1. (Dara) Describe the different anatomic layers of the true vocal fold and why they are important in voice production.


- stratified squamous epithelium
- basement membrane zone: a complex area anchoring the epidermis to the superficial layer of the lamina propria
  - subepithelial tissue (lamina propria)
    - superficial layer (Reinke’s space): composed of fibroblasts that produce proteins to form an extracellular matrix of loose connective tissue. Collagen type III and VII fibers intertwine and fix the basement membrane zone to the superficial lamina propria.
    - intermediate layer: composed mainly of elastin fibers
    - deep layer: collagen fibers
      - collagen fibers from the deep layer of the lamina propria blend into the underlying thyroarytenoid muscle, which forms the main bulk of the vocal fold.

Sound arises from a passive movement of the TVCs. Pitch, quality, and volume are altered by interaction of thoracic and abdominal muscles, intrinsic and extrinsic muscles of larynx, and the shaping and resonance of the upper airway and nasal passages. Contraction of the expiratory muscles produces a rise in subglottic air pressure causing rapid escape of air between the nearly apposed TVCs. Bernoulli’s effect and the elasticity of the cords causes medial displacement of the medial edges of cords and airflow is stopped. A rapid rise again in subglottic pressure causes the cords to part and the cycle is repeated. It is the escape of small puffs of air that produces the vibratory phenomenon interpreted as sound.

During phonation the lower margins of the true vocal folds separate first with formation of a volume of subglottic air. As the upper margins of the vocal folds separate a burst of air is released – the glottal puff. The lower fold then returns to midline, followed by the upper margin. This delay between closure of the lower and upper margins of the fold is termed the phase delay. The mucosal wave consists of both a horizontal movement of the folds and a vertical undulation. The body-cover theory helps explain this mucosal wave. It states that there are two layers of the vocal folds with different structural properties, the cover and the body. (Of note, different sources that I read divide the above layers into cover and body slightly differently.) The cover is composed of stratified squamous epithelium and the superficial layer of the lamina propria (Reinke’s space). The body of the fold is composed of the intermediate and deep layers of the lamina propria (vocal ligament) and the thyroarytenoid muscle. The cover is pliable, elastic, and nonmuscular; the mucosal wave occurs primarily in this loose cover of the fold.

3. (Deya) What is Reinke’s edema? What does it signify? How should it be managed?
- Etiology - strong association with cigarette smoking and heavy voice use.
- Hallmark - diffuse edematous changes of the vocal cords. The distinguishing feature of this condition is the diffuse nature of the swelling, which is an accumulation of fluid in the superficial layer of the lamina propria of the vocal fold.
- Clinical Findings - patients present with diffuse swelling of the vocal cords, which is usually bilateral. The cords feel boggy when manipulated during microlaryngoscopy, and the swelling can be rolled beneath the instruments.
- Treatment - smoking cessation is the key to resolving Reinke edema. In mild cases, speech therapy may also prevent the need for surgical treatment. However, severe Reinke edema, which is intractable to speech therapy, may have to be treated surgically. Surgical measures involve making a lateral incision on the superior aspect of the vocal fold and extravasating the fluid before carefully replacing the mucosa. Trimming the excess mucosa may be required, but care must be taken not to injure the underlying vocal ligament.

4. (Deya) Where and what is the saccule?
The appendix of the laryngeal ventricle (appendix ventriculi laryngis; laryngeal saccule) is a membranous sac, found between the ventricular fold and the inner surface of the thyroid cartilage, occasionally extending as far as its upper border or even higher; it is conical in form, and curved slightly backward. On the surface of its mucous membrane are the openings of sixty or seventy mucous glands, which are lodged in the submucous areolar tissue. This sac is enclosed in a fibrous capsule, continuous below with the ventricular ligament. Its medial surface is covered by a few delicate muscular fasciculi, which arise from the apex of the arytenoid cartilage and become lost in the aryepiglottic fold of mucous membrane; laterally it is separated
Dec 6: Benign Laryngeal Lesions (updated 08/06)

from the thyroid cartilage by the Thyreoepiglotticus. These muscles compress the sac, and express the secretion it contains upon the vocal folds to lubricate their surfaces. Interestingly, it is thought to be a vestigial structure, being a much larger structure interdigitating with the neck musculature in some of the great apes where it serves as a resonating chamber.

5. (Amy) Endoscopic or open approach for treatment of saccular cysts? Marsupialization or excision? The laryngeal saccule is a blind sac that extends upwards between the false vocal fold and the thyroid cartilage. It is a normal anatomical space that contains mucous glands that empty into the anterior ventricle via an orifice. Laryngoceles, saccular cysts, and laryngopyoceles are saccular disorders; all involve abnormal dilation of the saccule. In an air-filled laryngocele the orifice is patent. In contrast, saccular cysts are filled with granular secretions that accumulate due to an obstructed orifice. Saccular cysts are classified as anterior, lateral, or ductal. Saccular cysts may be approached either endoscopically or open, depending upon the location of the cyst. An open external approach is generally preferred for lateral lesions, although some authors report complete endoscopic excision even for large recurrent lateral cysts. Lateral saccular cysts are approached via the thyrohyoid membrane; a midline or lateral thyrotomy can be performed to increase exposure. Small lateral laryngeal cysts may be excised endoscopically. Complete excision is preferred whenever possible, although one study showed a low recurrence rate for endoscopic marsupialization of anterior cysts. Endoscopic marsupialization is sometimes performed in infants with congenital lateral saccular cysts.

6. (Amy) Describe the classification of laryngoceles and the management of each.
Internal: within the thyroid cartilage
External: traverses thyrohyoid membrane
Combined: internal and external

Combined laryngoceles are the most common type. They occur most commonly among white men in their 50's. Etiologies include obstruction of the saccular orifice by laryngeal ca, or frequent laryngeal use requiring high transglottic pressure (trumpet players, glass blowers). Common presentations include hoarseness and neck swelling. Stridor can occur with internal laryngoceles. Patients may also have dysphagia, sore throat, snoring, and cough. Physical exam may reveal a lateral neck mass if an external component is present. Diagnosis is confirmed with the finding of an air or fluid filled sac on CT.

Management is surgical with either endoscopic marsupialization or endoscopic excision. Most authors prefer an external approach, particular if there is an external component to the laryngocele. The laryngocele is traced through the thyrohyoid membrane and transected close to the orifice of the saccule. A lateral thyrotomy may be necessary to achieve adequate exposure. Endoscopic excision may be possible for small internal laryngoceles. Laryngeal cancer must be ruled out before surgical treatment, and some authors support endoscopy with multiple biopsies prior to excision of a laryngocele.

7. (Rosow) Discuss mucous retention cyst vs. epidermoid cysts of the vocal folds.

<table>
<thead>
<tr>
<th>Epithelial lining</th>
<th>Mucous retention cyst</th>
<th>Epidermoid cyst (aka inclusion cyst)</th>
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</thead>
<tbody>
<tr>
<td>Contents</td>
<td>Respiratory epithelium</td>
<td>Squamous epithelium</td>
</tr>
<tr>
<td>Etiology</td>
<td>Thinner, mucoid material</td>
<td>Thick, mushy cellular debris</td>
</tr>
<tr>
<td></td>
<td>Trauma or inflammation resulting in closure of glandular ducts</td>
<td>Possibly congenital (acc. to Bouchayer), or could be related to sulcus vocalis, which invaginates and ultimately leads to inclusion cyst formation</td>
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The term sulcus literally means a depression or furrow and does not describe a pathologic entity. Such depressions on the medial surface of the vocal folds can occur in patients without vocal complaints, and might be secondary to atrophic vocal fold changes from aging or paresis. These lesions are designated type 1 (physiologic sulcus) in the paper, and they can be distinguished clinically by noting preservation of vocal fold vibratory activity on videoendoscopy. Presence of mucosal wave activity indicates adequate functional separation of the vocal fold body and cover. Histologically, the superficial lamina propria is intact, which distinguishes type 1 sulcus from type 2 (vergeture) and type 3 (vocalis). Type 1 might be an incidental finding.
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9. (Kathy) The MICU has just consulted you for post-extubation hoarseness in a chronically intubated patient. What will you most likely find and how will you manage the problem?

The most likely pathology is an intubation granuloma, which occurs in patients who have undergone acute or chronic intubation, or any other direct laryngeal manipulation. Granuloma after intubation can occur because of direct abrasion of the arytenoids perichondrium, a break in the mucosa covering it as a result of coughing on an endotracheal tube, or long-term pressure necrosis of the vocal process area. The resulting reparative granuloma may initially progress from fairly sessile to large and pedunculated, but it may regress with maturation over several months. Antibiotics or voice therapy may be helpful with intubation granulomas, but over time they usually mature and “fall off”. Direct microlaryngoscopy with corticosteroid injection into base of granuloma before removal can be done if it does not regress.

Other possibilities in a chronically intubated patient include post-intubation edema of the RLN, which may manifest as transient unilateral vocal cord paresis on endoscopy, and usually improves with time. Arytenoid dislocation is a complication of traumatic intubation. The cause is either extreme force applied directly to the arytenoids by a laryngoscope or endotracheal tube, or careless extubation with an inflated cuff. Diagnosis is made by microlaryngoscopy with palpation of the arytenoids.

10. (Kathy) What are the most common types of human papilloma virus in respiratory papillomatosis? Which types are associated with squamous cell carcinoma?

Respiratory papillomatosis is a disorder involving HPV infection of the aerodigestive tract resulting in benign proliferation of the hyperplastic squamous epithelium. HPV types 6 and 11 are most common, but HPV types 16 and 18 are known to degenerate into SCC. The aim of treatment is to develop a satisfactory voice, and maintaining the structure and function of vocal folds as well as a patent airway. Management involves CO2 laser treatment, which vaporizes the papillomas while minimizing damage and scarring to the vocal folds.

11. (Caroline) How would you recommend resecting laryngeal papillomas? Laser, microdebrider, etc.?

<table>
<thead>
<tr>
<th>PROS:</th>
<th>CONS:</th>
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<tbody>
<tr>
<td>Laser</td>
<td>Microdebrider</td>
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<tr>
<td>Hemostasis</td>
<td>Intact pathology specimen</td>
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<tr>
<td>Less OR time</td>
<td></td>
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<td></td>
<td>OR need special training</td>
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Other techniques: coblation, cold excision

12. (Caroline) What is cidofovir? What are the results of intralesional cidofovir injection in laryngeal papillomas? Any side effects?

Cidofovir: anti-viral agent, inhibits viral DNA polymerase at intracellular concentrations 50-fold to 1000-fold lower than those required to inhibit cellular DNA synthesis. High selectivity such that, there are three orders of magnitude more absorption in papilloma cells vs. non-disease cells.

Chadha et al. 2007 (otoHNS journal)

Systematic review to include randomized controlled trials (RCTs), comparative studies, case series, and case reports. The strongest evidence was for intralesional cidofovir, with 17 studies including 158 patients. Of these, 90 patients (57%) demonstrated complete resolution, 55 patients (35%) a partial response, and 13 patients (8%) showed no improvement. CONCLUSIONS: Insufficient evidence from controlled trials exists for reliable conclusions, but several series indicate intralesional cidofovir may have some efficacy

Side effects:
Toxicity to kidneys in large systemic doses.
Some irritation to laryngeal tissue. necrosis


This article details several different medical treatments for RRP. The standard treatment of RRP lesions of the airway is surgical excision via CO2 laser or microdebrider. However, several studies show some promise in medical adjuvant therapy. IFN-a n1 study of 34 patients showed 82% positive response, 47% complete response over 6 mo, 35% with partial response. 28 day loading dose followed TIW dosing produced better response than 21/28 day pulse therapy. Complete response were higher in juvenile onset RRP than adult onset.

Complications: fatigue, HA, fevers, elevated LFTs, alopecia, rash. Isotretinoin study of 5 patients treated after failure of IFN treatment. No significant clinical response noted. Complications: severe dry skin/lips. Methotrexate (antimetabolite) study of 3 patients treated after failure of IFN. Trach dependent, surgery qmouth. All had significant response to methotrexate with decreased need for surgery. No complete response. Complications: nausea
Scarring is the single greatest cause of poor voice after surgery. Fibrous replacement of natural layers cause loss of mucosal pliability and disrupts normal vibratory function. This often leads to glottal insufficiency due to increased effort. Scarring is related to size of deficit (which may lead to healing by secondary intention. Repeated surgery, anatomic site (anterior commissure, vocal ligament), untreated LPR and heavy smoking contribute to risk of scarring. To decrease risk of post-surgical scarring it is important to preserve the superficial and deep layers of the lamina propria and its mucosal pliability. Medical treatment post-surgery may include anti-reflux medications, diet modifications, steroids, antibiotics and/or voice rest. Voice therapy is an essential post-operative therapy course. With someone who has dysphonia, a strobe exam is essential to evaluate the VF vibratory dynamics (normal 250x/s while phonating at middle C). Strobe will note asymmetry, incomplete closure, non-vibrating segment. Treatment begins with voice therapy and helps patients with dysphonia from developing hyperfunctional compensatory behaviors that may lead to further worsening of the voice. Collagen injections may 'soften' the development of scarring and patients showed objective and subjective voice improvement after injections, although voice improvement was related to the amount of normal vocal tissue present. Autologous fat injection shows promise and improves the contour of the vocal fold as well as voice improvement and mucosal wave. Autogenous fat is minimally reactive and has been shown to be viable over 1 year in some patients. Postoperative therapy course. Medialization laryngoplasty has been used a great deal for unilateral VF paralysis but can be used in specific types of VF scarring. When the arytenoid has relatively normal mobility but the VF is adynamic and fibrotic with a large glottic gap. Medialization combined with a injection can improve the glottic closure and improve mucosal wave function.

15. (Tali) Guidelines for management of post-op vocal fold microsurgery (voice use, steroids, reflux prophylaxis, etc.)

Postoperative Medications
Some patients are given antibiotics during the period of mucosal healing (5 to 7 days), and some are treated with systemic steroids (prednisone or methylprednisolone dose pack) for 3 to 7 days postoperatively, particularly in cases involving resections of pyogenic granulomas, stenosis and scar, and in patients who experience perioperative swelling. Reflux must be controlled. To aid in this, a protein-pump inhibitor usually is prescribed at least until full vocal fold recovery has occurred. Some patients find guaifenesin B is a good mucolytic and is helpful following surgery.

Postoperative Voice Use
There is much controversy on the need for and nature of voice rest. Most laryngologists (especially those caring for professional voice users) agree that absolute voice rest is judicious following surgery on the vibratory margin. All evidence is anecdotal though with no prospective studies. Is need for close collaboration between the laryngologist and voice pathologist.

An underlying principle behind the use of voice rest is the notion that phonation should be avoided or limited until the epithelium has healed in order to provide biologic protection for the fibroblast-bearing layers of the lamina propria. As a matter of tradition and convenience, a period of 5 to 8 days of absolute voice rest usually is prescribed. The patient should be scheduled for postoperative evaluation by the surgeon at the earliest time the patient is expected to demonstrate healing sufficient to permit voice use. Spiegel et al [7] have begun looking at earlier return to voice use in selected cases, sometimes as early as the first to third postoperative day. Potential candidates are patients who have had limited surgical disruption of their vocal fold mucosa and are excellent voice users who have complied with preoperative therapy. Judgments regarding the time when voice rest is discontinued are always made based on stroboscopic examination revealing intact epithelium and usually early return of a mucosal wave. After about 3 to 6 weeks of gradually increasing voice use and postoperative therapy, most patients generally are cleared for unrestricted use of the speaking voice with the condition that they rest the voice periodically, especially if vocally fatigued. Stroboscopic examination at this time is necessary to look for evidence of return of the mucosal wave and to be sure that there is no sign of new injury. Return of mucosal wave is the parameter used for resumption of singing voice sessions for singers and nonsingers.