3 Upper Airway Anatomy and Physiology

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Nasal Cavity

The nasal cavity extends from the anterior nasal aperture to the beginning of the nasopharynx posteriorly and is divided into two separate cavities by the nasal septum. Broadly speaking, the nasal cavity has three key functions: respiration, protection, and olfaction. An average adult human inhales 10,000 L of air daily [1]. The upper airway has evolved to allow for both oral and nasal breathing, but in the absence of nasal obstruction, humans preferentially rely on the nasal airway for respiration. The large surface area of the sinonasal cavity has superior heat and moisture exchange capabilities, and is adapted to trapping impurities in inhaled air. The nasal cavity accounts for approximately half of total airway resistance—significantly greater than that of the oral cavity [2]. The nasal cavity accounts for the largest and greatest fluctuation in resistance to airflow; however, these fluctuations are not made as quickly as in other segments of the upper airway, such as the pharynx, oral cavity, and larynx [2]. Unlike these other segments of the upper airway, the nasal cavity is largely immobile save the contribution of facial mimetic musculature to flare nostrils and dilate the nasal valve. Rather, changes in nasal airflow are largely mediated by the autonomic control of the robust mucoperiosteal lining of the nasal cavity.

Anatomy

The external nose is pyramidal in shape, reflecting the paired nasal bones, paired upper lateral cartilages, and paired lower lateral cartilages supported in the midline by the nasal septum. The bony framework of the nasal cavity is comprised of several bones of the skull and midface. The lateral walls of the nasal cavity consist of the maxillary bones and lacrimal bones. The palatal processes of the maxilla and the horizontal processes of palatine bones form the floor, which is the nasal surface of the hard palate. And the roof of the nasal cavity has contributions from the cribriform plate, the ethmoid bones, the sphenoid bones, the nasal bones, and the frontal bones. The anterior bony entrance to the nasal cavity is called the pyriform aperture and is a heart-shaped opening formed by the nasal bones and maxillary bones. The external nasal opening or nostril is formed by the nasal ala, the nasal sill inferiorly, and the nasal columella medially. The columella is formed by the medial crura of the lower lateral cartilages. The nostril gives way to the nasal vestibule, which is lined with stratified squamous

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epithelium and houses hairs called vibrissae, which trap large particles in inspired air [3, 4]. From here, the nasal cavity extends posteriorly to the nasal choana or posterior nasal aperture. This space marks the boundary between the nasal cavity and the nasopharynx. It is bounded by the vomer, the sphenoid bones, the medial pterygoid plates, and the palatine bones (Figs. 3.1 and 3.2).

The midline nasal septum divides the nasal cavity into two separate cavities, thereby helping to increase surface area of the nasal cavity. In addition to dividing the airway, it provides structural support to the nasal dorsum and serves as one of the primary sources of nasal tip support. The nasal septum is divided into three segments: the membranous septum, the cartilaginous septum, and the bony septum. The membranous septum extends from the columella to the quadrangular cartilage where the cartilaginous septum begins. The quadrangular cartilage attaches superiorly to the perpendicular plate of the ethmoid bone, posteriorly to the vomer, and inferiorly to the maxillary crest of the maxilla. Here it is firmly adherent to the maxilla by way of decussating fibers which help to anchor it. Posterior to the quadrangular cartilage, the perpendicular plate of the ethmoid descends from the skull base to meet the vomer inferiorly and form the bony septum [4–6].

The septal perichondrium and periosteum carry rich vascularity to the overlying respiratory epithelium from the internal and external carotid artery systems via the ophthalmic, maxillary, and facial arteries. This robust vascularity has significant contributions to the physiology of the nasal airway, helping to regulate nasal airflow, heat exchange, and humidification. During endoscopic evaluation, one may notice the bilateral septal swell bodies on the anterior septum, just anterior to the level of the middle turbinate. While these may look like septal deviations, they are areas of thickened mucosa which are soft and compressible [7].

Along the lateral nasal wall are bony outcroppings called conchae. These form the bony scaffold for the respiratory epithelium-covered turbinates, which are fully developed by 24 weeks gestation [8]. The superior and middle turbinates stem from the ethmoid bone while the inferior turbinates originate from the maxilla. The primary purpose of the turbinates is to greatly increase the surface area of the nasal cavity to aid in humidification, heat exchange, and filtration. The inferior turbinate is the largest of the three with most robust

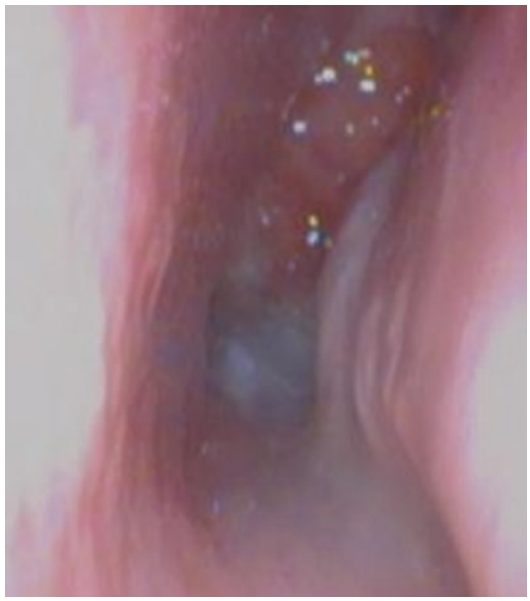

Fig. 3.1 Left choana showing partial obstruction by adenoid bed superiorly

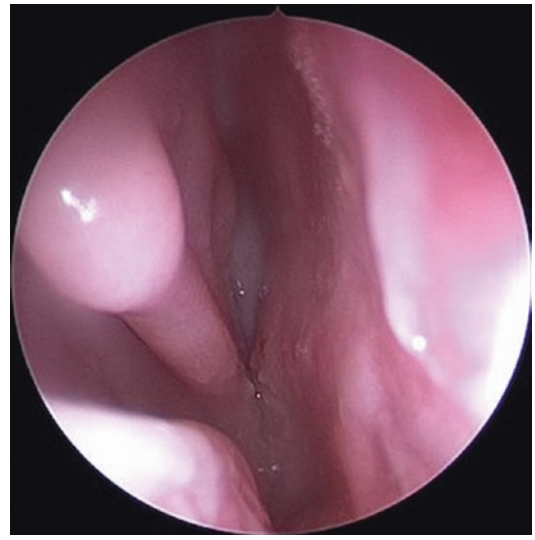

Fig. 3.2 Right choanal atresia. Notice the posterior septal deviation and blind-ended cavity

mucosal erectile tissue. This, in addition to its association with the nasal valve, makes it a major contributor to nasal obstruction and nasal airflow resistance. The spaces beneath the turbinates are referred to a meati and serve as drainage passages for mucocilliary clearance. The nasolacrimal duct drains anteriorly into the inferior meatus, channeling tears posteriorly into the nasopharynx. The middle meatus which is found beneath the middle turbinate, receives drainage from the maxillary sinus, frontal sinus, and anterior ethmoid sinuses. Obstruction of this region, which is often referred to as the ostiomeatal complex, leads to build up of mucus, infection, and sinusitis. Finally, the superior meatus receives drainage from the posterior ethmoid air cells [4]. When passing an endoscope through an adult nasal cavity, it is often most spacious along the floor of the nose; however, due to the relative sizes of the inferior turbinate and the nasal cavity of a child, it is often easier to pass through the middle meatus.

The blood supply to the nasal cavity is supplied by both internal and external carotid systems. The terminal branches of the external carotid system, which supply the nasal cavity, include the superior labial arteries off the facial artery, and the sphenopalatine, descending palatine, and infraorbital arteries off the internal maxillary arteries. The anterior and posterior ethmoid arteries are branches off the ophthalmic arteries from the interal carotid system. These two vessels descend from the skull base to supply the nasal septum. Temperature, pain, and touch sensation to the internal and external nose is provided by the first two divisions of the trigeminal nerve. However, olfaction is a function of the specialized olfactory bulbs of the first cranial nerve. Except for the keratinizing squamous cell epithelium of the nasal vestibule and the specialized lining of the olfactory cleft, the mucosa of the nasal cavity is pseudostratified, ciliated columnar epithelium.

Physiology

Nasal Cycle

Patients frequently report a fluctuating or alternating nasal obstruction. Indeed asymmetric nasal congestion and edema can often be seen on both physical exam and radiographic studies. This is the result of the normal nasal cycle, which is present in approximately anywhere from 20% to 80% of the population. The term nasal cycle is used to describe the asymmetric and occasionally periodic fluctuations in venous congestion of the venous sinuses along the nasal septum and inferior turbinates. With engorgement of the venous sinuses, the mucosal lining swells resulting in increased nasal airflow resistance. The typical nasal cycle takes anywhere between 30 min and 3 h to complete [3, 9–11]. Though the side of the nasal cavity experiencing the mucosal swelling experiences an overall increase in nasal obstruction, the total nasal airflow resistance remains stable throughout [10]. In patients with preexisting anatomic asymmetry of the nasal cavities, this phenomenon may lead to what is referred to as "paradoxical nasal obstruction," where the side that is perceived to be obstructed due to cyclic swelling may be more patent than the permanently narrowed side. In patients with a fixed anatomic asymmetry like a deviated septum, the total nasal resistance fluctuates depending on mucosal swelling.

Nasal Valve

The nasal valve is perhaps the most significant segment of the nasal cavity for understanding nasal airflow. The nasal septum forms the medial wall of the internal nasal valve. It is also bound by the upper lateral cartilages and head of the inferior turbinate laterally, and the nasal floor inferiorly (Fig. 3.3). The angle between the septum and upper lateral cartilages is typically cited as 10 to 15 degrees. Derangements in this angle have significant implications for airway patency. As the narrowest segment of the nasal airway, the nasal valve has the most significant control over nasal airflow and the greatest contribution to airflow resistance [3, 5, 6, 12]. Poiseuille's law helps to explain the dramatic effect even a small change in the cross sectional diameter of the internal nasal valve has on nasal airflow, as the airflow through the nasal cavity is proportional to the radius of the airway to the fourth power [12].

Inspired air enters the nasal cavity through the nasal vestibule and then is channeled through the

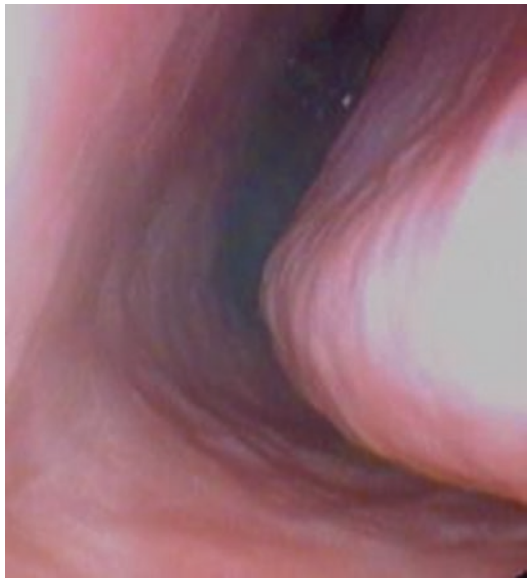

Fig. 3.3 Left nasal passage demonstrating the region of the nasal valve bordered by the nasal septum (left), the inferior turbinate (right), and the nasal floor

nasal valve where its flow is laminar. Air accelerates through the nasal valve reaching speeds of up to 18 m/s, and then upon reaching the turbinated nasal airway, airflow slows down to 2 m/s and becomes turbulent, allowing greater interaction with the nasal sidewall, turbinates, and septum [1, 3, 4, 12]. Turbulent airflow through the nose is critical for all major functions of the nasal cavity because it ensures more of the inspired air comes in contact with the turbinated nasal airway. By the time inspired air enters the nasopharynx, it has reached 37 degrees Celsius and approximately 85% humidity [13, 14]. Foreign particles have been filtered out of the air because turbulent airflow provides greater opportunity for inspired particles to become trapped in the mucous lining. Finally, greater turbulence ensures more airflow past olfactory epithelium.

A common reason for narrowed nasal valve is septal deviation. Nasal septal deviation may be present in anywhere from 75% to 90% of the population [8]. One explanation for this high prevalence may be deviation secondary to facial trauma during passage through the birth canal. Whatever the cause, a deviated septum can significantly reduce the angle of the nasal valve and result in dramatically increased resistance to nasal airflow. When septal deviation involves the quadrilateral cartilage, it may be evident as a resulting deflection of the external nasal dorsum. While a septal deviation at the level of the nasal valve may dramatically narrow the nasal airway, a posterior deviation involving the vomer in the posterior nasal cavity may have relatively little impact on airflow. Likewise, the endoscopist may find passing a flexible scope through the nasal passage difficult with an anterior deviation, but have relatively little difficulty with a posterior deviation.

Another common reason for nasal obstruction and narrowing of the nasal valve is turbinate hypertrophy. As was previously discussed, the nasal cycle leads to alternating nasal congestion. This is a repetitive and physiologically normal process which resolves at the completion of the cycle. However, turbinates are also commonly enlarged in the presence of allergy and vasomotor rhinitis. In these conditions, the sinusoids within the mucoperiosteum become engorged, leading to significant soft tissue swelling. The resultant edema reduces the cross sectional diameter of the nasal valve. On evaluation with fiberoptic scopes, engorged turbinates will often appear boggy and erythematous. This fullness may be accompanied by thin rhinorrhea. The swelling is soft and can often be pushed past with the telescope; however, application of topical decongestants such as oxymetazoline will greatly reduce this swelling by inducing vasoconstriction. While septal deviation is often perceived as ipsilateral nasal obstruction, a "paradoxical nasal obstruction" may occur due to contralateral turbinate hypertrophy. Unlike the edema seen in allergic rhinitis, the turbinate hypertrophy which accompanies deviated nasal septum is often bony in nature as well. In this case, it may be much more difficult for the nasal valve to accommodate a bronchoscope.

Allergic rhinitis is a common cause for alterations in nasal airflow. This IgE mediated hypersensitivity of the nasal lining is more common in children than in adults and has a strong familial predisposition. When an inhaled allergen lands on the nasal mucosa, it is engulfed by macrophages, dendritic cells, or Langerhans cells and

then through a series of immunologic signaling pathways, IL-4, IL-5, and IL-13 incite the production of IgE. Upon re-exposure to the antigen, an IgE-mediated release of inflammatory substances from mast cells results in the symptoms of allergic rhinitis. The swelling that results to cause nasal obstruction associated with allergic rhinitis is predominantly localized on the nasal septum and inferior turbinates [15, 16].

During sleep, as in wakefulness, humans are preferential nasal breathers. Despite evidence that recumbency causes nasal congestion in the ipsilateral nasal cavity as the gravity-dependent side, there is no significant change in total nasal airway resistance from wake to sleep [13]. The nasal cycle persists independent of posture, and the physiology of the nasal airway does not undergo the same derangements as the pharynx during sleep [17]. Oral breathing during sleep bypasses any nasal airway reflexes which participate in maintaining airway patency. In addition, with oral breathing, the mandible is displaced inferiorly and posteriorly counteracting actions of the pharyngeal dilators. These factors may contribute to greater incidence of obstructive sleep apnea with mouth breathing.

Mucociliary Clearance

The primary way in which the nasal cavity protects the lower airways is through mucociliary transport. As was previously stated, the lining of the nasal cavity is pseudostratified ciliated columnar epithelium. Goblet cells within the epithelium create a mucus blanket which covers the nasal cavity and traps inspired particles. Surrounding the cilia is a less viscous periciliary sol layer which permits the beating of the cilia. This motion of the cilia propels the thicker overlying gel layer toward the pharynx where it will be swallowed. The more gelatinous surface layer traps particles and also contains various antimicrobial proteins. The health of the mucociliary transport system within the nasal cavity is paramount to maintaining nasal airway patency and preventing disease. Failure of the mucociliary transport system, as seen in diseases like cystic fibrosis can lead to infections, inflammation, and obstruction of the nasal airway [1, 14, 18, 19].

Oral Cavity

Anatomy

The oral cavity begins at the lips and continues posteriorly to where the oropharynx begins at the junction of the hard and soft palate. It is bound superiorly by the hard palate, inferiorly by the floor of mouth, and laterally by the cheeks. The bony framework of the oral cavity is composed of the mandible and the hard palate. The hard palate consists of the palatine processes of the maxilla and the horizontal plates of the palatine bones. Together, they form the U-shaped roof of the oral cavity that separates it from the nasal cavity.

Within the oral cavity, there are several anatomic subsites—the lips, gingivae, teeth, oral tongue, buccal mucosa, floor of mouth, retromolar trigone, and hard palate. Forming the opening to oral cavity, the upper and lower lips meet at the oral commissures laterally. In addition to participating in speech formation and facial expression, the human lips act as a sphincter for mouth closure through action of the orbicularis oris muscle which encircles the mouth. Controlled by the facial nerve, this muscle is responsible for maintaining oral competence during mastication and swallowing. Deep to the buccal mucosa of the cheek, the buccinator muscle works in conjunction with the orbicularis muscle and other muscles of mastication to keep food aligned with the occlusal surfaces of teeth and prevent pockets of food from forming in the cheeks. The space enclosed by the lips, the teeth and alveolar processes, and the buccal mucosa is referred to as the oral vestibule. It is into the lateral oral vestibule that saliva from the parotid duct, or Stensen's duct, empties adjacent to the second maxillary molar.

The maxillary and mandibular alveolar ridges are lined with dense fibroepithelial mucosa, the gingiva. From these ridges arise the teeth whose primary function is to cut and grind food. In children, 20 deciduous emerge and are eventually replaced by 32 permanent teeth. Posterior to the third molars is the retromolar trigone, which occupies the space between the mandibular ramus, maxillary tuberosity, buccal mucosa, and tonsillar pillar.

The hard palate is divided into the primary palate, and secondary palate by the incisive foramen through which the nasopalatine nerve passes. The muscles of the soft palate attach to the posterior edge of the hard palate where the oral cavity merges with the oropharynx. At birth, the hard palate is generally broader and less arched than the adult palate. However, as teeth erupt along the alveolar ridge, the palatal arch deepens. Simultaneously, the oral surface of the palate enlarges while the nasal surface resorbs, and the volume of the nasal cavity increases [20]. In patients with a cleft palate, failure of the two maxillary prominences to fuse in the midline results in an open palate and common oronasal cavity. The hard palate is covered by a thick mucosal layer of keratinized squamous epithelium. Like the mucosa of the rest of the oral cavity, it houses many minor salivary glands which produce mucus to lubricate and prevent drying. The hard palate is supplied by the greater and lesser palatine arteries which pass through the greater and lesser palatine foramina and are branches of the internal maxillary artery.

The dominant structure within the oral cavity is the oral tongue. This occupies the greatest space and significantly contributes to respiration. The oral tongue, also referred to as the mobile tongue, is the anterior two-thirds of the tongue which lies anterior to the sulcus terminalis and circumvallate papillae. The bulk of the oral tongue is made up of 4 paired intrinsic tongue muscles. These include the superior longitudinal, inferior longitudinal, transverse, and vertical muscles. Together, they work to lengthen, shorten, flatten, and round the tongue, and it is through their contraction that the tongue is able to curl and roll. Protrusion, retraction, and changing the tongue position are controlled by the 4 paired extrinsic muscles which originate outside the main body of the tongue but attach to it. These include the primary tongue protruder, the genioglossus, and the styloglossus, hyoglossus, and palatoglossus, which retract the tongue. Each of these muscles is controlled by the hypoglossal nerve except for the palatoglossus, which is innervated by the vagus via the pharyngeal plexus. General sensation to the oral tongue is carried by the trigeminal nerve while taste is carried by the chorda tympani, a branch of the facial nerve. The surface of the tongue is covered with several hundreds of papillae, which house the taste buds responsible for allowing humans to detect sweetness, saltiness, sourness, bitterness, and umami [21]. The lingual arteries, which are branches of the external carotid arteries, supply blood to the tongue muscles. As will be discussed elsewhere in this chapter, in addition to assisting with speech formation, mastication, and swallow, the tongue plays an important role in maintaining airway patency.

Physiology

In addition to the saliva produced by the minor salivary glands within the oral cavity, the mouth receives additional contributions of saliva from the paired parotid, submandibular, and sublingual salivary glands. The largest of the salivary glands, the parotid glands, are located along the mandibular ramus and produce mostly serous saliva, which empties into the oral cavity via Stensen's duct in the buccal mucosa. The submandibular glands are slightly smaller and sit between the digastric muscle and mandible. These glands produce a more viscous saliva, which accounts for about 70% of salivary volume [22]. Submandibular saliva empties into the oral cavity via Wharton's ducts, which run along the floor of mouth before opening at papilla adjacent to the lingual frenulum. Finally, the sublingual glands can be found deep to the mucosa of the floor of mouth, just anterior to the submandibular glands. Adults may produce up to 1.5 L saliva daily which aids to prevent the oral cavity from drying, lubricate food, and initiate digestion. Maintaining a healthy flow of saliva is also crucial for prevention of dental caries and halitosis as saliva helps to regulate oral pH and remove bacteria and bacterial substrates [22]. Salivation is under autonomic control and can be triggered by the presence of food in the oral cavity as well as smell, taste, and even psychological stimuli [23]. During endoscopic evaluation of the airway, taking note of the presence and quality of saliva and

secretions can be an excellent indicator of health or disease status. While dry mucus membranes may be a result of various rheumatologic disease or iatrogenic influence, sialorrhea and pooling of secretions often points to dysphagia.

Like swallowing and breathing, chewing is controlled by central pattern generators (CPG) in the brainstem. CPGs are sensory and motor neuron circuits which coordinate rhythmic events in the body [24, 25]. The process of mastication is beyond the scope of this chapter. However, mastication contributes to the oral phase of deglutition and is essential for facilitating a safe and coordinated swallow, thereby protecting the lower airway from aspiration. The food bolus is mixed with saliva which initiates digestion and lubricates the food to facilitate the swallow. During formation of the bolus, the glossopharyngeal and lingual nerve reflexes help to protect the tongue from inadvertent bite trauma [26]. Once the oral preparatory phase is complete, the tongue elevates and propels the bolus posteriorly toward the oropharynx where the reflexive swallow will begin. This is discussed in greater depth later in this chapter.

At birth, the oral cavity is almost entirely occupied by the tongue, rendering the neonate an obligate nasal breather. This changes as the child grows, and after infancy, the oral cavity becomes a passive conduit for respiration. The nasal airway remains the primary airway; however, during times of heavy activity and with nasal or nasopharyngeal obstruction, mouth breathing predominates. Recall that the resistance to airflow though the oral cavity is much less than through the nasal cavity. While this is true, the oral cavity is not equipped to condition or filter inspired air in the same way that the nasal cavity is. Orally inspired air enters the lower airway cooler and drier than that which is inspired nasally; and oral breathing permits more aerosolized particles into the lower airway. During mouth breathing, the tongue is actively depressed by contraction of the intrinsic muscles and the hyoglossus muscle. This acts to open the pharyngeal airway. Simultaneously, the soft palate is contracted to close of the nasopharynx, worsening the nasal obstruction [27]. An additional physiologic reason for oral breathing is gasp breathing. Triggered by hypoxia, gasp breathing results in protrusion of the tongue by way of genioglossus contraction, which draws the hyoid and tongue anteriorly and opens the pharynx widely to minimal resistance to airflow [21]. With persistent hypoxia, however, research has shown that tongue protrusion fatigues. Thus, in patients with sleep apnea, as hypoxia worsens, so too may their ability to resist worsening pharyngeal collapse [28].

This highlights that perhaps the most important contribution the oral cavity has to upper airway physiology is through the interaction between the tongue and the pharynx. In addition to working toward a safe and coordinated swallow, the tongue musculature also helps to dilate the pharynx. This will be addressed further in the pharynx section. There are myriad anatomic variations and pathologic conditions that may impinge on the oral airway, however the role of endoscopy in their evaluation and diagnosis is fairly minimal. Generally, a direct oral exam using a tongue depressor, dental mirror, and manual palpation is of greater utility than endoscopy.

Pharynx

The pharynx is the largest and most compliant segment of the upper airway. As part of the alimentary and respiratory tracts, it serves as a conduit for both air and ingested food and drink. It is a "space" between the oral cavity and the laryngeal airway. As such, it has two opposing functions—to remain patent during inspiration, and to close and constrict to propel food into the esophagus. Roughly cylindrical in shape, the pharynx works as a muscular channel lined with mucosa that extends from the skull base to the esophageal inlet. In addition to serving as a conduit for ingested food and liquid from the mouth to the esophagus, the pharynx receives and swallows secretions from the nasal cavity and the middle ear. Additionally, the tonsillar tissue of the pharynx is positioned strategically at the portal of entry for air and ingested matter where it comes into contact with myriad antigens, especially

early in life. Though important in the immature immune system, the tonsillar tissue of Waldeyer's ring is more germane to this text for its influence on airway dynamics. Perhaps beyond the scope of this chapter, it is important to recognize the role the pharynx also plays in speech and sound formation, acting as a chamber to increase resonance as well as shape sound generated in the larynx.

At various stages of development, the human pharynx undergoes significant changes both anatomically and physiologically. Prenatally, the developing larynx is positioned high in the neck allowing the epiglottis and soft palate to first interlock at around weeks 23 to 25. When the larynx is high in the neck, the aerodigestive pathway is much like that in other mammals and primates, allowing the neonate to breathe and feed simultaneously. Centrally, a channel is maintained for passage of air, while milk is diverted laterally around the epiglottis, into the pyriform sinuses, then to the esophagus [29]. While this anatomic relationship is intact, the child is an obligate nasal breather. This relationship between larynx and pharynx continues until approximately 2 years of age, at which point the larynx begins its descent in the neck. The pharynx elongates, eventually reaching adult size by about age 6, resulting in the loss of the relationship between the epiglottis and uvula/soft palate [20, 30]. The epiglottis can no longer interlock with the palate, and for the first time, the pharynx is truly a common aerodigestive cavity. It is at this time that the child transitions from obligate nasal breather to being able to rely more on an oral airway when needed [30].

Anatomy: Endoscopic Evaluation

Nasopharynx

In examining the pharynx endoscopically, it is helpful to recall its tripartite configuration. The nasopharynx, oropharynx, and hypopharynx all share certain common anatomy and physiologic functions, but each has a distinct endoscopic appearance. The nasopharynx is the superiormost segment of the pharynx and directly communicates with the nasal cavity via the choanae as well as the middle ear spaces via the Eustachian tubes. The pharyngeal fornix forms the superior extent of the nasopharynx and lies along the occipital and sphenoid bones. Anteriorly, the nasopharynx begins at the choanae. Recall that the choana is the space through which the nasal cavity and nasopharynx communicate. It is bordered by the vomer, the sphenoid bones, the medial pterygoid plates, and the palatine bones. From here, the nasopharynx extends inferiorly to the pharyngeal isthmus—the space between the posterior border of the soft palate and the posterior pharyngeal wall. This marks the boundary between the nasopharynx and oropharynx.

Immediately posterior to the choanae, along the lateral walls of the nasopharynx sit two cartilaginous mounds known as the torus tubarius, which mark the Eustachian tube orifices. These structures serve as the attachment for the salpingopharygneus muscle, which merges inferiorly with the palatopharyngeus and forms the salpingopharyngeal fold. Posterior to this fold sits the fossa of Rosenmuller or pharyngeal recess, which is clinically significant when evaluating for nasopharyngeal carcinoma. Occasionally during routine endoscopic evaluation, a midline smooth, cystic-appearing mass may be observed in the posterior nasopharynx. Known as a Tornwaldt's cyst, this is generally attributed to abnormal notochord regression. Some series have quoted the incidence of these benign growths between 1.4% and 3.3% of the population, though a more recent radiographic study of incidentally found cysts suggested the incidence may be closer to 0.06% [31, 32]. Rarely, these cysts may become infected or grow large enough to cause airway obstruction, but predominantly, they are asymptomatic.

During endoscopic evaluation of the pediatric nasopharynx, one must pay special attention to the pharyngeal tonsil/adenoid bed. Located in the posterior, superior aspect of the nasopharynx, the adenoids comprise part of Waldeyer's ring, lymphoid tissue ideally situated for exposure to both airborne and ingested antigens [33]. Adenoid tissue first develops during gestation and continues to grow through the first 6 years of life after which it generally atrophies and becomes less

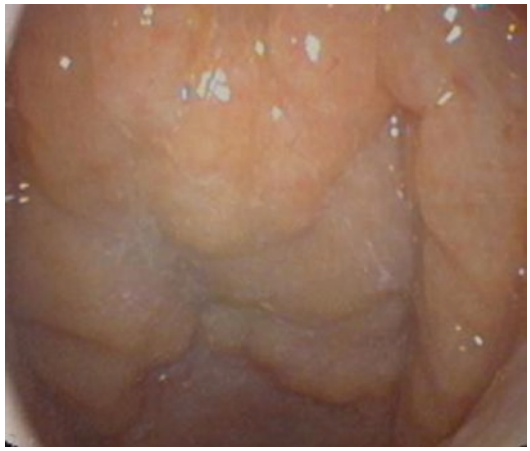

Fig. 3.4 Normal-appearing adenoid bed within nasopharynx

prominent. When hypertrophic, adenoid tissue may significantly obstruct the nasal airway and reduce nasal airflow. Adenoid hypertrophy is marked by symptoms of snoring, nasal obstruction, mouth breathing, and eventually alterations in facial development [34, 35]. Not surprisingly, the presence and degree of nasal obstruction symptoms has been shown to correlate closely with the size of adenoid tissue evaluated endoscopically (Fig. 3.4) [36–39].

The mucosa of the nasopharynx reflects its location between the respiratory epithelium-lined nasal cavity and the stratified squamous epithelium of the rest of the pharynx. Just posterior to the choanae, the mucosa is primarily respiratory, whereas at the level of the pharyngeal isthmus, it has transitioned to stratified squamous epithelium.

Oropharynx

The next segment of the pharynx following the nasopharynx is the oropharynx which communicates with the oral cavity, the nasopharynx, and the hypopharynx. As mentioned above, the oropharynx begins at the pharyngeal isthmus. Anteriorly, the oropharyngeal isthmus or isthmus of fauces encompasses the soft palate, the palatoglossal arches, and the posterior one-third of the tongue. The oropharynx extends from the junction of the hard and soft palate to the level of the hyoid, or the vallecular inferiorly. Within the oropharynx are several subsites that are easily examined endoscopically—the soft palate and uvula, the palatine tonsils, the posterior one-third of the tongue or tongue base, the posterior pharyngeal wall, and the vallecula. Due to the presence of the palatine and lingual tonsils as well as the base of the tongue, the oropharynx is often the source of obstruction in obstructive sleep apnea.

Tonsils

Two of the most significant structures for the endoscopist are the lymphoid collections referred to as palatine and lingual tonsils. The palatine tonsils are secondary lymphoid organs, which arise from the second pharyngeal arch, and can be found between the palatoglossus and palatopharyngeus muscles, bordered laterally by the superior constrictor muscle [33, 40, 41]. Like the adenoids, the tonsils are epithelial lined, highly cryptic structures which comprise part of Waldeyer's ring. Their highly cryptic surface structure maximizes surface area for interaction with antigens. Though the surface of the tonsils is epithelial lined, the crypts are lined with reticular epithelium with large open spaces filled with non-epithelial cells including T cells, immunoglobulin-producing B cells, dendritic cells, and Langerhans cells [40]. The underlying basement membrane is interrupted, allowing for easier delivery of antigen to the lymphoid tissue within the tonsillar tissue. In addition to the lymphoepithelial tissue, tonsils are made up of mantle zones, populated by dense, small lymphocytes; follicular germinal centers, where memory B cells and plasma cells are formed; and interfollicular areas, which are populated predominantly by T-lymphocytes and high endothelial venules which facilitate extravasation.

In palatine tonsils, primary follicles develop by 16 weeks gestation, and by 20 weeks, the crypts have begun to develop and are fully formed by 7 months gestation. Postnatally, tonsillar tissue continues to develop, but by around age 4–7, adenoid tissue has begun to involute, followed by palatine tonsillary tissue by the teenaged years, and finally, lingual tonsils during adulthood [40, 41]. The size and appearance of tonsillar tissue is widely variable in children, as are the ways in which the tissue influences disease status. Not all

hypertrophic tonsils result in sleep apnea or sleep disordered breathing.

Glossoptosis

During respiration, the tongue base is prevented from collapsing posteriorly into the vallecula by contraction of the tongue and cervical strap musculature. Anterior and superior forces on the tongue and hyoid bone help to stent open the pharynx during inspiration, thereby resisting powerful negative inspiratory pressures. Specifically, the genioglossus muscle has been shown to have increased electromyography (EMG) activity during inspiration [42, 43]. Despite this action, certain pathologic conditions result in loss of the oropharyngeal airway. This is especially true in patients with neuromuscular disorders, macroglossia, or micro/retrognathia [44]. Endoscopically, the tongue base may be seen crowding the oropharynx and pushing the epiglottis against the posterior pharyngeal wall, obstructing the airway. In these scenarios, a jaw thrust helps to pull the tongue and hyoid anteriorly, providing a wide open view of the hypopharynx and larynx. This maneuver may be helpful when determining whether or not a mandibular distraction will significantly alter upper airway dynamics.

Hypopharynx

Finally, the oropharynx gives way to the hypopharynx at the level of the epiglottis. The hypopharynx extends down to the posterior surface of the cricoid cartilage and laterally along the lateral surfaces of the larynx into the pyriform sinuses. These mucosa-lined pockets are formed by the aryepiglottic folds medially and the thyroid cartilage laterally. Like the oropharynx, the hypopharynx is lined with stratified squamous epithelium. Though squamous cell carcinoma may originate in the hypopharynx, there are few pathologies that arise here in the pediatric patient. However pooling of secretions observed endoscopically may provide information on the status of the swallow, aspiration, and airway protection.

Drug-Induced Sleep Endoscopy

Over the past several years, drug-induced sleep endoscopy (DISE) has become an important diagnostic tool for sleep doctors and endoscopists. Typically, DISE has been utilized in children who have previously had an adenotonsillectomy but have persistent OSA. By inducing a sleep-like state while evaluating the upper airway, the level of persistent obstruction may be identified [45, 46]. Common sites for obstruction are the velum or soft palate, oropharynx, base of tongue, and epiglottis (VOTE). The first three of these subsites are anatomic components of the pharynx while the epiglottis is part of the larynx. This procedure is also frequently used in patients with high likelihood of having persistent OSA despite adenotonsillectomy, including patients with trisomy 21, craniofacial abnormalities, obesity, and hypotonia. DISE may also help in identifying the site of obstruction in patients with OSA but clinically insignificant tonsils. In these patients, lateral pharyngeal wall collapse is infrequently identified, so adenotonsillectomy may not lead to improvement [47].

Pharyngeal Musculature

The three largest and most prominent pharyngeal muscles are the pharyngeal constrictor muscles, which, when activated, propel food into the esophagus. The superior constrictor muscle attaches superiorly to the skull base at the pharyngeal tubercle anterior to the foramen magnum, the medial pterygoid plate, the pterygomandibular raphe, the mylohyoid line of the mandible, and the lateral tongue. The middle constrictor attaches to the greater and lesser horns of the hyoid bone and the stylohyoid ligament. As it fans out posteriorly, it overlaps with fibers of both the superior and inferior constrictors. Finally, the inferior constrictor muscle attaches to the thyroid cartilage and the lateral aspect of the cricoid cartilage. The inferior constrictor fibers that originate on the cricoid cartilage insert on the circular muscle fibers of the esophagus creating the cricopharyngeus muscle. This muscle forms the upper esophageal sphincter, helping to prevent gastroesophageal reflux and regurgitation of ingested food. Posteriorly, each of the constrictors is attached to the cervical vertebrae in the midline at the pharyngeal raphe which is continuous with the pharyngobasilar

fascia—a dense fascial plane between the mucosa and muscular layer that attaches superiorly to the occipital and temporal bones. Though the pharyngeal constrictors form the cylindrical wall of the pharyngeal lumen, they do not play a role in maintaining patency of the pharynx during respiration. Rather, this task is accomplished by a host of other extrinsic muscles known as pharyngeal dilators, including the genioglossus, geniohyoid, tensor palatine, and anterior belly of the digastric [29, 48].

The three additional paired muscles of the pharynx are the salpingopharyngeus, the stylopharyngeus, and the palatopharyngeus. The salpingopharyngeus originates on the torus tubarius within the nasopharynx and then merges with the palatopharyngeus muscle. When activated, the salpingopharyngeus works to dilate the Eustachian tube opening, allowing for pressure equalization between the middle ear and pharynx. It also assists in elevation of the larynx during deglutition. The palatopharyngeus muscle, covered in mucosa forms the posterior tonsillar pillar, and as the name implies, it originates on the palate and then inserts into the pharynx. Here, it merges with the stylopharyngeus muscle which originates on the styloid process and inserts on the thyroid cartilage and merges with the pharyngeal constrictors. Together, these muscles help to elevate the pharynx and larynx during deglutition, and assist in propelling the food bolus toward the esophagus.

Motor innervation of the pharynx comes from the vagus nerve via the pharyngeal plexus. This is true for all pharyngeal musculature except for stylopharyngeus muscle, which receives motor input from CN IX (glossopharyngeal nerve) [29].

Pharyngeal Physiology

Airway Patency

The physiology of the pharyngeal airway has been studied extensively, especially in its relationship to obstructive sleep apnea [49, 50]. As previously stated, the pharyngeal constrictors have little impact on the maintenance of pharyngeal patency. This is instead accomplished by several extrinsic muscles with pharyngeal attachments referred to as pharyngeal dilators. The two most studied muscles of this group are the genioglossus and tensor veli palatini muscles. These two muscles are the most readily accessible for monitoring and EMG testing. The genioglossus, which attaches to the mandible and inserts on the tongue protrudes the tongue, and when activated during inspiration, it works to pull the posterior portion of the tongue down and anteriorly. This action results in the dilation of the pharyngeal airway. The tensor veli palatini, on the other hand, is innervated by the trigeminal nerve. Extending from the Eustachian tube to wrap around the Hamulus of the medial pterygoid plate and insert on the soft palate, contraction of this muscle dilates the pharyngeal airway at the level of the soft palate, pulling it away from the posterior pharyngeal wall [51, 52].

Much of what has been discerned about the genioglossus and tensor veli palatini contribution to pharyngeal physiology is extrapolated to other extrinsic muscles of the pharynx as well. Not surprisingly, neuromuscular control of the pharyngeal dilators is complex and is controlled by multiple factors including the pre-Boetzinger—a central pattern-generating complex within the brainstem, chemoreceptors, mechanical receptors, and wakefulness stimuli. The pre-Boetzinger complex, which is responsible for rhythmic control of the diaphragm, also provides motor stimulation to the hypoglossal nerve [50]. In both the genioglossus and tensor palatini muscles, there is a sharp decrease in motor activity at the onset of sleep, also referred to as the alpha-theta transition [53]. When the "wakefulness stimuli" that helps to maintain pharyngeal patency is diminished with sleep onset, the pharynx is more susceptible to obstructive collapse. This is implicated in the multifactorial etiology of OSA. Recently, the hypoglossal nerve stimulator has been employed to exploit this relationship, providing rhythmic stimulation to the hypoglossal nerve throughout sleep, thereby mitigating this loss of wakefulness drive [54, 55].

In addition to wakefulness stimuli, there are chemoreceptors within the brain that respond to increasing CO_2 and mechanical receptors that

respond to the negative airway pressure to increase genioglossus activity and increase upper airway tone [56]. This is demonstrated by the negative pressure reflex. With an increase in upper airway resistance, nasal obstruction for example, airflow decreases and the resulting negative pressure beyond the obstruction results in collapse of the pharyngeal airway. This change in pressure is detected by mechanical receptors which trigger the pharyngeal dilators to resist the collapse [50, 57] (Figs. 3.4, 3.5, 3.6, and 3.7).

The prevalence of OSA in children is as high as 1–4%, yet in obese children, this may be as high as 25–40%. In obesity, excess adipose stores build up in the soft tissues of the neck, resulting in smaller cross-sectional area of the pharyngeal airway secondary to extrinsic compression. Additionally, this tissue leads to increased compression during sleep when pharyngeal dilator tone decreases [58, 59].

Swallow

The primary function of the pharyngeal musculature is to participate in the complex process of swallowing. Humans typically swallow around 500 times daily, each swallow employing 30 muscles under the control of multiple cranial and peripheral nerves [24]. While advancing a food bolus from the oral cavity to the esophagus, the pharynx must also work to protect the airway. Breathing and swallowing are both governed by brainstem central pattern generators (CPG)—sensory and motor neuron circuits which coordinate rhythmic events in the body [24, 25, 60]. Communication between these two CPGs leads to coordinated movements of the pharyngeal musculature, tongue, and larynx. The swallow is initiated during the post-inspiration/expiration phase, followed by a brief apnea, and then an expiration. During the brief apnea, the laryngeal adductors are activated to close off the trachea. This sequence of events helps to safeguard against aspiration of food particles into the lower airway [61–63]. In the neonate, however, in

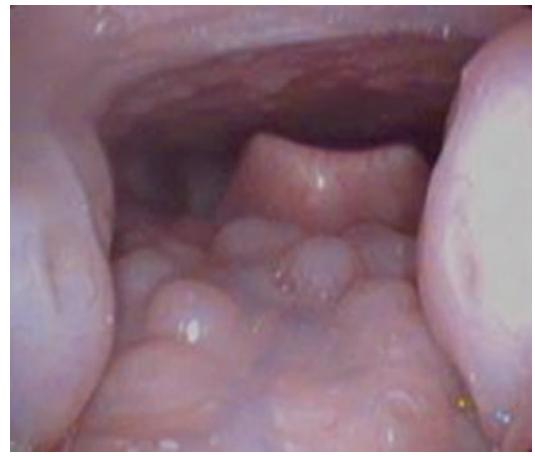

Fig. 3.6 Pharynx with tonsillar hypertrophy causing lateral crowding, and prominent lingual tonsils

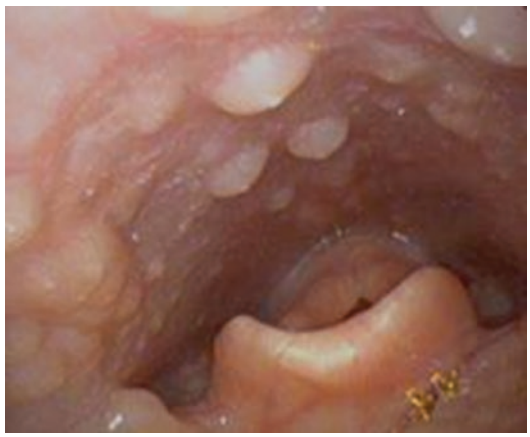

Fig. 3.5 Patent pharynx with cobblestoning of posterior pharyngeal wall

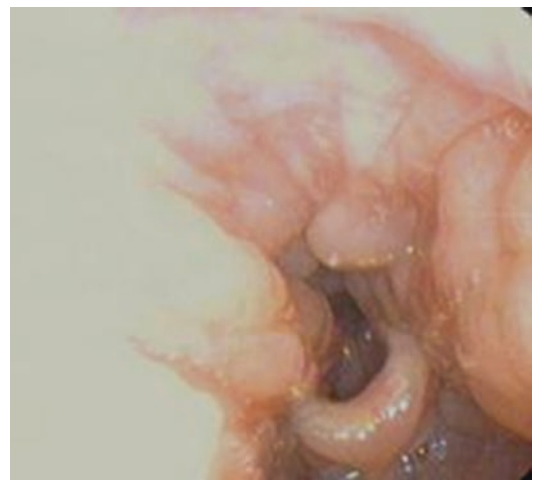

Fig. 3.7 Circumferential pharyngeal collapse

whom the airway is partially protected by its cephalad positioning and the relation between the epiglottis and uvula, this swallow pattern has not been established. Rather, there is a greater tendency to initiate swallow during inspiration [64]. The pharyngeal swallow in the neonate is often not initiated until the presence of a milk bolus in the valleculae [65].

In general, it is helpful to divide the swallow mechanism into four phases: the oral preparatory phase, the oral transit phase, the pharyngeal phase, and the esophageal phase. During the oral preparatory phase, food is chewed and mixed with saliva and salivary amylase, thereby beginning the process of digestion. The food bolus is then formed and positioned on the anterior portion of the oral tongue. Next, the soft palate elevates to contact the posterior pharyngeal wall and close off the nasopharynx and nasal cavity from the oropharynx. Simultaneously, the tongue elevates and pushes the bolus into the oropharynx [27]. This oral transit phase is followed immediately by the pharyngeal phase, which is initiated when the food bolus triggers tactile receptors of the anterior tonsillar pillars [66, 67]. In turn, a "leading complex" is initiated which entails contraction of the genioglossus, mylohyoid, hyoglossus, stylohyoid, and geniohyoid muscles. The end result of the leading complex is hyoid elevation and anterior displacement which draws the larynx up toward the tongue base and causes the epiglottis to retroflex over the larynx [24, 67]. In addition to protecting the lower airway, this anterosuperior displacement of the larynx helps to open the upper esophageal sphincter. In conjunction with a peristaltic pharyngeal wave, a negative pressure gradient is created, and the food bolus is pulled into the esophagus.

The pharyngeal swallow is modulated by several different stimuli detected by oropharyngeal receptors. Upon reaching the anterior tonsillar pillars, the food bolus triggers the swallow reflex [66, 67]. Additional tactile, thermal, and taste receptors within the oropharynx modulate the latency, and strength of the downstream swallow [24, 60]. In neonates, however, the trigger for swallow mechanism may be the accumulation of food in the vallecula rather than passage of food past the pharyngeal arch. Studies have shown that the speed of the pharyngeal swallow increases with age—4-year-old children take statistically significantly longer to swallow a bolus of water than their 12-year-old or adult counterparts [68]. The length of time it takes for the mature pharyngeal swallow to develop speaks to the complexity of the physiologic function and the degree of coordination required to maintain a safe common aerodigestive tract.

Larynx

The human larynx has evolved from a mere sphincter to protect the lower airway to a highly specialized organ with the elegant neuromuscular control required to produce the human voice. At birth, the immature larynx is anatomically optimized for respiration, not unlike our primitive mammalian ancestors. As the child matures, so too do the reflexes facilitating mature feeding, respiratory control, and phonation. This is mirrored by the anatomic position of the larynx. At birth, the larynx is positioned high in the neck with its inferior border at the fourth cervical vertebra. Throughout childhood, the larynx descends in the neck, reaching the level of C6-C7 by about 15 years of age [69, 70]. While this descent increases the length of the pharynx, and exposes the larynx to greater risk of aspiration, it also generates a resonance chamber for vocalization. Simultaneously, the laryngeal framework matures and sexual dimorphism becomes apparent during puberty. By this point, the three functions of the larynx—protection, respiration, and phonation—are fully developed and well-coordinated. This chapter will discuss the anatomy and physiology of the larynx, focusing on important considerations for the bronchoscopist.

Anatomy

Laryngeal Framework

The bony-cartilaginous framework of the larynx is comprised of the hyoid bone, the thyroid, cricoid, epiglottic, and arytenoid cartilages and the

sesamoid cuneiform and corniculate cartilages. The hyoid bone is a horse-shoe-shaped bone suspended from the skull base and the mandible by its many muscular and ligamentous attachments. It is oriented roughly horizontally with its open end facing posteriorly. Directly below the hyoid bone, attached by the thyrohyoid membrane sits the thyroid cartilage. Roughly shield-like, the thyroid cartilage houses the vocal folds, with the anterior commissure attaching to the inner surface of the thyroid cartilage via a dense collection of connective tissue known as Broyle's ligament [71, 72]. The thyroid cartilage is made up of two lamina which meet midline at a 120-degree angle in the infant larynx. During puberty, sexual dimorphism of the adult larynx becomes apparent and this angle becomes closer to 90 degrees in males [70, 73]. Like the hyoid, the thyroid cartilage is open posteriorly, where it attaches to the pharyngeal constrictors. The thyroid cartilage sits just above the signet ring-shaped cricoid cartilage, to which it is attached by the cricothyroid membrane and the cricothyroid joint. This joint allows contraction of the cricothyroid muscle to tilt the cricoid cartilage posteriorly, thereby elongating the vocal folds and changing vocal pitch [74]. Unlike both the hyoid and thyroid cartilage, the cricoid cartilage forms a complete cartilaginous ring. In the neonate, the airway at the level of the cricoid cartilage is the narrowest segment, measuring as narrow as 4–5 mm in diameter [75].

The paired arytenoid cartilages are roughly pyramidal in shape and articulate with the surface of the posterior cricoid cartilage via the ball and socket cricoarytenoid joints. All intrinsic laryngeal muscles, save the cricothyroid muscle, attach to the arytenoid cartilages, and it is to the vocal process of the arytenoid cartilage that the vocal ligament attaches. The cricoarytenoid joint allows movement classically described as rocking, gliding, and rotating, which results in the complex three-dimensional manipulation of the vocal folds [76, 77].

In addition to the arytenoid cartilages, the supraglottis is comprised of the epiglottis and two paired sesamoid cartilages, the cuneiform and corniculate. The epiglottis attaches to the internal and anterior midline surface of the thyroid cartilage and projects superiorly into the hypopharynx. The epiglottis is connected to the arytenoid cartilages by the aryepiglottic folds, which also house the cuneiform and corniculate cartilages. In the neonate, the arytenoids are often quite prominent on endoscopic view, and the epiglottis may appear highly curved, or omega shaped. Occasionally, this supraglottic tissue may become obstructive, leading to the clinical entity known as laryngomalacia. The prominence of the arytenoid cartilages diminishes by adulthood.

Aside from the bony-cartilaginous framework of the larynx, there are two fibroelastic structures which also contribute to the structure and function of the larynx. The first, known as the quadrangular membrane, attaches to the epiglottis anteriorly and then wraps around within the aryepiglottic folds to attach to the arytenoid cartilages. The quadrangular membrane also travels inferiorly along the medial wall of the pyriform sinus. The second fibroelastic structure known as the conus elasticus, helps to support the true vocal folds. Roughly conical in shape, it extends from the vocal ligament, anterior commissure and vocal process to the superior border of the cricoid cartilage inferiorly. In addition to providing structure to the larynx, these fibroelastic structures are also barriers for the spread of malignancy [78].

Musculature

The intrinsic musculature of the larynx is responsible for the control of the vocal folds by manipulating the arytenoid cartilages and laryngeal framework. Though vocal folds are generally thought of as opening and closing in a two-dimensional plane, over the past several years, research has elucidated much more complexity in vocal fold movement. In addition to opening and closing the glottic aperture, the laryngeal muscles also change the shape, volume, and tension of the vocal folds. Generally, the intrinsic muscles are described as adductors (lateral cricoarytenoid, thyroarytenoid, interarytenoid), abductors (posterior cricoarytenoid), and tensors (cricothyroid). The adductor muscles work to bring the vocal folds together in the midline. As the name implies, the lateral cricoarytenoid muscle originates on the lateral aspect of the cricoid cartilage and attaches to the muscular process of the arytenoid cartilage [29, 48,

72, 76, 77]. The paired thyroarytenoid muscles attach anteriorly to the inner surface of the thyroid cartilage and posteriorly to the bases of the arytenoid cartilages. Divided into two separate muscle compartments—the medial vocalis muscle and the lateral muscularis portion—the thyroarytenoid muscle is the bulk of the vocal folds and contributes to adduction. The sole unpaired laryngeal muscle, the interarytenoid, spans posteriorly between both arytenoid cartilages. In addition to being unpaired, it is also unique in that it receives bilateral innervation from the recurrent laryngeal nerve, and has been shown to contribute both to adduction and abduction of the vocal folds [79]. The primary vocal fold abductor is the posterior cricoarytenoid (PCA) muscle, which originates on the posterior cricoid cartilage and attaches to the muscular process of the arytenoid process. Recent work has shown that each PCA muscle is actually at least two distinct bellies with different histology and functions. However, broadly speaking, PCA contraction rotates the vocal process superiorly and laterally to open the glottis [80].

The only intrinsic laryngeal muscles that do not articulate on the arytenoid cartilages are the cricothyroid muscles which instead attach to the anterior surfaces of thyroid and cricoid cartilages. Cricothyroid contraction draws the two cartilages together anteriorly and tilts the cricoid cartilage posteriorly, which increases the distance between the anterior commissure and the vocal process of the arytenoid cartilage. The end result is a vocal fold elongation and increased tension [74]. This is also the only intrinsic laryngeal muscle which is not innervated by the recurrent laryngeal nerve.

Extrinsic laryngeal musculature includes the cervical strap muscles, the sternothyroid, sternohyoid, omohyoid, and thyrohyoid, as well as the mylohyoid, digastric, and stylohyoid muscle, which suspend the larynx from the skull base and mandible. This set of muscles primarily work to elevate and depress the larynx to assist with deglutition.

Innervation

The larynx is innervated by two branches of the vagus nerve—the superior laryngeal nerve and the recurrent laryngeal nerve. The intrinsic laryngeal musculature is innervated by the recurrent laryngeal nerve, named such because of its descent into the chest prior to looping back up into the neck. Because of its close association with the aorta and subclavian artery, vocal cord paralysis following cardiac surgery is a common occurrence in the pediatric population [81]. When assessing for paralysis on bronchoscopy, it is important that the anesthesiologist allow the child to maintain spontaneous respirations. Vocal fold movement should be symmetric, with abduction coordinated with inspiration. The best time to assess vocal fold motion, though, is during an awake exam as anesthesia can impair the interpretation of vocal fold motion.

As was previously mentioned, the only intrinsic laryngeal muscle that does not receive motor input from the recurrent laryngeal nerve is the cricothyroid muscle which instead is innervated by the external branch of the superior laryngeal nerve. The internal branch of the superior laryngeal nerve receives sensory stimuli from the larynx. The laryngeal mucosa is densely populated by mechanical, thermal, chemical, and taste receptors. As will be further discussed in the context of the physiology of the larynx, these sensory receptors play a role in the protective reflexes of the larynx as well as in the regulation of respiration.

Endoscopically Relevant Anatomy

A description of the topographic anatomy of the human larynx is an integral part of any endoscopic evaluation of the airway. It is helpful to do this in a sequential manner, in the order in which the structures and surfaces are encountered endoscopically. Here, it is important to understand the division of the larynx into three separate regions: the supraglottis, the glottis, and the subglottis. Depending on findings within the pharynx, a clear visualization of the laryngeal aperture—the area within the epiglottis, aryepiglottic folds, and interarytenoid space—may be challenging to obtain. Laryngomalacia, glossoptosis, vallecular cysts, vocal fold paralysis, or mass effect from extrinsic cervical pathology may distort laryngeal anatomy. Assessing for symmetry and ease of endoscopic exposure are critical initial components of the laryngeal evaluation.

Supraglottis

The supraglottis includes the epiglottis, the arytenoid cartilages, the false vocal folds, and the laryngeal surfaces of the aryepiglottic folds bilaterally. Special attention should be paid to the shape, size, and positioning of the epiglottis and arytenoid cartilages. In the neonate or premature child, it is not uncommon to see a highly curved epiglottis, often referred to as omega-shaped. The arytenoid cartilages may be especially prominent in the newborn larynx, prolapsing into the laryngeal airway with inspiration. The aryepiglottic folds may appear shortened, leading to a retroflexion of the epiglottis even during inspiration. At times, this constellation of features may lead to airway obstruction or feeding difficulties and is diagnosed as laryngomalacia.

Within the laryngeal aperture, the next structure to be examined should be the false vocal folds, which appear as symmetric mounded tissue immediately superior and lateral to the true vocal folds. These give way to the laryngeal ventricle—a mucosa-lined invagination that separates the true vocal folds from the false vocal folds. At the anterior extent of the ventricle bilaterally is the laryngeal saccule, a diverticulum lined with mucus and serous glands. Secretions from these glands help to lubricate the true vocal folds whose surface epithelium lacks mucus glands. The laryngeal saccule is not routinely examined endoscopically; however, rarely, it becomes dilated by air (laryngocele) or fluid (saccular cyst) and may appear as supraglottic asymmetry causing hoarseness, dysphagia, and airway obstruction [82, 83] (Fig. 3.8).

Glottis

The lateral aspect of the laryngeal ventricle marks the transition from supraglottis to glottis. Perhaps the most recognizable anatomic landmark of the endoscopically visualized larynx is the rima glottidis. The rima glottidis is the opening between the vocal folds and arytenoid cartilages extending from the anterior to posterior commissures. The anterior two-thirds of the vocal folds from the vocal processes to the anterior commissure are referred to as membranous glottis. The cartilaginous glottis lies posterior to the vocal processes. Viewed endoscopically, the vocal folds should appear symmetric and smooth with clean edges. Prominent vasculature, thickened mucus, irregular borders, lesions, and any asymmetry should be noted. More refined and specialized evaluation of vocal fold function and anatomy is best accomplished using videostroboscopy in the awake patient. However, gross motor function and the aforementioned qualities of the glottis should be remarked upon (Fig. 3.9).

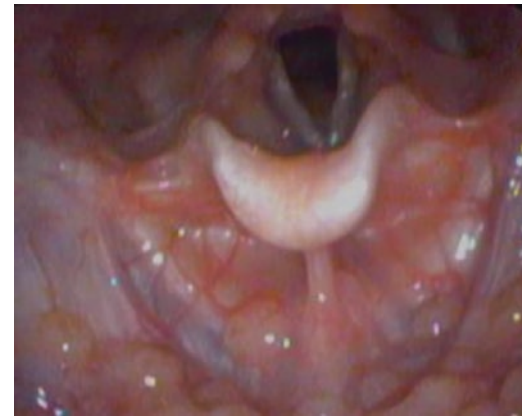

Fig. 3.8 Normal vallecular, supraglottis, and glottis. Notice the prominent median and lateral glossoepiglottic folds

Subglottis

Directly below the vocal folds, extending to the inferior edge of the cricoid cartilage is the subglottis. In the neonate, this is the narrowest segment of the airway and is a common site for airway pathology. The subglottis increases in size significantly during the first 3 years of life followed by a more linear pattern of growth until the adult larynx is reached [75]. Subglottic evaluation and pathology will be detailed extensively later in this volume.

Vocal Fold Histology

The membranous vocal fold, colloquially referred to as the vocal cord, spans the laryngeal opening from the inner surface of the thyroid cartilage at the anterior commissure to the vocal process of the arytenoid cartilage. Maculae flava at each attachment are responsible for the synthesis of the intervening vocal ligament. The area posterior to the vocal process is referred to as the cartilaginous glottis and does not play as significant a role in phonation.

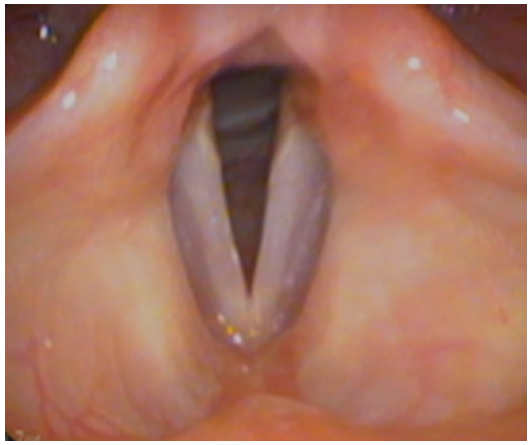

Fig. 3.9 Glottis, demonstrating true vocal folds, laryngeal ventricle, and false vocal folds

No discussion of the anatomy and physiology of the larynx would be complete without a description of the microstructure of the vocal fold. The vocal fold is a layered structure consisting of an epithelial surface layer, basement membrane, and a lamina propria, which is divided into three distinct layers over the vocalis muscle. While most of the larynx is covered with pseudostratified columnar respiratory epithelium, the vocal fold epithelium is stratified squamous. Immediately deep to the basement membrane of this epithelium is the superficial lamina propria, an acellular layer composed of extracellular matrix proteins and a few collagen and elastin fibers. This loose, gelatinous layer allows the overlying epithelium to vibrate freely and glide over the underlying muscle. The underlying intermediate and deep layers which together comprise what is referred to as the vocal ligament contain increasingly higher concentrations of collagen and elastin fibers. The deepest layer which is in contact with the underlying muscle is the most densely organized collagen fibers. The vocalis muscle, then, is immediately deep to the vocal ligament and makes up the bulk of the vocal fold. Anteriorly, the vocalis muscle attaches to the inner surface of the thyroid cartilage via a dense collection of connective tissue known as Broyles ligament. At this location, the inner perichondrium of the thyroid cartilage is absent [71, 72].

Whereas the neonatal larynx is primarily concerned with respiration there are several differences between the newborn and adult larynx which indicate the increasing importance of phonation and nuanced voice production with age. At birth, the vocal fold lacks any structure resembling the vocal ligament. The maculae flava are immature, but as the child develops, they begin to synthesize the collagen and elastin fibers that will contribute to the layered structure of the lamina propria [84–86]. Consequently, the newborn glottis does not have the layered structure required for mature phonation. Additionally, while the adult glottis is approximately 60–70% membranous, the neonate glottis is often closer to 30–40% membranous [75].

Physiology

Phonation

In addition to protecting the lower airway and helping to regulate respiration, the larynx has evolved in humans for phonation. The study of voice and phonation is a vast topic which is largely beyond the scope of this chapter. However, the basic concept behind voice production and the anatomy of the vocal fold and larynx will be reviewed here.

As discussed previously, the vocal fold is a layered structure consisting of an epithelial surface layer, basement membrane, and a lamina propria which is divided into three distinct layers over the vocalis muscle.

The myoelastic-aerodynamic theory of voice production was first introduced by Van den Berg and helps to described how subglottic air entrained over the vocal folds produces vibrations. The shape, size, and tension of the vocal folds are controlled by a complex interplay of neuromuscular control to produce vibrations. The passage of air from a high-pressure region (subglottis) to a low-pressure region (supraglottis) is controlled by muscular alterations in shape, size, and tension of the vocal folds to generate what is referred to as a mucosal wave due to the Bernoulli effect. This wave causes the inferior surface of the vocal folds to deflect medially to close. As the wave moves from inferior to superiorly, the surface is deflected first medially and then laterally, causing the folds to repeatedly

open and close [72, 87, 88]. Hirano's Body Cover theory explains the interplay between the muscular body of the vocal fold and the overlying lamina propria. Even while the vocalis muscle tightens and contracts, the overlying epithelium is able to freely move, deform, and vibrate [89]. This is only possible due to the previously described histologic make-up of the vocal fold.

Airway Protection

Perhaps the most critical function of the human larynx is to protect the lower airway from aspiration and inhalation of potentially harmful substances. Positioned at the distal end of the pharynx, and anterior to the esophagus, glottic closure is an integral part of the swallow mechanism, helping to safeguard from aspiration. Protective closure of the larynx in response to stimuli results in closure at three levels—at the level of the arytenoids and aryepiglottic folds, at the level of the false vocal folds, and finally at the level of the true vocal folds [90]. Accordingly, the surface of the larynx is populated by a large concentration of sensory receptors which respond to pressure, thermal, chemical, taste, and mechanical stimuli and participate in several protective reflexes [91, 92]. One such reflex that is especially salient during endoscopic evaluation of the larynx is that of laryngospasm, which can be triggered by various stimuli and causes the glottis to close forcefully—sometimes until long after the stimulus is removed [90, 93, 94]. Though protective in origin, laryngospasm has been hypothesized as the etiology behind Sudden Infant Death Syndrome (SIDS). Topical application of plain lidocaine over the larynx helps protect against laryngospasm during endoscopy.

Coughing, both reflexive and voluntary also demonstrates the larynx's role in airway protection. A cough helps to expel phlegm, mucus, or foreign material from airways and also helps to inflate the lower airways. The sequence of events that lead to a cough are a rapid and deep inhalation followed by glottis closure and initiation of expiration with resulting increase in intrathoracic pressure. The final stage in a cough involves opening the glottis rapidly, expelling air as quickly as 10 L/s [29, 95]. Both reflexive and voluntary cough share these three phases, though with voluntary cough, the amount and rate of inspired air have been shown to vary depending on strength of desired cough [95].

Respiratory Control

Finally, the larynx functions to control airflow. Acting as a valve, the glottis can control airflow and intrathoracic pressures by opening and closing. At the onset of inspiration, the posterior cricoarytenoid muscle fires to abduct the vocal folds prior to activation of the diaphragm. Similar rhythmic contraction of the cricothyroid muscle with respiration increases the anterior-posterior dimension of the larynx to facilitate inspiration [90, 96]. Again, the superior laryngeal nerve and its many sensory receptors on the laryngeal epithelium play a key role here.

Yet another example of the complex neuromuscular control of the larynx with respiration can be found in the laryngeal response to partial airway obstruction in the upper airway. The resulting decreased flow is detected by flow receptors of the superior laryngeal nerve. In response the posterior cricoarytenoid muscle contracts to open the glottis while the diaphragm simultaneously diminishes its inspiratory force. If not for these alterations, the negative pressure generated in the trachea and distal airways would result in airway collapse. [48] The laryngeal abductors again open widely and remain open longer during forceful expiration, whereas during panting, the abductors remain activated throughout.

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