic stimulation via cholinergic receptors or sympathetic stimulation of alpha-1 adrenergic receptors will result in production of watery, serous saliva. In contrast, sympathetic stimulation via beta adrenergic receptors produces thick, mucinous saliva [30–32]. Pharmacologic therapy has primarily focused on use of anticholinergics, with limited additional evidence regarding the use of adrenergic receptor antagonists. It is notable that salivary production is decreased in patients with PD [12], though use of dopaminergic medications increases salivary flow in PD patients. This appears to be a central effect of levodopa or carbidopa, such that peripheral blockade of the D2 dopamine receptor does not decrease salivary secretion for these patients [33].

It is important to understand that pharmacologic measures that alter salivary flow may also affect salivary consistency, with unintended consequences. Specifically, efforts to reduce drooling may focus on reducing the total volume of saliva produced (so-called whole mouth saliva).

However, if this is accomplished primarily by reducing the output of thin, serous saliva, the result may be a lower volume of thicker, more mucinous saliva. An increase in thick saliva can prove problematic for patients with impaired swallowing or difficulty clearing airway secretions. In such instances, it may be necessary to increase efforts to thin saliva and clear secretions via aggressive oral or tracheostomy care, moist sponges, increases in enteral hydration, and humidification of inspired air or supplemental oxygen. Topical glycerol-based saliva substitutes are commonly used to decrease symptoms of patients suffering from xerostomia, with limited success. If the use of medications to reduce drooling results in subjective xerostomia or overly thick saliva, then titration of the medication dose may prove more effective than addition of saliva substitutes, which do little to thin the consistency of existing saliva.

Anticholinergic Cholinergic muscarinic receptors may be targeted with a range of antagonists to reduce salivary production. The M3 subtype of cholinergic receptor has emerged as the most functionally active in the stimulation of serous salivary production [31]. However, the muscarinic receptor antagonists available for clinical use are not M3-specific, and the non-salivary effects related to cholinergic stimulation may limit tolerability for many patients. Significant side effects such as constipation, urinary retention, drowsiness, blurred vision, confusion, or even hallucination may limit the ability to achieve a dose sufficient to decrease salivary flow for some patients. Anticholinergic drugs are also contraindicated for many patients with history of cardiac disease, glaucoma, prostate hypertrophy, impaired gastrointestinal transit, or myasthenia gravis [7, 34, 35].

Glycopyrrolate does not cross the blood-brain barrier and is thus associated with minimal central side effects relative to other anticholinergics. Oral glycopyrrolate at a dose of 1 mg TID has been demonstrated to be superior to placebo in a randomized, double-blind crossover trial which evaluated drooling using a non-validated scoring scale in a cohort of PD patients [36]. No increase in adverse events relative to placebo was observed in this trial, though there was a trend of increased dry mouth seen with glycopyrrolate. No objective measures of salivary flow were recorded.

The antimuscarinic effects of *amitriptyline* (a tricyclic antidepressant) have been employed to reduce sialorrhea resulting from clozapine (an antipsychotic), at doses ranging from 10 to 100 mg per day [37–39]. Providers should be aware of this potential effect of amitriptyline in the management of patients with PD who suffer from depression and/or psychosis. However, there have been no trials evaluating amitriptyline for management of sialorrhea or drooling, and the potential for adverse effects including cognitive symptoms is not inconsiderable [40].

Transdermal drug delivery offers the ability to reduce peak serum concentrations, thus potentially limiting anticholinergic side effects related to higher doses. Transdermal *scopolamine* has been demonstrated to improve subjective and objective measures of drooling or sialorrhea in several small prospective and retrospective trials, though study populations were not limited to those with neuromuscular or neurodegenerative disease [41, 42]. A larger multicenter survey reported that although scopolamine patches were frequently used as first-line anticholinergic therapy for ALS patients, 60% of patients experienced adverse effects, most commonly including local skin reaction, excessively dry mouth, or thickened secretions. Of patients, 33% discontinued transdermal scopolamine due to intolerance of these effects [43]. The authors suggest that a balance of symptomatic benefit with limited side effects may be achieved by favoring the lowest dose preparations available and potentially by the addition of topical steroid cream to decrease the incidence of dermatitis.

The use of topical intraoral anticholinergic preparations may improve ability to target salivary symptoms while limiting systemic effects. Sublingual application of *atropine* eye drops to limit sialorrhea was first described for patients suffering the cholinergic effects of antipsychotics [44] and was subsequently evaluated in a small

pilot study of PD patients, with favorable results [45]. Open label use of a single drop of 1% atropine solution administered twice daily yielded significant declines in objective and subjective measures of drooling severity. However, systemic absorption may still elicit central effects such as delirium or hallucinations in susceptible patients. A more recent double-blinded RCT did not show sublingual atropine to be superior to placebo in a cohort of patients with drooling resulting from upper digestive tract cancer, though the pathophysiology of drooling in that patient population differs considerably from those with primary neurologic diseases [46]. *Ipratropium bromide* does not cross the blood-brain barrier and has low systemic absorption when administered topically, so promises to offer similar benefit to sublingual atropine with a more favorable side effect profile. However, a double-blinded RCT failed to demonstrate benefit of sublingual ipratropium over placebo for the primary outcome of saliva production in PD patients [47]. Use of a topical intraoral *tropicamide* film was also demonstrated to have no significant treatment effect in a pilot study of PD patients, though the small trial may have been underpowered to detect meaningful effect [48].

In summary, anticholinergic medications are commonly used to treat drooling and sialorrhea in patients with neurologic disorders, but the available evidence regarding such use of these drugs remains very limited, and side effects can be common and potentially serious. Anticholinergic drugs with central effects are contraindicated for patients with cognitive impairment or dementia, and a range of peripheral effects further limit use in those with heart disease, hepatic or renal insufficiency, prostate hypertrophy, or glaucoma, thus excluding use in many elderly patients. Moreover, patients with PD may suffer autonomic dysfunction making them even more sensitive to the unwanted effects of muscarinic blockade [49]. As such, these medications may not be sufficiently efficacious, safe, or sustainable to be considered standard of care therapy for this population and indication [31, 50]. If anticholinergic therapy is employed, a strategy of selecting the lowest possible starting dose and slowly titrating to effect is recommended, with appropriate patient education and observation for potential side effects.

Beta Blockade Selective blockade of beta-adrenergic receptors could reduce production of the thick mucinous saliva which can remain a significant complaint even if anticholinergic or other therapy is successful in reducing total salivary production. A small, single arm pilot study evaluated the use of *propranolol* and *metoprolol* in ALS patients complaining of thick, tenacious secretions while on "maximal" anticholinergic therapy [32]. Seventy-five percent of patients reported initial subjective benefit in symptoms, though the response did not always prove durable. There have to date been no trials of beta blockade for management of saliva or respiratory secretions, so the evidence is not sufficient to support this use.

Botulinum Neurotoxin Botulinum neurotoxin (BoNT) prevents release of acetylcholine from the presynaptic axon, allowing therapeutic use as a longer-term inhibitor of cholinergic activity. Direct injection of BoNT into salivary tissue disrupts muscarinic stimulation and decreases salivary production, with a slow reversal of this effect as the toxin degrades and fusion proteins regenerate over subsequent months. Of the eight serotypes A–H, botulinum toxin types A and B have been employed for medical use. The majority of available evidence for salivary gland injection involves use of *onabotulinumtoxin A* (Botox®; Allergan, Madison, NJ), *abobotulinumtoxin A* (Dysport®; Medicis, Bridgewater, NJ), and *rimabotulinumtoxin B* (Myobloc®; Solstice, Louisville, KY), with a small but growing body of literature on *incobotulinumtoxin A* (Xeomin®; Merz, Raleigh, NC).

Specific indications, procedural details, outcomes, and complications of botulinum toxin use for management of drooling and sialorrhea will be detailed in subsequent sections.

Radiation

The radiosensitivity of salivary tissue is frequently associated with toxicity for patients undergoing oncologic therapy, but this effect can be favorably employed for selected patients with sialorrhea or drooling. The application of external beam radiation therapy (EBRT) for management of sialorrhea in patients with PD or ALS has been evaluated by a handful of prospective and retrospective studies. A systematic review reported outcomes and complications of over 200 patients treated in 10 studies which evaluated EBRT in patients with either PD or ALS [51]. Photons or electrons were used, delivering a median of 12 Gy total dose and a median of 2 fractions. The field arrangements most commonly targeted the entire SMG and caudal two-thirds of the parotid gland bilaterally. Long-term subjective success rates of approximately 80% are reported, with no suggestion of variable effect based upon particle or extent of fields. Initial symptomatic success rates do not suggest a dose response curve, though rates of long-term relapse of symptoms are higher in cohorts receiving total dose of 15 Gy or less.

Radiation-related toxicity is a primary concern of many patients and providers. The available evidence suggests that acute toxicity is common, though primarily related to xerostomia (19%) rather than mucositis (10%) or dermatitis (6%) [51]. The majority of long-term toxicities were related to xerostomia or thickening of salivary consistency. The risk of secondary, radiation-induced malignancy is also an important consideration. Significant increased risk of neural tumors has been reported in association with doses as little as 1–2 Gy administered to the head and neck region in childhood for benign conditions [52]. Newer techniques such as intensity modulated radiation therapy (IMRT) can minimize the dose to critical structures as compared to use of parallel opposed fields, but the risk of radiation-induced sarcoma remains problematic for any tissue receiving >10 Gy regardless of the technique [53]. As a consequence, few would recommend EBRT for sialorrhea or drooling in younger patients, though it may be a reasonable option for those with life expectancy of less than several decades.

Surgery

Surgery can provide an effective and permanent solution for drooling or sialorrhea, though invasive and irreversible measures are only considered once less-invasive approaches have failed. A number of surgical options are available, ranging from limited approaches such as neurectomy, ductal ligation, or ductal rerouting, to complete excision of the submandibular and/or sublingual glands. There is no single procedure that has been demonstrated most effective, and the largest meta-analysis to date reported that, although the overall subjective success rate for surgical procedures is over 80%, the available evidence is low quality and heterogeneous [54]. It is also notable that the majority of the available evidence regarding surgery for management of saliva is limited to a pediatric population, focusing primarily on children with cerebral palsy. The availability of quality evidence regarding surgical management of sialorrhea or drooling in adults with neurologic disease is even more limited.

Neurectomy Division of the tympanic plexus and chorda tympani nerve is historically noteworthy but has largely fallen out of favor due to the associated morbidity and variable success rates. Surgical approach via the external auditory canal provides access to the middle ear to section both Jacobson's nerve as it crosses the cochlear promontory and the chorda tympani nerve under the tympanic membrane, interrupting parasympathetic innervation of both the parotid and SMGs. However, this results in loss of taste sensation to the anterior two-thirds of the tongue, which is generally considered unacceptable, particularly by patients for whom oral intake may already be limited or problematic. Additional risks of permanent xerostomia, hearing loss, and even facial nerve injury all bear consideration. Significant variability in results may result due

in part to extensive anastomoses of the tympanic plexus [31, 54–56]. More recent reports have described transoral division of the submandibular ganglion, which promises parasympathetic denervation of the SMG while preserving lingual nerve sensation [57, 58]. This approach merits further evaluation to better define associated outcomes, complications, and patient selection.

Ductal Ligation Surgical ligation of the paired submandibular or parotid ducts or all four ducts offers a simple surgical option with relatively low morbidity. Under general anesthesia, each duct is cannulated, and intraoral mucosal incisions are created around the circumference of the ductal papilla (Fig. 26.1a, b). The distal duct is ligated with permanent suture, and the overlying mucosa is closed primarily. Duct ligation results in immediate decrease in intraoral salivary volume and long-term atrophy of the associated glands. Up to one-third of patients experience persistent or recurrent postoperative facial swelling, generally managed successfully with conservative measures such as warm compresses, facial massage, and oral antibiotics [59]. Postoperative ranula has also been reported [60]. Improvement in salivary flow and quality of life outcomes are generally reported at greater than 70%, with mean duration of effect greater than 4 years [59]. A minority of patients may experience recurrence of sialorrhea or drooling, likely due either to recannulation at the site of ligation or fistulization of the proximal duct(s).

Ductal Rerouting Transposition of the parotid ducts to decrease drooling by diversion of saliva into the pharynx rather than the oral cavity was first described in 1967 [61]. Submandibular duct rerouting was subsequently described as another means of diverting salivary drainage into the pharynx and thus diminishing pooling in the anterior floor of mouth [62, 63]. Positioning the transposed papilla just posterior to the anterior tonsillar pillar to drain onto the adjacent base of tongue may also stimulate a swallowing reflex, further improving salivary clearance [34]. Reported outcomes are excellent, with a meta-analysis of 21 studies estimating overall subjective success rate at 85% [54]. The procedure is technically straightforward, though more involved that simple duct ligation (Fig. 26.1b, c). Complications are rare, consisting primarily of ranula formation; this risk is reduced considerably if the sublingual glands are removed at the time of duct relocation (Fig. 26.2) [64]. Retrospective data has also suggested increased risk of dental caries when duct relocation is employed in a pediatric population [65, 66].

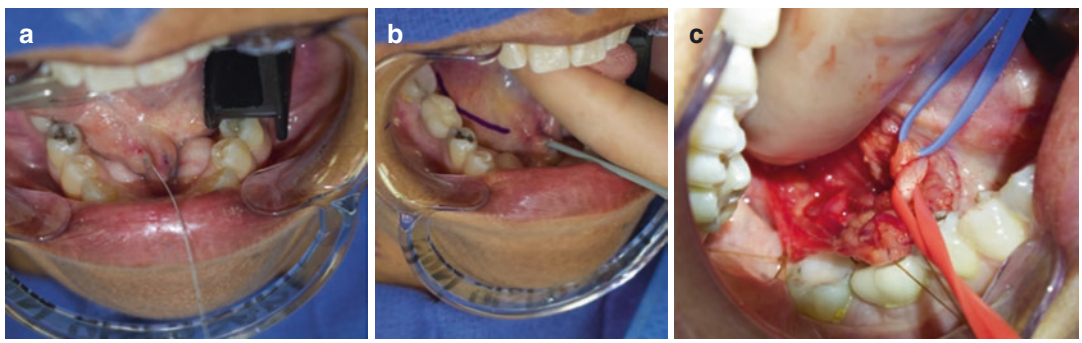

Fig. 26.1 The submandibular duct is identified, cannulated, and mobilized. (**a**) A 0.015 inch guidewire is atraumatically inserted via the native papilla. (**b**) A flexible dilator is passed over the wire to define and protect the duct during dissection. If duct relocation is planned, a linear incision along the floor of mouth (*purple line*) can optimize exposure and visualization, though the papilla and duct can also be tunneled under the mucosa via separate anterior and posterior incisions. (**c**) During submandibular ductal relocation, it is important to preserve the lingual nerve (*red loop*) adjacent to the duct (*blue loop*). (© Charles Coffey, with permission)

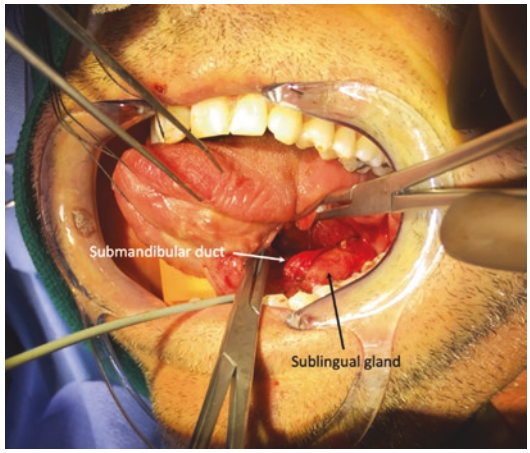

Fig. 26.2 Removal of the sublingual gland (*black arrow*) at the time of submandibular duct relocation (*white arrow*) can reduce the risk of postoperative ranula. The sublingual gland can generally be dissected free of the adjacent duct, lingual nerve, and loose fascia with a combination of blunt dissection and bipolar cautery. (© Charles Coffey, with permission)

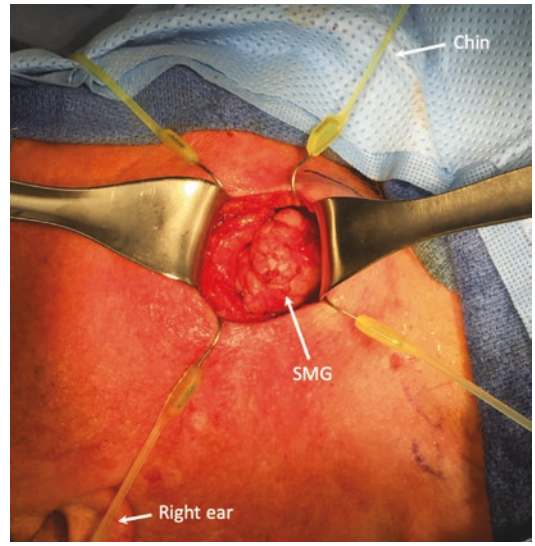

Fig. 26.3 The right submandibular gland is exposed and dissected via a horizontal incision in the overlying skin, at least two fingerbreadths below the border of the mandible (*ear and chin labeled for orientation*). The lingual nerve, hypoglossal nerve, and marginal mandibular branch of the facial nerve are preserved, while the facial artery and vein and the submandibular duct and ganglion are ligated and divided. (© Charles Coffey, with permission)

Gland Excision Parotid gland excision for management of sialorrhea is not an attractive option, primarily due to the risk of facial nerve injury which could add considerable additional morbidity for any individual, particularly those with baseline neurologic dysfunction. In contrast, the risks associated with SMG excision are low, and the combination of SMG excision (Fig. 26.3) with either rerouting or ligation of the parotid ducts has yielded subjective success rates of 85–88% by meta-analysis [54].

It is important to note the vast majority of data supporting surgery for management of sialorrhea or drooling in neurologic disorders is based upon level 4 evidence, with no randomized control trials of any surgical technique in the adult population [54]. The majority of available evidence also focuses on pediatric populations and may thus be less generalizable for adults with neurodegenerative or neuromuscular disease. Recommendations for treatment must thus be based upon the best available evidence and clinical judgment, including consideration of the degree of potential benefit and relative risk. Surgical management offers the potential for long-term or even permanent control of symptoms, in contrast to available pharmacotherapies. The lack of significant systemic or cognitive side effects may make surgical management especially appealing for patients unable to tolerate anticholinergic effects. Most of the available surgical options do, however, require general anesthesia, which confers increased risk for those with significant medical comorbidities. Ligation of the submandibular +/− parotid ducts appears to be a relatively effective, minimally invasive, reversible technique with potential for long-lasting benefit and as such may be considered a good first-line option for patients failing medical management. More invasive approaches such as duct relocation with or without submandibular or sublingual gland excision can be employed for patients failing to improve after ductal ligation. Salivary duct rerouting may prove most attractive for patients whose primary complaint is drooling rather than aspiration, as diversion of additional saliva posteriorly into the pharynx could in theory be problematic for patients suffering from aspiration.

Assessment and Indications for Therapy

There is no broadly agreed upon clinical measure or assessment tool for drooling or sialorrhea and thus no standard means to objectively determine when intervention is indicated or which approach to employ. Although objective assessment of salivary flow volume is possible, the various methods of saliva collection and volumetric or weight measurement all require significant time, are prone to imprecision, and are impractical for general clinical use [3, 67]. Several patient-reported outcomes measures have been developed to assess drooling and sialorrhea in patients with neurologic disorders [9, 10, 68, 69]. However, external validation and breadth of clinical application of these measures is limited, and they are rarely employed in the clinical setting [67]. Finally, there can be large variability of drooling throughout the day for any one individual based upon posture, diet, time, level of wakefulness or attention, and any number of other factors, making even the most strenuous efforts at objective assessment problematic. As such, a consortium which reviewed management of drooling in a pediatric population ultimately concluded that objective quantification was not required to implement or assess interventions [70]. An international consensus statement argues that the single most important factor in determining whether intervention to reduce drooling or sialorrhea is indicated is the wishes of the individual or caregiver to improve quality of life [71]. The majority of clinical management in the adult population is thus symptom-driven, and measures of success in clinical practice are frequently subjective and based upon patient or caregiver reports of success or failure.

Timing of Intervention

Behavioral therapy, swallowing therapy, and other relatively conservative measures may be employed at any point in the disease process and should be considered as soon as management of saliva has been identified to be problematic. If systemic pharmacotherapy is used, initial dosing should be minimal, with slow-dose escalation titrated to effect. If behavioral measures prove insufficient, or anticholinergic side effects too intolerable, BoNT should be considered as next-line therapy.

Botulinum Neurotoxin Injection

BoNT injection is relatively well-tolerated by most adults, and unlike surgery or radiation therapy, the effects resolve over time. Response to salivary gland BoNT may also prove useful in predicting whether more invasive management may prove beneficial. Surgery could be considered for a patient who experiences favorable symptomatic results following BoNT injection but desire a more permanent solution, while a patient for whom BoNT causes xerostomia without significant improvement in aspiration might be predicted to have a similarly suboptimal surgical outcome. Duration of action in salivary tissue may vary based upon BoNT serotype and subtype, though direct comparison suggests similar effective duration for commonly used subtypes [72, 73]. The effects of salivary BoNT injection may be expected to last from 2 to 8 months, generally a longer duration than is seen with intramuscular use. Timing of re-dosing for serial use is guided by patient response, with an average of 4–6 months between treatments. Seasonal variations may also be taken into account; treatment of patients at increased risk of respiratory infections should aim to optimize salivary control during winter months when infections are more common [71]. The formation of antibodies to BoNT may result in decreased sensitivity or treatment failure in a minority of patients. Avoiding repeat injections within a 3-month period has been suggested as one means to reduce risk of developing antibodies and treatment resistance [71, 74]. Serial BoNT injection can remain effective for many years, with one report documenting a failure rate of only 11% in up to 8 years of repeated treatments [62].

Table 26.1 Botulinum toxin formulations [49, 72, 75, 78]

Toxin	Serotype	Trade name (USA)	Estimated dose equivalency (range)[a]	Commonly reported total salivary dose	Preparation/storage
Onabotulinumtoxin A	A	Botox®	–	100 units	Powder/refrigerate
Incobotulinumtoxin A	A	Xeomin®	1:1–1:1.2	100 units	Powder/room temp.
Abobotulinumtoxin A	A	Dysport®	1:2–1:3	250 units	Powder/refrigerate
Rimabotulinumtoxin B	B	Myobloc®	1:30–1:50	2500 units	Solution/refrigerate

[a]Relative to onabotulinumtoxin A

Description of Procedure

Salivary Gland BoNT Injection BoNT injection into the major salivary glands can be performed in a clinic setting for most adults. Injection is frequently tolerated with little or no local anesthetic, though application of a topical anesthetic cream 60 minutes prior to the procedure may prove beneficial for some patients. Commercially available forms of BoNT-A require reconstitution with normal saline. Only preservative-free normal saline should be used, as reconstitution with sterile water may be associated with intense injection site pain, and anaphylaxis has been reported when BoNT is reconstituted with lidocaine [75]. The only available preparation of BoNT-B, rimabotulinumtoxin B, is supplied as a sterile solution for injection, though it may be diluted as needed to achieve desired concentration.

Preparation of BoNT for injection is performed according to manufacturer instructions. A range of dilutions are reported, with at least one small series suggesting a lower rate of swallowing dysfunction associated with concentrated preparations (100 units/1 ml) compared to more dilute solutions, with speculation that diffusion of toxin into adjacent muscles may result from increased injection volumes [76]. Use of 1 ml syringes for injection allows for precise dosing in small increments. This is particularly important when using relatively concentrated solutions of toxin.

There is no established optimal dose for salivary BoNT injection, though there is evidence that total doses >50 units are clinically superior to doses <50 units [77]. Selecting a BoNT dose can be challenging not only due to wide ranges reported in the literature but also because the unit doses of the individual products are not interchangeable and there is variation in the estimated dose equivalency ratios [75, 78]. Clinical dose equivalency ratios of the four commercially available products are reported in Table 26.1. Contemporary reports indicate standard dose ranges of 15–50 units of BoNT-A (onabotulinumtoxin A, or equivalent) into each parotid gland and 10–30 units per SMG [71, 72]. The author recommends initial treatment in the lower to middle portion of that range, with the ability to titrate dose upward with subsequent injections if indicated based upon patient response. Outcomes of a recent blinded RCT demonstrate that, although therapeutic effects increase with the number of glands injected (4 > 3 > 2), there is no apparent difference based upon which glands are injected (both parotids, both SMG, or some combination of each) [79].

Ultrasound guidance is increasingly employed for salivary BoNT injection and may yield improved outcomes resulting from more reliable distribution of the drug within the gland [80]. If a "blind" technique is used, the injection sites are defined according to external anatomic landmarks (Fig. 26.4), with the gland grasped and stabilized between two fingers if possible. Having patients clench their teeth can help to better identify the posterior border of the masseter muscle and avoid intramuscular injection. The precision provided by ultrasound allows for easier distribution of the dose across multiple anatomic sites, theoretically increasing the volume of salivary tissue affected while limiting the risk of improperly injecting adjacent tissues. The SMG dose is frequently divided between the anterior and posterior halves of the gland and parotid dose between the superior and inferior halves, or superior, middle, and inferior thirds.

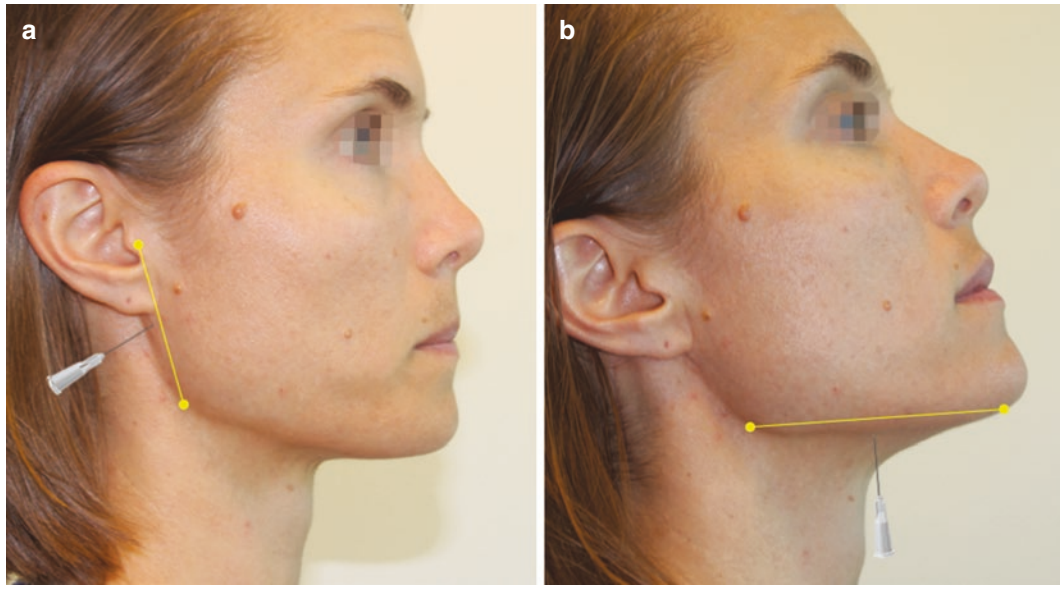

Fig. 26.4 If ultrasound is not employed, BoNT injection can be performed based upon anatomic landmarks. (**a**) Site for parotid injection is at the midpoint of a line drawn between the tragus and angle of the mandible. The parotid tail can frequently be grasped between two fingers just posterior to the mandibular ramus. (**b**) Site for submandibular gland injection is halfway between the mandibular angle and the menton (most anterior-inferior aspect of the mandible), and 1 cm medial to the body of the mandible. The contour of the SMG may be visible with the neck gently extended. (© Charles Coffey, with permission)

Patients should be comfortably seated or reclined, and the room arrangement should allow the provider to work from both sides of the patient and easily access a clean prep space and the ultrasound unit. The planned dose and corresponding injection volume should be reviewed prior to each injection. Skin sites are cleaned with alcohol pads immediately prior to injection. Sterile 27- or 30-gauge needles are affixed to a 1 ml Luer lock syringe. If ultrasound guidance is used, either in-plane or out-of-plane needle visualization can be effective, though patient anatomy and limitations of cervical mobility may favor one technique over the other in certain instances (Fig. 26.5).

Complications

One of the primary benefits of BoNT in comparison to other medications for management of sialorrhea is the low incidence of adverse effects. The most commonly reported side effects in patients with neurologic disorders receiving BoNT injections include increased saliva thickness (3.9%), dysphagia (3.3%), and xerostomia (3.3%) [77]. This compares quite favorably to the 30–60% of patients who discontinue anticholinergics due to side effects. Injection-related adverse events such as pain, hematoma, and jaw muscle weakness are also quite rare (1.5%) [72]. More significant effects such as dysphagia and pneumonia have been reported, though in many instances it is difficult to distinguish the medication effects from progression of underlying neurologic disease [72]. Transient facial nerve paralysis has also been reported, but is exceedingly rare [81].

Outcomes

Multiple-blinded, randomized, and placebo-controlled trials have demonstrated significant improvement in subjective and objective measures of drooling and sialorrhea in patients with PD, ALS, multiple system atrophy, and corticobasal degeneration, with additional open-label non-randomized series reporting benefit in progressive

Fig. 26.5 Ultrasound guidance can improve the ease and accuracy of salivary gland injection. The author prefers to use an "in-plane" needle visualization technique in the parotid (**a**) and submandibular gland (**b**) when possible. The needle may be introduced from either end of the transducer, depending upon provider preference and patient comfort. An out-of-plane technique is equally appropriate and in some instances may be required for parotid (**c**) or SMG (**d**) injection due to the patient's body habitus or limited neck mobility which can interfere with the hand and needle orientation of an in-plane technique. (© Charles Coffey, with permission)

supranuclear palsy, dementia with Lewy bodies, stroke, and cerebral palsy [72, 77, 79, 82–84]. The majority of patients undergoing injection demonstrate benefit, with 80–90% of patients in several randomized trials demonstrating significant decrease in saliva production and corresponding patient satisfaction with the outcome [72, 79, 82]. The magnitude of effect varies based upon the objective assessment measures and the nature of intervention (total dose, number of glands, baseline severity, etc.). A meta-analysis of eight randomized placebo-controlled trials reported a

significant overall effect size, with standard mean difference of −1.5 compared to placebo [77].

Onset of action following injection is generally 1–2 weeks for maximal efficacy. Duration of benefit of up to 8 months is reported [85], with a mean duration of about 3 months [72]. As pertains to management of sialorrhea, there is to date no clearly defined benefit of any one BoNT-A or BoNT-B toxin over the other preparations in regard to potency, duration, or adverse event profile [7, 72, 73, 77]. It appears that ALS patients may experience less benefit than those with PD, stroke, or CP, primarily related to decreased duration of effect [72, 79]. The reason for this is uncertain, though it may be related to more pronounced worsening of dysphagia over time in ALS patients or the increase in oral motor dysfunction in ALS relative to other disorders.

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Management of Glottic Incompetency

27

Vaninder K. Dhillon and Lee M. Akst

Introduction

Glottic incompetency, synonymous with glottic insufficiency, is the condition of incomplete vocal fold closure. It has a number of potential causes, including complete neurologic motion impairment of one or both vocal folds (paralysis), partial neurologic motion impairment of one or both vocal folds (paresis), change in contour of a vocal fold (atrophy or presbylarynges), or reduced motion of the vocal folds on the basis of mechanical fixation such as in stenosis. Because closure of the vocal folds is an essential laryngeal function, incomplete closure – glottic incompetence – can negatively affect a person's ability to breathe, cough, voice, and swallow. Symptoms often depend on the size of the glottic gap and can include reduced vocal projection, increased vocal effort, early vocal fatigue, coughing and choking with oral intake, and aspiration pneumonia. Both surgical and nonsurgical treatments exist. Treatment decisions should account for the etiology of glottic incompetency, potential for spontaneous recovery, size and configuration of the glottic gap, degree of patient voice and swallow handicap, patient comorbidity, and patient goals and expectations.

This chapter discusses symptoms, evaluation, and treatment of glottic incompetence. The thought process that helps to guide decision-making and literature concerning outcomes of treatment for glottic incompetence will be highlighted to demonstrate the importance of recognizing and addressing this condition in patients with neurologic and neurodegenerative diseases of the larynx.

Evaluation

Evaluation of glottic incompetency encompasses a variety of techniques, all designed to help establish potential etiology for the incomplete glottic closure, to assess the patient's laryngeal function and characterize the size of the glottic gap, and to understand the impact that the glottic incompetency has on symptoms. Comprehensive understanding of these concepts helps guide appropriate management as described subsequently.

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History

Patients with glottic incompetence can have a multiplicity of symptoms affecting voice and swallow. It is important to evaluate voice quality and nature of voice use, as each patient's vocal demands are different. Voice can become breathy, and even if conversational projection is intact, patients with incomplete vocal cord closure may be aware of increased vocal effort and early vocal fatigue. There is a spectrum of presentations when it comes to patient's voice complaints. For patient with symptomatic paralysis, breathiness and increased work of breathing with voice use may be noted in an acute period of time. For others with vocal fold atrophy, there may be a more of a gradual change in volume and increased vocal effort over time. The etiology of the glottic incompetence ultimately impacts vocal complaints differently.

Patients can experience trouble swallowing, coughing, and choking with solids and liquids. Aspiration pneumonia and weight loss may accompany the dysphagia found in glottic incompetency, both because vocal cord closure is an important part of airway protection during the oropharyngeal phase of swallowing and because patients with neurologic causes of glottic incompetency may have pharyngeal weakness and/or loss of laryngeal and/or pharyngeal sensation. Incomplete glottic closure often leads to an inefficient cough and throat clear. This can manifest as persistent sensation of phlegm in the throat, chronic throat clearing, and a "wet" sounding voice.

During evaluation, it is important to inquire about onset and duration of the voice and/or swallowing changes and whether these symptoms have been stable or progressive. This information provides clues as to etiology of the glottic incompetence and may inform diagnostic workup and treatment decisions. The clinicians should also glean the relationship between onset and upper respiratory infections, trauma, and recent surgeries that might put recurrent laryngeal nerve function at risk (e.g., cervical spine, thyroid, and other head, neck, and chest operations). Additional questions should elicit the presence or absence of any associated neurologic defects, such as tremor, change in gait, change in handwriting, or involuntary motor tics of other head and neck structures. Glottic incompetency in the absence of vocal fold paralysis may be a consequence of some neurodegenerative conditions, and other neurologic symptoms may provide insight as to whether there is concern for underlying neurologic disorder. The most common causes of glottic incompetency is presbylaryngis which is age-related loss of volume and bowing of the vocal fold inner edges. Presbylaryngis is a relatively chronic change to the voice and is important to consider in the history taking process.

Laryngoscopy and Stroboscopy

Assessing the size of the glottic gap with laryngeal examination (laryngoscopy and/or stroboscopy) is an important part of the assessment. Severity of voice complaints are associated with the size of the glottic gap [1]; that is, the larger the gap between vocal folds during phonatory closure, the more disability experienced by the patient. In fact, the *size* of the gap is more predictive of patient symptoms than is the *etiology* of the gap [2]. Moreover, the size of the glottic gap also influences choice and timing of treatment, as will be discussed later.

Even though flexible laryngoscopy can assess for lesions of the vocal folds and can evaluate vocal fold motion, stroboscopy is necessary for comprehensive assessment of glottic closure and the evaluation of the mucosal wave. In this way, stroboscopy allows visualization of the open-closed phases of glottic closure providing more accurate assessment of the size of the glottic gap and allowing for direct evaluation of the impact of reduced glottic closure on the physiology of voicing.

Additional Testing

Laboratory testing is rarely indicated in patients with glottic incompetency [3], though

some patients with reduced vocal fold motion may benefit from evaluation of Lyme disease and a comprehensive autoimmune workup in the appropriate clinical settings.

In contrast, radiologic testing is often indicated in cases of glottic incompetency – if a patient presents with vocal fold paralysis of unknown etiology, then computed tomography scanning along the course of the recurrent laryngeal nerve is recommended to assess for occult lesions [4]. If vocal fold paralysis is associated with palatal weakness, deviation of the tongue with protrusion, or other cranial nerve findings, then imaging should include the skull base and brainstem to evaluate for lesions that might affect the vagus nerve proximal to the takeoff of the recurrent laryngeal nerve. Imaging is also a consideration for patients with vocal fold paresis [5]. Serial exams showing progression should prompt cross-sectional imaging to evaluate for lesions along the nerve.

If aspiration is a concern, a modified barium swallow or fiber-optic endoscopic evaluation of swallowing (FEES) can be ordered for evaluation. Moreover, further testing beyond the scope of this chapter may be required.

Other Evaluations

Speech-language pathology (SLP) evaluation that assesses the functional contribution to voice and swallowing complaints is an important part of the workup of patients with glottic incompetency [6]. Select patients may be stimulable for improved voice or swallowing with voice or swallow therapy alone. Glottic incompetency that is concerning for an underlying neurodegenerative disorder should prompt a neurology referral. An accurate neurological diagnosis and treatment may benefit voice and swallowing complaints and can help with prognosis, which in itself may affect treatment decisions made by the patient and the otolaryngologist [7].

Treatment Options

The primary tenet of treatment is to reduce or eliminate the phonatory glottic incompetence. This is most often accomplished via coordinated vocal fold augmentation/medialization and voice therapy. Vocal fold augmentation/medialization can be done either through injection laryngoplasty or framework surgery such as medialization laryngoplasty with implant, with or without arytenoid repositioning, or laryngeal reinnervation, as discussed in Chap. 30, [8].

Injection Laryngoplasty

Injection laryngoplasty can be done in the office or the operating room (OR). The advent of distal chip and high-definition scopes has improved the feasibility of in-office-based procedures, without the need for general anesthesia and operating room time. Office injection can be done through multiple approaches, including either transoral or transcervical needle placement [9]. Transoral approaches involve placement of a curved injection cannula through the mouth, behind the tongue, and directly into the affected vocal fold (Fig. 27.1). Conversely, percutaneous injection techniques involve placement of a needle through the neck via the cricothyroid membrane, thyrohyoid membrane, or thyroid cartilage. For both transoral and transcervical injection approaches, the larynx is typically anesthetized with topical lidocaine prior to injection [10] and visualization of the larynx is maintained throughout the procedure with either a rigid or flexible laryngeal endoscope.

Injection in the OR, typically performed under general anesthesia, is most often done through direct laryngoscopy approaches. The needle is passed via the operative laryngoscope directly into the affected vocal fold allowing for precise needle placement. Patients may prefer general anesthesia for comfort purposes, and therefore procedures done in the operating room should be discussed as an alternative to office-based injections.

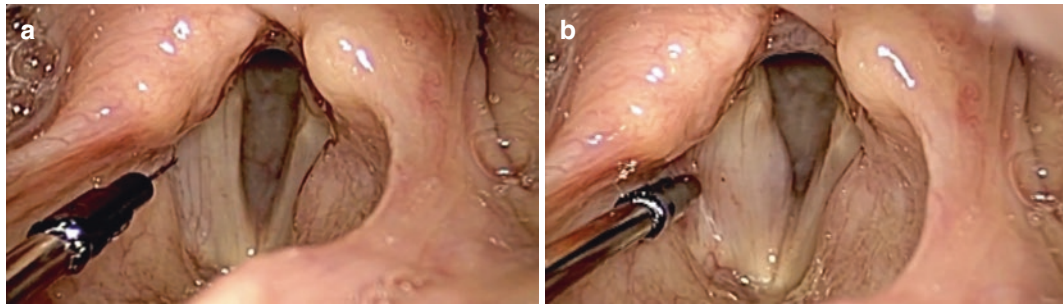

Fig. 27.1 (**a**) Pre-vocal fold injection augmentation (transoral approach); (**b**) post-vocal fold augmentation with medialization (transoral approach)

Table 27.1 Type of injectables used in injection laryngoplasty

Injectable	Expected duration of action (mo)
Carboxymethylcellulose	1–2
Hyaluronic acid	1–3
Micronized alloderm	2–12
Calcium hydroxylapatite	12–24
Autologous fat	12 or longer

When opting for injection augmentation in the treatment of glottic incompetency, the physician must choose from among a variety of possible injectable fillers. Among off-the-shelf options, temporary fillers such as carboxymethylcellulose or hyaluronic acid may allow for approximately 1–3 months of augmentation, while long-term durable fillers such as calcium hydroxylapatite can last up for approximately 12–24 months [11, 12] (Table 27.1).

Autologous fat may also be used for vocal fold injection augmentation, though donor site harvest and pressure needed for injection limit lipoinjection to the OR [13]. None of the injectable options are considered permanent, though injection can be repeated as necessary if material resorbs and the glottic incompetency returns.

Medialization Laryngoplasty

Medialization laryngoplasty was described by Isshiki in 1974 [14]. Also known as type I thyroplasty, this technique is in which an implant is placed into the paraglottic space through a window made in the thyroid cartilage via an external neck approach. Medialization laryngoplasty is done in an operating room setting with patients awake or under conscious sedation, allowing patients to phonate during placement of implant in order to fine-tune voice results. Once in place, the implant (most often expanded polytetrafluoroethylene or silastic) is expected to permanently correct the glottic incompetence.

Type I laryngoplasty involves creating a window in the thyroid cartilage that is measured just posterior to the midline with an inferior strut based upon whether the patient is male or female. The implant is either carved and fitted within the window if silastic or placed as a ribbon strip of polytetrafluoroethylene within the window. The choice of implant is most commonly dependent on surgeon preference and experience.

Medialization implants alone are best for moving the membranous vocal folds; if a gap in the posterior larynx is contributing meaningfully to glottic incompetency, then an arytenoid procedures can be done to close a posterior gap and address height mismatch between the vocal folds. While medialization alone can be done in mobile vocal folds to address contour change and vocal cord paralysis, arytenoid repositioning procedures are done only in cases of vocal fold paralysis in which there is no prospect for spontaneous recovery of nerve function.

The two main approaches to arytenoid repositioning are arytenoid adduction [13] and adduction arytenopexy [15]. These procedures are preferred in cases where there is a large posterior glottal gap or vertical misalignment between the

vocal folds. Arytenoid adduction is accomplished by passing a suture between the muscular process of the arytenoid cartilage and the thyroid cartilage [16]. This rotates the arytenoid cartilage and adducts the vocal fold. In contrast, adduction arytenopexy is where the lateral aspect of the cricoarytenoid joint is opened widely and the body of the arytenoid is manually medialized along the cricoid facet [16]. The arytenoid is rocked internally on the cricoid facet, and suture tension is adjusted appropriately to simulate normal cricoarytenoid adduction [17].

Speech-Language Pathology Intervention

While injection laryngoplasty and medialization laryngoplasty aim to change glottic configuration, voice and/or swallow therapy with a speech-language pathologist (SLP) offers behavioral approaches to improving function. Interventions encompass direct and indirect treatment strategies improving the vocal efficiency and quality, safer swallowing function, or both. Behavioral strategies emphasize optimal use of the muscles of voice and swallowing to help patients best compensate for the glottic incompetency, and depending on the size of the glottic gap, many patients benefit from SLP interventions alone even in the absence of injection laryngoplasty or medialization laryngoplasty.

Evaluation of a patient who has glottic incompetency by a SLP with expertise in voice and swallowing disorders can best determine if therapy is likely to be helpful and what type of therapy is indicated. The involvement of a SLP can also allow for the differentiation between presbylaryngis and presbyphonia. Presbylayngis, or age-related vocal fold atrophy, is different than presbyphonia, which is age-related vocal changes. With an increase in the aging population, not all voice-related changes with age are due to pathologic vocal fold atrophy. Presbyphonia can be multifactorial, related to other systemic factors including breath support, vocal hygiene, and conditioning. The role of the SLP is important in addressing these factors beyond vocal fold atrophy alone. These interventions are also beneficial after medialization procedures, in order to optimize voice quality, where behavioral strategies can improve voice and swallow efficiency.

Decision-Making

Decision-making to improve glottic incompetency begins with a series of questions, keeping in mind the patient's voice and swallowing needs and goals, as well as consideration of the etiology of the incompentency. Ultimately it is the provider's role to perform an intervention that the patient desires and one they will tolerate.

When considering vocal fold medialization, factors to consider include:

- Will medialization be helpful; that is, is the sole problem one of incomplete vocal fold closure, or are there coexisting issues with laryngeal function that may limit voice and/or swallow function even after medialization is performed?
- How much medialization is required? Is unilateral or bilateral medialization needed?
- What is the etiology of the glottic incompetence – is it likely to get better on its own?
- What is the patient's tolerance for an office-based procedure?
- Is the patient a good candidate for the procedure? Does the patient have any other comorbidities?

The consideration of whether medialization will be helpful or not depends on the nature of the glottic incompetency, size of the glottic gap, coexistence of other issues that might lead to voice or swallowing handicap like neurologic, pulmonary or musculoskeletal disorders, and patient preference. In general, the degree of benefit to a vocal fold medialization is in direct proportion to the size of the gap being closed.

The nature of the glottic incompetency is important, and etiology helps inform the appropriate medialization performed. In the setting of an acute unilateral vocal fold paralysis, it is important to determine whether it is temporary or

permanent. Vocal fold paralysis related to idiopathic causes may be transient, as compared to an iatrogenic transection of the recurrent laryngeal nerve during surgery resulting in a permanent vocal fold paralysis. This influences the decision for a temporary versus permanent medialization laryngoplasty. Injection laryngoplasty can use either short- or long-term materials, while only medialization laryngoplasty with an implant can be considered lifelong. In a patient with potential for recovery of laryngeal function as in an idiopathic vocal fold paralysis, a short-term procedure may be indicated – for instance, if status of the recurrent laryngeal nerve is unknown in a patient presenting with acute-onset unilateral paralysis after thyroid surgery, it is possible that vocal fold motion or position may improve spontaneously over time; thus, a temporary material is best. Repeated injections of temporary material can be provided every few months as indicated until nerve recovery has occurred or until it is thought that motion impairment is permanent, at which time switching to a longer-lasting injectate or to a permanent implant may be indicated.

If the condition for glottic insufficiency is not associated with the prospect of spontaneous improvement in vocal fold contour and glottic closure, then it may be reasonable to choose a longer-lasting procedure first. There is one caveat to this situation, and it reflects those patients with uncertain benefit from medialization/injection as mentioned above. If a patient is uncertain as to whether or not they want a long-term medialization, or if the treating physicians are uncertain as to degree of benefit that might be obtained from medialization, then a temporary injection laryngoplasty is appropriate and can provide information that might help both the patient and physician decide about longer-term options.

The size of the glottic gap is important for both injection laryngoplasty and medialization laryngoplasty. Injection laryngoplasty may be good for mild/moderate glottic incompetency, while medialization laryngoplasty has been shown to be sufficient for larger glottic gaps [18]. Additional procedures including possible arytenoid repositioning may be required beyond medialization for patients with foreshortened vocal folds, posterior glottic gaps, or anterior and posterior gaps [19]. Those in favor of medialization with laryngoplasty argue that, unlike injection augmentation, the technique allows for additional arytenoid procedures at the same time as the primary procedure [20, 21]. In patients with a permanent etiology for their glottic insufficiency such as patients with large posterior gaps in the setting of unilateral vocal fold paralysis, it may be best addressed with a framework procedure that includes arytenoid repositioning, as injection approaches largely address only the membranous vocal folds [19]. In the case of preblarynges, where reduced closure exists secondary to age, weakness, reduced coordination, or other contour defect, then a bilateral procedure with small amounts of material on each side might help preserve vocal fold symmetry as each vocal fold achieves a straighter edge (Fig. 27.2).

It is important that when planning for implants or injection, the possibility of progression of vocal fold motion impairment is considered. There may be unique cases whereby a patient may have progressive bilateral vocal fold paresis and demonstrate poor abduction as well as poor closure, and any augmentation to improve voice might worsen the airway, either now or in the future. In this setting, augmentation should be conservative and if there is a concern for narrow glottic airway, a patient should be counseled on the potential plan for tracheotomy.

Patient preference as well as individual patient candidacy for in-office or OR procedures is also a part of the surgical decision-making process. A

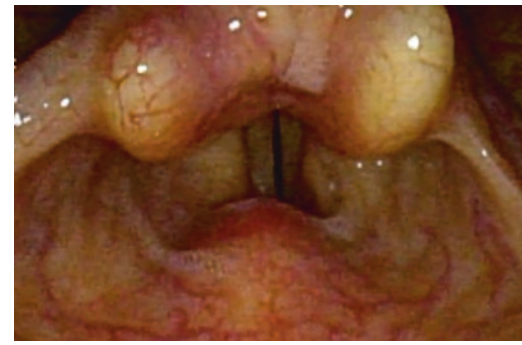

Fig. 27.2 Spindle-shaped glottic gap seen in vocal fold scarring and/or vocal fold atrophy (glottic incompetency)

Table 27.2 Treatment options for glottic incompetency

	Injection laryngoplasty	Medialization laryngoplasty (with or without arytenoid procedures)	Speech language pathology (SLP)
Candidates	Idiopathic vocal fold paralysis Vocal fold paresis Progressive glottic incompetency Airway concerns Patient's unable to have general anesthesia (in office-based procedure)	Permanent vocal fold paralysis	Poor surgical candidates Neurologic etiologies for glottic insufficiency- possible speech impediments and intelligibility concerns Refractory to medialization
Considerations	Can be done in the operating room or in office	Posterior glottic gap/ anterior and posterior gap, height mismatch Possible arytenoid repositioning required Requires good cervical spine extension Anticoagulation therapy	Patient compliance and ability to attend therapy sessions Good SLP/laryngology team (multidimensional approach)

frank discussion with the patient of the risks, benefits, and alternatives of office-based and OR procedures is necessary for the most informed decision. If the goal is to avoid general anesthesia, given an individual patient's co-morbidities, then an office-based procedure would be appropriate. Other factors that may influence injection laryngoplasty over medialization laryngoplasty include poor neck mobility, cervical spine instabilities, and anticoagulation therapy. From a cost standpoint, multiple authors have demonstrated cost savings for in-office versus OR injection augmentation [22, 23]

Lastly, underlying functional issues should be addressed with an SLP. Comorbid exacerbating factors – deconditioning, reduced breath support, rapid fatigability as with multiple sclerosis, reduced motor coordination as with Parkinson's disease – can make compensation harder for patients. In some cases of vocal fold scarring and loss of the native vocal fold tissues, medialization procedures often prove unsatisfactory in terms of voice improvement, and therefore speech therapy is required [24]. Neurologic diagnoses can limit and can also require more than just efficiency training but also strength training, given the underlying diagnosis. SLP completes medialization in that it allows a patient to have a voice whereby the adjunct requirements for glottic competency are addressed and a patient has an overall healthy voice. The treatment options are summarized in Table 27.2.

Results

Literature about the impact of treatment of glottic incompetency is robust for paralysis, is fair for paresis, and is fairly limited for neurodegenerative disorders. We will give a brief overview of these results, mainly to show what degree of voice/swallowing improvement is possible when glottic incompetency is identified and treated.

In patients with glottic incompetency secondary to acute unilateral vocal fold paralysis (UVFP) in a traumatic or iatrogenic setting, early medialization is effective not only from a voice standpoint, but in allowing for enhanced safety of swallow function [25]. Early injection laryngoplasty has been shown to decrease risk for aspiration pneumonia and allow for safer swallow and earlier discharge from the hospital [26, 27].

In addition to intervention in the acute setting, medialization can be beneficial in a more long-term fashion for voice outcomes. Many studies have indicated the voice benefits of medialization in its various forms, with both patient-reported and listener-observed improvements in vocal

roughness, projection, strain, and effort [28]. Patients who receive early injection augmentation have also been shown to have good voice outcomes according to measurable voice parameters [29]. While the data on *how* early injection laryngoplasty may prevent need for long-term medialization is controversial, it appears that it may change glottic closure according to some papers [29, 30]. On the other hand, other studies demonstrate that patients may benefit from more than one procedure in their lifetime, whereby an early injection laryngoplasty is followed up with a long-term medialization laryngoplasty [31].

The evidence is fair for medialization of vocal fold paresis. Vocal fold paresis has been treated with steroids and antivirals, voice therapy, injection augmentation and medialization, as well as treatment of any considered underlying systemic causes [32]. There is no systematic appraisal of treatment for paresis with injection augmentation or medialization, although reports on injection augmentation for cough and glottic incompetency have demonstrated improvement in symptoms [32]. The variability in the literature on the definition of vocal fold paresis makes systematic review of treatment difficult.

The role of medialization in patients with neurologic etiologies for voice and speech complaints is limited. More than 70% of Parkinson's patients demonstrate problems with speech and voice [33]. Retrospective studies evaluating the efficacy of injection laryngoplasty in patients with underlying neurologic disorders like Parkinson's have demonstrated a benefit, although non-significant, in voice outcomes [34]. Injection laryngoplasty has been found to improve cough and prevent aspiration pneumonia for this subgroup [34]. Speech attributes like strength and intelligibility were not affected by medialization. The role of SLP, including Lee Silverman Voice Treatment (LSVT LOUD®), may play an equal if not more substantial role for these patients [35, 36]. Studies concerning treatment of voice complaints in multiple sclerosis [37], multiple system atrophy [38, 39], and ALS [40] are more limited and create a foundation for further research.

Lastly, SLP intervention is a viable option for glottic competency, as a primary treatment modality, both prehabilitative and rehabilitative, before and as an adjunct to medialization. While the documentation of SLP benefits is limited by lack of standardization in the reporting of SLP methods or outcomes measures, it has been shown to be beneficial for patients with incompetency for many reasons. Multiple studies demonstrated improvement from voice therapy for UVFP patients in a multidimensional approach, using both visual-perceptual and audio-perceptual scales to demonstrate improvement [41]. Standardized approaches to timing and frequency of therapy have strengthened the robustness of SLP outcome measures for these patients [42, 43]. Standardized approaches to SLP management may aid in future data collection demonstrating benefit of voice and swallowing therapy for this subgroup of patients.

Conclusion

This chapter serves as a roadmap for the decision-making process involved in determining how to treat patients with glottic incompetency using available techniques in medialization including injection laryngoplasty and framework surgery, along with SLP. The chapter outlines etiologies of glottic incompetency in relationship to vocal fold paralysis, and paresis and secondary to vocal fold atrophy and underlying neurodegenerative disorders. The role of medialization is to improve glottic incompetency, understanding that the decision-making tree involves not only etiology and size of glottic gap but also patient expectations and the tolerability of the approach. SLP is an important adjunct to addressing functional and rehabilitation issues beyond medialization alone. Our aim is to help outline current practice paradigms and the results based upon the literature available. The hope is that readers will be able to identify treatments available for patients with glottic incompetency in an informed and organized manner in order to improve patient-centered care.

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Laryngeal Diversion Procedures

28

William E. Karle and Joshua S. Schindler

Introduction

Each laryngeal diversion procedure aims to achieve mechanical separation respiration from deglutition. Their sole indication is intractable aspiration that has failed conservative management. Although laryngeal diversion procedures are much more commonly performed in the pediatric population, for the purpose of this chapter, our discussion will focus on these procedures in the adult patient.

Within the pediatric literature, the ability to reverse the procedure is an important consideration; however this is much less appropriate for adults. Here we will discuss the ability to reverse certain procedures, yet we strongly urge providers to use discretion if reversal is a possible consideration. Patients who may be considered for a reversal most commonly include those with traumatic, ischemic, or iatrogenic brain injuries [1]. Strong consideration should also be given to the patients' ability to phonate preoperatively, as they will lose this function following the surgery. Laryngeal diversion procedures have become more uncommon as conservative management continues to improve, but the information provided here should be helpful for any medical professional providing care to patients with intractable aspiration.

History of Procedure

Until the 1970s, the standard of care for intractable aspiration that failed conservative management was total laryngectomy (TL). Surgeons had been thinking of less destructive methods for treating these patients, and in 1972 Habal and Murray published their description of an epiglottic flap to occlude the supraglottis [2]. However, it was not until 1975 that Lindeman described the first laryngeal diversion surgery, which he called the tracheoesophageal diversion (TED) [3]. His intent was to produce a nondestructive separation of airway and alimentary tract that was reversible. The following year he went on to describe the laryngotracheal separation (LTS), which he performed on patients who could not undergo a tracheoesophageal diversion due to a prior "high tracheotomy" [4].

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Surgical Indication

Within the adult population, intractable aspiration is the only indication to perform a laryngeal diversion. To be considered "intractable," first-line conservative management must have been attempted and failed. This management includes comprehensive medical treatment for any underlying causes following a thorough workup. The underlying cause of the aspiration in these patients is often multifactorial. Causes may include neurologic insult with an absence of a cough reflex or a severely impaired mental status. Patients who have suffered from a cerebral vascular accident or have a degenerative neurologic disorder are the most common indication for this type of surgery within the adult population. Alternatively, the cause may be structural subsequent to major head and neck surgery, radiation, or trauma. Even a single major aspiration episode may lead to aspiration pneumonia, chemical pneumonitis, or an acute airway obstruction, each of which may be fatal [5].

In most cases of intractable aspiration, patients can be managed with more conservative measures such as using a gastrostomy or jejunostomy tube and prohibiting anything by mouth. Management may include care in a medical facility with aggressive oral suctioning and pulmonary toilet capability. Swallow assessment by a speech-language pathologist should be a prerequisite of all patients with severe pharyngeal dysphagia, and therapy—even without resuming oral intake—may prove adequate to prevent complications of chronic aspiration without a separation or diversion procedure. While some attempt to manage chronic aspiration with an inflated cuff on a tracheotomy tube, we strongly discourage this practice as a cuffed trach tube has not been shown to decrease the incidence of aspiration pneumonia [6, 7]. Although a tracheostomy provides easier access for pulmonary toilet, it can impair swallowing function by inhibiting laryngeal elevation and—most importantly—markedly weakening a productive cough when not valved or capped.

Surgical Options

There are only a few laryngeal diversion surgeries, yet each has several modifications available. These procedures, when done successfully, eliminate aspiration, avoid negatively affecting deglutition, and provide a safe airway. Although important, allowing phonation may be considered a secondary goal in certain patients. These procedures also do not provide any certainty of allowing a patient to resume an oral diet, as the ability to tolerate an oral diet post-op is heavily reliant on the patient's ability to swallow and overall condition prior to surgery. Whether the indication for this surgery is a cerebrovascular accident, advanced neurologic disease, or other neurologic insult, all aspects of swallowing may be affected within this patient population. It is important to assess which specific aspects of swallowing are affected and how much benefit these procedures could offer. If aspiration alone is the main component of their inability to safely swallow, then one would expect an enormous benefit from any one of these surgeries. However, if a patient also suffers from other deficits with pharyngeal constriction, cricopharyngeal relaxation, or oral control, the ability to safely swallow after the procedure may be limited.

The most commonly performed surgery for intractable aspiration is a near-field laryngectomy (NFL). Its popularity over laryngeal diversion procedures is likely due to simplicity and, maybe in part, surgeons' unfamiliarity with other laryngeal diversion procedures. Many surgeons are comfortable performing a total laryngectomy (TL) for oncologic necessity, and this is easily adjusted to become a near-field laryngectomy. The step-by-step details will not be provided here as there are numerous sources for this surgical procedure. To adjust a TL to a NFL, the incision may be shortened and dissection should only proceed medial to the great vessels. The hyoid, strap muscles, and hypopharyngeal mucosa all should be preserved. In our experience, the NFL may produce more reliable phonation with a tracheoesophageal puncture or electrolarynx as opposed to alternative laryngeal diversion procedures. However, the strongest argument against

performing a NFL is its inability to be reversed. Neither a TL nor a NFL are considered laryngeal diversion procedures.

The main alternative to a laryngectomy is a diversion procedure, either a LTS or TED. Both of these procedures have the potential to be reversed, have shorter operative times, and have been shown to have lower leak rates compared to a TL [8]. When performing a LTS, a tracheostoma is created in a similar fashion to a TL, but the larynx is left in situ. Instead, the first couple of rings below the cricoid are closed to create a blind pouch (Fig. 28.1) [9]. As with a TL or NFL, there exists the risk of wound breakdown and salivary fistula. This procedure also has the added risk of injury to the recurrent laryngeal nerves (RLN), which is something that is inconsequential if there is no possibility of reversal in the future.

A variation of the laryngotracheal separation is TED. Again, like all previously described procedures, a tracheostoma is created. However, with this modification, instead of creating a blind pouch, the most proximal tracheal rings are sutured end-to-side with the cervical esophagus (Fig. 28.2). The decision between performing a LTS with or without a diversion is largely based on surgeon preference and experience. However, if the patient presents with a previous high tracheotomy, tracheoesophageal diversion will not be a technically feasible option due to the short proximal tracheal segment. Some surgeons also argue that TED should be the preferred method, as it avoids subglottic pooling of secretions and food. A TED also provides a longer proximal tracheal segment and avoids resection of any tracheal rings, making an easier airway reconstitution in the rare event that a reversal is warranted. Creating a blind pouch will collect laryngeal secretions and presumably food and liquids until the patient lies supine. There is also a theoretical higher risk of wound breakdown during healing, although this also has not been demonstrated in any published studies.

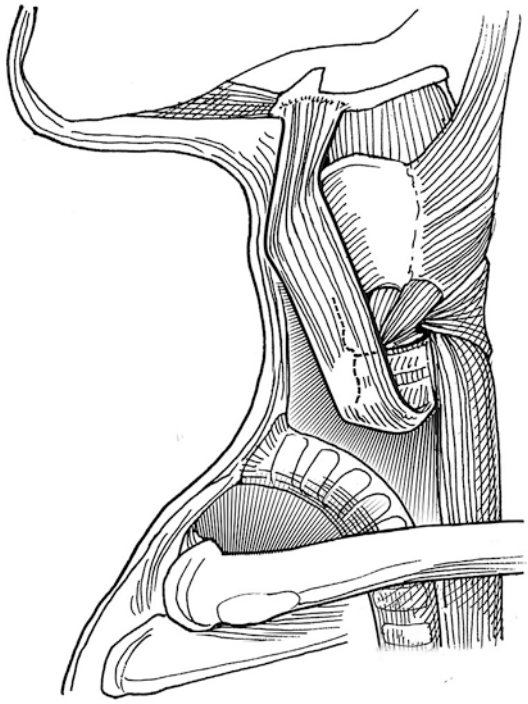

Fig. 28.1 Laryngotracheal separation procedure with creation of a blind pouch (LTS or Lindeman type II procedure). (From Pletcher and Eisele [9] with permission)

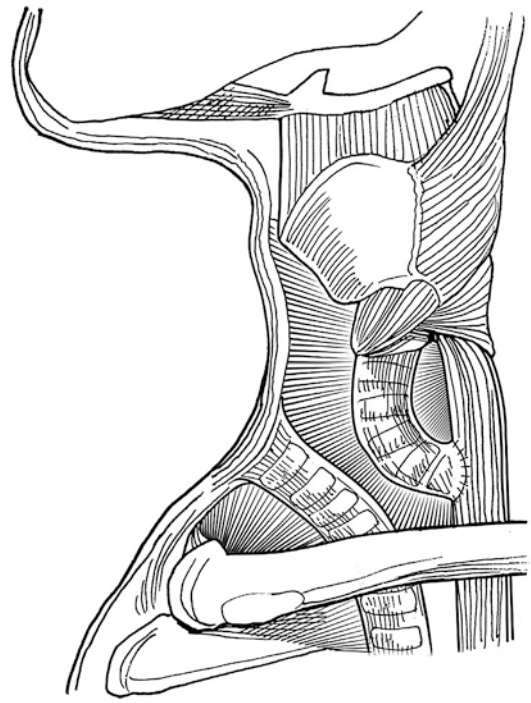

Fig. 28.2 Tracheoesophageal diversion procedure (TED or Lindeman type I procedure). (From Pletcher and Eisele [9] with permission)

Although a laryngeal diversion may be a life-saving surgery for certain patients, the morbidity associated with it is significant as this surgery will leave the patient aphonic. Various means of speech may be available including tracheoesophageal puncture or electrolarynx; however, results are highly variable [10]. Any potential patient should understand that lifelong inability to speak is a significant risk. For this reason, these procedures are often only performed on patients who have already lost their ability to speak.

Although not commonly performed, another alternative treatment for intractable aspiration is performing a tracheotomy followed by laryngeal obliteration. The laryngeal obliteration can be performed using any technique to cause complete stenosis of the subglottis, glottis, or supraglottis. This may be difficult to achieve if there are copious oral secretions with continual aspiration. Laryngeal obliteration would also preclude phonation or reversibility.

Procedures

Laryngotracheal Separation with and Without Esophageal Diversion

If the patient does not have a tracheotomy, they should be orotracheally intubated with a 5.5 or 6.0 endotracheal tube. The surgeon should consider starting with a rigid or flexible esophagoscopy. Although a modified barium swallow and esophagram should have been performed prior to the surgery, more information may be gained from direct inspection and palpation of tissues. The preoperative esophagram should show any strictures, and, if present, they should be dilated at the time of surgery. Although several methods are available, the authors of this chapter prefer Maloney dilators in the majority of cases.

Next a direct laryngoscopy is performed. A preoperative flexible videolaryngoscopy should have been completed prior to the procedure, and intraoperative evaluation can add additional information. This is especially important in patients who have been previously treated with radiation therapy. During the direct laryngoscopy, it is important to palpate the arytenoids to assess their mobility.

A curvilinear incision is marked out at the level of the second tracheal ring or two fingerbreadths above the sternal notch. The planned incision is extended bilaterally to the sternocleidomastoid muscles. If a tracheotomy is present the incision should include it, with an elliptical excision of the scar. A stoma site is marked out at the midline with a half-circle extending inferiorly from the marked incision with a height of approximately 1 cm.

The patient is then prepped and draped with exposure of the mentum to midsternum. It is the authors' preference to use a clear, drape with coverage of the mandible superiorly. This allows access to the mouth later in the case if needed and makes access to the oral endotracheal tube easier by the anesthesiologist. The incision is made and subplatysmal flaps are raised superiorly to 1 cm above the hyoid and inferiorly to the sternal notch. Strap muscles are then separated at the midline raphe. The thyroid isthmus is divided and ligated and reflected laterally. Care should be taken to avoid injury to the RLN during this maneuver.

The trachea is then mobilized by dissecting through the pretracheal fascia at approximately the level of the second tracheal ring. The dissection will need to be done at a more inferior ring if a prior tracheotomy exists. The plane between the trachea and pretracheal fascia is relatively avascular and blunt dissection can proceed inferiorly. This may begin with a clamp and then switch to an index finger in order to reach the carina. Care must be taken to stay in this plane in order to avoid inadvertent damage to the great vessels. Dissection can proceed 270 degrees around the trachea without risking injury to its blood supply. By keeping the dissection in the correct plane, injury to the RLNs will also be avoided. There is no indication for a suprahyoid or infrahyoid release during this procedure, and conducting either procedure will have unnecessary adverse effects on the patient's swallow.

At this point the anesthesiologist is instructed to remove the oral endotracheal tube (if a prior tracheotomy is not present). A tracheal incision is then performed, typically between the second and third tracheal rings for a LTS or fourth and fifth

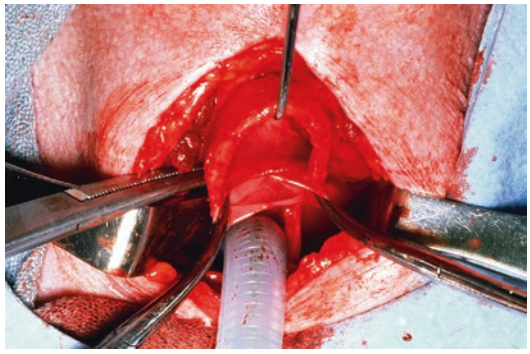

Fig. 28.3 Division of trachea for laryngotracheal separation. Note that the dissection is taken immediately against the cartilage to prevent injury to the recurrent laryngeal nerves. (Photo courtesy of Paul W. Flint, MD, Department of Otolaryngology–Head & Neck Surgery, Oregon Health and Science University, Portland, Oregon)

when performing a TED (Fig. 28.3). If a tracheotomy is present, the tracheal incision should include it with an excision of the first inferior tracheal ring to the stoma. Beveling this incision superiorly is unnecessary and should be avoided. Instead, an incision should be made parallel to the tracheal ring. A sterile 6.0 armored endotracheal tube and sterile circuit are then inserted into the distal end of the trachea. Hook retractors or a suture can be used to loosely secure the tube into place.

Completion with Diversion Procedure (Tracheoesophageal Diversion) Approximately 3 cm of esophagus is separated from the posterior tracheal wall of the distal segment. This is performed by dividing along the common party wall using a 15 blade. Insertion of an esophageal bouge is optional and based on surgeon preference. A 1½–2 cm vertical incision is made along the anterior wall of the esophagus. The location of this incision should be placed at the location to which the proximal tracheal stump will extend, without placing any tension on it. The proximal tracheal segment is then sutured to the esophagostomy in an end-to side fashion. This should be performed with interrupted 3-0 Vicryl® sutures (Ethicon, Bridgewater, NJ).

Completion Without Diversion (Laryngotracheal Separation) The submucosa, including and superior to the second tracheal ring, should be preserved. If the original tracheal incision was made between the third and fourth ring, then another incision should be made just superior to the third ring and that ring excised. The second tracheal ring is incised vertically at the midline, and using a cottle or periosteal elevator, the submucosa is elevated in a subperichondral plane. The two pieces of incised tracheal ring are discarded. Approximately 2 cm of submucosa should be available for closure at this point (Fig. 28.4). The submucosa should be inverted and sutured with 4-0 Vicryl® using a Connell or Cushing closure (Fig. 28.5) and then oversewn with 3-0

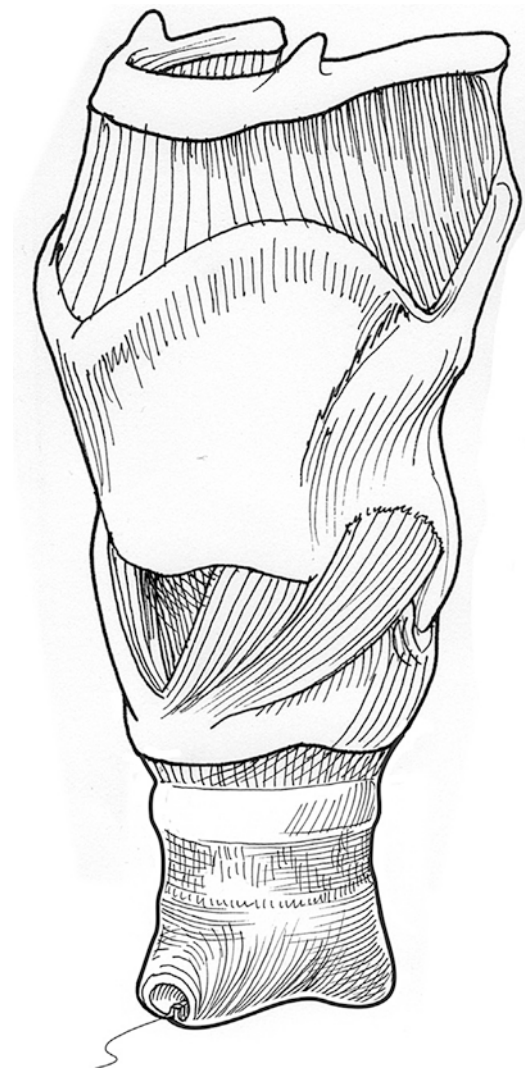

Fig. 28.4 Preparation of the proximal trachea. This is performed with a length of tracheal mucosa spanning 2 rings. (From Pletcher and Eisele [9] with permission)

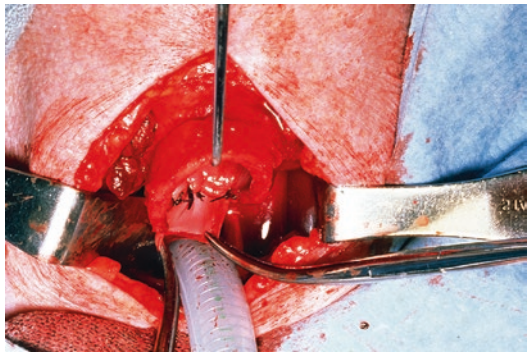

Fig. 28.5 Proximal tracheal mucosa is closed within the trachea with judicious dissection to allow reconstruction in the future. (Photo courtesy of Paul W. Flint, MD, Department of Otolaryngology–Head & Neck Surgery, Oregon Health and Science University, Portland, Oregon)

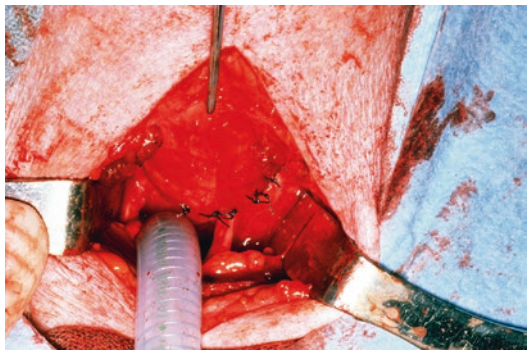

Fig. 28.6 The proximal tracheal mucosa is sewn to the distal posterior tracheal wall. (Photo courtesy of Paul W. Flint, MD, Department of Otolaryngology–Head & Neck Surgery, Oregon Health and Science University, Portland, Oregon)

Vicryl® . The blind pouch may either be left in place or sutured to the posterior wall of the distal tracheal segment (Fig. 28.6). A third layer of closure may also be included using the distal cut end of the sternohyoid or sternothyroid muscles.

Closure The closure for both procedures is the same. A 10Fr Jackson-Pratt drain is placed on each side and later set to bulb suction. The strap muscles should be closed at the midline superior to the stoma. The platysma is closed with 3-0 Vicryl® followed by skin closure. The tracheal stoma is finalized with half mattress sutures to the inferior and superior skin flap (Fig. 28.7). A laryngectomy tube is used until healing has completed. If the patient does not already have a feeding tube, a nasogastric feeding tube is placed prior to closure. The patient should receive nothing by mouth for 1 week if unirradiated or for 2 weeks in patients with prior neck radiation. A swallow study with gastrografin will be performed prior to commencing an oral diet.

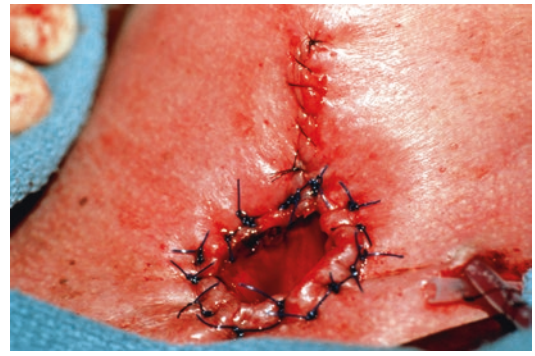

Fig. 28.7 Tracheostoma fashioned for either separation or diversion procedure. (Photo courtesy of Paul W. Flint, MD, Department of Otolaryngology–Head & Neck Surgery, Oregon Health and Science University, Portland, Oregon)

Of note, a voice prosthesis may be placed at a later date into either the LTS or TED procedures. If the geometry is suitable, following TED procedure, the voice prosthesis may be placed from the posterior wall of the tracheostoma into the end of the proximal trachea. This offers the possibility of glottic instead of tracheoesophageal voicing in some patients (Fig. 28.8).

Modifications There are several variations of the above-mentioned procedures. Described below are two adjunct procedures that may be used independently or in conjunction with the LTS or TED. Both eliminate the possibility of reversing the procedure at a later date. We have not found these procedures to be successful when performed alone and typically find them unnecessary when performing a LTS or TED.

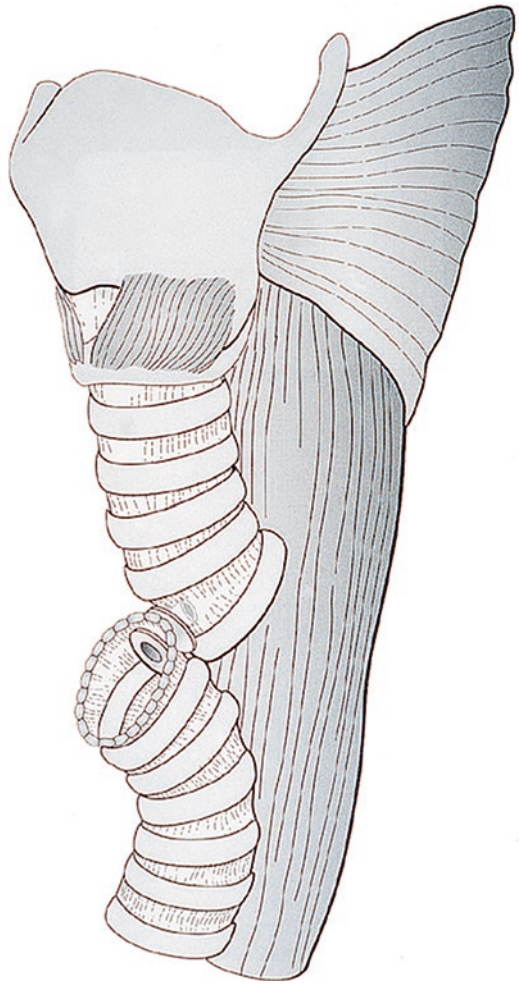

Fig. 28.8 Voice prosthesis may be placed from tracheostoma into proximal trachea to allow glottic voicing if geometry is suitable. (Image courtesy of Elsevier, with permission)

Supraglottic Closure

The procedure, also called the epiglottic flap or "epiglottic sew down," may be performed either through a laryngofissure, lateral pharyngotomy, or endoscopically. It proceeds with denuding the mucosa of the laryngeal surface of the epiglottis, interarytenoid space, arytenoids, and aryepiglottic folds. Following this, the arytenoids are sutured together. The epiglottis is then folded posteriorly and sutured to the aryepiglottic folds and the arytenoids. To decrease tension on the suture line, the hyoepiglottic and thyroepiglottic ligaments may also be transected [11]. Botulinum toxin may also be injected into the thyroarytenoids to decrease tension [12].

Glottic Closure

Exposure may be obtained either endoscopically or via laryngofissure. The mucosa of the true cords, false cords, and posterior commissure are denuded. Sutures with full thickness bites are placed through the true cords and tied before proceeding with closure of the false cords. Five interrupted Vicryl® or non-absorbable sutures should be sufficient for each layer. Finally, the posterior commissure should be sutured together. When performed alone, the success rate of this procedure is much higher than that of the supraglottic closure [13].

Complications

The most common complication of any laryngeal diversion procedure is a salivary leak secondary to breakdown of the proximal tracheal closure or its anastomosis to the esophagus [14]. Like those occurring with a TL or NFL, the salivary leak often leads to a tracheocutaneous fistula, which may necessitate packing or revision surgery. More significant concerns include inferior extension for mediastinitis or erosion of the great vessels causing a tracheoinnominate fistula. Both of these more significant complications are less frequently seen than in those patients undergoing TL, in part due to the absence of prior radiation or persistent cancer. Studies looking at patients who have undergone laryngeal diversion procedures, excluding laryngectomies, have shown leak rates ranging from 0% to 38% [15–18]. One factor shown to increase the risk of a leak in these patients was a prior tracheotomy [17, 19]. Injury to the recurrent laryngeal nerve (RLN) is another potential complication in laryngeal diversion

procedures. This risk is thought to be higher for a TED compared to a LTS. However, if there is no intent on reversing the procedure, injury to the RLN is inconsequential.

Conclusions

Intractable aspiration in the adult population may be surgically treated with a near-field laryngectomy or a laryngeal diversion procedure. These procedures should only be considered after failure of conservative management. Although not frequently performed, laryngotracheal separation and tracheoesophageal diversion options that allow possible reversal should be considered more frequently.

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Deep Brain and Vagal Nerve Stimulation

29

Sungjin A. Song, Pawan Mathew,
Farid Hamzei-Sichani, and Phillip C. Song

Introduction

Neurostimulation is the deliberate excitation modulation (excitation or inhibition) of neural activity to elicit a downstream neurological change for therapeutic or diagnostic purposes. The concept of neurostimulation has been present for centuries and has been in clinical practice in the medical field for over 100 years in the form of electroconvulsive therapy, pacemakers, electromyography, nerve conduction studies, and cochlear implants. In the late 1990s, both the vagal nerve stimulator (VNS) for intractable epilepsy and the deep brain stimulator (DBS) for the control of Parkinsonian tremor received the US Food and Drug Administration (FDA) approval. The indications for use in these devices have expanded considerably since then, and the increasing frequency of implantable stimulators to treat neurologic diseases had revealed both beneficial and negative effects on laryngeal function. We highlight two neurostimulators in this chapter, vagal nerve stimulators and deep brain stimulators. The critical role of the vagus nerve on laryngeal function and the expanding role of VNS in the treatment of seizures to headaches and recently to inflammatory diseases make understanding the impact of this device on laryngeal function important. DBS has been used for central nervous system (CNS) disease, and potential effects are highly dependent on the indication, target, and CNS placement. DBS for treatment of essential tremor has demonstrated to consistently improve vocal tremor. However, current targets for DBS with PD and spasmodic dysphonia (SD) do not seem to improve voice and speech consistently. The lack of understanding of the role of various neuromodulation targets and how to engage them in the central and peripheral nervous system reflects the variable effect on laryngeal function seen after DBS and VNS implantation.

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Vagal Nerve Stimulation

The vagus nerve (cranial nerve X) has the most extensive course and distribution of all the cranial nerves and originates in four distinct nuclei in the medulla oblongata. These nuclei exert autonomic function on the viscera, gastrointestinal tract, and heart (dorsal nucleus, nucleus tractus solitarius);

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motor neurons to the CN IX, X, and XI (nucleus ambiguus); and sensory function via the trigeminal nerve (spinal nucleus of trigeminal nerve). These brainstem functions coordinate swallowing and phonation; digestive, cardiac, and pulmonary function; taste and cutaneous sensation; and visceral sensitivity from the neck, chest, abdomen, carotid, and aortic bodies. It was recognized in the early 1930s that peripheral stimulation of the vagus nerve can cause measurable changes of cortical function on electroencephalogram (EEG), evoke responses in regions of the thalamus, and inhibit certain neural processes [1]. In 1985, VNS was found to have a role in terminating seizures in canines [2]. In 1997, VNS was approved in the United States for the treatment of medically refractory partial-onset seizures in adults and adolescents. The efficacy of VNS on depression followed after clinical observations of improvement of depression in implanted patients. This expanded the clinical use of VNS from drug-resistant epilepsy to treatment-resistant major depressive disorder, migraines, and cluster headaches [3, 4]. More recently, VNS was shown to elicit electrophysiological changes in the hippocampus and amygdala responsible for memory and learning, stimulation of neurogenesis, and appetite suppression for morbid obesity.

Mechanism of Action of Vagal Nerve Stimulation

The mechanism of action of VNS is not completely known. Recent research studies have proposed mechanisms beyond simple excitation or inhibition of neural activity in the form of complex interactions with neuronal oscillations across different brain networks. Studies have looked at the specific pathways affected by VNS. Ramsay et al. [5] demonstrated that the activation of the reticular system by stimulation of the vagus nerve may increase the threshold for initiation and propagation of seizures. Animal and human studies have also implicated the central autonomic network, the limbic system, and the diffuse noradrenergic projection system as possible areas of influence of the antiseizure effects of VNS [6]. In addition, several groups have looked at the effect of VNS on electroencephalogram (EEG). Animal experiments have demonstrated that repetitive vagal stimulation can cause synchronization or desynchronization of the EEG, depending on stimulus frequency and current strength [7–9]. High-intensity, high-frequency (>70 Hz) vagal stimulation produces desynchronization of the cortical EEG in cats, but lower-intensity stimulation at the same rate causes synchronization, presumably because only larger myelinated fibers are recruited. EEG desynchronization is also caused by high-intensity, slower stimulation in the range of 20–50 Hz. Furthermore, slower stimulation (1–17 Hz) also causes synchronization [10]. These studies suggest that careful control of the intensity and frequency of vagal stimulation is necessary to disrupt seizures in animals by desynchronizing interconnected regions.

The mechanism and effects of VNS have also been studied in humans using positron emission topography (PET) scanning. However, the results of such studies have been inconsistent. In one study, increased flow in the ipsilateral anterior thalamus and cingulate cortex was reported [11]; in another, increased flow was shown in the contralateral thalamus and temporal cortex and ipsilateral putamen and cerebellum [12]. These studies did, however, have some limitations. In the study by Garnett et al. [11], two of the five patients had an electrographic seizure during image acquisition, and it is not known if the stimulator was activating the same fiber subset in all patients. Furthermore, VNS may alter cerebral blood flow in ways that are different from changes in local neuronal activation. In addition, it can be challenging to localize anatomical structures (e.g., putamen, insular cortex) with PET technology.

Other studies have investigated the biological mechanism by which VNS exerts its effects. VNS has been shown to result in a long-lasting (greater than 80 min) increase in the release of noradrenaline in the basolateral amygdala, through stimulation of the locus coeruleus or through stimulation of the nucleus of the solitary tract [13]. It can be argued, however, that much of the evidence linking noradrenaline to VNS is circumstantial as

noradrenaline is certainly involved in many brain functions. VNS has also been shown to increase levels of free GABA, the major inhibitory neurotransmitter in the central nervous system, in the cerebrospinal fluid [14]. In epileptic patients receiving VNS for a year, GABA A receptor density in the hippocampus was shown to significantly increase in the responsive patients compared to controls and nonresponders [15]. The authors conclude that GABA A receptor density may contribute to the therapeutic effects of VNS via CNS inhibition.

Subsequent studies have also examined if VNS can exert its effects through an immunemodulatory mechanism. Afferent vagal signals can activate the cholinergic anti-inflammatory pathway upon inflammation [16]. The downstream efferent vagal neurons then inhibit the release of pro-inflammatory cytokines and in this way reduce inflammation. Recent studies have suggested that seizures can be a consequence of inflammation [17]. Several studies have demonstrated that VNS can in fact affect the anti-inflammatory markers. The study by Hosoi et al. [18] demonstrated that stimulation of the left vagus nerve at 10 Hz in rats induced an increase in the expression of IL-1beta mRNA in the hypothalamus and hippocampus as well as an increase in the expression of CRF mRNA in the hypothalamus and an increase in plasma levels of ACTH and corticosterone. Although the mechanism behind VNS remains largely unknown, these studies together suggest that the mechanism is multifaceted and involves various interacting pathways.

VNS and Voice

VNS is generally associated with detrimental effects on laryngeal function. The device is surgically implanted under the skin of the chest and a wire is threaded under the skin to the left vagus nerve. The right vagus nerve is not used as it is more associated with cardiac stimulation [19]. The most commonly reported adverse event after vagal nerve stimulator activation was voice changes (33–66%), coughing (33–45%), and less frequently shortness of breath (25–33%) [20, 21]. In a retrospective study of four VNS patients, Zalvan et al. [22] found that all patients had vocal fold paresis postimplantation. VNS-implanted patients have been found to have a significant increase (worsening) in mean voice handicap index (VHI-10) score, for example, from a score of 2.1 increase in the control group and 27.5 increase in the VNS-implanted group. Hoarseness in VNS-implanted patients is thought to be related to active stimulation, surgical manipulation needed for dissection near the vagus nerve, a tight fitting electrode causing ischemia, or excessive stimulation resulting in nerve cell death [20, 23]. Vocal cord paralysis occurs almost twice as often when stimulator lead coil diameters are 2 mm compared to 3 mm across all age groups. Interestingly, the voice deterioration for most patients is not present immediately after implantation or device activation but occurred after an event such as battery replacement and device reprogramming well after initial implantation [20]. Two exceptional cases of self-inflicted traction injuries by rotating the pulse generator in the subclavian pocket have been reported [24]. As mentioned above, vagal nerve stimulators are almost always placed on the left vagus nerve because of an increase in cardiac slowing seen with the right VNS in the canine model. This occurs because the right vagus nerve innervates the sinoatrial node. Accordingly, the majority of laryngeal manifestations will be seen in the left hemilarynx.

After vagal nerve stimulator implantation, patients often have objective and subjective abnormalities of their vocal folds. VNS patients have been reported to have asymmetrical true vocal fold movement, decreased left vocal fold mobility, and shortened length compared to opposite side on videolaryngoscopy [20]. Vocal fold palsy has been reported to occur in 1–5.6% of cases [19, 25]. Charous et al. [26] noted that in all patients examined, upon stimulation, the vocal fold was fixed in the paramedian position regardless of breathing or vocalization, with normal vocal fold movement returning after stimulation ended. Ghanem et al. [23] observed vocal fold immobility and temporary supraglottic spasm

with vocal fold paresis with device activation in the symptomatic patients. Felisati et al. [27] described that, even with the VNS not stimulating, 78.6% of patients demonstrated a left vocal fold palsy at rest, but most of these patients compensated with hyperadduction of the contralateral vocal fold. Ardesch et al. [28] reported that the vocal fold electromyographic (EMG) saturation levels were reached between 0.75 and 1.0 mA but found that the ipsilateral vocal fold adductory spasm did not correlate with hoarseness symptoms. Although voice change is the most common symptom related to VNS, the incidence of patients who complain of voice impairment after VNS implantation seems to be much lower than those with actual laryngeal manifestations.

Unsurprisingly, higher levels of VNS stimulation correspond with increased laryngeal dysfunction. Handforth et al. [21] found in 194 patients studied with high (30 Hz)- versus low-stimulation (1 Hz) VNS that high-stimulation treatment had a statistically increased incidence of voice alteration (66% versus 30%) and dyspnea (25% versus 11%). Similar frequency-dependent changes have been reported with increased laryngeal dysfunction with higher stimulation. Lundy et al. observed consistent changes in the larynx and increasing stimulation with vocal fold immobility at 20 Hz and 40 Hz, impaired vocal fold mobility and torsion of the larynx at 59 Hz, and increased tetanic contraction of the entire left hemilarynx at 83 Hz. Even with the high incidence of laryngeal adverse effects from VNS, patients who underwent VNS implantation for epilepsy universally reported that they would have the device implanted again knowing the vocal side effects they would have [26]. The laryngeal dysfunction seen with VNS can negatively impact the voice, but patients are willing to cope with the voice alterations to have better seizure control. Recently FDA-approved indications for VNS now include cluster headaches and migraines, and whether patients are willing to accept the laryngeal dysfunction for treating these diseases remains to be seen.

Patients undergoing vagal nerve stimulator placement can benefit from perioperative evaluation of laryngeal function. Shaw et al. [29] found that all patients with abnormal laryngeal EMG findings preimplantation developed prolonged left vocal fold paresis 3 months after implantation. An abnormal preoperative laryngeal EMG was shown to be a statistically significant predictor of long-term vocal fold dysfunction. Preoperative visualization of the larynx to assess for right-sided vocal cord immobility/paralysis or obstructing endolaryngeal lesions may be a prudent recommendation as vagal nerve implantation could theoretically result in airway complications. Professional voice users and elite vocal performers should be well counseled on the risks and possible long-term laryngeal dysfunction associated with VNS. Reasonable recommendations include a postimplantation examination and subsequent reevaluation with any changes such as device reprogramming or battery replacement. Perioperative laryngeal evaluation and close communication with the neurosurgeon can help with calibrating the programming and stimulation levels to optimize seizure control while minimizing laryngeal dysfunction.

VNS and Swallowing

Vocal fold paresis and paralysis associated with VNS have been well reported in the literature; however, the associated risk for aspiration and dysphagia is uncertain. Aspiration can occur with seizures without VNS, and it may be difficult to differentiate the contribution of VNS to the underlying disease effect. Aspiration has been reported with VNS [22, 30]. Lundgren et al. [30] reported transient swallowing difficulties in five out of seven children and two children with increased aspiration scores when the stimulator was set to continuous mode. Contradictory findings were reported by Schallert et al. [31], who found that preoperative laryngeal penetration was present in three of eight children who were receiving intermittent left VNS, but no development of aspiration in any of the children implanted. In both studies, the most severely mentally disabled children were at highest risk of developing swallowing problems associated with the VNS.

Deep Brain Stimulation

Physicians have understood that selective ablation of key regions of the brain can be used therapeutically to control seizures since the 1940s. Wilder Penfield and other pioneering neurosurgeons developed techniques to electrically stimulate different areas of the cerebral cortex using stereotactic localization. Gradually, a functional brain map was created using these techniques, and neurosurgeons expanded these procedures for other indications including psychiatric disorders, movement disorders, and chronic pain. Moreover, it was noted that the pacing of electrical stimulation could achieve different clinical effects; higher-frequency stimulation could suppress certain motor areas, whereas lower-frequency stimulation could exacerbate motor symptoms in patients with movement disorders. The feasibility of electrical stimulation to elicit therapeutic changes for movement disorders was shown in the 1960s; however, it was not until the widespread availability of the cardiac pacemaker that a commercially implantable pacer could be repurposed for neurological conditions. DBS was coined by Medtronic (Dublin, Ireland) in the 1970s to describe neurostimulation for the treatment of chronic pain. For movement disorders like PD and tremor, the thalamus and subthalamic nucleus (STN) became the region of focus. Thalamic stimulation for the clinical goal of tremor reduction was first reported in 1991 by Benabid et al. [32]. Many reports since have described the successful use of DBS for movement disorders, including PD, essential tremor, and dystonias.

Functional neurosurgeons have continued to refine and develop the clinical efficacy of neurostimulation for a variety of movement disorders. Location, stimulation frequency, and surgical approaches can have potential impact on laryngeal function. PD and essential tremor were among the first diseases to be studied using DBS. In 1999 Taha et al. [33] showed the efficacy of bilateral thalamic DBS for head, voice, and bilateral limb tremor in patients with PD (six patients), essential tremor (15 patients), and multiple sclerosis (two patients). Majority of the patients with severe head tremor (90%) and voice tremor (86%) showed improvement with a mean follow-up of 10 months. Over the past decade, research has intensified in the study of STN electrostimulation for the management of PD. D'Alatri et al. [34] studied the effect of bilateral STN stimulation and medication on PD and dysarthria. They found that STN improved motor function and voice tremor noting a "major stability to glottal vibration." However, similar to other reports, they noted that STN had a greater effect on the motor dysfunction of extremities than on the voice dysfunction. In 2010, Hammer et al. [35] studied the aerodynamic measures of speech and respiration in PD patients after STN DBS. Their findings showed that high-frequency STN DBS often caused "respiratory overdrive and excessive vocal fold closure," which further helps refine how we use DBS in the management of this disease.

For essential tremor, up to 25% of patients who have the disease also have a voice tremor. As essential tremor is the most common form of movement disorder, this affects the quality of life of many individuals. Kundu et al. [36] found that DBS of the ventralis intermedius nucleus (Vim) of the thalamus is effective at treating not only the motor component but also dramatically decreased the amplitude of voice tremor in the patient group.

Multiple groups have published reports on the efficacy of DBS for various types of dystonia. They found that DBS was effective in focal hand dystonia, oromandibular dystonia, and blepharospasm. DBS use in dystonia has primarily been used in patients who do not achieve adequate benefit with medical treatment. Two important DBS targets are the globus pallidus internus and the thalamus. At this time, the consensus is that patients with primary (familial or sporadic) generalized or segmented dystonia and patients with complex cervical dystonia are the best candidates for pallidal DBS [37].

More recently, studies have demonstrated the efficacy of DBS in the management of chronic pain and psychiatric illnesses including obsessive-compulsive disorder and depression. Denys et al. [38] showed that bilateral DBS of the

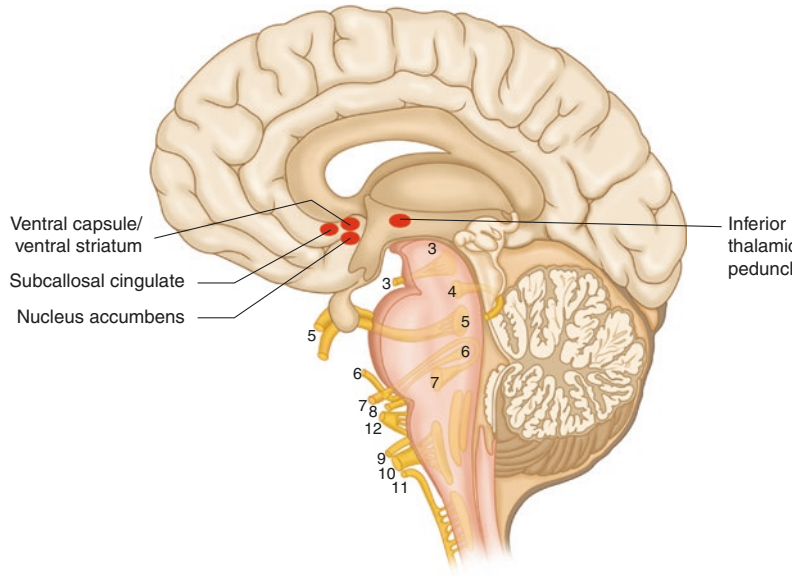

Fig. 29.1 Common anatomical targets for treatment-resistant OCD and depression include the nucleus accumbens, ventral capsule/ventral striatum, subcallosal cingulate, and inferior thalamic peduncle. The numbers indicate the cranial nerves

nucleus accumbens in obsessive-compulsive disorder (OCD) patients decreased their Yale-Brown Obsessive-Compulsive Scale and that depression and anxiety improved significantly. Other anatomical targets for treatment-resistant OCD and depression include the ventral capsule/ventral striatum, subcallosal cingulate, and inferior thalamic peduncle (Fig. 29.1).

DBS has become a treatment option for multiple neurological conditions. In 1997 FDA approval was granted for DBS for severe tremor and PD. In 2003, approval was granted in Europe and the United States for dystonia. DBS is now used routinely as a treatment option for patients with advanced PD, dystonias, and essential tremor [39]. In 2018, Medtronic was granted approval for marketing DBS for the treatment of epilepsy, with plans to expand use for depression and OCD.

Mechanism of Action

DBS has been used for many years for the treatment of several movement disorders, but despite widespread use, the exact mechanism of action remains unknown. Understanding the effects of DBS has presented a paradox to investigators as they attempt to understand how stimulation (traditionally thought to activate neurons) can result in similar therapeutic outcomes as ablation [40]. This has led to two strongly debated philosophies about DBS: DBS generates a functional ablation by suppressing or inhibiting the stimulated nucleus [40] or DBS results in activation of the stimulated nucleus that is transmitted throughout the network. Based on these philosophies, four general hypotheses have been developed to explain the mechanisms of DBS: depolarization blockade, synaptic inhibition, synaptic depression, and stimulation-induced modulation of pathological network activity. Overall, the therapeutic mechanisms that underlie DBS most likely represent a combination of several phenomena [41, 42]. McIntyre et al. [40] examined these general hypotheses and suggested that, although depolarization blockade and synaptic inhibition represent attractive hypotheses to explain the similarity between the therapeutic benefit of ablation and DBS for the treatment of movement disorders, their limitation is that they do not take into account the possible independent activation of the efferent axon of projection neurons as seen in other studies [43, 44]. The theory of synaptic depression is also an attractive explanation. In this theory, the neurons activated by the stimulus train are unable to sustain a high-frequency activation of efferent targets due to depletion of neu-

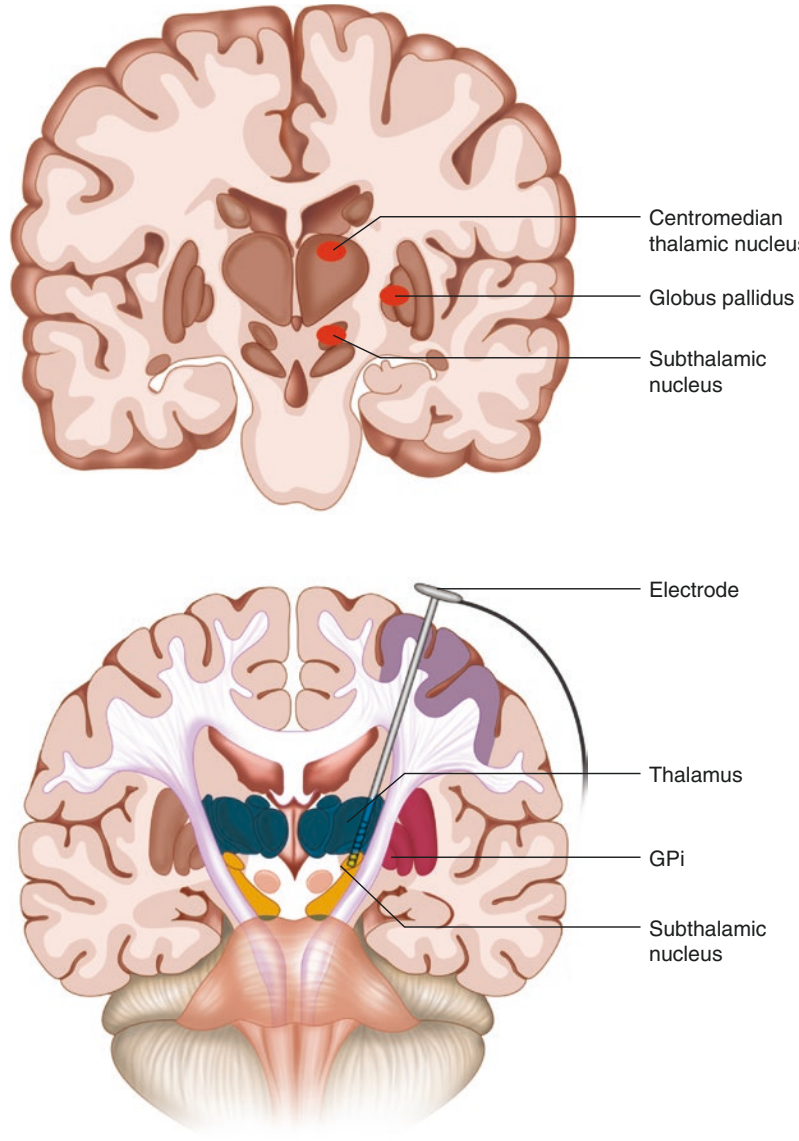

Fig. 29.2 Regions for deep brain stimulation implantation for movement disorders include the thalamus, globus pallidus, and subthalamic nucleus

rotransmitter. However, several in vivo experiments have demonstrated increases in neurotransmitter release in neuron firing consistent with activation [43, 45, 46]. Therefore, the review concludes that the only general hypothesis on the mechanisms of DBS that is consistent with all of the available data on the effects of DBS is stimulation-induced modulation of pathological network activity. For example, DBS activity in the STN, GPe (external segment of the globus pallidus), and GPi (internal segment of the globus pallidus, or globus pallidus internus) can lead to changes in their firing that can be therapeutic for patients suffering from PD (Fig. 29.2). Thus, while ablation and DBS result in similar therapeutic outcomes, it is likely that they achieve their results via different mechanisms.

Benabid et al. [41] also looked at how frequency of stimulation affects the function of certain structures such as the thalamus, basal ganglia, STN, and hypothalamus. They found that high-frequency stimulation (>50 Hz, 130–180 Hz) mimics the effect of ablative procedures and that low-frequency stimulation generally

results in an excitatory process. Other studies have used functional imaging experiments to better understand DBS. Perlmutter and Mink [47] showed that during DBS, there was an increase in metabolic activity and thus blood flow throughout the brain. Overall, DBS fMRI studies have been limited, but many have shown that STN DBS generates activation throughout the network, with activation of the globus pallidus and thalamus being common across most patients [48, 49]. PET studies from the Eidelberg laboratory have also shown that suppression of their PD-related spatial covariance patterns is seen not only in dopaminergic therapy and STN lesioning but also in STN DBS [50, 51]. These studies suggest that DBS not only has local effects around the electrode but rather affects many parts of the brain [52].

Deep Brain Stimulation and Voice

DBS in patients with essential vocal tremor can reduce symptoms by targeting various areas of the thalamus in patients with severe medication-resistant disease (Table 29.1). Voice tremor reduction with DBS of the Vim in essential tremor patients was first reported in 1998 with voice improvements seen in those with greater severity of disease [53]. Yoon et al. [54] found, in an essential vocal tremor patient implanted with bilateral DBS placement in the Vim, the tremor was completely controlled when both stimulators were active based on strobovideolaryngoscopy and objective voice analysis. Kundu et al. [36] showed in a retrospective study that 19 out of 20 patients with voice tremor had an average of 80% reduction in voice tremor after Vim DBS. Hagglund

Table 29.1 The effect of deep brain stimulation on laryngeal and swallowing functions

Site of placement	Physiological function of region	Common indication	Effect on laryngeal function	Effect on swallowing function
Subthalamic nucleus	Component of the basal ganglia, involved in scaling and focusing movement, motor learning	Parkinson disease (PD) Essential tremor	Improved vocal parameters in, PD but no benefit in overall speech perception May impair voice and deteriorate speech intelligibility	Variable response, but in general no worsening of swallowing in PD patients Improved self-reported swallowing symptoms
Ventralis intermedius nucleus (Vim)	Relay nucleus of the thalamus with input from the cerebellum and basal ganglia with output to various areas of the motor cortex	Essential tremor PD Multiple sclerosis (MS)	Improved essential vocal tremor Strained phonation under stimulation in MS patients	None reported
Caudal zona incerta (cZi)	One of the four major sectors of the cZi associated with motor functions	PD Essential tremor	Improved essential vocal tremor Subgroup of severe PD had considerable voice tremor reduction	None reported
Ventral oralis anterior nucleus (Voa)	Relay nucleus of the thalamus with input from the cerebellum and basal ganglia with output to various areas of the motor cortex	MS Essential tremor	Case study showed improvement in spasmodic dysphonia vocal dysfunction with Vim and Voa stimulation	None reported
Globus pallidus internus (GPi)	Component of the basal ganglia involved in scaling and focusing movement, motor learning	PD Primary dystonia	As a group, no negative effect on speech and communication Individuals reported stimulation-induced stuttering and dysarthria	No change in swallowing or increase in aspiration or penetration

et al. [55] discovered that stimulating the caudal zona incerta (cZi) reduced voice tremor substantially in those with essential tremor without the adverse effects such as dysarthria, gait disturbances, and paresthesias. Studies suggest that bilateral DBS may reduce vocal tremor more than unilateral DBS but is also associated with more adverse effects [33, 53, 56, 57]. This observation is most likely due to the bilateral neural input necessary for laryngeal function and controlled voice production. Sydow et al. [58] reported no significant voice tremor reduction in unilateral and bilateral Vim DBS 6 years from implantation. A case report showed voice normalization in a patient with disabling Holmes' tremor after bilateral Vim stimulation [59].

Neuromodulation in SD does not show a clear benefit with divergent voice outcomes. A case study of a patient with ET and adductor SD revealed improvement in SD vocal dysfunction with unilateral Vim and ventral oralis anterior (Voa) nucleus stimulation [60]. Risch et al. [61] showed that GPi DBS for primary dystonia does not negatively affect speech and communication scores as a group, but there were individuals that developed stimulation-induced stuttering and dysarthria. Vidailhet et al. [62] reported no change in speech for patient with generalized dystonia following GPi DBS.

DBS of the STN in PD seems to improve some measurable vocal parameters but without observed benefit in overall speech perception. A promising early study by Gentil et al. [63] described that in PD patients who had bilateral STN DBS there was "longer duration of sustained vowel, shorter duration of sentences, more variable fundamental frequency in sentences" corresponding with better intonation and more natural-sounding speech. Small study of DBS in PD patients showed variable response with stimulation with improvement and impaired precision of the glottal and supraglottal articulation as well as phonatory function [64]. High-frequency STN DBS has been shown to result in "respiratory over-drive and excessive vocal fold closure," thus not mirroring the improvement with motor dysfunction [35]. Voice quality improvement, pitch variation, and range in PD patients who underwent STN DBS have been reported, whereas cZi DBS showed no beneficial effect [65]. Karlsson et al. [66] found that voice tremor generally showed a mild improvement in PD patients who underwent STN DBS but a variable effect on those with cZi DBS. In a subgroup of cZi DBS patients with severe voice tremor ratings, voice tremor reduced considerably. In comparing STN versus cZi DBS, one study [67] found a statistically significant although small increase in mean voice intensity in the STN group and decrease in the cZi group.

Voice intensity can increase with STN DBS but does not correlate with improved speech intelligibility. Dromey et al. [68] investigated STN DBS on acoustic measures on voice and found that although vocal intensity variability increased the overall functional change was imperceptible. Often PD patients who undergo STN DBS suffer a more strained voice and spastic dysarthria and stimulation may worsen stuttering and breathiness. Tsuboi et al. [69] studied voice outcomes in 76 PD patients after STN DBS and found that improvements in voice tremor and increase in volume did not correspond with improved speech intelligibility and in fact deteriorated overall speech intelligibility in most patients. Klostermann et al. [70] found that STN DBS in PD patients leads to improvement in glottic tremor frequency but significantly worsened speech performance. Similar observations were seen by D'Alatri et al. [34] for patients who underwent bilateral STN DBS with improvements in glottal vibration and vocal tremor but with no significant gain in speech intelligibility. Of 32 PD patients who underwent subthalamic stimulation, 78% reported deterioration in speech intelligibility 1 year after implantation. STN DBS does not appear to be as effective in improving speech outcomes as it does in reducing motor symptoms in PD [71]. Tanaka et al. [72] reported that PD patients who underwent STN DBS revealed overall impairment of voice and significantly poorer voice handicap index (VHI) scores compared to those who received medical therapy alone. Putzer et al. [63, 73, 74] observed that in PD patients there was a relative deterioration of the glottal cycle, whereas for multiple sclerosis

patients, there was more hyperfunctional phonation changes. In PD patients, current DBS targets to improve voice and speech functions do not seem to have the consistent beneficial effects seen with motor symptoms.

Putzer et al. [75] found that phonation has a greater tendency to be strained under stimulation with Vim DBS in multiple sclerosis. Notably, there was impaired adduction of the vocal cords without stimulation. In general, there was a higher degree of perceptual hoarseness in the individuals.

Deep Brain Stimulation and Swallowing

The effect of electrical neuromodulation on deglutition is variable. The majority of studies show that there is no worsening of swallowing symptoms or objective swallowing studies in PD patients after various types of DBS. On videofluoroscopic exams, studies have shown improved pharyngeal transit time and pharyngeal composite score after STN DBS in PD. In the largest study evaluating the effect of DBS on swallowing function (n = 18), Lengerer et al. [76] found that even 2 years after implantation the pharyngeal phase transit time remains decreased when compared to preoperatively and that there was no worsening dysphagia secondary to DBS. Kitashima et al. [77] reported contradictory findings with no change in videofluoroscopy after DBS in PD patients compared to preoperatively. Olchik et al. [78] found that there were no significant changes in swallowing in the 10 PD patients after DBS. The PD patients implanted with cZi DBS also seem to have no negative effect on swallowing, aspiration, or decrease in swallowing-specific quality of life [79–81]. Only one study [82] has directly compared STN DBS to GPi DBS with regard to their effect on swallowing function and found that patients who underwent GPi DBS had no change in swallowing safety (i.e., no increased penetration or aspiration risk).

Although DBS may not provide significant changes in objective swallowing function, it does seem to improve self-reported swallowing symptoms after DBS in PD patients. Kulneff et al. [83] reported the effect of DBS on swallowing with fiberoptic endoscopic evaluation of swallowing and self-estimated evaluations and found significant subjective improvements but no objective changes on swallowing or aspiration assessment. Interestingly, Silbergleit et al. [84] also found a discrepancy between the perceived improvement in swallowing by advance PD patients who underwent DBS and the lack of objective improvement in swallowing function seen with videofluoroscopic swallowing studies. It is unclear why PD patients in these two studies perceived an improvement in swallowing, but better overall motor function, placebo effect, or emotional condition could contribute to this paradox. A recent prospective, crossover, double-blind study by Xie et al. [85] evaluated low-frequency stimulation of the STN compared to high-frequency DBS and found 79% reduced frequency of aspiration on videofluoroscopy swallowing studies and improved perception of swallowing when patients were on low-frequency stimulation. The lack of understanding of the role of various neuromodulation targets and how to engage them in the basal ganglia reflect the variable effect on deglutition seen after DBS implantation.

Conclusion

VNS and DBS elicit neuromodulation through electrical stimulation of the brainstem and midbrain via central and peripheral approaches, but the fundamental mechanism of action is unclear. The efficacy of these implants suggests a paradigm shift in our view of brain organization, blurring the traditional distinction between the peripheral and central nervous system. With growing commercial availability, implantable neurostimulators will continue to rapidly grow in scope and indications, and the prevalence of these devices in medicine will continue to expand. In 2017 and 2018, VNS received approvals for cluster headaches and migraines by the FDA. The development of neurostimulation is

based on clinical observation and therapeutic research, not basic science and in vitro experiments, and this trend continues as experience grows. Clinical trials for VNS are underway for neurogenesis, memory, autism, obesity, alcoholism, anxiety, and even autoimmune disorders. Deep brain stimulators now have indications for PD, tremor, dystonia, and epilepsy, with possible new indications for chronic pain and headaches.

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Laryngeal Reinnervation

30

Kenneth R. Feehs, Richard W. Thomas, and Michael I. Orestes

Introduction

Permanent recurrent laryngeal nerve (RLN) injury is an uncommon but well-documented complication of anterior neck and thyroid surgery and anterior neck trauma. Incidence of permanent RLN injury in benign thyroid surgery ranges from 1.1% to 2.3% [1–3], while reported incidence for patients undergoing thyroid surgery for malignancy is considerably higher at 1.8%–5.3% [4, 5]. Optimal treatment for unilateral vocal fold paralysis following permanent RLN injury would ideally restore vocal fold movement, position, mass, and tension. Improved positioning of the paralyzed vocal fold can be achieved with static medialization procedures such as thyroplasty, arytenoid adduction, and injection laryngoplasty (IL), while laryngeal reinnervation (LR) allows for improved vocal fold mass, tension, and—in select cases—motion.

The concept of laryngeal reinnervation is over a century old with Horsley describing the first successful vocal fold reinnervation in 1909 [6]. Today, the term laryngeal reinnervation encompasses an array of surgical techniques that seek to restore neural connection to denervated portions of the larynx. These techniques include direct anastomosis or neurorrhaphy, nerve-muscle pedicle (NMP), direct implantation of a nerve into muscle, and muscle-nerve-muscle (MNM) transfer. These techniques may be utilized in isolation or in combination. Considerations regarding technique include unilateral vs. bilateral vocal fold paralysis (BVFP), preservation of the distal RLN and donor various nerves, treatment goals, life expectancy, and age at presentation.

Anatomy of the Recurrent Laryngeal Nerve

Knowledge of the anatomy of the recurrent laryngeal nerve is critical to understanding how to properly perform RLN reinnervation and is described more thoroughly by Orestes et al. [7]. While most otolaryngologists understand the extralaryngeal anatomy of the nerve, the intralaryngeal component is not as well known. The nerve becomes intralaryngeal as it passes under the cricopharyngeus, posterior to the cricothyroid joint (Fig. 30.1). This is also one of the most common areas to injure the nerve. In cases of injury, the distal nerve segment can be exposed by dividing the cricopharyngeus. The nerve typically becomes smaller in diameter at this point,

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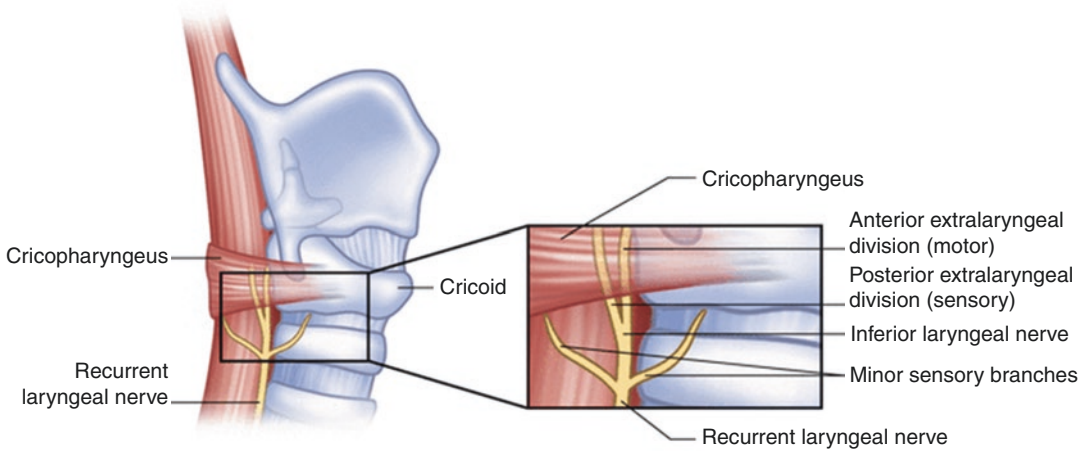

Fig. 30.1 Intralaryngeal transition of the recurrent laryngeal nerve. (From Orestes and Berke [7], with permission)

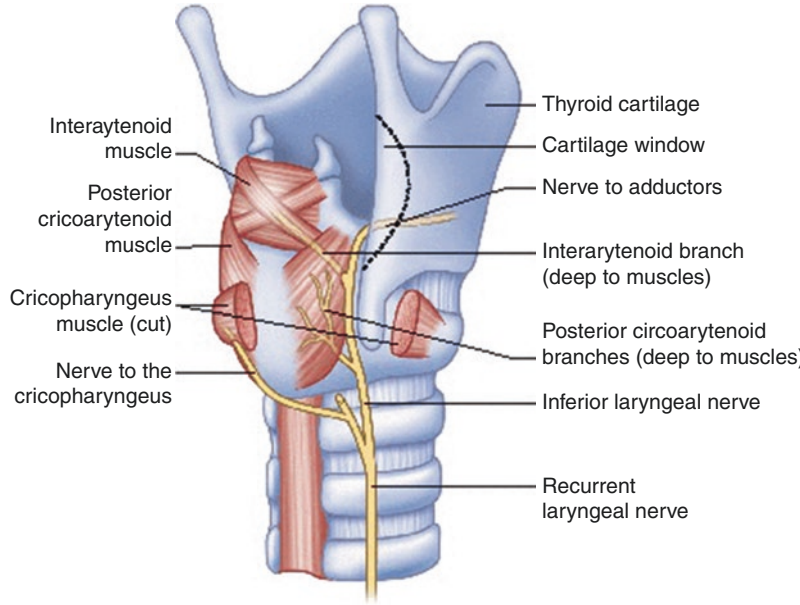

Fig. 30.2 Intralaryngeal anatomy of the abductor branch of the recurrent laryngeal nerve. (From Orestes and Berke [7], with permission)

as it gives a branch to the cricopharyngeus muscle itself.

Once passing through the cricopharyngeus, the nerve gives branches to the posterior cricoarytenoid (PCA) muscle; in humans, these nerves travel deep to the muscle (Fig. 30.2). A variable branch is given to the interarytenoid (IA), after which the nerve curves anteriorly innervating the lateral cricoarytenoid (LCA) and thyroarytenoid (TA) muscles (Fig. 30.3). It is possible to perform the neurorrhaphy along this distal segment, selectively reinnervating the distal musculature to prevent synkinesis. Unfortunately, it is difficult to isolate the nerve to the interarytenoid muscle, which would otherwise permit straightforward reinnervation of this muscle without creating inadvertent connections to the PCA. These techniques allow for selective reinnervation for treatment of spasmodic dysphonia and bilateral vocal cord paralysis described later in this chapter.

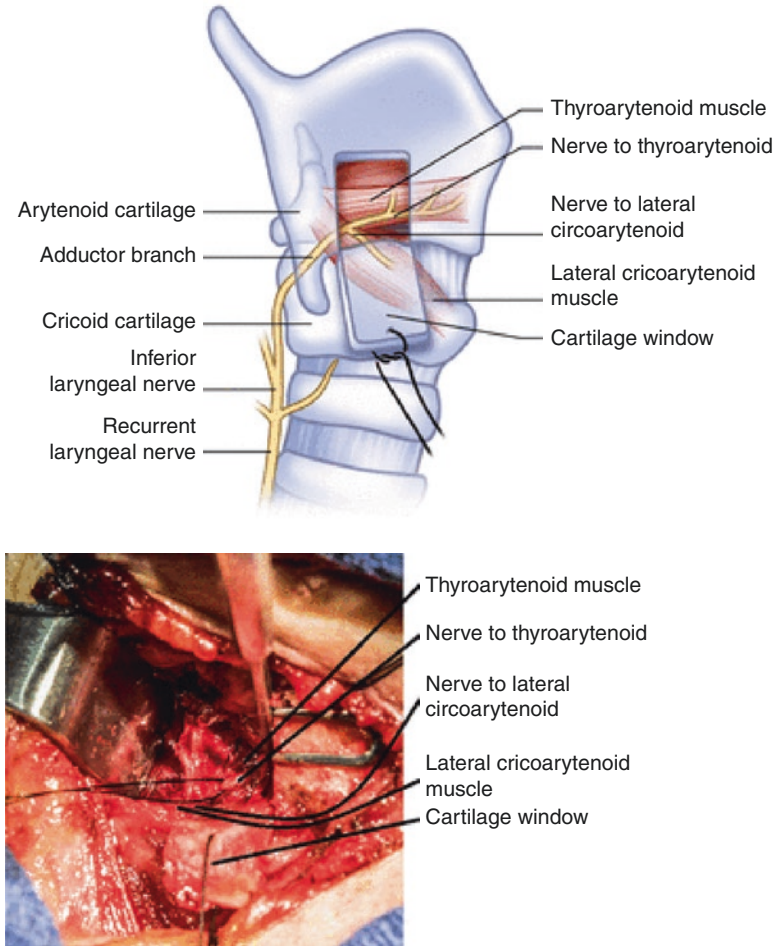

Fig. 30.3 Intralaryngeal anatomy of the adductor branch of the recurrent laryngeal nerve. (From Orestes and Berke [7], with permission)

Laryngeal Reinnervation: Unilateral Vocal Ford Paralysis

The goal of reinnervation in patients with unilateral vocal fold paralysis (UVFP) is improvement of the voice. This is primarily achieved by adductor reinnervation, which increases the bulk and tone of the hemilarynx, and in particular the thyroarytenoid muscle, which provides fine control of the phonating edge of the vocal fold. The majority of the reinnervation techniques for UVFP provide some degree of reinnervation to the posterior cricoarytenoid as well likely increasing the stability of the cricoarytenoid joint [8]. Reinnervation furthermore allows for appropriate medialization of the vocal fold and results in the potential for near-normal vocalization. Optimal timing of reinnervation is controversial; however, it is typically delayed until spontaneous recovery is deemed unlikely.

Direct Neurorrhaphy

While Horsley and several others [9, 10] have described successful reinnervation and recovery of laryngeal function by primary neurorrhaphy of the RLN, reinnervation of the RLN at the nerve trunk has not gained wide acceptance due to laryngeal synkinesis. As the RLN trunk contains both adductor and abductor fibers, primary RLN anastomosis produces nonselective innervation—termed laryngeal synkinesis—of the laryngeal musculature [11, 12]. If significant

synkinesis does occur, the TA can protrude into the airway on inspiration, causing significant obstruction due to inappropriate innervation by abductor axons [13]. Although controversial, primary RLN reanastomosis is predominately utilized when the RLN is transected, recognized, and repaired during the same procedure [14]. For delayed laryngeal reinnervation, the primary method of direct neurorrhaphy utilized today is an end-to-end anastomosis of the ansa cervicalis nerve to the distal stump of the extralaryngeal RLN or anterior motor branch of the RLN (ansa-RLN).

The ansa cervicalis presents a compelling compilation of traits that makes it the most commonly selected nerve for laryngeal reinnervation for UVFP. The ansa cervicalis is anatomically in close proximity to the RLN and is typically of sufficient diameter and length to permit neurorrhaphy, and donor site morbidity is minimal. The ansa has approximately the same number of myelinated fibers and motor fibers as the RLN branches to the TA and LCA [15] allowing it to accurately replace the function of the original RLN. Additionally, the strap muscles innervated by the ansa share reasonably comparable contraction times and muscle fiber composition to the laryngeal musculature [16, 17], which is significant, because a donor nerve changes the fiber type and contraction pattern of reinnervated muscle [18]. For UVFP, adductor reinnervation of the sternohyoid branch of the ansa is frequently selected, as it has no phasic activity [19]. While animal studies have demonstrated active vocal fold adduction with ansa-RLN neurorrhaphy [20, 21], this result has rarely been replicated in human studies.

Frazier [22] first reported the ansa-RLN transfer with successful laryngeal reinnervation in 1924. Over the past four decades, studies on ansa-RLN transfer have consistently produced near-normal vocal quality results in the overwhelming majority of patients with UVFP who underwent laryngeal reinnervation with this technique. In 1986, Crumley reported excellent voice quality following ansa-RLN in two patients [23]. Five years later, Crumley reported a larger series of 20 patients who underwent ansa-RLN transfer in which excellent to normal phonatory quality was achieved in 18 [24]. Of note, multiple patients in this study had significant delays (>8 years) between RLN injury and successful reinnervation. Subsequent reports by multiple authors have demonstrated successful ansa-RLN reinnervation with favorable voice results. Zheng et al. [15] reported good vocal results in seven of eight patients who underwent ansa cervicalis anastomosis to the adductor branch of the recurrent laryngeal nerve for UVFP and additionally demonstrated appropriate reinnervation of the adductor musculature by EMG in five patients. Olson et al. [25] reported significant improvement in voice quality, dysphonia, breathiness, and asthenia in 12 patients who underwent ansa-RLN transfer and noted that the greatest degree of improvement was seen in patients with isolated UVFP. In a large study of 237 patients, Wang et al. [26] reported effective laryngeal reinnervation with ansa-RLN transfer in 235 (99.2%) of patients with improvement in glottic closure, vocal fold position, and phase symmetry. Several studies have additionally demonstrated the comparatively efficacious use of the contralateral ansa cervicalis in ansa-RLN transfer [27, 28].

In 1999, Paniello et al. [29] first proposed the use of the hypoglossal nerve and an alternative donor nerve to the ansa cervicalis for laryngeal reinnervation by direct neurorrhaphy. Stated advantages include increased axon number, increased temporal activity during phonation and deglutition, and frequency of preservation in patients with prior history of neck surgery. Paniello et al. [30] furthermore reported a series of 25 patients with UVFP, in which 12 ultimately underwent laryngeal reinnervation via hypoglossal-RLN anastomosis with excellent voice results. Notably, this study reported definite vocal fold adduction and sphincter-like glottic closure during the swallowing reflex. The role of the hypoglossal nerve in laryngeal reinnervation remains to be established and is not commonly used in clinical practice.

Nerve-Muscle Pedicle Transfer

Laryngeal reinnervation with neuromuscular pedicle (NMP) transfer was first developed and studied in animal models in the 1970s [31]. In this technique, the donor nerve and a small section of muscle at the distal end of the donor nerve containing intact motor units are harvested. This muscle block is then sutured into the target denervated muscle, allowing for transplanted axons to permeate recipient muscle fibers and innervate the motor endplates of the denervated muscle. As with direct neurorrhaphy, the ansa cervicalis is most often selected as the donor nerve with the muscle pedicle taken from the anterior belly of the omohyoid. In patients with UVFP, the muscle pedicle is sutured into the lateral cricoarytenoid.

Tucker first reported the use of NMP in 1976 for patients with bilateral vocal fold paralysis [32] and the following year reported use of NMP in nine patients with unilateral vocal fold paralysis [33]. All nine patients had recovery of adduction function within 12 weeks; however, just six of the nine patients demonstrated satisfactory improvement in voice quality. Later studies both by Tucker and others utilizing NMP for UVFP demonstrated significantly higher success rates (88%–100%) regarding voice improvement [34–37]. Despite the high rates of success in restoring vocal function reported by multiple authors, NMP has not developed widespread use in laryngeal reinnervation for UVFP. NMP transfer has developed a larger role in laryngeal reinnervation for BVFP as described below.

Additional Laryngeal Innervation Techniques

Two additional laryngeal reinnervation techniques that have been utilized predominately in animal models are direct nerve implantation and muscle-nerve-muscle (MNM) transfer. In direct nerve implantation, the donor nerve is sutured directly into the denervated, recipient muscle. The nerve is ideally sutured into the muscle at the site with the highest concentration of motor endplates to increase the likelihood of establishing axonal-endplate connection. Su et al. [38] reported a series of 10 patients who underwent direct nerve implantation of the ansa cervicalis into the thyroarytenoid for UVFP with improvement in voice quality in eight patient and near-normal voice quality in six. The MNM technique is similar in that a donor nerve graft is sutured directly into the denervated muscle on one end and an innervated muscle on the other, allowing axons to transverse the graft from the innervated side and reinnervate the opposite side. El-Kashlan et al. [39] reported a study of three patients with UVFP who underwent both ansa-RLN anastomosis and selective cricothyroid reinnervation via MNM. All three patients recovered near-normal vocalization with EMG evidence of cricothyroid reinnervation.

Medialization Versus. Reinnervation for UVFP

Medialization procedures such as injection laryngoplasty, arytenoid adduction, and thyroplasty are commonly used in the treatment of unilateral vocal fold paralysis. Since the advent of modern laryngeal reinnervation, numerous studies have aimed to assess the comparative validity of medialization and reinnervation for UVFP both in isolation and in combination [40–44]. Noted advantages of reinnervation include restoration of bulk of the TA, improved vocal fold positioning as a result of LCA, interarytenoid and PCA contraction, reversibility, and elimination of dysphonia due to synkinesis, and it does not preclude future use of static methods. Conversely, disadvantages of reinnervation consist of the need for an intact donor nerve and RLN stump, increased time to vocal improvement, and increased cost [24, 41]. Considerations that influence postoperative outcomes regardless of surgical intervention include patient age, glottal gap, anatomical location of RLN lesion, and dysphonia severity.

Chhetri et al. [40] reported a review of 19 patients, 9 of whom underwent arytenoid adduction alone and 10 of whom underwent combined

arytenoid adduction and RLN anastomosis. The study reported no significant differences in videostroboscopic parameters, aerodynamic measures, or perceptual rating between groups. Tucker [44] studied the long-term preservation of voice improvement in patient with UVFP who underwent surgical medialization alone with those receiving combined medialization and nerve-muscle pedicle reinnervation. He found 28% voice deterioration at 6–24 months in patients receiving medialization alone vs. 4% at 24 months in those who received combined therapy. In 2011, Paniello et al. [43] published a prospective trial in which 24 patients with untreated UVFP were randomized to undergo medialization laryngoplasty (ML) or laryngeal reinnervation (LR). The study found no significant differences regarding perceptual rating, blinded speech pathologist GRBAS (grade, roughness, breathiness, asthenia, strain) scores, and voice-related quality of life (RUL) scores. However, the study did note that, for patients aged <52, the LR subgroup had significantly better RUL and GRBAS scores than the <52 ML subgroup, and the converse was true for >52 subgroups with ML demonstrating significantly better results compared to LR. In 2018, Lee et al. [42] analyzed and compared long-term voice outcomes for 62 patients with UVFP, 19 of whom underwent ansa-RLN reinnervation and 43 of whom received injection laryngoplasty (IL). The study reported that, while both LR and IL demonstrated statistically significant voice improvement up to 36 months postoperatively, after 36 months, patients who had IL experienced significant deterioration of voice parameters, while the LR group improvements remained stable after 36 months.

Laryngeal Reinnervation: Bilateral Vocal Fold Paralysis

Bilateral vocal fold paralysis (BVFP) is a rare, potentially life-threatening condition that results in airway compromise frequently necessitating tracheotomy. RLN injury following thyroidectomy is the most common cause of BVFP [45]. Static treatments of BVFP, including laser posterior cordectomy, arytenoidectomy, and laterofixation of the vocal fold trade, improved airflow for the potential of increased aspiration risk and decreased voice quality. Laryngeal reinnervation in BVFP with resultant return of abductor function during inspiration carries the potential benefit of both airway and voice preservation. The disadvantage of reinnervation over static methods is the duration of time until improvement and decannulation, which can be a significant deterrent to patients and the potential of failure of the reinnervation.

Laryngeal reinnervation in patients with BVFP requires the selective reinnervation of the posterior cricoarytenoid to re-establish vocal fold abduction during the inspiratory phase of the respiratory cycle. In humans, the native innervation of the PCA from the intralaryngeal RLN is highly variable. Nguyen et al. [46] described three main variations of PCA innervation in cadaveric dissections, demonstrating that the interarytenoid branch and PCA branch occasionally share a common trunk from the intralaryngeal RLN (see Fig. 30.2). Further studies by Prades et al. [47] and Maranillo et al. [48] demonstrated that the PCA branch and IA branch share a common trunk in up to 88% of cadaveric specimens. This variability of intralaryngeal nerve patterns poses a challenge to selective reinnervation of the PCA by allowing for synkinesis from adductor axon innervation. Several donor nerves with phasic inspiratory activity have been proposed, including the phrenic nerve, the external branch of the superior laryngeal nerve (EBSLN), and the omohyoid or sternothyroid branch of the ansa cervicalis.

The anatomy and inspiratory phasic activity of the phrenic nerve make it a considerable candidate for PCA reinnervation. Multiple animal studies have demonstrated the successful use of the phrenic nerve to reinnervate the PCA by direct neurorrhaphy [49, 50] and direct nerve implantation [51] with return of normal abductor function in 75–89% of cases. Concerns of donor site morbidity with transection of the phrenic nerve have prompted animal studies of split-phrenic grafts [52] and cervical root phrenic grafts [53]; however, these studies demonstrated

a lower rate of phasic inspiratory muscle contraction. Human studies on phrenic reinnervation of the PCA are limited, and initial efforts were unsuccessful at demonstrating active abduction [54]. More recently, Marie et al. [55] have demonstrated active vocal fold abduction in three of six patients who underwent PCA reinnervation with phrenic nerve root and interpositional free nerve graft.

The EBSLN supplies efferent motor axons to the cricothyroid and has been shown to be active in respiration [56], corresponding to the phasic activity of the PCA [57]. EBSLN use in PCA reinnervation was first reported by Maniglia et al. [58] in canines. Dogs in which an NMP harvested from the cricothyroid was sutured into the PCA demonstrated approximately half-normal vocal fold abduction. In 2015 Orestes et al. [59] published the first use of the EBSLN in selective PCA reinnervation in humans. Two patients underwent direct neurorrhaphy of the EBSLN-RLN along with adduction reinnervation of the ansa cervicalis to distal adductor nerve trunk. In both patients, either the interarytenoid nerve or muscle was sectioned to present synkinesis. Both patients demonstrated improvement in abduction at seven months with excellent voice quality.

As with UVFP reinnervation, the ansa cervicalis has multiple aforementioned characteristics that make it a reasonable candidate for BVFP reinnervation. For BVFP the branch to the anterior belly of the omohyoid or to the sternothyroid is selected for appropriate phasic activity. Tucker has published multiple studies utilizing ansa-NMP technique for PCA reinnervation in patients with BVFP. In a long-term review of over 200 patients, successful reinnervation of the PCA was demonstrated in 74% [36]. This high success rate of reinnervation using the ansa has not been redemonstrated in smaller series [60].

Pediatric Consideration Regarding Laryngeal Reinnervation

In children, UVFP is often a sequela of vagal damage from pediatric chest or cardiac procedures, specifically the ligation of the patent ductus arteriosus. Smith et al. [61] demonstrated that patient weight at the time of surgery had significant implication on the rate of UVFP and found that infants weighing less than 1250 g at time of PDA ligation had 24% risk of UVFP. Initially, feeding and airway protection are primary concerns, while voice and speech become the areas of greatest concern in older children [62]. While static interventions have been reported in children with UVFP [63–65], there is a paucity of well-documented treatment outcomes [62]. Several factors, including future laryngeal growth, absence of a well-defined vocal ligament, and softness of laryngeal cartilage, make static treatment options for UVFP less ideal in the pediatric population.

Several small case series and reports have consistently shown efficacy of laryngeal innervation in children via ansa-RLN neurorrhaphy [62, 66, 67]. In 2015 Butskiy et al. [68] published a systematic review of pediatric surgical intervention for UVFP comprising 15 studies and 79 children. All 36 of the children who underwent laryngeal reinnervation had improvement or complete resolution of dysphonia, which was significantly better than in children who underwent injection laryngoplasty and thyroplasty, leading the authors to suggest that reinnervation may be the most effective surgical intervention in children with UVFP and dysphonia. In 2018 Bouhabel et al. [69] published a survey of pediatric otolaryngologists with special interest in pediatric laryngology. They note a significant shift in practice, reporting more than 20% of respondents considered ansa-RLN as first-line treatment of patients with symptomatic UVFP, whereas only injection medialization laryngoplasty was considered in the past.

Developing Advances in Laryngeal Reinnervation

Gene therapy using viral and nonviral vectors to introduce neurotrophic and growth factors into the nucleus ambiguus, RLN, and laryngeal musculature has been an ongoing, promising area of inquiry for the past two decades. Shiotani et al.

[70] studied the introduction of insulin-like growth factor I (IGF-I) gene into denervation laryngeal musculature via a muscle-specific, non-viral vector and demonstrated a significant increase in motor endplate number, length, and muscle fiber diameter. Araki et al. [71] demonstrated neurological RLN recovery in rats following adenoviral glial cell-derived neurotrophic factor (GDNF) gene transfer with treated animals showing higher nerve conduction velocity, larger axonal diameter, and improved remyelination compared to controls. Several animal studies have shown improved recovery of vocal fold movement compared to controls in rat RLN-crush models using gene transduction of GDNF [71], vascular endothelial growth factor [72], and zinc finger protein gene [73], which stimulates endogenous secretion of IGF-I. A thorough review of gene therapy pertaining to RLN injury is presented by Araki et al. [74].

Recent studies of the use of calcium channel blockers to promote axonal regeneration [75, 76], tacrolimus to improve recovery of GDNF of laryngeal muscle fiber types [77], microtubule inhibitors and vincristine to suppress synkinesis [78, 79], and placing of a conduit such as a portion of a vein over the anastomosis to maintain neurotrophic factors in the region of the neurorrhaphy have shown significant potential as developments in laryngeal reinnervation. Further investigation will allow for determining which developing techniques hold the most promise for the future of laryngeal reinnervation.

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31 Management of the Cricopharyngeus

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Introduction

Anatomy

Situated between the inferior pharyngeal constrictors and the cervical esophageal musculature, the cricopharyngeus muscle (CPM), together with these muscles, comprises the upper esophageal sphincter (UES), also referred to as the pharyngoesophageal segment (PES). The UES is between 2 and 4.5 cm in length in humans, separating the pharynx and esophagus [1, 2]. The UES is mobile, moving superiorly and inferiorly with swallowing, respiration, belching, and vomiting. The UES accommodates increased pressures to prevent reflux of esophageal contents and aerophagia while also permitting decreased pressures for swallowing, belching, and vomiting. Opening of the UES is also facilitated by the superior and anterior motion of the hyolaryngeal complex by the action of suprahyoid muscles during swallow that stretch the UES.

The CPM is a bilateral "C"-shaped muscle arising from the lower portion of dorsolateral aspect of the cricoid cartilage without a distinct posterior raphe [3]. The upper oblique portion termed the *pars obliqua* fuses superiorly with the thyropharyngeus, and the lower horizontal portion is termed the *pars fundiformis* and blends with the circular muscle layer of the proximal esophagus [2, 4, 5]. The CPM is approximately 1–2 cm wide and composed of predominately type-I, slow-twitch skeletal muscle and about 40% connective tissue by volume supporting and surrounding the muscle fibers [4]. The relatively larger portion of connective tissue compared to limb musculature in the CPM is thought to contribute to the muscle's elastic features. A study in cats suggests the CPM functions similar to cardiac muscle, with maximal tension at 1.7 times its basal length compared to maximal tension at basal length in other skeletal muscles [6]. This tension relationship allows for passive stretching open of the CPM in this elastic range during passage of a food bolus without active relaxation or inhibition of the CP muscle [3, 4].

Unlike the well-described CPM anatomy, the innervation pattern of the CPM remains less well elucidated. Despite lacking a prominent central or posterior aponeurosis, the human CPM is a bilateral muscle receiving bilateral innervation [3]. The CPM receives innervation contributions from the recurrent laryngeal nerve (RLN), superior laryngeal nerve, pharyngeal branch of the vagus nerve, and glossopharyngeal nerve based on human anatomic studies [3, 7–9]. Electromyography (EMG)

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CPM recordings identified RLN activation of the CPM, confirming a motor contribution from the RLN, with the pharyngeal plexus contributions suggested as a sensory or mixed contribution [10].

Knowledge of fascial planes and potential spaces surrounding the CPM is crucial in considering implications of interventions addressing cricopharyngeal muscle dysfunction (CPD). The buccopharyngeal fascia, part of the middle layer of the deep cervical fascia, resides immediately posterior to the CPM, blending with the carotid sheath bilaterally, fibrous pericardium inferiorly, and extending to the skull base superiorly. The retropharyngeal space lies behind the buccopharyngeal fascia, a potential space of areolar tissue bounded posteriorly by the alar fascia. As part of the deep layer of the deep cervical fascia, the alar fascia fuses with the buccopharyngeal fascia in the superior mediastinum at the level of T1/T2. The alar fascia serves as a boundary between the retropharyngeal space and the danger space and prevertebral fascia posteriorly [11].

Diagnosing Cricopharyngeal Muscle Dysfunction

CPD occurs from CPM fibrosis or other histologic changes, hypertonicity, and/or altered neural signaling from a stroke, such as a lateral medullar stroke, or neuromuscular diseases. Neuromuscular conditions that affect the pharynx, esophagus, or neck musculature can cause CPD and include amyotrophic lateral sclerosis, oculopharyngeal muscular dystrophy, other forms of muscular dystrophy, or abdominal myoclonus to name a few. Stenosis of the UES second to external beam radiation may also lead to CPD. Patient-reported symptoms of CPD vary from a mild globus sensation and throat clearing to more significant solid food and liquid dysphagia and, in some cases, cough and aspiration. Therapeutic decision-making relies on careful assessment of dysphagia complaints and a thorough swallow evaluation to delineate CPD from dysphagia second to other etiologies such as reduced hyolaryngeal elevation, pharyngeal weakness, and esophageal dysmotility.

In clarifying the etiology, a history and full head and neck exam are often suggestive of CPD and drive further testing. In general, patients with suspected CPD undergo a clinical swallow evaluation prior to additional instrumented exams. In this setting, it is possible to palpate hyolaryngeal motion during swallow and identify potential signs of CPD such as throat clearing and repeat swallows. As no single test exists explicitly for CPD, data from fiberoptic endoscopic evaluation of swallow (FEES), EMG, manometry, and videofluoroscopy can aid in diagnosis and decision-making. As many of these studies rely on multidisciplinary efforts, it is important to recognize that diagnostic and evaluation patterns vary and can impact both study results as well as tests performed [12]. Diagnostic tests are summarized in Table 31.1.

Similar to a clinical swallow evaluation, FEES is both easy to perform in the office but not very specific for CPD. Identification of pooling within the piriform sinuses and subsequent spillage into the laryngeal inlet can be a sign of CPD, especially with an intact pharyngeal squeeze [2, 13]. FEES also permits evaluation of the anatomy and muscle of the larynx and pharynx.

CPM EMG has traditionally been reserved for research purposes but is possible both in the office setting and in the operating room and is sometimes used during CPM botulinum toxin (BTX) injections in treating CPD [6, 7]. More recently, evidence suggests differences in EMG patterns in patients with CPD and history of a cranial nerve palsy [14, 15]. Interestingly, while a link exists between increased UES pressure recordings and the presence of acid within the esophagus, a small 24-patient study of CPM EMG found normal EMG recordings of the CPM [16].

Manometry continues to evolve as a mechanism for CPM and UES evaluation with improved technology and smaller, smoother catheters more comfortable for patients. Current high-resolution manometry (HRM) and newer probes allow for more specific UES evaluation, overcoming early challenges arising from variations in measured values based on differing probe positioning within the asymmetric UES [17]. Manometry pressure measurements allow for the assessment of pharyn-

Table 31.1 Advantages and disadvantages of cricopharyngeal muscle dysfunction interventions

Diagnostic tool	Uses	Limitations
Clinical swallow evaluation	Can easily be performed in office. Can suggest PES dysfunction	Not very sensitive or specific
Functional endoscopic evaluation of swallow	Office-based procedure. Allows assessment of laryngeal and hypopharyngeal anatomy. Able to assess pharyngeal squeeze	White out during swallow and view from nasopharynx limits assessment. Generally, still requires additional testing for diagnosis of UES dysfunction
High-resolution manometry	Provides objective measure of UES and can also evaluate for other esophageal motility disorders. Can be combined with VFSS for comprehensive UES evaluation	Less pharyngeal HRM normative values for interpretation. The UES dynamically sliding superiorly during swallow can confound and limit data value
Electromyography	Allows for objective measurement of CPM function	Generally reserved for research. Can be technically challenging, particularly in patients with larger necks. Relatively sparse normative data
Videofluoroscopic swallow study (VFSS)	Allows visualization of oral phase, pharyngeal phase, UES, and cervical esophagus to compare hyolaryngeal elevation, pharyngeal contraction, and presence of CPM abnormalities. A follow-through can also provide information on esophageal function	A cricopharyngeal bar is found in nearly one-third of elderly patients and does not always correlate to symptoms. Radiation exposure

PES pharyngoesophageal segment, *UES* upper esophageal sphincter, *CPM* cricopharyngeus muscle

geal strength, CPM, and upper esophageal sphincter relaxation and pharyngeal coordination. Results that are suggestive of CPD include normal pharyngeal contraction with elevated upper esophageal residual pressure during deglutition as well as reduced relaxation times [2]. Increased CPM tone may also occur in response to acid within the esophagus and esophageal distention [18, 19]. Continued development of pharyngeal manometry and HRM with a simultaneous videofluoroscopic swallow study (VFSS) and/or EMG recordings will improve overall UES evaluation [1].

VFSS is an adaptation of a barium esophagram focusing on the oral, pharyngeal, and PES regions using varying solid food and liquid consistencies mixed with barium and is particularly suited for evaluation of the UES and CPD [20]. VFSS illustrates CPM function in relation to hyolaryngeal elevation and pharyngeal contraction, ultimately allowing for the identification of patients who may benefit from treatment for CPD [2]. Decreased distention of the UES and retained bolus above the UES after swallow suggest CPM dysfunction [21]. VFSS can be misleading, though, as radiographic evidence of a "cricopharyngeal bar," or posterior soft tissue outpouching in the UES region on maximal distention occluding at least one-third of the passage with a bolus, occurs as frequently as 30% of patients over the age of 60 [22, 23]. Various techniques are employed to objectively evaluate VFSS results, including the calculation of pharyngeal constriction ratio; measuring the opening in lateral and anteroposterior views above, at, and below the UES; and calculating the UES cross-sectional area [2, 24, 25]. Figure 31.1 illustrates common CPD findings on VFSS.

Treatment

Patient Selection

When selecting patients appropriate for the treatment of suspected CPD, the decision to move forward with a procedure is dependent on presenting symptoms and the quality of life impact to the patient. In general, for patients who present with CPD, therapies targeting the CPM are indicated when there is impaired UES opening, adequate

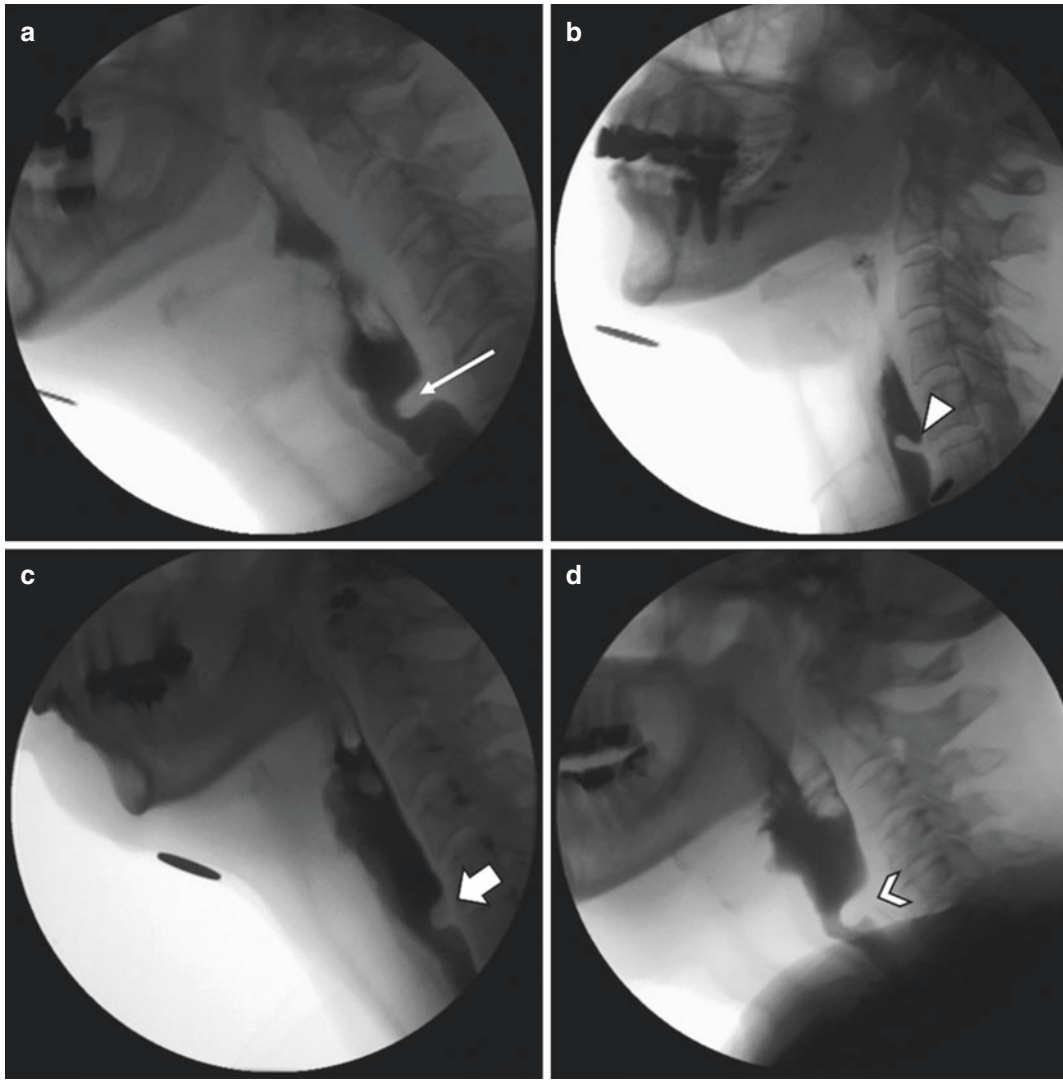

Fig. 31.1 Sample videofluoroscopic swallow study images illustrating the range of cricopharyngeal muscle dysfunction. (**a**) Moderately obstructive cricopharyngeal bar (*thin white arrow*) protruding from the posterior pharyngeal wall in the upper esophageal sphincter region impairing bolus motion. (**b**) Cricopharyngeal bar developing into a small Zenker's diverticulum (*white arrowhead*). (**c**) Small, mildly obstructing cricopharyngeal bar (*thick white arrow*). (**d**) Large, mostly obstructing cricopharyngeal bar (*white chevron*) impeding bolus motion

laryngeal elevation, and acceptable oral and pharyngeal propulsion [13]. In addition, underlying etiologies for increased UES pressures should be first treated; esophageal acid exposure from reflux and esophageal distension as might occur from underlying lower esophageal sphincter achalasia or severe dysmotility both can increase UES pressures [18, 19]. This may include a trial of anti-reflux medications, 24-hour pH study, and/or a traditional esophagram; in some locations, an esophageal follow-through during the VFSS may provide this information.

Management of CPD ranges from nonsurgical exercises and biofeedback techniques to minimally invasive procedures to chemically denervate and/or dilate the CPM to endoscopic and open cricopharyngeal myotomy [1]. Limited evidence exists for swallowing exercises improving UES opening and is specific to Mendelsohn's maneuver, an exercise designed to increase the extent and duration of

Table 31.2 Uses and limitations of common diagnostic tools for cricopharyngeal muscle dysfunction

Treatment approach	Advantages	Disadvantages
Balloon dilation—general anesthesia	Ability to palpate CPM. Option of rigid dilators or balloon dilation. Can be combined with BTX injection	Requires brief general anesthetic/intubation. Not permanent
Balloon dilation—sedated transnasal	Avoids general anesthetic. Quick procedure with shorter recovery. Some authors suggest that it can be performed outside operating room	Relies on balloon dilations. Requires transnasal esophagoscope. Not able to palpate CPM. Not permanent
CPM BTX injection—general anesthesia	Ability to palpate CPM and carefully direct BTX injection without need for electromyography. Can be combined with balloon or rigid dilation (if combining, dilation should occur first to prevent forceful distribution of injection to unintended local structures with dilation)	Requires brief general anesthetic/intubation. Not permanent. Risk of worsening swallow if BTX extrudes to inferior pharyngeal constrictors. Not permanent
CPM BTX injection—EMG guided transcervical	Avoids general anesthetic. Confirmation of ideal BTX placement with aid of EMG guidance. Can be performed in clinic to avoid expense associated with operating room	Necessitates access to EMG machine and expertise in EMG-guided BTX injections. Can be technically challenging, particularly in patients with unfavorable anatomy (larger neck circumference, thick neck musculature, etc.). Not permanent
Endoscopic CPM myotomy	Permanent procedure. No neck incisions. Symptom resolution in well-selected patients	Requires overnight observation for air/fluid leak through buccopharyngeal fascia. Requires CO_2, thulium, or KTP laser access
Open, transcervical CPM myotomy	Permanent procedure. Ideal if challenging endoscopic exposure. More easily allows for longer myotomy and direct visualization of musculature prior to myotomy. Symptom resolution in well-selected patients	Requires, at minimum, overnight stay in the hospital to assess for any pharyngeal leak. Requires neck incision and puts RLN and deep neck structures at risk

BTX botulinum toxin, *CPM* cricopharyngeus muscle, *EMG* electromyography, *KTP* potassium-titanyl-phosphate, *RLN* recurrent laryngeal nerve

laryngeal elevation during swallowing [26]. This approach may be useful in situations where the patient is apprehensive about a surgical intervention or is a poor candidate for general anesthesia or a sedated procedure. Interventions for CPD are summarized in Table 31.2 and described below.

History of Surgical Intervention for Cricopharyngeal Muscle Dysfunction

In 1950, Asherson introduced the term cricopharyngeal achalasia while assessing neurologic CPD leading to the first reported CPM myotomy in a patient with polio-related complications [7, 27–29]. Sutherland described successful transcervical CPM myotomy for CPD in eight patients [30]. In parallel, variations of a transmucosal CPM myotomy via diathermy were performed and popularized in 1958 by Dohlman [31]. The use of a carbon dioxide (CO_2) laser for myotomy was introduced in 1981 and a potassium-titanyl-phosphate (KTP) laser in 1992 [32, 33]. BTX for chemical denervation of the CPM emerged as an alternative to surgical CPM myotomy in 1994 [34]. Passive and active CPM dilations have longed been performed [35]. Today, interventional options remain largely similar to historical procedures and include passive dilation, active dilation, chemical denervation with or without dilation, endoscopic myotomy with or without mucosal closure, and open, transcervical CPM myotomy. Myotomy remains the only permanent treatment for CPD.

Cricopharyngeal Muscle Dilation

CPM dilation can be performed under general anesthesia or minimal sedation using either fixed

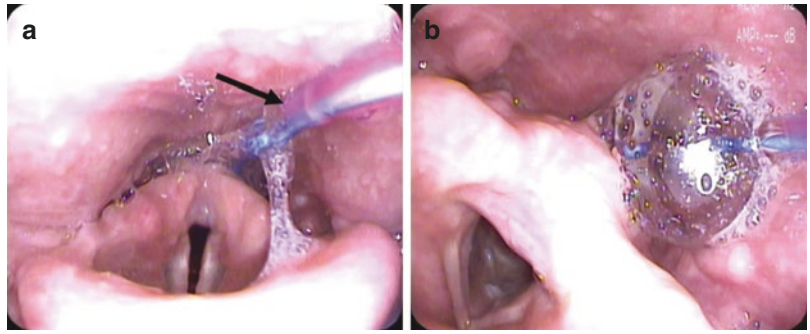

Fig. 31.2 Transnasal esophagoscopy with balloon dilatation. (**a**) Balloon passed over a guidewire entering the esophagus (*black arrow*) visualized from the transnasal esophagoscope resting in the nasopharynx. (**b**) Balloon inflated, stretching open the upper esophageal sphincter

diameter bougies or balloon catheters. The decision to proceed with either approach depends on surgeon comfort, available equipment, a patient's ability to undergo general anesthesia safely, and mitigating factors that may make exposure of the UES challenging, such as poor neck extension after radiation therapy. Under general anesthesia, the UES is identified and the prominent CPM visualized. Depending on dilation approach, the patient is either placed in suspension and undergoes balloon catheter dilation or serial passage of fixed diameter bougies is performed. Balloon catheters are inflated to the manufacturer's recommendations, deflated, and then removed [35, 36].

When performing CPM dilation under sedation, a transnasal esophagoscope is passed through the nares and into the esophagus. A guidewire for the selected balloon catheter is then passed through the channel in the esophagoscope and the esophagoscope removed while advancing the guidewire to remain within the esophagus. The balloon is then passed over the guidewire and into the UES region under visualization with the esophagoscope after which the balloon is inflated to the desired dimension (Fig. 31.2).

Whether using the awake transnasal approach or under general anesthesia, a double balloon technique with side-by-side balloons (Fig. 31.3) can allow for additional dilation dimensions as well as better approximate the natural shape of the UES [37, 38]. Reported outcomes in the literature suggest that dilation is an effective treatment option for CPD, with a majority of patients having at least short-term success [39, 40]. Benefits of CPM dilation include a very low complication risk and the ability to perform serial dilations, particularly useful for radiation stenosis of the UES, and ability to perform future interventions.

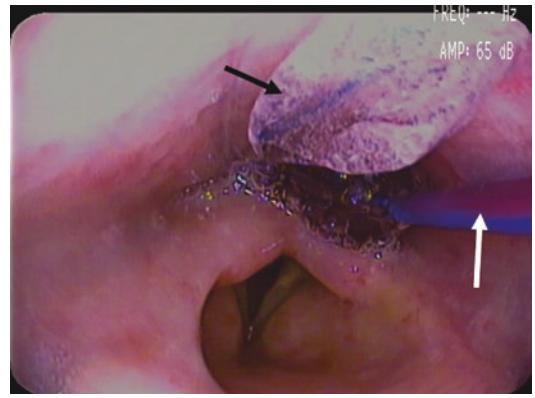

Fig. 31.3 Transnasal esophagoscopy with double balloon dilation with an inflated (white arrow) and partially inflated (*black arrow*) balloons in the upper esophageal sphincter

Botulinum Toxin Chemical Denervation of the Cricopharyngeus Muscle

Chemical denervation of the CPM with BTX can also be, like balloon dilation, injected awake or under general anesthesia as well as with or without EMG guidance [41, 42]. As in its use for

other otolaryngologic applications, BTX functions by blocking release of acetylcholine from presynaptic nerve terminals into the neuromuscular junction. Operative chemical denervation involves direct visualization of the CPM. The injection can be performed as an isolated procedure or in conjunction with CPM dilation [15, 34, 43]. When performing the injection, it is important to inject the horizontal portion of the CPM and not the caudal fibers of the inferior pharyngeal constrictor muscle, which risks reduction in pharyngeal contraction and potential worsening of dysphagia. Visualization of the horizontal portion of the CPM can be accentuated by passing a rigid suction through the UES under direct visualization and applying a small amount of lateral stretch. Under this visualization, BTX can reliably be administered without EMG guidance (Fig. 31.4). In the percutaneous approach to CPM BTX injection, EMG guidance plays an essential role in localization and is technically more challenging [41].

BTX dosing for CPD injection varies widely between studies and types of BTX. Reported onabotulinumtoxinA dosing ranges between 2.5 and 100 units, and abobotulinumtoxinA dosing ranges between 60 and 300 units with no correlation between dose and success rate for either [42]. Literature outcomes for BTX injection for CPD are equally as variable, partly as a result of differing inclusion criteria, outcome measures, dosing, and length of follow-up [42, 44]. However, overall reports are generally positive for the use of BTX for CPD, and the procedure has a favorable risk profile. Most complications from BTX injection for CPD relate to diffusion of the toxin to surrounding inferior pharyngeal musculature that can worsen dysphagia and place the patient at risk for aspiration.

Cricopharyngeal Myotomy

CPM myotomy, either endoscopically or transcervically, remains the only current permanent surgical treatment for CPD. The most common approach to endoscopic cricopharyngeal myotomy involves the CO_2 laser performed under direct visualization [11]. As imaged in Fig. 31.5, a diverticuloscope or laryngoscope exposes the esophageal inlet and CPM, and under binocular microscopy, a CO_2 laser incises the mucosa and CPM while taking care not to violate the yellowish-appearing buccopharyngeal fascia deep to the CPM overlying the areolar tissue of the retropharyngeal space [11, 45]. Knowing that the inferior constrictors contribute to nearly two-thirds of the UES pressure measurements, an extended myotomy is commonly performed. Some authors advocate for mucosal closure after myotomy and possibly even CPM myectomy both to prevent the muscles from scarring together and provide additional protection to the buccopharyngeal fascia [46]. More recently, endoscopic CPM myotomy has been described through flexible instrumentation [47].

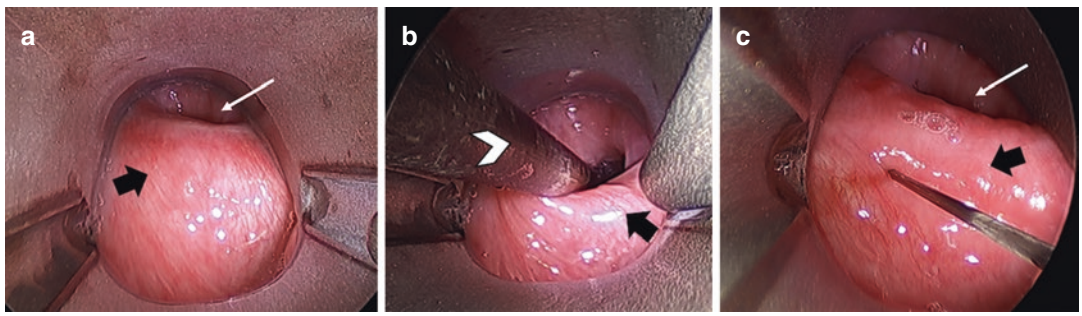

Fig. 31.4 Endoscopic botulinum toxin (BTX) injection. (**a**) Visualization of cricopharyngeal bar (*short black arrow*) and esophageal inlet (*thin white arrow*). (**b**) Rigid suction cannula (*white chevron*) stretching the cricopharyngeus muscle (CPM) (*short black arrow*). (**c**) BTX injection into the CPM (*short black arrow*) just posterior to the upper esophageal sphincter opening (*thin white arrow*)

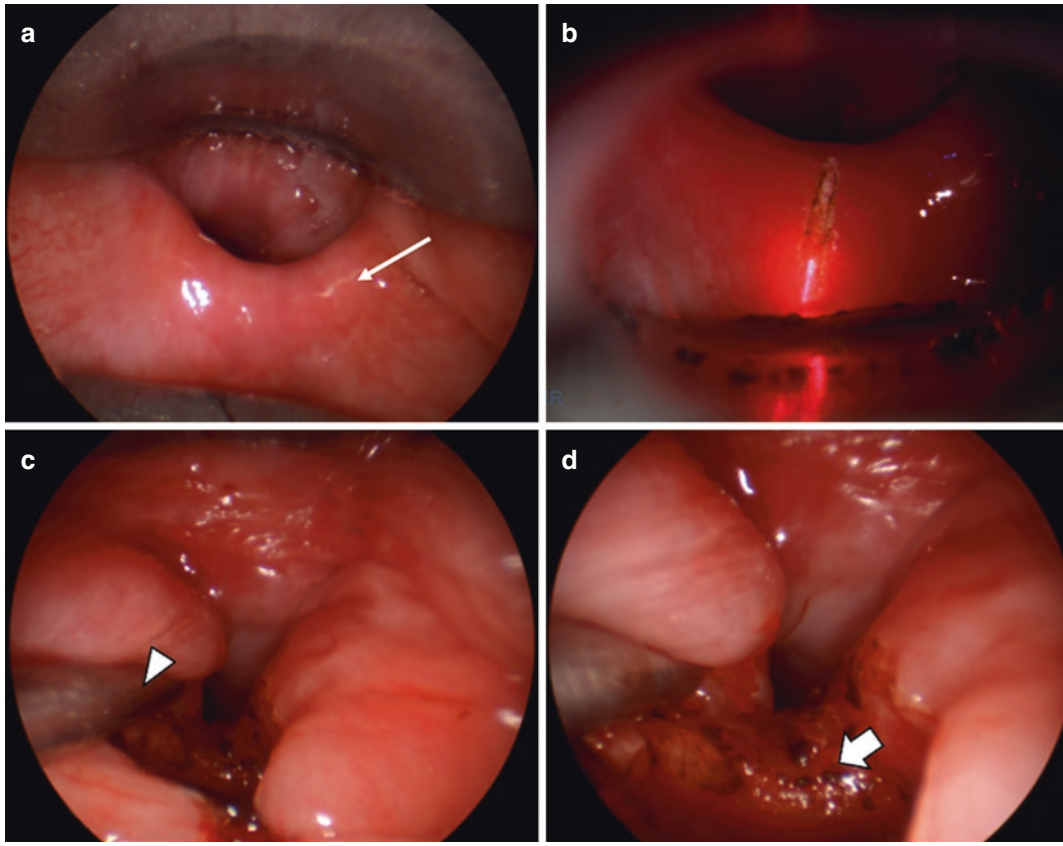

Fig. 31.5 Images from endoscopic cricopharyngeal myotomy. (**a**) Exposure of the cricopharyngeus muscle (CPM) (*thin white arrow*). (**b**) Mucosal and CPM incision via the CO_2 laser in an anterior to posterior fashion. (**c**) Opened upper esophageal sphincter by rigid suction cannula (*white arrowhead*). (**d**) Complete CPM myotomy with intact, visualized buccopharyngeal fascia (*short white arrow*)

The external approach for CPM myotomy is commonly performed in conjunction with a Zenker's diverticulectomy. The procedure begins with an incision along the anterior border of the left sternocleidomastoid muscle, retraction of the carotid sheath laterally and laryngotracheal structures anteromedially, and rotating the larynx to the right, exposing the pharyngoesophageal junction. The horizontal CPM may appear as either a soft muscle mass or more firm cord-like structure. A nasogastric or orogastric tube placed in the esophagus will aid in the recognition of the CPM. A posterior vertical midline CPM myotomy is performed to protect the RLN and nearby structures, and the wound is closed in layers [30].

Outcome data for endoscopic and open CPM myotomy suggest overall improvement in symptoms with both approaches without one approach providing clinically better results [46–51]. These studies, however, are limited by an overall lack of randomized controlled trials and varying diagnostic criteria, treatment approaches, and no outcome measurement uniformity impairing meta-analyses of many small studies [52]. A small number of studies suggest favorable CPD response to BTX injection may suggest positive outcomes from future CPM myotomy, but these studies are limited in numbers and lack randomization [49, 53].

CPM myotomy is generally safe, though potential complications can be devastating, particularly in an older population where prolonged swallowing difficulties can lead to inadequate oral intake and malnourishment. Complications are specific to the surgical approach selected. External CPM myotomy complications can

include recurrent laryngeal nerve paralysis, hemorrhage or hematoma formation, subcutaneous emphysema, pharyngocutaneous fistula, parapharyngeal abscess, aspiration pneumonia, and mediastinitis [54]. Endoscopic CPM myotomy is similar, except that there is no risk to the recurrent laryngeal nerve, and hemorrhage, aspiration pneumonia, and mediastinitis are far less common. Minor subcutaneous emphysema is more common than in the external approach. In cases where an unintentional pharyngotomy is created during CPM myotomy, avoiding positive pressure ventilation at the end of the surgery can help to minimize the chances for subcutaneous emphysema and mediastinitis.

Summary and Future Directions

The CPM plays a key role in the UES, and dysfunction of the CPM originates from histological tissue changes or neuromuscular alterations. Diagnosis typically combines patient-reported symptoms with videofluoroscopy and possibly manometry or EMG to evaluate anatomy and isolate CPD from pharyngeal weakness or poor hyolaryngeal elevation. CPM myotomy is generally considered the definitive treatment of CPD, although dilation and chemical denervation can be used as trial therapies or in those patients who are otherwise deemed not surgical candidates for a CPM myotomy. Continued advancement in pharyngeal HRM, combined manometry and VFSS, and newer manometry probes with variable measurement capacity in the axial plane will enhance UES evaluation and CPD diagnosis. Newer flexible endoscopic treatments for Zenker's diverticulum and, more recently, application to CPD are likely to continue shifting the landscape of CPD management in the coming years.

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Voice Therapy

32

Emerald J. Doll and Brienne Ruel

Introduction

Behavioral voice therapy administered by the speech language pathologist (SLP) focuses on improving the voice and upper airway within the constraints of the abnormal anatomy and/or physiology rather than achieving a "normal" voice. An understanding of normal physiology and how the disorder affects function will influence the overarching goal of voice therapy for neurolaryngeal disorders and further guide the therapeutic intervention. Behavioral intervention should target improved vocal function, efficiency, quality, and endurance, through coordination of respiration, phonation, and resonance. Incorporating tactile, visual, auditory, kinesthetic, modeling, and negative feedback will aid in the acquisition of therapeutic techniques. People with a neurologic disorder can benefit from additional strategies of muscle rebalancing, masking symptoms, and encouraging glottal efficiency. Therapy should be individualized, considering age, gender, personality, stress, hearing acquisition, cognitive abilities, emotional distress, vocal awareness, vocal load, and vocal priorities in social, occupational, and personal situations to encourage patient motivation, adherence, and acquisition of voice techniques.

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Focal Dystonia

Botulinum toxin (Botox®) is the current gold-standard pharmaceutical treatment for focal dystonias of the larynx and has been used since the mid-1980s [1]. Effectiveness has been well documented for adductor spasmodic dysphonia (ADSD), abductor spasmodic dysphonia (ABSD), and some cases of essential tremor depending which of the intrinsic laryngeal muscles are impacted [2–4]. A trial of voice therapy is worth implementing in the following instances:

1. A patient does not want to receive Botox® shots 3–5 times per year.
2. SD symptom presentation is mild.
3. They have concomitant airway or swallowing comorbidities that would benefit from SLP intervention.
4. They experienced inconsistent or less than satisfactory success with Botox® due to a mixed presentation of SD and tremor.
5. They have extended side effect periods of a weaker, breathier voice.
6. If the improved voice duration is too short.
7. To optimize their voice between treatments.

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The benefit of voice therapy is to educate the patient about their voice disorder, the subsystems of voice production, and provide voice exercises and strategies that optimize their communication. In some cases, voice therapy is necessary to tease out the possible maladaptive behaviors, such as compensatory muscular tension, that may have developed in response to the chronic spasms. Additionally, education is paramount to ensure the patient understands the chronic nature of the disorder, the variability in voice and treatment effects, and how to lessen the impact of the vocal symptoms on their quality of life while enhancing their communicative participation [5, 6].

Spasmodic Dysphonia

Therapy techniques and facilitators for SD are designed to reduce the severity and frequency of the voiced or voiceless spasms, but, like Botox®, are not curative nor permanent solutions [2, 7]. Therapy targets the subsystems of respiration, phonation, and resonance coordination to optimize function and minimize negative compensatory behaviors, such as overlaying muscle tension dysphonia. Patient-centered goals are important, since the persistent nature of this disorder can be extremely frustrating for people with SD. Patience and understanding are crucial because of the nature of these disorders. Traditional voice therapy exercises (e.g., resonant voice, vocal function exercises, airflow-based facilitators, laryngeal manual manipulation therapy, relaxation, vocal hygiene) are useful to increase patient's awareness of their voice production and breathing patterns and techniques for optimizing voice production despite a chronic impairment. Additionally, strategies specifically designed for this population to reduce the perception of the sound-specific voice breaks can be temporarily or situationally useful [8–10]. For example, in ADSD, easy onsets, breathier quality, or varying intonation can mask the strained-strangled voice breaks, while, in ABSD, voiced onsets (such as a slight hum prior to voiceless stimuli) can ease the sound transition. Additional sensory-motor tricks can temporarily relieve the disruption from the spasms, such as an accent, inhalation phonation, or speaking right after a yawn or laughter [11]. While these have minimal long-term effects and would not be expected to generalize, they can provide the patient some ways to explore what their voice is capable of, empower them to get creatively comfortable with their voice, and provide some relief, all of which may positively impact perceived quality of life [6]. For example, a patient at our clinic who is a traveling preacher discovered that he produced voice much more consistently during sermons when using an Irish accent and, since he was often new to the congregation, did not mind trying it out with each place he visited.

For those receiving botulinum toxin injections, the cyclic nature of the symptom relief and exacerbation also needs to be handled with empathy and education by the SLP and adjunct professional counseling offered as indicated [12, 13]. In our clinic, for example, we find that even many years after diagnosis, people with SD continue to ask questions about the nature of the disorder and seek new ways to cope. Additionally, it is imperative to view the patient holistically, suggest options for seeking supportive professional counselors, and be transparent with them about all available treatment options, such as intensive voice therapy programs, neuroplasticity training, and even alterative wellness modalities to enhance their autonomy to choose what they feel is best.

Vocal Tremor

Vocal tremor can benefit from a few potential treatment pathways. Pending accurate diagnosis of type, directionality, severity, and amplitude of tremor, the approach to essential tremor of the voice can be with systemic medication, botulinum toxin, behavioral voice therapy, or a combination. In severe multisite tremor or neurodegenerative disease cases, deep brain stimulation (DBS) is another option; however, if

any comorbidities exist that are treated with DBS, the current sparse literature suggests less efficacy and reduced long-term gains from voice-specific behavioral interventions [14, 15].

Patients with vocal tremor who present with mild to moderate dysphonia severity can respond favorably to behavioral tremor-specific reduction therapy if responsive to therapeutic probes. However, very few reports exist in the literature on behavioral treatment [16]. Behavioral therapy can be used as an initial conservative approach or in conjunction with medical and pharmaceutical treatments. Due to the co-occurrence of tremor in patients with Parkinson disease (PD), some clinicians prefer to use Lee Silverman Voice Treatment (LSVT) in addition to articulatory goals to improve vocal volume [17]. For essential tremor affecting the glottal and supraglottal levels, tremor-specific voice therapy is symptom-based approach aimed at improving overall intelligibility [18]. Barkmeier-Kraemer demonstrated that mild-moderate severe vocal tremors are suitable for attempting the strategies she describes such as vowel clipping, faster speaking rate, elevated pitch, voiceless easy onsets, and modulating intensity or frequency or both. Thus by targeting vowels, which carry the bulk of the acoustic information/tremor characteristic perceptually, the overall intelligibility may improve. Objective outcomes data, however, is lacking although patient-perceived improvement has been documented [18]. For more detailed education in this area, the reader is encouraged to explore online courses and in-person training opportunities.

Multiple Sclerosis

Voice quality impairment in MS [19] exists as part of the constellation of dysarthria symptoms that patients experience [20]. Bauer et al. [21] reported that quality of life was hindered by changes in voice, finding that 55% had dysphonia as determined by expert clinicians and a corresponding significant correlation of higher VHI scores to the GRBAS qualities of asthenia and strain.

Respiratory weakness occurs, with lower maximal expiratory pressure. Use of expiratory muscle strength training devices has been suggested and found not to have a statistically significant impact on voice or speech production in patients with MS [22].

There is a paucity of data related specifically to voice therapy outcomes in the MS population, for both progressive and relapsing-remitting subtypes. Speech, language, and cognitive goals are most common. The deficits of a voice with MS depend on whether there is upper motor neuron, lower motor neuron, or cerebellar damage, and thus, the voice can present with variations of spasticity and roughness to glottic insufficiency, breathiness, vocal fatigue, loss of vocal power as well as pitch, and volume instability [23–25]. Cortical level treatments, such as DBS, while addressing the more systemic issues of gross motor deficits, can sometimes be counterproductive to the fine motor control of voice.

Thus, voice therapy would target aspects to improve glottic closure, elicit more easeful voicing in the cases of spasticity, and, when indicated, increase the vocal power and energy in the case of weakness. The aim is to improve voice and speech clarity and consistency, with the understanding that the treatment goals may need to evolve as the disease progresses or in other cases relapses. If the dysphonia and dysarthria become too severe, an evaluation for alternative-augmentative communication options is strongly encouraged.

Kennedy Disease

A lower motor neuron disease process also known as spinal-bulbar muscular atrophy can present clinically with paradoxical vocal fold motion (PVFM), and approximately 44% of this population experience laryngospasm [26]; therefore, voice and upper airway assessment and treatment are warranted. Therapy targets include respiratory retraining exercises, sniff-pursed lip breathing techniques, and postural modifications where appropriate, such as during eating or reading so that head flexion or extension does not

trigger an episode. Voicing exercises for a patient at our clinic diagnosed with Kennedy disease improved his voice projection and resonant focus. Speech deficits were not present in this patient. If a speech impairment is part of the presentation, depending on the severity level, treatment focused on upper airway patency and dysarthria may become a priority.

Poststroke and Amyotrophic Lateral Sclerosis

Voice therapy as a single treatment modality is rarely used or effective for communication impairments in poststroke and amyotrophic lateral sclerosis (ALS) patients. Typically, the speech mechanism is impaired at varying levels of severity. In ALS, some of the early preclinical signs are reduced maximum pitch range and phonatory instability prior to the more obvious altered speech rate or reduced intelligibility, loss of laryngeal fine motor control from generalized spasticity, hypophonia, or a combination [27, 28]. Additionally, metalinguistic elements such as prosody can be impaired; thus, a patient may be able to use discrete pitch-changing tasks in a session; however, generalization to using more normalized inflection pattern to improve intelligibility is unlikely. Additionally, lack of pitch inflection does not impede the listener to the degree that imprecise articulation or impaired resonance (hyper- or hyponasality), tends to. Therefore, to maximize intelligibility, addressing the articulatory deficits and rate of speech should take precedence [27]. Vocal fold (VF) incomplete closure and compensatory hyperfunction, as well as reduced abduction, have been documented as primary visual findings in videostroboscopy of patients with ALS [29]. Treatment focuses on symptom management (e.g., vocal fold augmentation to improve glottic closure) or behavioral intervention to improve vocal efficiency, reduce background noise, reduce negative compensatory behaviors, modify the environmental noise, and improve body positioning to optimize posture for respiratory support and speech strategies for dysarthria [30, 31].

Parkinson Disease

Idiopathic Parkinson disease (PD) is a neurodegenerative disorder resulting in motor function impairments and hypokinetic dysarthria, including hypophonia. Voice disorders have been reported in 89% of 200 individuals with PD [32]. Hallmark voice symptoms are reduced vocal intensity, monoloudness, monopitch, increased fundamental pitch, reduced pitch range, breathiness, and hoarseness [32–39]. As the disease progresses, the voice can deteriorate further and some experience onset of tremor [34].

Behavioral therapy, in combination with medical management, has been shown to be the most efficacious method for speech and voice intervention in those with PD [40], with intensive-type therapies having the greatest impact on improving hypophonia [40–42]. One highly efficacious intensive behavioral approach is Lee Silverman Voice Treatment (LSVT), now known as LSVT LOUD® developed by Ramig and colleagues [43, 44]. LSVT is a high-intensity, voice-building regimen that consists of voice therapy 4 days a week for 4 weeks and daily home practice. One simple task of increasing vocal loudness is the primary goal of LSVT. The clinician models the target loudness, shaping as needed to avoid strain or yelling, and provides verbal reminders to "think loud" throughout a prescribed hierarchy of tasks. LSVT has demonstrated immediate pre- and posttreatment improvements in vocal intensity (SPL) [44, 45], 6–7 months posttreatment [46, 47], and 2 years posttreatment [48] in individuals with PD. In addition, a pre-post outcome study found further improvements in intelligibility, articulation, and pitch [49].

SPEAK OUT! ®, similar to LSVT, is an intensive voice therapy regimen based on patient progress, ranging from three times a week for 4 weeks, with prescribed twice-a-day home practice for 25 consecutive days [50]. SPEAK OUT! ® focuses on speaking with intent, including elevated vocal intensity and intonation variability during a series of hierarchical tasks, with prompted cues of "speak with authority," "use your CEO voice," and "say it with gusto" [51]. SPEAK OUT! ®

was found to be an effective treatment for those with hypophonia related to PD in a retrospective study of 78 patients with PD 12 months posttreatment [51] and 3 prospective studies of 12 patients with PD immediately posttreatment [52], 16 patients with PD one to three weeks posttreatment [50], and 6 patients with PD 12 weeks posttreatment [53].

In some cases, those with PD receive DBS to improve tremor, gait, rigidity, and bradykinesia [54]. Despite improvements in global motor limb dysfunction, voice is often negatively impacted following DBS [55–57]. Outcomes of LSVT in combination with DBS have been variable. One study demonstrated improvements in SPL up to 6 months post LSVT [58], whereas another study results were variable, including deterioration in some subjects [59].

When treating patients with PD, clinicians should not ignore the possibility of any concomitant underlying vocal pathology that may also be contributing to the dysphonia diagnosis, such as vocal fold tissue changes and/or maladaptive compensatory behaviors. Additional considerations should be given when selecting an intensive and/or loud voice-building approach in these cases. Further, encouraging an individualized treatment approach including a resonant or elevated airflow approach may aid in maintaining a healthy vocal mechanism and avoid onset of maladaptive compensatory behaviors.

Progressive Supranuclear Palsy

Parkinson plus syndromes encompass progressive supranuclear palsy (PSP) and multiple systems atrophy (MSA), a group of heterogenous neurodegenerative diseases that deviate from idiopathic PD. Due to the similarities PSP and MSA have to idiopathic PD, they are often misdiagnosed as PD. Symptoms of dysarthria and dysphonia in PSP and MSA are increasingly more progressive and severe as compared to PD [60].

Due to the multisystem deficits, there unfortunately is very little literature related to voice therapy for people with PSP. Concomitant symptoms, including gait disturbance, tremor, rigidity, apraxia, aphasia, cortical sensory loss, dystonia, and bradykinesia, tend to present themselves first and often take precedence in treatment over dysphonia. One PSP case study attempted treatment with a delayed auditory feedback device and reported improved loudness, rate, and overall intelligibility [61]. Unfortunately, the subject did not have carry over and was only able to target these improvements while using the device. A case series without statistical analysis was completed on three individuals receiving LSVT therapy, one patient with MSA, Shy-Drager syndrome (SDS), and PSP [62]. The subject with MSA improved initially but declined to worse than pretreatment status 6 months later, and the subjects with SDS and PSP maintained improvements 6 months later. Comparatively, the authors indicated these patients were less successful as compared to those with idiopathic PD. In another study, 16 inpatients with PSP had significant improvements immediately post LSVT treatment; however, improvements were less than those experienced by matched PD controls [45]. Unfortunately, this study only assessed immediate posttreatment and did not assess for maintenance of treatment effects.

Sadly, PSP is often diagnosed late in the disease progression [63], and therapy as it relates to voice does not yield much benefit. In the realm of potential areas to target treatment, typically, dysphagia and dysarthria predominate, with voice addressed as a secondary target, if addressed at all. If voice therapy is pursued, the goal is usually directed at improving quality of life through communicative function, rather than for curative purposes.

Vocal Fold Paralysis/Paresis

Vocal fold (VF) paralysis or paresis is often characterized by abnormal habitual pitch, changes in frequency range, reduced phonation time, strain, and vocal quality changes, including diplophonia, reduced loudness, vocal fatigue, and/or vocal effort [64]. The result of the voice disorder is extremely dependent upon the individual communicative needs and the impact the VF paralysis

or paresis has on glottic configuration. For example, a nonprofessional voice user with a VF paralysis in the median position may not be aware of any vocal limitations due to their low vocal demands. A VF paresis in a paramedian position, in a teacher, may result in a larger vocal deficit with perceptual changes of breathiness, roughness, diplophonia, and vocal effort and fatigue. And finally, reduced vocal fold tension and loss of elongation of the vocal fold during high frequencies, with normal abduction and adduction of the arytenoids in a singer, may be devastating to their career. These patients experience changes in their vocal quality, lower habitual pitch, diplophonia, reduced tone, range, pitch control, loudness, and/or ability to sustain phonation, as well as vocal effort and/or fatigue.

Patients with this voice pathology do well with voice therapy, and as such, it is strongly recommended particularly if glottic closure can be obtained through behavioral voice exercises. Conversely, if no glottic closure can be obtained, therapy should be geared to improve patient complaints of vocal fatigue, effort, and/or strain and provide education and recommendations for communication alternatives and/or aids and as an adjunct to medical/surgical intervention [65–67]. Therapy only has been beneficial in those with a RLN injury [68–70] or SLN injury [71]. In many studies, individuals with VF paralysis who received voice therapy had improved vocal quality and function [68, 69, 72–74] and reduced or eliminated maladaptive behaviors [75]. Additionally, voice rehabilitation should be initiated as soon as possible following the nerve insult [72, 74–78], as it can reduce the rate of voice problems [79], can improve glottic closure, and may reduce glottal insufficiency [74, 80]. Voice therapy should continue until vocal recovery, the patient has satisfaction with current/improving vocal function, or the patient has maximized therapeutic gains.

Voice therapy consists of both indirect and direct therapeutic intervention including explanation of the pathology, how it relates and affects vocal function and efficiency, vocal hygiene recommendations, and specific voice exercises. Voice exercises are individualized to the patient and are geared to encourage optimal vocal mechanics; coordinate respiration, phonation, and resonance; and reduce maladaptive compensatory behaviors.

The following therapy strategies have been used in voice treatment for those with a VF paralysis or paresis: vocal function exercises [71, 74, 78, 81]; pitch glides [69, 76, 82] with semi-occluded vocal tract exercises, including humming, straw phonation, trills [72], and bubbles (i.e., la vox) [69]; resonant voice techniques [69, 74], including forward focus and twang [72]; accent method [72, 74, 80]; and manual circumlaryngeal therapy. The relative effectiveness of each type of therapy has not been specifically studied.

Of note, voice therapy strategies of hard glottal attacks or pushing-pulling strategies are not recommended in an effort to avoid inducing compensatory hyperfunction. However, some studies used these techniques in the short term [74, 80] to encourage further glottic adduction. To avoid inducing supraglottic hyperfunction, these studies monitored use of these techniques through auditory perceptual voice analysis [80] and with endoscopic visualization [74, 80]. However, it is unclear when monitoring occurred during the study.

In cases where medical/surgical intervention is considered, discussion with the patient by the interdisciplinary voice team, including a laryngologist and SLP, is advised. The Clinical Practice Guidelines for Hoarseness published by the American Academy of Otolaryngology – Head and Neck Surgery stated voice therapy is "an important component of any comprehensive surgical treatment of dysphonia" [67]. When glottal incompetency due to VF paralysis or paresis is too significant to overcome with voice therapy only, voice therapy can be an adjunct to vocal fold augmentation [65] or thyroplasty [66]. Patients receiving pre-procedural voice therapy for benign vocal fold lesions with or without post-procedural therapy had statistically improved VHI scores as compared to those who received only post-procedural voice therapy [83]. Pre-procedural therapy provides patient education about voice physiology and surgical

expectations as it relates to their vocal pathology, identifies communication alternatives during periods of voice rest, manages patient expectations of their vocal function and change immediately post-procedure and over time, and provides an opportunity to teach voice exercises to encourage optimal vocal mechanics when phonation is resumed.

Post-procedural care for VF paralysis/paresis is important for voice rehabilitation [68]. Post-procedural therapy should assess patients' communication and vocal function and application of learned voice exercises [75], aid in vocal recovery and improved phonatory efficiency, and avoid and/or eliminate maladaptive compensatory behaviors. Patients often acquired maladaptive behaviors due to presenting pathology; therefore, it is inaccurate to assume that maladaptive behaviors will resolve on their own despite improved glottic closure. Pre- and post-procedural therapy may only require 2–3 sessions if the patient is satisfied following the procedure. However, continued therapy may be warranted if dysphonia persists.

Despite a few studies showing long-term efficacy of voice therapy for those with VF paralysis [72, 76], it is unknown whether vocal improvements were due to voice therapy and neurologic recovery [81] and/or if voice rehabilitation aided in that neurologic recovery. Additionally, there is very limited literature as to what type of voice therapy should be implemented [84, 85], as VF paralysis or paresis can result in different vocal features and impact on each individual. Therefore, voice therapy should be individualized and patient-centered until further research is completed.

Paradoxical Vocal Fold Motion

Clinical studies have demonstrated that behavioral voice therapy in the form of respiratory retraining and rescue breathing techniques are efficacious in the management of paradoxical vocal fold motion (PVFM) [86–88]. Often, by the time a patient sees an SLP, they have been through exhaustive assessment by other specialties and may still be confused as to the nature of their symptoms. The therapy the SLP provides is a notable turning point in the patient's ability to control laryngeal breathing and make gains in resuming activities they had previously avoided. Education on normal respiration, types of breathing patterns (at rest vs exertion), and techniques to incite more control over breathing are primary therapeutic targets. Another key factor is to reduce the potential for an episode of upper airway dyspnea by identifying symptom triggers (such as smells, chemicals, exercise, air temperature, humidity, talking or laughing, postural changes) and avoiding those triggers when possible, to allow the upper airway mechanism an opportunity to desensitize.

When indicated, collaboration with the pulmonologist for adequate concomitant asthma management is crucial [89]. As patients progress through the behavioral treatment, they become adept at distinguishing between breathing symptoms that reflect the asthma diagnosis (chest tightness, chronic dyspnea, wheezing) and the symptoms that are related to PVFM (throat tightness, episodic dyspnea, and occasionally stridor). This helps them be more effective in the choice and implementation of action plans for each disorder [90].

Treatment can include the following:

- Elimination of triggers
- Variations on nasal-oral breathing such as sniff inhale and pursed lip exhale, oral-straw sip inhale and exhale, nasal only inhale and exhale (for patients who are prone to cough on forced exhale or don't report relief with oral resistance exhale)
- Neutral or anterior positioning of the tongue as often patients will report perceived relief of breath restriction
- Voice exercises for laryngeal control and modulation
- Panting gently
- Visual biofeedback
- Pairing nasal inhale-oral gasp

Additionally, it is important to address and improve the multifactorial features of this disor-

der [91–95]. Psychotherapy support can be very worthwhile for stress management intervention and thoroughly addressing the social-emotional triggers of PVFM episodes [86, 96].

Swimmers are a special consideration given that rescue breathing techniques need to be executed orally. Pursed lip or straw sip inhale and pursed lip exhale are beneficial [97].

A more recent treatment approach, albeit somewhat controversial, is the use of inspiratory muscle strength trainer devices [98, 99].

The reader is encouraged to review the reference list for resources as to the specific breathing techniques and options mentioned.

Chronic Cough

Behavioral therapy has shown to be an efficacious treatment for chronic cough (CC) [87, 96, 100–102] and has shown to improve patient quality of life and reduce cough reflex sensitivity [102, 103]. A randomized control study of behavioral therapy administered by an SLP for those with CC had significantly more improvement in symptoms as compared to those who received healthy lifestyle education [104].

The goals of CC therapy are to increase conscious control over cough by reducing the frequency and severity of the behavior and reducing reflex sensitivity and irritation that triggers cough [105]. Chronic cough therapy is most successful with individual buy-in, self-efficacy, and adherence, and therefore, behavioral modification therapy should consist of the following elements as stated by Vertigan and colleagues: (1) Education about the voluntary control over the cough [106] and focus on symptom control rather than looking for a cause. (2) Identify precipitating sensations or warning signals prior to cough onset, followed by a cough suppression strategy or avoidance technique.

Patient education should include information about the laryngeal mechanism and how it relates to the pathophysiology of CC. Often patients will express "why shouldn't I cough if it feels like I have to?" Psychoeducational counseling is important to increase patient adherence, motivation, and awareness. The SLP must reframe the perception that cough is a controllable physiologic response to stimuli that protects the body by expelling material and secretions from the lungs or the airway and explain that there is no physiologic benefit of cough if the airway does not require anything to be expectorated [107]. Further explanation that cough can be both an automatic and controllable response triggered by throat irritation, such as a sensation of mucus, rather than irritation from the lungs and the habitual and cyclical nature of cough on the laryngeal mechanism can cause negative effects, such as laryngeal trauma, exacerbation of irritation, and perpetuation of a coughing cycle [105, 108].

Cough suppression strategies or avoidance techniques for cough can include the following:

- Non-phonotraumatic behaviors, such as a distinct, effortful, and deliberate hard swallow with or without liquids or with a chin tuck
- Nasal-oral breathing variations, such as one or two sniffs followed pursed lip exhale, pursed lip breathing, or relaxed throat breathing
- Laryngeal relaxation techniques, such as semi-occluded vocal tract exercises or resonant voice exercises, specifically humming if the cough is triggered by phonation [107]
- Yawning, whistling, manual circumlaryngeal therapy, and reduction in laryngeal constriction, including developing an awareness of any head, neck, and trunk tension [96, 100, 105, 108–110]

When the act of coughing is unavoidable, then cueing and training to use one or more of the aforementioned replacement strategies are recommended, or a very gentle cough with an open glottis "ha," with the emphasis on the /h/, can be suggested for the interim. These substitute behaviors are intended to distract from the urge or cease the cough while offering an alternative to the chronic impactful behavior of hyperadducting the vocal folds repeatedly during episodic periods of coughing and/or frequent throat clearing throughout the day.

Therapeutic education should also include vocal hygiene education including superficial

hydration, non-mentholated lozenges, and identification of triggers and aggravating factors of cough. Once triggers are identified, they can initially be avoided to enhance desensitization and then gradually be reintroduced pending the patient's success with using a replacement strategy to cease a cough response.

All techniques should be practiced outside of the clinical setting; when asymptomatic and when symptomatic; and can be used in the clinical setting during deliberate exposure to a trigger.

Habitual chronic cough can also manifest in the setting of a cough induced by other etiologies, such as upper airway cough syndrome, laryngeal neuropathy, gastroesophageal reflux disease/laryngopharyngeal reflux disease, asthma, non-asthmatic eosinophilic bronchitis, cardiovascular disease, chronic obstructive pulmonary disease, and/or obstructive sleep apnea. Therefore, CC therapy in conjunction with medical and pharmaceutical treatment may be advantageous to eliminate any co-occurring habitual cough to provide additional symptom relief.

Cough suppression therapy delivered by the SLP is an effective treatment modality and should be considered in the multidisciplinary treatment protocol and as an adjunct to medical care to optimize patient outcomes, provide much needed relief, and restore an improved quality of life.

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Swallow Therapy

33

Linda M. Rowe and Michelle R. Ciucci

Introduction to Treatment

The development of an appropriate treatment plan for patients with neurolaryngeal swallowing disorders begins before the clinician enters the patient's room. Prepared with data from a thorough chart review, interdisciplinary communication, and background knowledge of relevant pathophysiology, the clinician forms hypotheses regarding likely sensorimotor deficits that are causing the physiologic consequence of dysphagia. The same hypothesis-driven, evidence-based approach to evaluation should also guide treatment.

Underlying impairments may be related to deficits in sensation, movement (strength, range of motion, coordination), sensorimotor integration, or airway protection. Treatment relies on a comprehensive evaluation, including thorough chart review, patient/caregiver interviews, analysis of sensory and motor function (cranial nerve examination), clinical swallowing assessment, airway assessment, and instrumented diagnostic examination such as videofluoroscopy, fiberoptic endoscopic examination of swallowing, or high-resolution pharyngeal manometry. Determination of the most critical underlying impairments to target for management will vary with etiology, but care should always be taken to address deficits in the context of patient and caregiver goals. The objective of swallowing treatment is to improve and/or to compensate for underlying impairments in order to optimize (or, more often, balance) safety and quality of life.

This chapter will cover common management approaches for dysphagia, as they relate to laryngeal impairment. We encourage the reader to review the other chapters relevant to anatomy and neurophysiology related to laryngeal function, especially with regard to swallowing. Because anatomy and physiology are covered in Chaps. 1 and 2, we are highlighting respiratory-swallow coordination, as this is impaired in many conditions. Basic background on breathing and swallowing central pattern generators (CPGs) is provided. Next, we discuss common neurologic diseases that affect sensory and motor functions of the larynx. We end this chapter with treatment options.

Respiratory-Swallow Coordination

The larynx is a complex organ involved in many overlapping and sometimes competing behaviors (see review by McCulloch et al. 2011) [1]. The

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most critical function is as an upper airway valve in the aerodigestive tract, with shared neural substrates for coordinating tidal breathing, swallowing, respiratory phase resetting, cough, and Valsalva to optimize airway protection. Integration of these processes is achieved via oppositional gating of excitatory and inhibitory input to central pattern generators (CPGs) in the brainstem [2]. The dorsal respiratory group (DRG) in the medulla and pons is a crucial region for inhalation. The ventral respiratory group (VRG) in the medulla is considered the expiratory center and includes the nucleus ambiguus and a cluster of interneurons called the pre-Bötzinger complex, which sends rhythmic output to the diaphragm and hypoglossal nucleus [3]. The respiratory CPGs have reciprocal connections to the swallowing CPGs: nucleus tractus solitarius and nucleus ambiguus (for details, see Chap. 28, Laryngeal Diversion Procedures). Importantly these swallowing CPGs use ongoing sensory feedback to elicit pharyngeal swallowing, which includes elevation and closure of the larynx and coincides with cessation of breathing (described below). Oropharyngeal swallowing is a rapidly occurring activity (700 ms), and timely closure of the larynx during the appropriate period in the respiratory cycle is important for airway protection.

In tidal breathing, the tongue and pharynx optimize airway patency, and the diaphragm and intercostal muscles contract and relax to alter the volumetric properties of the pleural cavity, which induces respiration via pressure differential [4]. Coordinated activation of upper and lower airway functions is achieved through central integration of afferent signals from several receptor types with specific sensitivities and conduction thresholds (Table 33.1 for a summary of lower airway sensory fibers [5–7]). Mechanoreceptors, such as slowly adapting receptors (SAR) innervating the lower airway and visceral chemoreceptor and baroreceptors, project to the brainstem, where regions in the medulla and pons regulate responses. Some responses are deeply reflexive – for example, the Hering-Breuer reflex which prevents overinflation of the lungs – while others are partly reflexive, and partly under volitional control, as in the case of apnea. The onset, duration, and offset times of the apneic period of the swallow (i.e., "swallow breath") are a critical component of airway protection.

When a bolus or aggregated secretions are sensed in the posterior oropharynx, a swallow is triggered, and the apneic period (defined by duration of glottal closure and cessation of respiration) can occur during any point in the respiratory cycle. Normative data show that healthy individuals typically exhale after single swallows [8]. The volume of air in the lungs prior to swallow initiation is larger for liquids than for solids [9]. The volume exhaled post-swallow is dependent on lung volume prior to swallow initiation, and apneic period duration may vary with bolus volume in single sips [10]. Swallow apnea is followed by hyolaryngeal elevation in healthy individuals [4]. Even in patients who have undergone total laryngectomy, the same apnea pattern is preserved, indicating that glottal closure and breathing cessation are related but independent functions [11].

Several conditions can alter the typical swallow-exhale pattern of respiratory-swallow coordination in a healthy system. For example, in sequential swallows, which demand a prolonged apneic period, approximately 80% of healthy individuals exhale after the swallow, and 20% inhale after the swallow [12, 13]. With aging, there is greater heterogeneity of normal patterns (inhale-exhale, inhale-inhale, exhale-exhale, exhale-inhale), as well as alteration of apnea duration and offset [13]. Despite these normative data being collected in persons without a history of dysphagia or aspiration, it is thought that a swallow-inhale pattern may predispose these individuals to aspiration events [14, 15]. As such, assessment of respiratory-swallow coordination, typically with instrumented evaluation, is crucial for appropriate management.

Impaired Respiratory-Swallow Coordination

Impaired respiratory-swallow coordination can be caused by a variety of underlying deficits,

Table 33.1 Characteristics of lower airway sensory fibers [5–7]

	C-fiber	Widdicombe "cough receptor"	Rapidly adapting receptors (RAR)	Slowly adapting receptors (SAR)
Location	Bronchopulmonary; airway epithelium, airway wall effectors	Extrapulmonary airway (trachea, main stem, segmental bronchi). Airway mucosa, between epithelium and smooth muscle	Intrapulmonary airways (possibly within/beneath epithelium)	Peripheral intrapulmonary airways (alveoli, bronchioles)
Myelination	Unmyelinated	Myelinated	Myelinated	Myelinated
Axon conduction velocity (m/s)	< 2	5	≥ 15	≥ 15
Reflex involvement; physiology	Cough reflex, apnea, airway mucous secretion, bradycardia	Cough reflex, apnea, airway mucous secretion, bradycardia	Active during dynamic inspiratory phase of respiration; gasp reflex, modulate inspiratory volume/rate, airway mucous secretion	Constituently active during respiration; Hering-Breuer reflex, tachycardia
Receptor type	Nociceptor	Mechanoreceptor	Mechanoreceptor	Mechanoreceptor
Sensitivity (general)	Bradykinin, ion channel activators, TRPV1 (e.g., capsaicin, protons), TRPA1 (e.g., ozone)	Mechanical stimulation; protons (acid-sensing ion channels)	Mechanical stimulation, spasmogens, autacoids; ATP, adenosine, neurokinin A, substance P	Mechanical stimulation; sustained lung inflation/distension
Sensitivity (specific)	Prostaglandin E2, ozone, nicotine, adenosine, serotonin	Punctuate mechanical stimulation, low pH	Punctuate mechanical stimulation, bronchospasm, lung collapse, negative intraluminal pressures	Stretch mechanical stimulation, sustained lung inflation, hypercapnia
Insensitive to	Mechanical stimulation	Chemical irritants (e.g., capsaicin), spasmogens, autacoids; e.g., ATP, adenosine, neurokinin A, substance P	–	–
Inhibitors	Capsaicin desensitization, neurokinin receptor antagonists, local anesthetics, ion channel blockers	Local anesthetics; Cl- channel blockers, Na+/K+ ATPase inhibitors	Integrated sensory signals from NTS; phasic (glycine) and tonic (GABA) inhibition during inspiration	Integrated sensory signals; hypercapnia inhibition of Hering-Breuer reflex

ATP adenosine triphosphate, *NTS* nucleus tractus solitarius

including alterations in oropharyngeal or laryngeal sensation, intrinsic and extrinsic laryngeal muscle function, and lesions affecting sensorimotor integration in the central nervous system. The timing and coordination of airway protection and swallow is crucially dependent on accuracy and efficiency of sensation. Below, we will discuss disease-specific factors related to impaired sensorimotor function in neurodegenerative diseases (Figs. 33.1 and 33.2 *and* Table 33.1) [16].

Many diseases/conditions are associated with dysfunctional respiratory-swallow patterns, such as "swallow-inhale" patterns, including chronic obstructive pulmonary disease (COPD), Parkinson disease (PD), head and neck cancer, cerebral palsy, and stroke [17–20]. This aberrant patterning is thought to increase vulnerability to

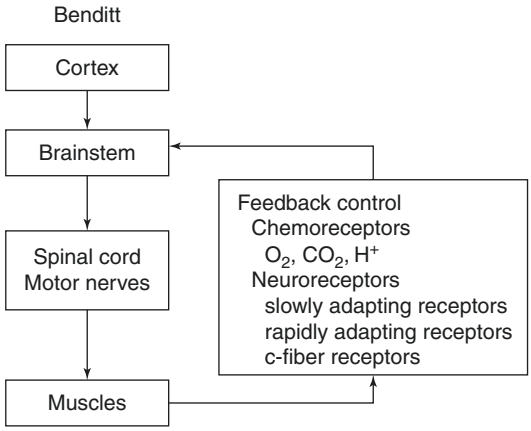

Fig. 33.1 The two major effects of neuromuscular disease on the respiratory system. (From Benditt [16], with permission)

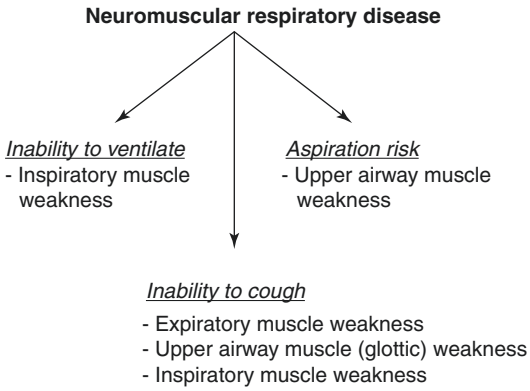

Fig. 33.2 Schematic of respiratory system, including controllers, effectors, and receptor feedback inputs. (From Benditt [16], with permission)

airway invasion through inhalation of post-swallow residue, which may elevate risk of aspiration pneumonia [21]. In addition to abnormal breathing-swallowing patterns, there are also other abnormalities such as the duration of swallow apnea. For example, in patients with amyotrophic lateral sclerosis (ALS), there is a prolonged apneic period during water swallowing [22]. Similarly, a prolonged swallow apneic period was found in patients with stroke that aspirate (versus non-aspirators). Interestingly, stroke patients who aspirate had an apneic period that is twice as long compared to healthy controls. This occurred across the majority of liquid bolus volumes and solid textures trialed [23]. In PD, aspiration is associated with inhalation after swallow and shorter apneic period [20].

Effects of Neurologic Disease on Laryngeal Sensorimotor Function

Safe and efficient swallowing relies on intact sensory and motor functioning. Naturally, any disease/disorder/condition/surgery that disrupts these functions along the afferent or efferent (or both) pathways will affect laryngeal physiology, including airway protective maneuvers such as throat clearing and cough [24–26]. Understanding the presenting etiology will then help the clinician to make informed predictions about how these conditions will affect laryngeal sensorimotor control and how the specific dysphagia will present.

Swallowing Deficits Observed in Testing

One of the most difficult aspects of swallowing treatment is that often the impairments (e.g., silent aspiration, laryngeal penetration, weakness in pharyngeal constriction, post-swallow residue, premature bolus spillage into oropharynx) are not visible to the patient, caregiver, or clinician. If a patient is in the early stages of swallow function decline, has not yet suffered deleterious effects such as pneumonia, or has altered sensory processing and is thus not sensate to penetrants or residue, it can be difficult to explain future risks and justification of recommendations. Impairments identified in diagnostic imaging will be helpful both for educating patient/caregivers of underlying deficits and triaging sensory and motor aspects of the swallow to target. Please see Table 33.2 for a reference of deficits on instrumented examination per common neurogenic condition [26–33].

Table 33.2 Deficits on instrumented examination per common neurogenic condition [26–33]

Pathology	Oral	Pharyngeal	Esophageal
Amyotrophic lateral sclerosis	Tongue fasciculation, lingual and palatal weakness, reduced mastication	Delayed swallow trigger, disordered and eventually absent volitional swallow	Hyper-reflexive and hypertonic CP, loss of coordination with voluntary swallow and laryngeal protection, nasal regurgitation during swallow
Parkinson disease	Impaired tongue and jaw movement, lingual pumping, drooling or dry mouth, reduced bolus control, delayed swallow onset, oral residue	Delayed swallow onset, reduced hyolaryngeal elevation and pharyngeal peristalsis, valleculae and pyriform sinus residue	UES relaxation dysfunction, reduced esophageal peristalsis, gastroesophageal reflux
Multiple sclerosis	Reduced lingual bolus control, reduced tongue base retraction	Delayed swallow trigger, reduced laryngeal closure and pharyngeal contraction	Reduced UES compliance
Huntington disease	Mandibular rigidity, disorganized tongue movement	Delayed swallow reflex, solid food residue in valleculae and pyriforms, spillage pre-post swallowing, irregular VP contractions	UES dysfunction
Myasthenia gravis	Delayed bolus formation and slow transit, piecemeal deglutition	VF paresis, aspiration especially liquids, delayed swallow initiation, reduced tongue base retraction, reduced epiglottic mobility, weak pharyngeal constriction	CP function typically normal
Advanced dementia	Impaired preoral phase (appetite and self-feeding), oral stasis, oral transit delay >5 sec, perseverative mastication, overfilling mouth, inattention to bolus, impaired tongue base retraction	Significant delay in swallow onset, impaired hyolaryngeal excursion and epiglottic inversion, silent aspiration	Impaired UES opening

CP chricopharyngeus, *UES* upper esophageal sphincter, *VP* velopharynx

Intervention: General

As mentioned in the introduction to this chapter, the objective of swallowing treatment is to improve and/or to compensate for underlying impairments, in order to optimally balance safety and patient quality of life. This involves merging clinician knowledge of underlying disease pathology with the patient's dynamically changing medical status, swallowing function, and personal goals. In the sections below, we will discuss factors impacting intervention, general and disease-specific compensatory strategies, sensory and motor exercises, and surgical interventions for neurolaryngeal swallowing dysfunction.

Information obtained from videofluoroscopy, fiberoptic endoscopic examination of swallowing, high-resolution manometry, and pulmonary and cough testing will serve as the basis for recommendations, in conjunction with other factors discussed below. Importantly, neurogenic disease may have a variable time course and be affected by medications. There may be multiple areas where impairment is identified; however, the prudent clinician will tailor therapy to target primary deficits most significantly impacting patient risk, in the context of patient's overall fatigue, social support, cognitive level, and motivation to perform exercises and compensatory strategies.

Disease Progression

The rate of progression, central and peripheral pathways affected, and current status of swallowing and airway protection mechanisms are all crucial elements of the treatment plan. Typically, clinicians assess these factors using a combination of chart review and clinical (bedside) or diagnostic imaging evaluations. However, there may be times during initial or follow-up assessments when more subtle signs and symptoms are missed, which could indicate a change in function. For example, a patient may report swallowing is "the same" but may have a recent history of modifying textures, taking smaller boluses, or swallowing pills differently. Previously recommended modifications and strategies may not be as effective. It is helpful to ask family and caregivers if they have noticed any differences as well. Many neurologic diseases can affect sensation and/or cognition, which may alter a patient's perception or recall of potential aspiration/penetration events; additionally, self-reporting systems may not consistently correlate with aspiration events observed in diagnostic imaging [34, 35].

Impact of Other Diagnoses

While specific impacts of neurogenic disease on swallowing function and airway protection may be our focus here, it is important to consider the patient in the context of their other diagnoses, which may inhibit use of certain treatments. For example, a patient with a history of cardiopulmonary disease, chronic obstructive pulmonary disease, and smoking may have difficulty generating sufficient subglottic pressure for a hard cough, desaturating oxygen levels, or increased respiratory rate during the meal [36]. A patient with upper extremity tremor/weakness may have difficulty acquiring a liquid bolus and risk premature spillage into the pharynx leading to aspiration before the swallow is triggered [37]. Patients with gastroesophageal reflux disease (GERD) may need additional positioning precautions or adaptations to exercises. Other diagnoses can also affect a person's ability to self-feed, maintain mealtime endurance, and tolerate an upright position among others. Unfortunately, the list of potential complications can become complex quickly.

Interdisciplinary Care: A Team Approach

An interdisciplinary approach to care may include nutrition, physical therapy, respiratory therapy, occupational therapy, gastroenterology and otolaryngology, and head and neck surgery specialists, among others. Nutritionists are able to calculate a patient's daily energy requirements by adjusting for factors such as metabolic status, energy expenditure (which may be elevated in spasticity-type diseases such as multiple sclerosis [MS] and ALS), and change in ambulation level [38]. Occupational therapy is imperative for patients with spasticity, weakness, or discoordination, who benefit from adaptive equipment to facilitate self-feeding. Such interventions that enable oral intake have been demonstrated to improve nutritional intake and quality of life in patients with Alzheimer disease, Multiple Sclerosis, motor neurone disease, and other neurogenic impairments [39–41]. Physical therapists are an excellent resource for patients with upper airway constrictor weakness (pharynx, larynx) and reduced trunk support, to improve postural stability during oral intake and efficiency of airway protection attempts [42, 43].

Patient and Caregiver Goals

Finally, jointly developing short- and long-term goals with the patient and caregivers is an essential component to treatment. Involving caregivers is particularly important when a patient's cognitive status affects their self-efficacy or accuracy in performing recommended exercises and precautions. Information regarding the patient's current and anticipated functional status, and potential risks, must be conveyed in a way that is comprehensible for all parties. Patient motivation and education are crucially important for setting realistic, achievable goals and for increasing

follow-through with therapeutic recommendations by virtue of a shared knowledge of rationale. Transparent, concrete goals help to promote rapport and reduce patient anxiety and frustration [44]. Ultimately, the aim is to provide sufficient education regarding effects of disease on swallowing/airway protection, anticipated functional decline, and options for intervention, such that patients can make informed decisions about their future oral or non-oral means of intake.

Intervention: General Compensatory Strategies

Overview

In order to compensate for impaired biomechanics, current practice engages several strategies to alter bolus kinematics through direct modification of texture, head position and swallowing maneuvers for bolus propulsion, as well as behavioral techniques to enhance oral and pharyngeal clearance of material. Depending on the individual patient's underlying physiology, specific deficits, nutrition/hydration demands, and personal goals, different combinations of strategies described below can be useful in facilitating optimal oral intake.

Texture Modification

One of the most common interventions in swallowing disorders is the modification of food and liquid textures in order to compensate for underlying sensory/motor deficits and improve safety of oral intake. The International Dysphagia Diet Standardization Initiative (IDDSI) was recently founded to standardize terminology and define parameters of solid food qualities (e.g., hard, cohesive, slippery) and liquid viscosities [45, 46]. Based on a patient's overall presentation and most salient difficulties in deglutition, a clinician can trial different consistencies and identify an optimal texture and viscosity to reduce the patient's risk of aspiration. The IDDSI pyramid is shown in Fig. 33.3. It demonstrates that as one moves down in the hierarchy, the solid consistencies are progressively more easily masticated and swallowed. Similarly, progressive thickening of liquid viscosities from 0 (water) to 4 (thick puree) allows for more time for patients to coordinate bolus control [46].

The literature generally agrees that thickened liquids prolong phases of the swallow and reduce aspiration events on diagnostic imaging evaluations [45]. However, thickened liquids are also correlated with deleterious effects, such as dehydration, reduced quality of life, urinary tract infection (UTI), and pharyngeal residue – which itself increases the risk of aspiration on subsequent swallows [21]. It is suspected that individuals with a swallow-inhale pattern may be predisposed to post-swallow aspiration of residue [14, 15]. Additionally, while many studies attempt to objectively quantify biomechanics of liquid swallows within a single videofluoroscopy session, few studies provide a longitudinal analysis to understand efficacy of prolonged use of thickener. One study conducted by Robbins et al. (2008) randomized patients with dementia or PD into three intervention groups: chin tuck with thin liquid, chin neutral with "nectar thick" liquid, and chin neutral with "honey thick" liquid. They found that at 3 months of follow-up, there was no significant difference in incidence of pneumonia between thin versus thickened conditions. However, there was a greater incidence of fever, UTI, and dehydration in the thickened liquid groups compared to thin with chin tuck [47]. Ultimately, the long-term biological, physiological, and systemic effects of thickener are not yet known.

Frazier Free Water Protocol

The Frazier Free Water Protocol is a procedure in which a patient can consume thin water between meals using recommended swallowing maneuvers and practicing aggressive oral care. However, they must continue to adhere to thickened liquids for mealtimes (Panther, 2005). This protocol has been implemented with dysphagic patients to improve hydration, with the rationale that pure, thin water contains fewer pathogenic bacteria and

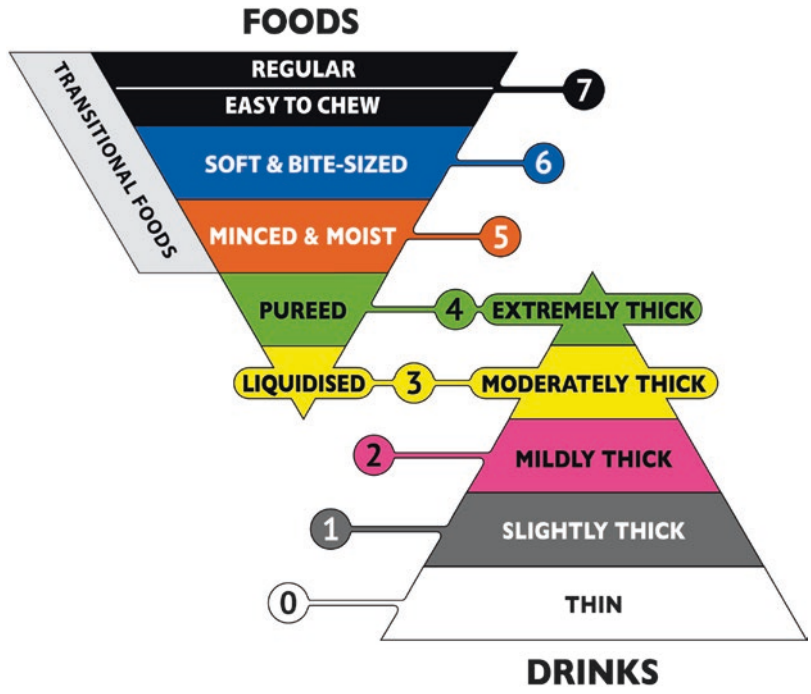

Fig. 33.3 Visual representation of solid and liquid texture hierarchy. The IDDSI framework. (© The International Dysphagia Diet Standardization Initiative 2016 @https://iddsi.org/framework/, with permission; The IDDSI Framework and Descriptors are licensed under the Creative Commons Attribution-ShareAlike International 4.0 License https://creativecommons.org/licenses/by-sa/4.0/legalcode. Attribution is NOT PERMITTED for derivative works incorporating any alternations to the IDDSI Framework that extend beyond language translation. Supplementary Notice: Modification of the diagrams or descriptors within the IDDSI Framework is DISCOURAGED and NOT RECOMMENDED. Alterations to elements of the IDDSI framework may lead to confusion and errors in diet texture or drink selection for patients with dysphagia. Such errors have previously been associated with adverse events including chocking and death)

can be absorbed from the lungs to the bloodstream in small amounts [48, 49]. However, there are several contraindications to the Frazier Free Water Protocol per recent systematic reviews. Recommended exclusionary criteria include neurodegenerative disease, immobility, respiratory compromise, medical instability, and impaired cognition [50].

Swallowing Maneuvers

Table 33.3 lists common swallowing maneuvers that we train patients to use during the swallow to increase swallow efficiency and reduce risk of aspiration/penetration events [51, 52]. Choice of maneuver(s) is tailored to overcome or mitigate underlying impairments in physiology. Most maneuvers target glottal closure and/or bolus propulsion by affecting timing and relative anatomical position of swallowing structures to compensate for underlying deficits. In addition to Table 33.3, training patients with biofeedback and explicit cueing (faded to autonomous) for swallowing mid-exhale and exhaling after the swallow has been shown in the head and neck cancer population to improve laryngeal vestibule closure, base of tongue retraction, and pharyngeal residue, as well as penetration/aspiration score [18]. Training in performing an exhale-swallow-exhale pattern may be beneficial for patients with uncoordinated laryngeal movements or reduced respiratory support in neurogenic disease. Identifying a swallowing maneuver that effectively and consistently improved function may circumvent the need for imposing restrictions on diet textures and liquid

Table 33.3 Common swallowing maneuvers to increase swallow efficiency and reduce risk

Technique	Performance	Intent	Physiology	Outcomes
Side-lying	Lie down with stronger side lower	Slow bolus Provides time to adjust and protect airway	Emphasizes pharyngeal constriction	Less aspiration
Chin-up	Elevate chin	Propel bolus to back of mouth	Widens oropharynx Increases PES pressure	Better oral transport
Chin-down	Lower chin	Improves airway protection	Narrows oropharynx	Reduced aspiration
Head-turn	Turn head to right or left	Reduces post-swallow residue and aspiration	Redirects bolus to stronger side of the pharynx Lowers PES pressure	Increased amount swallowed Less residue and lower risk of aspiration
Supraglottic swallow	Hold breath, swallow, cough gently	Reduces aspiration by increasing glottal closure	Horizontal glottal closure Increased movement of swallowing structures	Reduced aspiration Increased laryngeal excursion
Super-supraglottic swallow	Hold breath, bear down, swallow, cough gently	Reduces aspiration by increasing glottal closure	Horizontal and anteroposterior glottal closure Increased movement of swallowing structures	Reduced aspiration Increased laryngeal excursion
Mendelsohn maneuver	Squeeze swallow at apex	Improves swallowing coordination	Increased and prolonged hyolaryngeal excursion Improves UES opening and bolus flow [52]	Improved swallowing coordination Less post-swallow residue Less aspiration
Effortful swallow	Swallow harder	Increases lingual force on bolus	Increased tongue-palate pressures Increased duration of swallow Increased tongue base movement	Less residue

From Groher and Crary [51], with permission
PES pharyngoesophageal sphincter, *UES* upper esophageal sphincter

viscosity, which could have an impact on nutrition/hydration status and quality of life.

Behavioral Feeding Techniques

As mentioned above, solid foods follow a diet texture hierarchy, reflected on the IDDSI as an increase from uniformly smooth puree up to challenging textures that require significantly more mastication to form a cohesive, digestible bolus. During oral preparation, the bolus undergoes a physical and chemical breakdown, augmented by saliva for reduction of friction and promotion of bolus cohesion [53]. Local mucosa of the upper aerodigestive tract is also important for appropriate sensation and clearance of material. Many of the behavioral feeding techniques for solids are compensating for impairments in bolus formation (affecting pharyngeal clearance) or reduced coordination of breathing and swallowing due to impaired respiratory capacity, or sensorimotor processing.

Protecting the airway during liquid swallows is a primary aspect of care in neurolaryngeal dysphagia. As mentioned above, several common interventions include thickening liquids and training patients in swallowing maneuvers to optimize airway protection (e.g., chin tuck, Mendelsohn maneuver). In terms of

Table 33.4 Common behavioral feeding strategies to increase swallow efficiency and reduce risk

Bolus type	Techniques	Description	Target effect
Solid	Slow rate Texture–appropriate bite size Extra sauce/moistening agents	Allow longer time for mastication, process one bite at a time Reduce volume of challenging textures to ensure chewing, lingual coordination, and salivary qualities adequate for mastication	Adequate bolus cohesive and adhesive qualities to optimize oropharyngeal clearance
	Self-pacing Imposed breaks Liquid wash Dry swallows	Monitor respiratory rate and O2 saturation (pulse-ox) during meal to identify frequency and duration of respiratory recovery breaks Alternate solids and liquids to achieve oral and pharyngeal clearance of bolus and residue Nonliquid (saliva) swallows (i.e., lingual sweep-reswallow) to clear residue	Compensate for impaired respiratory support to reduce risk of desaturation or aspiration of pharyngeal residue Pacing and dry swallows also helpful to improve esophageal transit for patients with GERD
Liquid	Single sip No straws (cup rim only)	No sequential sip bursts Patient restricted from drinking by straw due to elevated demand on respiratory coordination. May sip from cup rim or adapted cup. Typically combined with single sip precaution	Respiratory support inadequate for prolonged apnea or elevated demand on respiratory-swallow coordination

GERD gastroesophageal reflux disease

feeding-related strategies, the goal for the oral phase is to improve control of a rheologically challenging bolus (liquid) to reduce risk of premature spillage into the airway prior to swallow initiation (see Table 33.4). The goal for the oropharyngeal and pharyngeal phases is to improve the timing and duration of airway closure to improve airway protection during the swallow. Single sips are recommended over consecutive bursts, and cup rim over straw, due to the elevated physiological demand for coordination of breathing and swallowing [54]. OT can be an excellent resource for identifying adaptive equipment to improve upper extremity stability bringing cup to mouth for bolus acquisition, as well as cups modified to restrict maximum bolus size for patients with difficulty self-regulating (Table 33.4).

Intervention: Exercises

Overview

The basic components of functional movement are appropriate strength, range of motion, and coordination to execute motor plans and achieve a goal. In neurogenic diseases, any aspect of this can be compromised: atrophic changes to muscle fibers or altered neuromuscular junction morphology affecting peripheral contraction, lower motor neuron dysfunction, upper motor neuron dysfunction, damage to the brainstem (e.g., lesion of nucleus tractus solitarius) affecting motor plan of the CPG itself, and other central nervous system cortical and subcortical control. Often with neurodegenerative diseases such as Multiple sclerosis, Huntington disease, and Alzheimer disease, the goal is not necessarily to make significant gains in function, but to maintain function for as long as possible. Knowledge of underlying pathophysiology will help the clinician identify appropriateness, frequency, and intensity of exercises to improve swallow function. Understanding disease progression is also important for identifying when it is contraindicated to continue with physiological exercises and transition to more compensatory strategies to optimize safety and intake [27]. As always, we must also keep in mind the role of sensory processing in appropriate muscle contraction.

Swallowing Exercises

Swallowing exercises relevant for the oropharyngeal and pharyngeal phases of swallowing are listed in Table 33.5 [55]. Of note, it is generally inadvisable to perform swallowing exercises with a bolus, due to the increased demand and potential for discoordination and subsequent aspiration of material. Several of these are described above as compensatory maneuvers for laryngeal motor impairment, but repetitions/sets are also prescribed clinically as exercise. With a few exceptions, the majority of swallowing and voice exercises have varying, or not well-described, recommendations regarding optimal effective dose (i.e., frequency, intensity, duration). Most dose recommendations are based on literature from studies on skeletal muscle of the limbs; however, limb and cranial skeletal muscles have very different properties and may not respond the same way to exercise [56, 57]. Translational research is currently being conducted into the biological, physiological, and functional response of cranial skeletal muscles to voice and swallowing exercises [58–61]. Table 33.5 contains doses only for extant described programs [55].

Laryngeal Closure and Range of Motion

Several of the exercises in Table 33.5, including supraglottic swallow, super-supraglottic swallow, and Mendelsohn maneuver, are targeting intrinsic laryngeal strength/range of motion/coordination for glottic closure. There is also overlap with respiratory exercises described below. Voicing exercises that target vocal fold adduction for coordination and strength include maximum phonation time (MPT) exercises, vocal function exercises (VFE; VF warm-up, stretching, contracting, and low-impact adduction exercise), hard glottal attack, and "pushing" and "pulling"

Table 33.5 Exercises to increase strength, range of motion, and coordination of the pharyngeal phase of swallowing

Swallow type	Directions	Targets
Supraglottic	Hold breath, swallow, cough gently	Horizontal glottal closure, laryngeal ROM
Super-supraglottic	Hold breath, bear down as if about to lift something heavy, swallow, cough gently	Horizontal and AP glottal closure, intrinsic laryngeal strength and ROM
Mendelsohn	Swallow and squeeze muscles to hold larynx at the apex	Increased and prolonged hyolaryngeal excursion, swallow coordination
Effortful	Swallow hard, as if you are trying to swallow down a big pill or a golf ball	Lingual force for bolus propulsion, tongue-palate pressure, and base of tongue movement
Masako (tongue-hold)	Protrude tongue and gently hold it in place with teeth, swallow with tongue protruded	Anterior movement/increased contraction of the posterior pharyngeal wall (base of tongue to posterior pharyngeal wall is important for bolus propulsion)
Shaker	Lie supine and lift head off of the mattress high enough to be able to see your toes, without lifting shoulders off of the mattress. Hold for 1 minute. Rest for 1 minute. Repeat hold and rest 2 more times. Then perform same maneuver in sort lift repetitions (1–2 sec holds) × 30 reps *Modifications:* For patients with positioning restrictions, chin tuck against resistance (CTAR) in which a patient is seated with an inflatable rubber ball tucked under their chin and compresses the ball as hard as possible for × 30 reps per set and 3 sets/day [55]	Increase anterior laryngeal movement, increase AP diameter opening of UES

ROM range of motion, *AP* anteroposterior, *UES* upper esophageal sphincter

while phonating to increase glottal closure [62, 63]. Generally, laryngeal closure is targeted in a functional activity, leveraging the neuroplasticity concept of activity-specific activation of neural substrates [64].

Respiratory

Neurogenic diseases can have profound effects on respiration, and the efficiency of airway protection in this population has been correlated with risk of aspiration and severity of dysphagia [24, 65–67]. Aspiration itself can have deleterious effects on the respiratory system, including inflammation and atrophy to the thyroarytenoid and diaphragm muscles, which may further weaken cough force [68]. Additionally, sleep-disordered breathing (including obstructive and central sleep apneas, chronic hypoxia) is common in neuromuscular diseases and can affect functional capacity for exercise, reduced pulmonary performance, and daytime fatigue [69].

Inspiratory and expiratory muscle strength trainings (IMST, EMST) are regimented paradigms in which resistance is applied against patient inhalation and/or exhalation in order to improve contractile strength of respiratory muscles and potentially cortical plasticity [70]. Many studies have identified positive effects of IMST/EMST in neurogenic diseases, including PD, MS, ALS, and stroke [71–75]. Outcomes include improvements in inspiratory/expiratory muscle strength, reduced fatigue, longer survival times, and reduced frequency of respiratory complications.

In addition to respiratory muscle strength and efficiency, exercises specifically targeting coordination of breathing and swallowing demonstrate effective improvements in improving swallowing kinematics. Although analyzed in a different population, recent work applying respiratory-swallow therapy (RST) to head and neck cancer patients with oropharyngeal dysphagia has shown significant improvements in laryngeal vestibule closure, tongue base retraction, pharyngeal residue, and PEN-ASP scores [18]. The program specifically trains patients to swallow during the exhale using biofeedback, with improvements in respiratory-swallow coordination maintained at 1-month follow-up. Given known impairments in optimal phase resetting for the neurogenic population (swallow-inhale pattern), RST may be a promising route for reducing aspiration.

Velopharyngeal Closure

Closure of the velopharyngeal (VP) port requires adequate range of motion for palatal elevation and coordination in timing of the pharyngeal components of the swallow. VP closure serves as a valve to obstruct flow of air, liquid, or solids from passing to or from the nasal cavity. Deficits could result in nasal regurgitation, reduced bolus propulsion through naso- and oropharynx, and post-swallow residue. VP closure can be affected by elements of cortical, upper motor neuron, and lower motor neuron impairments in a neurodegenerative diseases and sequelae (e.g., obstructive sleep apnea), including progressive supranuclear palsy, ALS, stroke, and PD [76–78]. Please refer to Chap. 7, Evaluation of Swallow, regarding more specific function and treatment of the soft palate.

Intervention: Sensation

The goals of intervention targeting laryngeal sensation are to improve or to compensate for impaired perception of residue and infiltrates. You may observe that a patient has an audible wet vocal quality, without independent attempts to clear. Cueing the patient to cough, assuming this is effective enough to clear, will likely demonstrate little carryover beyond that moment. Increasing self-monitoring for airway protection will rely on explicit identification of multisensory biofeedback to improve awareness of residue/infiltrates. For example, you might ask the patient the following:

- Can they feel it, even if no urge to cough?
- Can they hear it (wet-sounding quality on breathing or vocalization)?
- Can they clear it on their own power with hard cough or hard throat clear reswallow?
- Can they hear/feel difference now?

A recent study targeting upregulation of reflexive and voluntary cough in the PD population identified increased efficiency of airway protection with modulated (participant-blinded 25% increase in baseline average peak expiratory flow rate) visual and verbal biofeedback [79]. Therapy incorporating explicit identification of alternative sensory information may therefore facilitate improved airway protection and reduced risk of aspiration.

Sensory Exercise

Mechanoreceptor activation related to increased airway pressure may therefore be a potential avenue of treatment to improve laryngeal sensation for airway protection. Exercises using thermal, tactile, and gustatory stimulation have been demonstrated to improve initiation of oropharyngeal swallow [80]. Increasing sensory information for swallow initiation (with gradual reduction of stimuli) may improve timing and coordination of swallow central pattern generators for reduced risk of silent aspiration in pharyngeal phase. Sensorimotor integration is also crucial for airway protection. Although there are many studies exploring cough reflex testing with noxious stimuli (e.g., aerosolized capsaicin), relatively few discuss exercises for rescue. A recent study demonstrated that through verbal cueing and visual biofeedback, subjects with PD and age-matched controls were able to upregulate both reflexive and voluntary cough efficiency [81].

Sensory Compensations

Feeding techniques to compensate for impaired laryngeal sensation similarly include boluses with added element of simulation (e.g., hot or cold, sour, carbonated) to amplify afferent signaling of bolus throughout the aerodigestive tract. Compensatory techniques for impaired laryngeal sensation are generally intended to elicit a relatively spared swallow CPG through increased bolus awareness before, during, and after the swallow. In advanced cases of neurodegenerative disease, where motor and/or cognitive functions are affected such that sensory exercises are not sufficient to maintain or improve function, alternative compensatory strategies can be engaged to optimize nutritional intake.

Techniques leveraging increased sensory stimulation to improve mastication and swallow onset time include alternating temperatures/tastes, sour bolus, and increased pressure with utensil when administering bolus (mechanical sensory input). With patients for whom volitional control and cognition are significantly affecting coordination of deglutition, explicit, highly automatic cues and biofeedback techniques may improve elicitation of mastication and swallowing [82]. Such cues may be helpful in diseases with cognitive sequelae, including Alzheimer disease, stroke, and PD [82, 83]. Techniques include integrating visual information during preoral stage for increased sensory preparation of bolus via hand-under-hand feeding and cues for patient to look at bolus (present at eye-level, then hand-under-hand to bring to mouth) [84]. Presentation of dry utensil or cue to open mouth and say “ah” may improve automaticity of organizing or reinitiating oral processing and swallow initiation in cases of oral stasis and inattention to bolus.

Oral Care

Primary risk factors for aspiration pneumonia include inadequate oral care, dependency on others for oral feeding, dysphagia, and tube feeding status [85]. Poor dental hygiene can alter the local microbiome of mucosa in the oral tract, which subsequently generates colonizing pathogens that are aspirated via inhalation of secretions [86]. These factors are crucial even in non-neurogenic populations but are elevated

in patients with underlying risks from disease-specific sensory and physiological deficits. Overproduction of saliva (see Chap. 26, Saliva Management) as in patients with ALS, coupled with reduced swallowing efficiency and laryngeal sensitivity, can lead to airway vulnerability through oral bacteria. In patients with underproduction of saliva (xerostomia), as in Sjögren's syndrome or PD, the drying of mucosa can alter viscosity (thickness) quality, profile of oral microbiota (clonal bacteria), movement of bolus, and sensation of material. We recommend rigorous oral care regimen be implemented for patients at risk for aspiration of secretions [87–90].

Intervention: Surgical

Overview

When improvement is limited by anatomical factors, muscle innervation changes (spasticity, atrophy), or profoundly impaired sensorimotor functioning, surgical intervention may be recommended to enhance functioning. Surgical approaches include botulinum toxin (Botox®) injections for CP dysfunction, CP dilation or myotomy, vocal fold medialization, deep brain stimulation, and alternate forms of nutrition and respiration in the treatment of neurogenic dysphagia [92] . Note that each procedure may be accompanied by concurrent and subsequent dysphagia therapy but can be beneficial when underlying pathological changes are unresponsive or minimally responsive to other therapies. A recent systematic review on the effect of DBS in PD concluded that DBS to the subthalamic nucleus (STN) may improve timing of the pharyngeal phase of the swallow and subjective patient self-assessments (not necessarily correlated with physiologic improvements) [91]. However, the study encouraged caution of interpretation due to inconsistencies in reporting of "on/off" medication status, unilateral versus bilateral stimulation, and location (STN versus globus pallidus internus). Given heterogeneity in study reporting, symptom severity, disease progression, and medication status at time of testing, further study is needed to investigate the short- and long-term efficacy of brain stimulation therapies.

Enteral Nutrition

While exercises and compensatory strategies to optimize oral intake of food and nutrition may be sufficient to prevent functional decline in stages of neurogenic dysphagia, there is typically a point in the disease progression where impairments are too significant to allow for nutrition and hydration needs to be met with oral intake alone. Enteral feeds, in which a liquefied bolus is administered directly to the gastric system, bypassing the oropharyngeal swallow entirely, are an option for patients with severe dysphagia. Depending on the patient's medical and surgical history, different tube port placements may be indicated – e.g., a jejunostomy (J-tube), rather than a more common gastronomy tube (G-tube) placement.

A patient may receive total nutrition (i.e., nutrients, hydration, and medications) directly through the tube or may use the tube for supplemental nutrition while continuing to consume a modified amount/texture by mouth. Additionally, patients who receive total enteral nutrition may wish to have "pleasure feeds"/tastes of small negligible quantities by mouth for quality of life reasons. It is important to educate the patient and caregivers that, although nutrition is being supplemented or replaced by tube feeding, the patient is still at risk of aspirating secretions or aspirating "from below" (gastric reflux). Therefore, positioning and oral care, in addition to strict adherence of PO safety strategies for those still consuming some intake by mouth, is crucial to avoid aspiration.

Mechanical Ventilation and Tracheostomy

In advanced stages of disease, laryngeal-tracheal separation and mechanical ventilation may be

considered to improve pulmonary gas exchange for patients with intractable aspiration (see Chap. 3, Neuroanatomy of Voice and Swallowing). Ventilators have a physiologically different effect on the pulmonary system; while normal breathing is induced by negative pleural/thoracic pressure drawing air into the lungs, mechanical ventilation uses positive pressure from the upper airway into the thorax, which reduces load on the respiratory muscles. Tracheostomy permits a direct gas exchange between the lungs and the tracheal stoma, bypassing the upper airway. This adaptation can be used long-term and in conjunction with supplemental oxygen administration as needed.

Conclusion

The goal of dysphagia treatment is to optimize swallow safety and efficiency to meet nutrition and hydration needs while considering patient goals and maintaining the best possible quality of life. The success of treatment then depends on hypothesis-driven evaluation and evidence-based treatment. Underlying these clinical processes is a deep understanding of the anatomy and physiology as it pertains to normal and disordered swallowing. While swallowing is a vital function of the larynx, we must consider that this organ also participates in a range of automatic and skilled behaviors, and these behaviors are sometimes competing. Swallowing is coupled to breathing and airway protection (cough), and as such, these interlinking behaviors should be considered in both evaluation and treatment. Understanding the complexities of laryngeal function and dysfunction within the context of each patient and approaching management with an interdisciplinary team is vital to successful management.

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Augmentative and Alternative Communication

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Many patients could benefit from speech/language intervention that incorporates augmentative and alternative communication (AAC) systems [1], including, but not limited to, the full range of neurologic and neurodegenerative disease etiologies discussed in this book. AAC has been defined as a set of tools and strategies used to maximize functional communication [2, 3]. AAC systems and strategies are used to supplement, or in some cases to replace, natural speech with aided (e.g., graphic or written symbols) or unaided symbols (e.g., manual gestures and signs). The main goal of AAC systems and strategies is to improve functional and effective communication. For some individuals, AAC is a long-term need because of the nature of the underlying disease; for others, AAC is a short-term need to support functional communication during the recovery process. AAC systems and strategies are useful for any patient who is unable to use speech to meet all of his or her communication needs across all of the partners and contexts of daily life. AAC systems can be low tech or high tech. Examples of AAC systems include communication books and boards that may incorporate photographs or other picture symbols; written words, phrases, or messages; or even just the alphabet. High-tech options include voice output apps for personal computers, tablets and phones, and dedicated voice output devices that have sophisticated alternative access options such as eye gaze or switch access. Many patients benefit from a combination of low- and high-tech systems and strategies, depending on the communication context and the partner. It is critical to note that use of AAC systems and strategies and use of natural speech are not mutually exclusive communication options. AAC can be used to support the usefulness of natural speech and can be a powerful communication support in the recovery process.

In this chapter, we focus on a broad overview of AAC systems and strategies, with an emphasis on (1) types of AAC systems and strategies, (2) integration of AAC with natural speech, (3) the role of AAC for different disease courses, and (4) the role of intervention in supporting AAC implementation.

Types of AAC Systems and Strategies

There are generally four types of AAC tools:

1. Low or no tech
2. Simple digitized devices
3. Application-based tools for personal devices
4. Dedicated AAC devices

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Low-tech systems include, but are not limited to, paper-based communication books and boards, remnant books (e.g., photo albums, scrapbooks), calendar or day-planner books, and gestures or manual systems. These systems can be straightforward to develop, inexpensive, and often easily replaceable. Low-tech systems can be important communication tools in acute settings or for short-term use, particularly alphabet boards or simple message boards. See Fig. 34.1 for a sample alphabet board. Low-tech systems can vary markedly in complexity. For example, in its simplest form, a low-tech communication system could consist of a limited array of individual symbols or written messages or basic communication boards. On other end of the continuum, a low-tech communication system could consist of an elaborate, carefully organized, and multipurpose notebook of messages expressing wants and needs, small talk, conversational scripts, personal narratives, maps, photographs, and so forth. Low-tech "backup" systems are important for all individuals who use high-tech devices, as there are always situations where use of technology is not practical or feasible.

Simple digitized devices feature voice output and contain a limited number of messages, usually pre-recorded by another speaker. Examples include simple switches such as the BIGmack (AbleNet Inc., Roseville, Minnesota). These devices, by their nature, tend to have limited capability and are relatively inexpensive. Most simple digitized systems can store a limited number of message, and some systems can hold only one or two messages. However, simple digitized systems can be very useful for individuals with limited voice output needs and may serve as a powerful tool for getting attention or for supporting basic, predictable conversation.

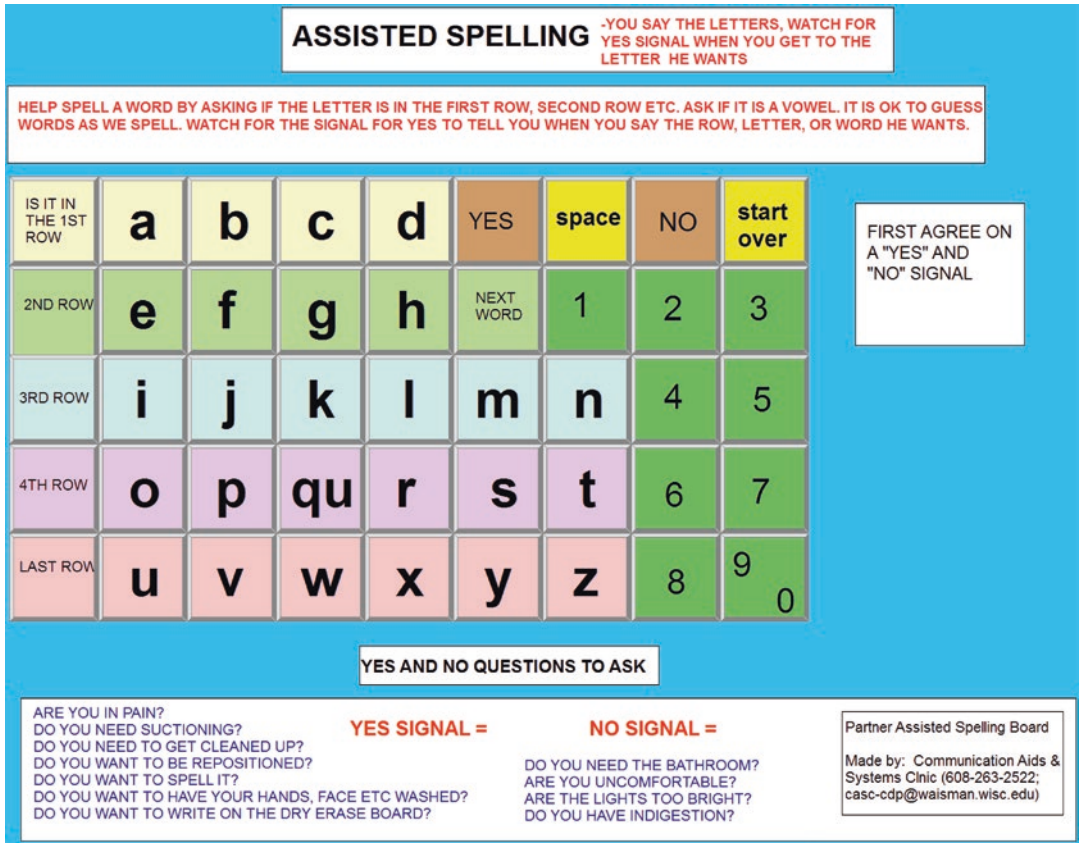

Fig. 34.1 Sample alphabet board used for assisted spelling. The board also includes frequent questions requiring yes/no responses that partners might use to help the patient communicate

There are a wide range of application-based AAC tools for personal devices, including apps for tablets and phones that feature voice output capability. These apps are readily available, are low cost, and thus provide an attractive option to many patients. In addition to apps for mobile personal technologies, there are also apps for personal computers. Computer-based tools include voice output options and can range from relatively simple to very complex. However, there are some important caveats related to app-based tools whether for tablets, phones, or personal computers. Specifically, considerable expertise is necessary to match capabilities and needs of the patient with features of particular AAC software. Thus, purchasing an app that looks attractive and loading it onto a phone or tablet is unlikely to yield success without expertise to guide the decision-making process. In addition, ongoing intervention to teach functional use of tools and to integrate the system into the individual's life is critical to success [4].

Dedicated voice output AAC systems are highly specialized electronic devices developed for the exclusive purpose of AAC, and, as such, they generally do not offer the capabilities of personal computers, tablets, or phones. Several such systems are available, with each offering slightly different features. Dedicated systems frequently offer more sophisticated access methods such as eye gaze or scanning capability (although app-based tools are increasingly expanding to include external hardware that offers alternative access features such as scanning). See Fig. 34.2 for an example of a Tobii Dynavox dedicated communication device (Tobii Dynavox, Pittsburgh, Pennsylvania). Dedicated systems are often the most appropriate AAC system for individuals with severe motor impairment or more complex communication needs such as those with amyotrophic lateral sclerosis (ALS). Many dedicated systems have dynamic displays and large preprogrammed dictionaries. Because these devices are highly specialized, they are costly. As with app-based systems, considerable expertise is necessary to match the capabilities and needs of the individual with the features of dedicated devices. A comprehensive AAC evaluation followed by a trial with multiple devices is recommended prior to making a final decision regarding which system is best for a given individual.

Fig. 34.2 Page set for eating-related vocabulary shown on a Tobii Dynavox i-15+ dedicated communication device. This device can be accessed by the patient using eye gaze, and scanning or through pointing with hands

Regardless of the particular type of AAC system, there are many important considerations in the assessment process in addition to the person's capabilities and needs. A few of these include the personal investment of significant others, the individual's own motivation, his or her life experiences (e.g., previous computer competence), his or her desire to use the telephone, and his or her ability to use multimodal communication. In addition, switches and other peripherals are often necessary to facilitate physical access to different types of devices. These include a wide range of different microswitches, head mice, trackpads/trackballs, alternative keyboards, optical pointers, and mounting devices for the AAC system. See Fig. 34.3 for an example of a mounting device for a dedicated communication system. Assessment of access needs is a highly specialized component of AAC. Usually this is completed by an occupational or physical therapist with expertise in human factors and assistive technology. Many new access technologies are on the horizon for people with severe motor restrictions such as those with ALS [5], including movement-sensing technologies, brain-computer interface, and multi-input eye tracking + switch

Fig. 34.3 Mounting system for communication device to ensure that the patient can access their AAC system across a range of physical positions

scanning. Such technologies are expanding the possibilities for access to AAC systems for individuals with the most severe motor impairments.

Integration of AAC with Natural Speech

AAC systems and natural speech are not mutually exclusive communication options. In fact, they are complementary modes of communication. The role that AAC may play with any given individual is largely dependent on the patient's functional speaking abilities. Speech intelligibility is an important clinical construct used to quantify functional speaking ability [6]. Intelligibility refers to the how well a speaker is able to produce an acoustic signal that can be accurately recovered by a listener. Intelligibility is dyadic in that it depends on both speaker and listener. It is influenced by a host of variables related to the speaker and his or her impairment(s), the listener and his or her ability to make sense of a distorted speech signal, and contextual factors such as the communicative environment and shared knowledge between speaker and listener. Intelligibility is a key component of functional communication and must be considered across contexts and partners.

AAC can play a variety of roles in an individual's communication repertoire and can serve as an important means to support the functionality of natural speech abilities. The interactive relationship between AAC systems and strategies and natural speech can be conceptualized along a continuum with three anchor points: those who can meet most communication needs using speech alone, those who can meet some of their communication needs using speech alone, and those who can meet few or none of their communication needs using speech alone.

Those who can meet most communication needs across the full range of communication partners and life contexts using speech alone generally have mildly reduced intelligibility that sometimes results in difficulty in adverse communication situations (e.g., competing for the floor in groups, in noisy or reverberant environments, or in situations where there is a misunderstanding or communication breakdown with a communication partner). These individuals benefit from AAC as a backup strategy to supplement speech, and it is used primarily in situations where communication difficulties arise or are expected to arise. Speech is the primary mode of communication for these patients; AAC is a secondary, supporting mode.

Those who can meet some communication needs across partners and contexts using speech alone generally have moderately reduced intelligibility. These individuals may have speech that is functional with familiar communication partners or in quiet one-on-one situations but may have difficulty with less familiar partners or in real-life noisy situations. For these patients, AAC serves as an important support to enhance speech intelligibility and may be used simultaneously

with natural speech [7, 8]. AAC plays an important role in supporting social participation and may even be a primary communication strategy in specific settings where there is less tolerance for communication breakdown. For these patients, AAC and speech can both be considered primary modes of communication, depending on the partner and the setting.

Those who can meet few or no communication needs across partners and contexts using speech alone may be able to produce a few words or vocalizations that very familiar communication partners can interpret; they also may be able to communicate to some extent using facial expressions, gestures, and vocal intonation, but their communication using these modes is extremely limited. For these individuals, comprehensive AAC systems are necessary for nearly all communication interaction to enable participation.

While the population of people who may benefit from comprehensive AAC systems as a replacement for speech is very heterogeneous, the common feature across individuals is the need for an AAC system that is versatile and can stand alone, independent of any residual natural speech. Individuals who require comprehensive AAC systems may present with a range of issues that make thorough, high-quality AAC assessment and intervention very complex. These include, but are not limited to, physical access problems, cognitive and language problems, and sensory problems. Each of these variables and the extent of its presence can have a critically important impact on the AAC options that are most appropriate for a given individual. In addition, whether or not the underlying problem is expected to be stable, degenerative, or improving also has an important impact on AAC options.

The Role of AAC for Different Disease Courses

At the most basic level, the course of a patient's underlying disease can be improving, degenerating, or chronic/stable. In addition to intelligibility, AAC decision-making is directly influenced by the expected course of the disease and the host of possible outcomes. Using this information, a series of interventions can be developed and implemented at appropriate junctures where changes in speech are observed. Yorkston and colleagues [6, 9] described a staging framework for considering both current and future intervention needs for patients with neurogenic speech disorders. The framework consists of five different intervention stages based on the person's level of intelligibility. Moving from least to most involved, these are the following: no detectable communication disorder, obvious disorder with intelligible speech, mildly reduced intelligibility, moderately reduced intelligibility, and no functional speech. Regardless of the course of the underlying disease, speakers may persist at any stage. For patients who are in the mildly reduced intelligibility stage, the moderately reduced intelligibility stage, and the no functional speech stage, intervention should include an AAC component, regardless of the course of the disease.

In those who have an improving course, it is expected that the underlying impairment will resolve or be rehabilitated to some extent so that the severity of the speech impairment and associated intelligibility reductions will be reduced over time as will the need for AAC. Stroke is one common etiology addressed in this book that is likely to show improvement with recovery. For those recovering from stroke, time post-onset is an important factor in the recovery of speech. Speakers with an improving course are likely to progress the stages described by Yorkston and colleagues [6, 9], moving from greater need for AAC to lesser need for AAC. Some individuals may make a full recovery. Others may progress to a point and then plateau with substantial communication limitations remaining. The limits of improvement will vary based upon individual circumstances. For the former group, AAC interventions are likely to be short term; for the latter group, AAC interventions will likely be a long-term solution to communication difficulties.

In speakers who have a degenerating course, it is expected that the underlying impairment will worsen over time so that speech impairment and

associated communication problems worsen with the progression of the disease. Common etiologies include ALS, Parkinson disease, and multiple sclerosis. Patients with these diseases begin with normal speech and may progress through the aforementioned stages toward greater impairment, ending with complete anarthria. The course of the disease, including the rate, extent, and limits of deterioration, will vary with the specific disease and the individual person. However, for some speakers in this group (particularly those with ALS), return to "normal" is not possible. For these patients, it is important that AAC systems are flexible and able to accommodate increasing needs to meet greater portions of the communication load for the speaker.

In speakers who have a chronic/stable course, it is expected that underlying impairment will be grossly static or unchanging over time. As a result, speech production and associated reductions in intelligibility will be relatively consistent. Common etiologies for chronic dysarthria include stroke and congenital neurologic disease such as cerebral palsy. Again, time post-onset is an important factor for acquired diseases. Because improvements in underlying impairments generally are not expected for patients with chronic diseases, AAC systems and strategies are often intended for long-term use to improve functional communication and participation. These interventions can range from simple alphabet boards to more complex AAC systems.

Role of Intervention in Supporting AAC Implementation

AAC interventions are broad in scope and can range from very simple to multifaceted and complex. In addition, the specific role that AAC plays with any given patient varies along with their functional speaking abilities and the course of their underlying disease (i.e., prognosis for improvement). Although the technology is an important tool, the focus of AAC assessment and intervention should always be on the *person* and his or her ability to communicate successfully. It is critical to remember that the technology is nothing more than a tool to bridge the gap between the person's capabilities and his or her communication needs. Technology alone is only part of the solution. Accordingly, the main aim of AAC assessment is first to identify the individual's physical, perceptual, speech, language, and cognitive capabilities and his or her communication needs and then to identify technology that is consistent with the person's profile of needs and capabilities. To accomplish this, thorough assessment of the person and knowledge of and access to current technology are necessary. In addition, it is not sufficient to simply provide a patient with AAC tools without a period of speech/language therapy that is focused on learning to use AAC systems and strategies.

The low cost and easy availability of many app-based AAC tools designed for personal technologies have revolutionized the possibilities of AAC [10] for people with neurologic and neurodegenerative diseases. However, the widespread availability of tools also presents a threat to patient care and to communication outcomes because provision of AAC intervention services is considerably more complex than simply choosing the most attractive app and presenting it to the patient. Appropriate app selection requires a thorough understanding of the patient and his or her communication needs and abilities (including whether the patient requires alternative access and, if so, what type of access works best for the patient). This thorough understanding of the patient must be carefully considered in light of a thorough understanding of the features of any given AAC tool to determine which tools match the needs of the patient. Thus, clinical expertise is required to ensure that feature matching between apps and the patient's needs is conducted before purchases are made and that treatment is provided to ensure that the patient learns to use AAC systems and strategies.

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