Title

Otolaryngology in Critical Care

Permalink

https://escholarship.org/uc/item/41d323mr

Journal

Annals of the American Thoracic Society, 15(6)

ISSN

2329-6933

Authors

Joshua, Jisha
Scholten, Eric
Schaerer, Daniel
et al.

Publication Date

2018-06-01

DOI

10.1513/annalsats.201708-695fr

Peer reviewed

Otolaryngology in Critical Care

Jisha Joshua[1,2]*, Eric Scholten[1,2]*, Daniel Schaerer[3], Mahmood F. Mafee[4], Thomas H. Alexander[3], and Laura E. Crotty Alexander[1,2]

[1]Pulmonary and Critical Care Section, Department of Medicine, Veterans Affairs San Diego Healthcare System, San Diego, California; and [2]Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, [3]Division of Otolaryngology, Department of Surgery, and [4]Division of Neuroradiology, Department of Radiology, University of California–San Diego, San Diego, California

ORCID ID: 0000-0002-5091-2660 (L.E.C.A.).

Abstract

Diseases affecting the ear, nose, and throat are prevalent in intensive care settings and often require combined medical and surgical management. Upper airway occlusion can occur as a result of malignant tumor growth, allergic reactions, and bleeding events and may require close monitoring and interventions by intensivists, sometimes necessitating surgical management. With the increased prevalence of immunocompromised patients, aggressive infections of the head and neck likewise require prompt recognition and treatment. In addition, procedure-specific complications of major otolaryngologic procedures can be highly morbid, necessitating vigilant postoperative monitoring. For optimal outcomes, intensivists need a broad understanding of the pathophysiology and management of life-threatening otolaryngologic disease.

Keywords: epistaxis; Ludwig's angina; retropharyngeal abscess; laryngectomy; epiglotittis

Otolaryngologic emergencies are commonplace in the intensive care unit (ICU). Because there is frequently a need for urgent management owing to airway involvement, it is important for intensivists to be familiar with standard treatment options for a diverse contingent of diseases. This knowledge will facilitate expeditious head and neck surgery consultation and prompts intensivists to start appropriate treatment before consultation. This focused review provides intensivists with state-of-the-art clinical management recommendations for common otolaryngologic disorders.

Artificial Airway Management Concerns

Endotracheal Intubation
Placement and maintenance of an artificial airway can result in various otolaryngologic complications. Endotracheal intubation damages teeth or lacerates pharyngeal structures in less than 1% of operating room intubations, but these complications occur more frequently with ICU intubations (1). Pharyngeal lacerations can lead to significant bleeding and serious infections resulting from subsequent descending mediastinitis (1). Repeated intubation attempts, prolonged duration of intubation, female sex, large tube sizes, and unplanned extubation are all risk factors for laryngeal edema, which manifests as postextubation stridor (2). Preextubation assessment of laryngeal edema is controversial. Recent practice guidelines suggest restricting the use of the cuff-leak test to individuals with the aforementioned risk factors. In high-risk individuals without a cuff leak, guidelines recommend a trial of extubation 4–6 hours after systemic steroid administration (in contrast to the more traditional 24-h delay) (3). Although commonly used, bedside fiberoptic laryngoscopy and fiberoptic bronchoscopy do not contribute much to the evaluation of laryngeal edema before extubation, owing to compression of structures by the endotracheal tube. Direct laryngoscopy with the patient under sedation can provide visible evidence, or lack thereof, of laryngeal edema, but there are no data to support this practice. In subjects who have risk factors, extubation over an airway exchange catheter or bronchoscope can maintain airway patency and provide a guide for rapid reintubation if laryngeal edema leads to airway collapse once the endotracheal tube has been removed. Airway exchange catheters can be left in place for minutes to days,

depending on patient factors (4). The catheter lumina can be used for oxygen insufflation or jet ventilation (5), but reintubation should not be delayed; success rates for reintubation over airway exchange catheters are 86 to 92% (4, 6).

Vocal cord paralysis presents similarly to laryngeal edema, with postextubation stridor or hoarseness. Risk factors include increased duration of intubation, older age, diabetes mellitus, and preexisting hypertension (7). In general, management is supportive, and gradual return of vocal cord function is not uncommon (functional recovery can take up to 1 yr). Finally, tracheal stenosis is a well-known complication of pronged intubation and is discussed in detail in the TRACHEAL DISORDERS subsection below.

The Difficult Airway

Preexisting otolaryngologic disease frequently contributes to "difficult airways," defined as difficulty with face mask ventilation and failure to obtain an airway after three attempts. Management of anticipated difficult airways centers on awake fiberoptic intubation with the patient prepped for surgical airway access. If an airway cannot be secured by using the various airway adjuvant and fiberoptic techniques, the quickest emergent surgical access is achieved via a cricothyroidotomy (8). The complication rates of emergent tracheotomy and cricothyroidotomy are similar (9). After tube placement, cricothyroidotomy should be converted to a tracheostomy when patients are anticipated to require long-term invasive airways (10). In nonemergent situations, bedside percutaneous tracheostomy placement has the advantages of lower cost and avoiding logistical transportation issues compared with operating room procedures (11).

Tracheostomy Issues

Tracheostomy emergencies are of importance to the intensivist. Creation of an unintended tract from the tracheostomy stoma to the mediastinal tissues or esophagus can occur after initial placement or replacement of a tracheal tube. This risk of tube misplacement is higher if the tracheal tube is dislodged in the immediate postoperative period, because the tracheal stoma has not had time to heal and endothelialize. If a "fresh trach" falls out, oral endotracheal intubation should be attempted. Alternatively, flexible

laryngoscopes can be used to replace the tracheostomy tube, with the tracheostomy tube loaded on the endoscope before visualization of the tracheal lumen, followed by advancement of the tracheostomy tube off of the endoscope in a Seldinger-technique. Fiberoptic endoscopy allows confirmation of intratracheal tube placement and should be liberally used (12).

More chronically, granulation tissue can lead to significant airway bleeding or difficulty removing the tracheostomy tube (12). If limited, granulation tissue and bleeding can be managed at the bedside with silver nitrate cauterization. However, granulation lesions that are more advanced may require operative debridement with the patient under general anesthesia. If nonhumidified gas is inspired, respiratory secretions become desiccated and thick, and they can obstruct the bronchi or the tracheal tube. Finally, tracheoinnominate artery fistulas can occur when the cuff or device erodes into the innominate artery, which overlays the anterior ninth tracheal ring. This massive airway hemorrhage syndrome is rare (<1% of all tracheostomies), typically occurs within 4 weeks of tube placement, and has a very high mortality (despite salvage maneuvers such as digital pressure on the artery while transporting the patient to the operating room for arterial ligation) (13).

Tracheal Disorders

Infections of the trachea in a critical care setting are related to immunodeficiencies, prolonged intubation, or underlying airway diseases such as cystic fibrosis and chronic obstructive pulmonary disease. Infection of the trachea by *Aspergillus* spp. can lead to necrotizing tracheobronchitis and is a cause of bronchial anastomotic dehiscence after lung transplant (14). Endotracheal lesions in patients with acquired immunodeficiency syndrome are commonly caused by *1)* herpes simplex virus and cytomegalovirus (ulcerative tracheitis), *2)* *Pasteurella multocida* and *Bartonella henselae*, *3)* tuberculosis and nontuberculous mycobacteria, *4)* Kaposi's sarcoma (caused by the oncogenic virus human herpesvirus 8), and *5)* *Aspergillus* spp. (15–18). *Pseudomonas* spp., *Corynebacterium* spp., *Staphylococcus aureus*, and *Klebsiella* spp. are nosocomial pathogens that can infect and damage the trachea in patients with prolonged endotracheal intubation (19). Viral infection with human papilloma virus

(HPV)-6 and HPV-11 are associated with diffuse tracheal papillomatosis, which is generally approached via rigid bronchoscopy using laser or microdebrider instruments to avoid malignant transformation. These lesions are now prevented with routine quadrivalent HPV vaccination (20).

Malignant tracheal diseases are rare and can elude early detection because they are often not apparent on routine radiographs of the chest (only 66% were identified in on series) (21). Metastatic lesions of the trachea are far more common than primary tracheal tumors (22). Squamous cell carcinoma, the most common primary neoplasm of the trachea, is associated with smoking and predominantly affects the lower two-thirds of the trachea (23). Adenocarcinoma of the trachea derives from small salivary glands of the trachea and generally affects younger patients without a smoking history (24). Mucoepidermoid carcinoma of the trachea also derives from glandular tissue and often shows calcification on imaging studies, a feature it shares with the more vascular neuroendocrine carcinoid tumor types (25). Mediastinal lymphoma may compress and involve the trachea and is occasionally diagnosed by endobronchial biopsy. In addition to the aforementioned Kaposi's sarcoma and respiratory papillomatosis, a multitude of rarer benign and malignant neoplastic tracheal lesions are detailed in a recent review by Wu and colleagues (22). In general, tracheal lesions are managed optimally with surgical resection. Radiation and bronchoscopic therapies are second-line, adjunctive, or palliative therapies.

Tracheal stenosis is most commonly caused by local trauma, inflammation, and mucosal ischemia related to endotracheal intubation or tracheostomy placement (26). Routine monitoring to keep endotracheal balloon cuff pressures less than 30 cm H_2O prevents luminal mucosal hypoperfusion, thereby avoiding mucosal necrosis, scarring, and subsequent luminal stenosis (27). Rarer systemic inflammatory diseases affecting the trachea include relapsing polychondritis, granulomatosis with polyangiitis, fibrosing mediastinitis, sarcoidosis, amyloidosis, rheumatoid arthritis, and inflammatory bowel disease (28). Management of tracheal stenosis centers on appropriate immunosuppression for ongoing inflammatory diseases, as well as serial endoscopic dilation procedures (and/or

surgical tracheal resection) to restore luminal patency (26, 29).

In the setting of trauma, crepitus and subcutaneous or mediastinal air can suggest rupture of the larynx or trachea. These lesions can generally be repaired operatively after an appropriate endotracheal or surgical airway is established to bypass the damaged site (27). Malignant tracheoesophageal fistulas are typically managed with endoluminal stenting and nothing-by-mouth status to allow for closure, whereas traumatic fistulas are typically repaired operatively (30, 31).

Angioedema

Angioedema refers to the rapid development of localized edema of the oral, laryngeal, and gastrointestinal tissues, which places patients at risk for airway obstruction (32). Identification of the mechanism of angioedema (anaphylactic/allergic, angiotensin-converting enzyme inhibitor [ACEI] related, hereditary or acquired deficiencies of C1 esterase, or idiopathic) is critical because this mechanism will dictate treatment. In addition, clinical management is stratified by the location of the affected tissues, with lip and soft palate edema being treated more conservatively and lingual or laryngeal swelling requiring ICU admission with a cricothyrotomy and tracheostomy kit kept at the bedside (33). Unfortunately, hereditary, ACEI-associated, allergic/anaphylactic, and acquired angioedema all have a wide distribution across affected sites, without clear associations between type of angioedema and the location of the swelling.

Anaphylactic angioedema is the classic type 1 hypersensitivity reaction, with immunoglobulin E–mediated mast cell activation and degranulation leading to massive histamine release (34). Angioedema may occur in isolation or as part of anaphylactic reactions (defined as angioedema plus any combination of hypotension, urticaria, bronchospasm, throat tightness, and nausea or gastrointestinal colic). The diagnosis is clinical, with angioedema plus urticarial lesions occurring in 50% of cases and hypotension frequently occurring as an additional defining feature. Owing to mast cell degranulation, serum tryptase concentration is markedly elevated in anaphylaxis and can be a diagnostic clue (34). Common allergic triggers include

insect bites, food proteins, opiates, β-lactams, aspirin, and nonsteroidal antiinflammatory drugs (35). Anaphylactic reactions require immediate treatment with epinephrine administered intramuscularly or subcutaneously (0.2–0.5 mg of a 1:1,000 solution) or intravenously (0.1–0.25 mg of a 1:10,000 solution as a slow infusion, followed by 1–4 μg/min intravenous infusion); delays are strongly associated with death (32, 36). There is no evidence that epinephrine is superior to other vasopressors for anaphylactic shock, but it is traditionally used (37). Additional management centers on discontinuing exposure to the inciting antigen; fluid resuscitation (starting with 1–2 L of lactated Ringer solution or normal saline, with frequent reassessment of intravascular volume status); glucocorticoids (methylprednisolone 40–200 mg intramuscularly/intravenously every 4 h; hydrocortisone 100–500 mg intramuscularly/intravenously every 6 h); antihistamine (H1 antagonist diphenhydramine 50–100 mg intramuscularly/intravenously every 2–4 h for severe cases, 25–50 mg by mouth/intramuscularly/intravenously every 2–6 h for moderate cases, and 25–50 mg by mouth/intramuscularly/intravenously once daily plus an oral H2 antagonist for mild cases); and in the setting of bronchoconstriction, inhaled β2-agonist to treat laryngeal edema (38, 39). After stabilization, prolonged observation should be considered because up to 20% of anaphylactic attacks manifest a biphasic presentation, with recrudescence of symptoms 8–12 hours after the initial episode (35).

ACEI- and angiotensin receptor blocker (ARB)-related angioedema is not accompanied by urticarial lesions (40). Inhibition of ACE or blockade of the receptor leads to accumulation of bradykinin, which has variable effects, including chronic cough, vasodilation, and increased vascular permeability (41). ACEI-related angioedema occurs in 0.1 to 0.7% of patients, with ARB-related angioedema occurring three times less frequently. ACEI- and ARB-related angioedema most often occurs within the first weeks or months of treatment initiation. Risk factors include African ancestry, prior history of drug rashes, and advanced age (42). Angioedema can also occur in delayed fashion, months to years into treatment (43–45). Medical therapies targeting histamine and mast cells (glucocorticoids, antihistamines, and

epinephrine) are generally unhelpful in ACEI-induced angioedema (40), but they can be given if the diagnosis of ACEI- and ARB-related angioedema is not clear. Recently, a bradykinin B2-receptor antagonist, icatibant, has been shown to significantly shorten the time to symptom relief (2 vs. 11.7 h) in patients with suspected ACEI-related angioedema (46), as well as in ARB-related angioedema (5–7 vs. 27–52 h) (47). If icatibant is not available, fresh frozen plasma (which contains ACE) can be administered, although the efficacy of this therapy has not been studied in rigorous prospective trials (43). Patients with confirmed angioedema receiving ACEI therapy may have a 0 to 9.2% risk of subsequent angioedema if started on an ARB (48).

The clinical presentation of hereditary angioedema (HAE) features *1*) repeated angioedema attacks within a family, typically inherited in an autosomal dominant fashion; *2*) a somewhat slower onset and resolution of symptoms (typically over 2–5 d); and *3*) the lack of urticaria, pruritus, or shock (with the absence of these three symptoms distinguishing this condition from anaphylactic angioedema). There is no strong association with a particular race or sex, and the age at onset is variable. A distinguishing feature is the relatively frequent recurrence of the attacks of HAE; most untreated patients with HAE will have at least one attack per month (49). Inherited mutations cause dysfunction of the C1 esterase inhibitor (a suppressor of complement activation), leading to unchecked complement activation, inflammation, increased bradykinin concentrations, increased vascular permeability, and angioedema (50). In the context of lymphoproliferative disorders, acquired autoantibodies targeting C1 esterase manifest as an acquired version of "hereditary" angioedema (51). Measuring the serum C4 concentration, C1 esterase concentration, and C1 esterase activity can help distinguish hereditary or acquired cases, during or between angioedema events (50). As with ACEI-related angioedema, glucocorticoids, antihistamines, and epinephrine have minimal therapeutic benefit (52). Acute attacks can be managed with pooled plasma–derived C1 esterase inhibitor concentrate or a recombinant version of the protein (52–54). Icatibant, ecallantide, and fresh frozen plasma have also demonstrated therapeutic efficacy in the

acute setting (55–57). Chronic prophylactic therapy for HAE is an active target of drug development. Currently, evidence of prophylactic efficacy exists for androgens (e.g., danazol), tranexamic acid, twice-weekly subcutaneous C1 esterase replacement, lanadelumab, and avoralstat (57–61). Referral to an allergy and immunology specialist is imperative for all cases of angioedema to select an appropriate prophylactic medication.

Upper Airway Hemorrhage

Epistaxis of sufficient severity to require medical attention occurs in approximately 10% of cases (62). Epistaxis is often primary or idiopathic (85%); secondary causes include postsurgical, trauma, neoplastic, inflammatory/vasculitic, infectious (fungal), and medication related (63). In the ICU, common causes of epistaxis include nonhumidified O_2 via nasal cannula, underlying coagulopathy, and trauma resulting from nasotracheal intubation (64–67). Ninety percent of nosebleeds are from the anterior plexus of Kiesselbach and are easier to control, and 10% of bleeds originate from the posterior Woodruff plexus (Figure 1) (68). Anterior speculum examination with suction usually identifies anterior bleeding, whereas posterior bleeds are best identified and managed with a rigid sinonasal endoscope. There are abundant

options to achieve hemostasis in the setting of ongoing epistaxis (69). Initial intervention should include application of pressure, liberal application of topical vasoconstrictive agents such as oxymetazoline, and appropriate reduction of blood pressure if elevated. The head should be kept elevated as far above the level of the heart as possible. Anterior pressure is applied to Kiesselbach's plexus (Figure 1) by constant pinching of the nose shut for at least 5 minutes, repeating for another 5 minutes if necessary. Nasal clips can also be used for prolonged pressure without requiring the constant presence of a medical provider (70). Anticoagulation should be reversed if possible. If these conservative measures fail, more invasive techniques may be warranted.

Application of cautery or nosebleed QR (BioLife) to the site of bleeding usually controls most bleeds. Use of oral or local tranexamic acid or aminocaproic acid has also shown benefit in control of acute epistaxis, especially in the setting of anticoagulation (71). A variety of hemostatic packing materials are available. For posterior epistaxis, a formal posterior pack can be placed by inflating a size 12- or 14-French Foley catheter in the nasopharynx and packing the anterior nasal cavity with strip gauze (72). Dual-balloon catheters that provide anterior and posterior nasal pressure, such as the Epistat, are particularly

useful for challenging bleeds. Patients who have posterior nasal packing require continuous cardiopulmonary monitoring owing to the trigeminocardiac reflex, which can lead to bradycardia, hypotension, and death (73). Because nasal packing materials are most often kept indwelling for 3 days or longer, to promote clot formation and epithelialization, these packs are a nidus for infection. It is common practice to initiate antibiotic coverage to prevent staphylococcal toxic shock syndrome at the time of placement (74).

Patients with continued epistaxis despite initial measures should be considered for more advanced techniques. Endonasal surgical ligation and endovascular embolization of the arterial supply to the bleeding are two options for intractable posterior epistaxis (75, 76). Sphenopalatine artery ligation has a very low rate of recurrent epistaxis but requires a surgeon comfortable with endoscopic equipment and this surgical technique. Endovascular embolization has a slightly higher rate of recurrent bleeding and carries a risk of stroke; however, it is useful in patients who are not good surgical candidates. Bleeding from the anterior ethmoid system cannot be addressed using embolization, owing to the risk of blindness. If the source is believed to be from this system, ophthalmologic intervention should
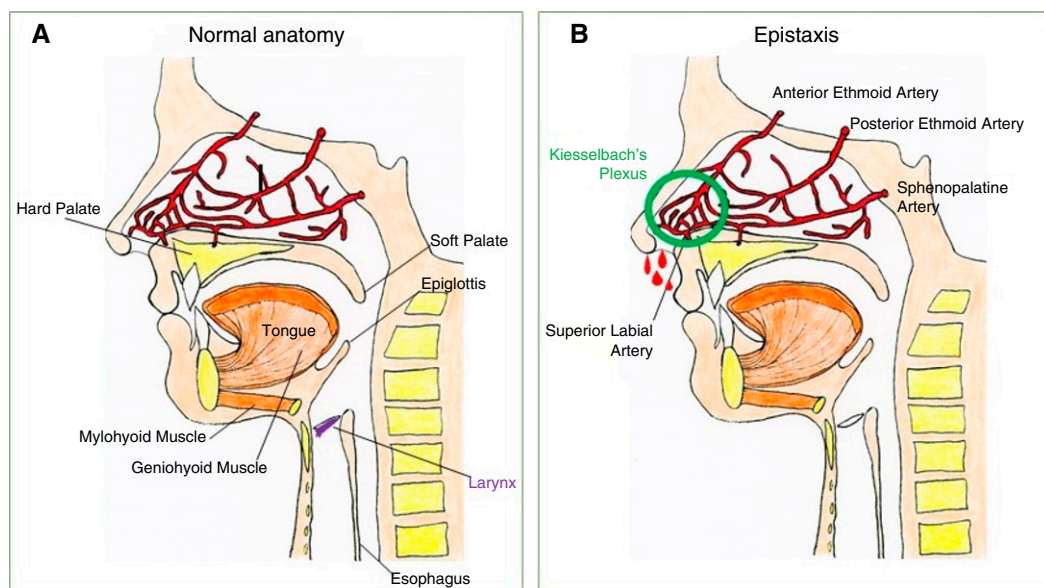

Figure 1. Vascular anatomy of the nose. (*A*) Schematic shows the anatomic blood supply to the nose. (*B*) Ninety percent of nosebleeds originate from the anterior plexus of Kiesselbach and are controlled mostly by conservative measures, whereas 10% of nosebleeds are from posterior sources, such as the sphenopalatine artery, and can require packing, endoscopic hemostasis techniques, and rarely endovascular embolization of the bleeding vessel.

be considered for a transconjunctival surgical ligation.

Other causes of upper airway hemorrhage, especially in the ICU setting, include retropharyngeal hematoma, sublingual hematoma, and nasal septal hematomas (commonly resulting from nasotracheal intubation) (77, 78). These enclosed hematomas occur in coagulopathic patients and can lead to upper airway obstruction. Large septal hematomas can compromise the vascular supply to the septum, leading to perforation; consequently, such hematomas are usually drained (79, 80).

Head and Neck Infections in the ICU

Sinusitis

Sinusitis in a critical care setting can be divided into nosocomial bacterial sinusitis (a common occult cause of fevers) and invasive fungal sinusitis (a surgical emergency in immunocompromised patients). Nosocomial bacterial sinusitis typically presents with isolated fevers; authors of a case series quoted a 7 to 40% prevalence in ICU patients with unexplained fevers (81–83). Nasogastric tubes impair drainage of the sinuses and are associated with a higher rate of nosocomial sinusitis than orogastric tubes (83, 84). Diagnosis traditionally is made by integrating computed tomographic (CT) imaging with culture data. Maxillary sinus ultrasound is a novel bedside technique that has a high negative predictive value (~95%) to exclude maxillary sinusitis but is far less useful in assessing the ethmoid and sphenoid sinuses (85). Plain films of the sinuses have low sensitivity (86). CT imaging of the sinus remains the gold standard for radiologic diagnosis; however, imaging alone is insufficient because nonpurulent sterile sinus fluid collections are common, accounting for 8 to 30% of sinus fluid samples in various series (82, 83). Management with bedside endoscopic transnasal puncture, followed by culture-driven antibiotic therapy, most often leads to resolution of fever (83). Gram-negative pathogens including *Pseudomonas* and *Klebsiella* were recovered in approximately 50% of cultures in one series; other commonly encountered bacterial pathogens include *Streptococcus*, *Staphylococcus*, and anaerobic species (82). Prophylaxis with nasal decongestants and nasal steroids can prevent radiographic occurrence of sinusitis (87).

Aggressive fungal sinusitis in immunocompromised patients causes rapid tissue destruction and morbidity over hours (88–90). The clinical presentation is commonly one of severe facial pain, but eschar formation, tissue necrosis, and cranial nerve involvement may be presenting features (88). Diagnosis can be made via clinical examination, including an insensate nasal cavity and necrotic appearance of the nasal mucosa, particularly on the middle turbinate. Biopsies of abnormal mucosa can be obtained for diagnosis. Because of their poor negative predictive value, frozen sections should not be relied on to exclude the diagnosis; fixed preparations are considered more reliable. This is a surgical disease; urgent and aggressive excision of all infected and nonviable-appearing tissue is the management priority. Often, the rapidly spreading infection and tissue necrosis necessitate wide surgical margins, as well as repeated debridement, which may leave patients with morbid functional and cosmetic defects. Adjuvant therapy includes systemic antifungals, reduction of immunosuppression, and glycemic control. Several general fungal resistance patterns are worth noting: *1) Mucor* is generally resistant to early-generation triazoles and echinocandins, necessitating amphotericin therapy; *2) Aspergillus* is susceptible to voriconazole and amphotericin; and *3) Scedosporium* is resistant to amphotericin and sensitive to triazoles (90, 91). Optimal empiric antifungal therapy has not been evaluated prospectively, but liposomal amphotericin B, together with a late-generation triazole (posaconazole or isavuconazole) is recommended on the basis of the aforementioned resistance patterns. Survival is highly correlated with the extent of invasion of the fungus, with central nervous system involvement portending a very poor prognosis.

Ludwig's Angina

Ludwig's angina is named for the sensation of asphyxiation accompanying the "woody" edema of perimandibular cellulitis (Figure 2). These infections typically arise from dental
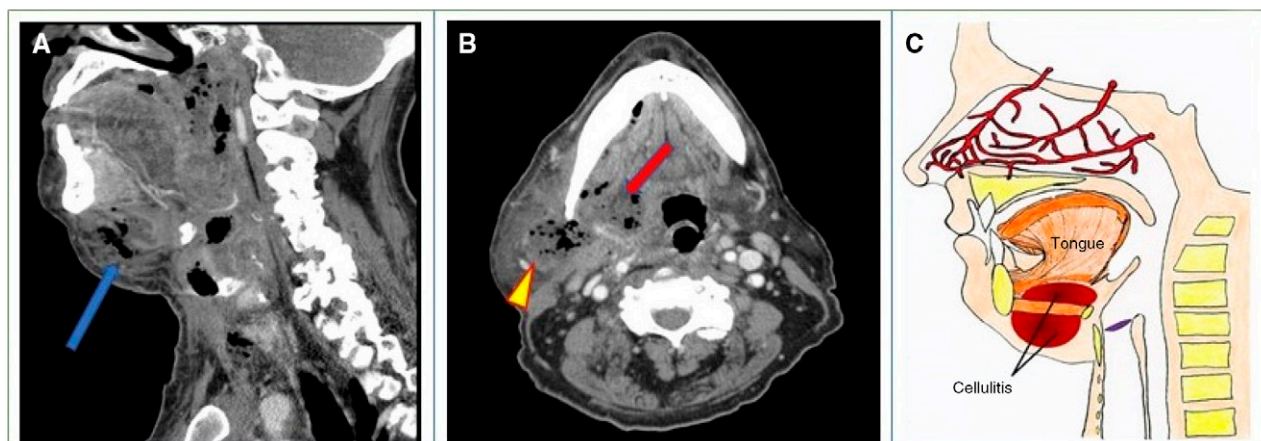

Figure 2. Ludwig's angina. (*A*) Sagittal computed tomographic (CT) scan of the neck shows a large, ill-defined region of hypodensity in the floor of the mouth/sublingual space (blue arrow) and diffuse fasciitis of the neck extending to involve the epiglottis and submandibular space. (*B*) Axial CT scan shows an abscess in the floor of the mouth (red arrow) and a right submandibular space abscess and soft tissue emphysema (yellow arrowhead). (*C*) Schematic diagram shows the sublingual and hypopharyngeal spaces involved in the infection, usually related to dental infection.

sources and can lead to airway compression resulting from lingual, epiglottic, or hypopharyngeal swelling (92). Human immunodeficiency virus infection and diabetes are recognized risk factors, but this syndrome can occur in immunocompetent patients, typically as a complication of dental procedures, untreated oral infections, or regional trauma (93).

For the critical care physician, airway management, antibiotic administration, and identifying drainable abscesses are priorities. When signs of airway compromise (drooling, muffled voice, stridor) are present, fiberoptic transnasal endoscopy to evaluate and secure an airway becomes necessary (94). Before or simultaneously with endoscopy, the patient should be prepared for surgical airway access, which is required in 30 to 60% of cases (93, 95, 96). Typical antibiotic regimens include intravenous ampicillin/sulbactam, which covers aerobic/anaerobic oral flora; severely immunocompromised patients should receive additional coverage for methicillin-resistant *S. aureus* and resistant gram-negative bacteria. CT imaging with an intravenous contrast agent is appropriate to evaluate for suppurative destruction, fascial gas, or drainable collections, as well as to assess the inferior margin of the infection (Figure 2). Airway compromise or multiorgan failure resulting from sepsis are typical causes of death, with a case fatality rate of 5 to 11% in the modern era (93, 95, 96).

Retropharyngeal and Parapharyngeal Abscesses: Deep Neck Infections

Unlike Ludwig's angina, deep neck infections (parapharyngeal and retropharyngeal abscesses) most commonly present in children owing to their abundant retropharyngeal lymph nodes, but these infections also occur in adults after instrumentation or in the context of poor dentition (97, 98). Other established risk factors for the development of deep infections include immunocompromised state, diabetes, intravenous drug abuse, older age, lower level of education, and smoking (97). Authors of a contemporary case series of adults with retropharyngeal or parapharyngeal abscesses described the frequency of presenting symptoms, which included localized swelling (93.2% of patients), throat pain (56.2% of patients), dysphagia (55.1%), neck stiffness (14.8% of patients), and trismus (14%). Airway obstruction requiring invasive airway management was reported in 8.5% of patients (97). A complicated course is predicted by a C-reactive protein concentration greater than 100 μg/ml, involvement of more than two deep neck spaces, female sex, and infection with streptococcal species (97, 99). Complications include descending mediastinitis, laryngeal edema requiring a surgical airway, bacteremia with septic emboli, dural vein thrombosis, parameningeal spread, and carotid artery

rupture (100, 101). Lateral neck plain films can be used for initial screening, but they have a lower sensitivity for detection of deep neck infections (83% sensitivity) than contrast-enhanced computed tomography. CT studies also precisely define the anatomic spaces involved, which assists in treatment planning, making contrast-enhanced computed tomography the diagnostic modality of choice (Figure 3) (102, 103).

These infections are typically polymicrobial, with anaerobes generally outnumbering aerobes by a factor of 10 to 1 (102). *Streptococcus milleri* is the most common isolate in the nondiabetic population, whereas the diabetic population was enriched with *Klebsiella pneumoniae* (97). Penicillin coadministered with metronidazole is the antibiotic regimen of choice for an odontogenic source of infection, but immunocompromised patients require a broader-spectrum antibiotic against organisms such as *S. aureus* and enteric gram-negative rods. Modern antibiotics have reduced mortality from 50% to less than 5% (104).

The role of surgery is evolving. Together with antibiotics, minimally invasive approaches such as ultrasound- and computed tomography–guided aspiration have the advantage of early specimen collection and avoidance of a neck scar, as well as drainage of the space. Recent studies suggest that surgical drainage is associated
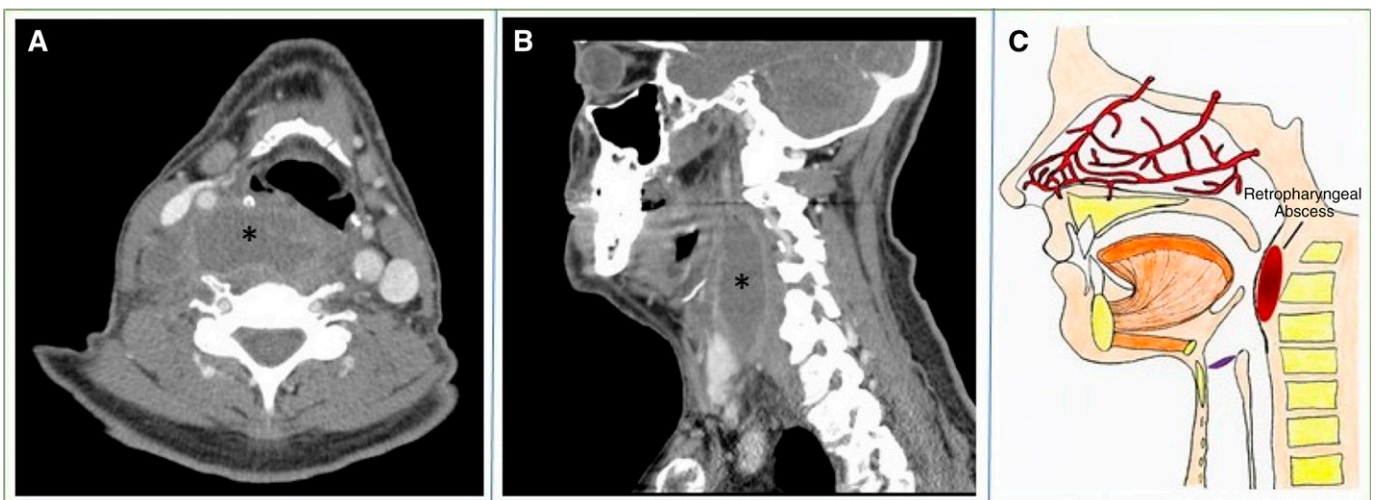

Figure 3. Retropharyngeal abscess. Contrast-enhanced (*A*) axial and (*B*) sagittal computed tomographic scans of a retropharyngeal abscess show a huge prevertebral space abscess associated with extensive soft tissue swelling, mass effect, and rim enhancement (asterisks). (*C*) Anatomic schematic shows the corresponding space involved.

with a longer length of stay and higher costs, without differences in complication rates or mortality (104). Patients with significant comorbidities often show lack of response to medical therapy alone (102). In these cases, as well as in patients with large or multiple infected spaces, a more aggressive surgical strategy is mandatory (104, 105). In one institution's experience, approximately one-third of cases required surgical drainage (97).

Epiglottitis

Routine *Haemophilus influenzae* type B vaccination has dramatically reduced the incidence of *H. influenzae* type B epiglottitis in children (106). In adults, the clinical course of epiglottitis is slower, with presentation occurring between 2 and 7 days in most cases. The most common presenting symptom is throat pain (>90% of cases). The gold standard for diagnosis is direct laryngoscopy, but lateral radiographs of the neck can be helpful in less symptomatic patients (Figure 4) (106). Beyond *H. influenzae*, a wide variety of bacterial pathogens have been implicated in adults, including all streptococcal species and *S. aureus*. Additional antibiotic

coverage for methicillin-resistant *S. aureus* should be administered in the critically ill. Dexamethasone is commonly given early in the course, and it is continued for at least 24 hours to treat the inflammatory component of the epiglottic swelling, but this practice is not data driven. The incidence of respiratory compromise requiring intubation is 30 to 40%, lower than that of children but still substantial, and the mortality rate is 6 to 7%. Because of these risks, affected patients should be monitored closely in the ICU (106, 107). Awake fiberoptic intubation is the ideal method of airway control in patients with stridor, anxiety, hypoxia, or inability to swallow secretions (drooling). A cricothyrotomy kit should be at the bedside with a provider ready to perform the procedure if intubation fails.

Postoperative Care in Head and Neck Surgery Patients in the ICU

Head and Neck Cancer

The incidence of head and neck carcinoma has declined in the United States over the

past 20 years, mirroring the decline in smoking (108). However, the incidence of HPV-related oropharyngeal cancer has risen considerably since the 1970s and now accounts for the majority of these malignancies (109). A minority of surgically treated patients require ICU admission, usually owing to surgical airway manipulation (total laryngectomy and tracheal resection). Total laryngectomy is indicated in *1*) patients with advanced cancer involving the larynx; *2*) as salvage therapy for patients in whom less invasive treatments fail, such as radiation or partial laryngectomy; *3*) in patients with a nonfunctional larynx that predisposes them to aspiration. In this procedure, the larynx is removed, and the trachea is diverted to an anterior neck stoma. The neopharynx is closed in a tube that leads to the esophagus only. This completely separates the patient's swallowing and respiratory tracts. It is critical to differentiate this procedure from a standard tracheostomy, where the patient's swallowing and airway tracts still share a common pathway (Figure 5).

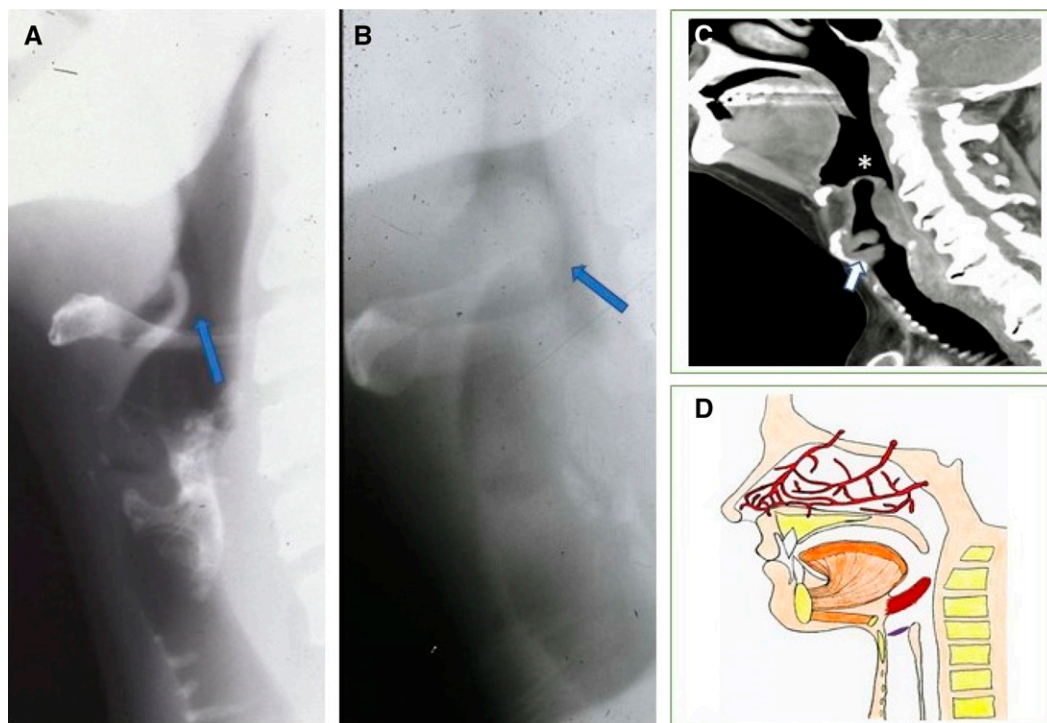Patients who have had a total laryngectomy cannot be intubated

Figure 4. Epiglottitis. Lateral radiographs of the neck show (*A*) normal-sized epiglottis and airway and (*B*) markedly swollen epiglottis and narrowed airway in the epiglottitis (blue arrows). (*C*) Sagittal computed tomographic scan of the neck shows folding of the epiglottis (white asterisk) and marked edema/thickening of the aryepiglottic fold, true and false cords (white arrow). These findings represent supraglottitis. (*D*) Schematic diagram shows the inflamed epiglottis in the context of the hypopharyngeal space.
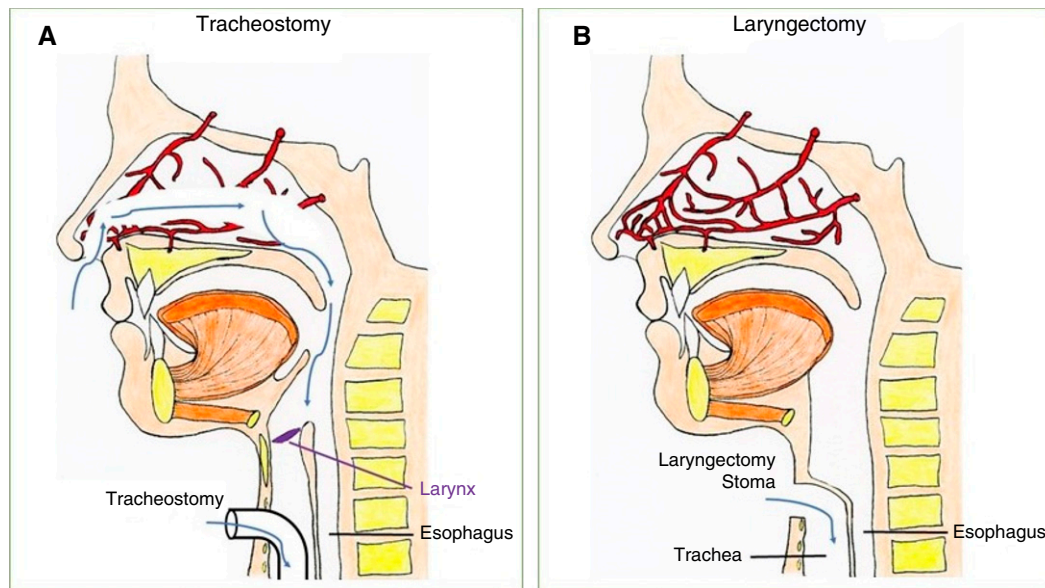
Figure 5. Tracheostomy versus laryngectomy. Anatomic comparison of airflow in the setting of (*A*) regular tracheostomy versus (*B*) through a stoma after total laryngectomy. Importantly, transoral or transnasal intubation of the trachea is impossible in patients who are status postlaryngectomy (*B*).

transorally, and obstruction of their tracheostoma will completely seal off their airway. It is generally recommended to place a sign above these patients' beds that reads, "Cannot intubate transorally!" If a postlaryngectomy patient requires ventilatory assistance, an endotracheal tube or cuffed tracheotomy tube can be inserted directly through the stoma and secured to the neck or chest. The distance from the stoma to the main carina is typically about 11 cm or less in a postlaryngectomy patient (110).

Tracheal resections are performed for postintubation tracheal stenosis and, less commonly, malignancies of the trachea (111). One of the most concerning postoperative complications is separation of the anastomosis, occurring in approximately 9% of patients, with an accompanying mortality rate of 7% (112). To help avoid this, a "guardian" stitch with a heavy monofilament between the anterior chest wall and the submental crease is placed to facilitate cervical flexion and is left in place for 1 week. Management of postoperative nausea is critical because retching or vomiting can lead to neck extension and/or potential aspiration. Prophylactic antiemetics and avoidance of narcotic pain medications are recommended for this reason (113).

Although most patients who undergo neck dissections do not require ICU level of care, carotid artery rupture is a complication of this procedure that requires rapid recognition and management. Carotid artery rupture is known as *carotid blowout syndrome* and occurs in approximately 3 to 4% of patients who undergo neck dissection. It was historically associated with a 40% mortality rate, but this has declined considerably with modern management (114). Patients with large cutaneous defects and high-output pharyngocutaneous fistulas, as well as patients who have previously received radiation, are at particularly high risk for carotid blowout syndrome. If blowout occurs, prompt control of hemorrhage with direct pressure, control of the airway, and fluid resuscitation are of paramount importance in order to stabilize the patient while mobilizing surgical and interventional teams for immediate surgical ligation or endovascular stenting to occlude the defect (114–116).

Flaps

Transfer of distant tissue flaps with microvascular anastomosis is used to cover the large tissue defects associated with operative management of head and neck cancers. The radial forearm free flap, anterolateral thigh flap, iliac crest flap, and fibula flap generally require ICU postoperative care, given the need for frequent flap checks to monitor flap viability and perfusion. Close observation of these

flaps is critical because immediate intervention is required to maximize the chance of salvaging the flap if perfusion is compromised. Approximately 50% of flaps with vascular compromise present within the first 4 hours of admission to the ICU, with 95% presenting within the first 72 hours (117).

Flaps are often checked hourly for the first 24 hours, then every 2 hours until 48 hours postoperatively, and every 4 hours after that (118). Flap monitoring is usually performed by clinical assessment and use of monitoring devices. A healthy flap should appear pink and warm with brisk capillary refill and should bleed after pinprick. Doppler flow is also commonly used to assess for viability of the vascular pedicle, and the site of maximal flow is often marked on the skin for ease of assessment. Surface temperature probes, transcutaneous oxygen tension probes, plethysmography, near-infrared spectroscopy, and tissue oxygen tension have also been used (119). Other important considerations include avoiding compression of the flap (such as with circumferential neck ties), proper head position, maintaining adequate blood pressure, avoiding hypothermia, and maintaining anastomosis patency with use of anticoagulants such as aspirin or heparin.

Flaps typically fail either by failure of arterial supply or by venous congestion. Arterial insufficiency usually presents as a

cold, pale flap without evidence of Doppler flow. Venous congestion creates edema and ecchymosis. Whereas arterial insufficiency will require either anticoagulation or surgical exploration, venous congestion can sometime be treated with leech therapy to help drain the excess venous blood (120).

Skull Base Tumors

Patients who have undergone skull base tumor resection are frequently admitted to the ICU postoperatively. Two key concerns in the management of these patients are cerebrospinal fluid (CSF) leaks and cranial neuropathies. CSF leak carries a high risk of meningitis. Patients should be assessed for clear rhinorrhea, otorrhea or discharge from the incision site. This fluid can be tested for β-2 transferrin, which is both sensitive and specific for CSF (121). However, this test commonly must be sent to an outside facility for analysis and can take several days for a result, limiting its utility. A quicker, simpler method by which to identify CSF is measurement of the glucose concentration of the nasal discharge, because CSF is composed approximately two-thirds of serum glucose (122). Conservative strategies

for prevention and management of CSF leaks include head-of-bed elevation, use of stool softeners, and avoidance of activities that increase CSF pressure. Lumbar drains are often used to lower CSF pressure, facilitating closure of the operative defect. In one study, 87% of CSF leaks after acoustic neuroma surgery were controlled with these measures alone (123).

Cranial neuropathies are caused by the tumor itself or by iatrogenic damage during resection. Damage to the inner ear labyrinth or the vestibular nerves can cause significant vertigo, nausea, and vomiting, which typically slowly resolve spontaneously over the course of several weeks. After an acute loss of peripheral vestibular function, vestibular suppressants such as meclizine or benzodiazepines should generally be avoided. Although these medications can provide some relief from acute vertigo, they will delay central compensation for a peripheral vestibular loss and can significantly prolong the recovery process (124). These patients can be reassured that their symptoms will improve and should be treated as needed with antiemetic

medications that do not suppress the vestibular system, such as ondansetron.

Facial nerve dysfunction is important to recognize. When significant weakness of the facial nerve is noted postoperatively, assessing eyelid closure is critical. Failure to fully close the eye places the patient at risk for exposure keratitis, which can lead to corneal ulceration and blindness. Aggressive application of artificial tears while the patient is awake and lubricating ointments at bedtime can help prevent these complications. Taping, patching, or padding of the eye is controversial because this can prevent adequate examination and lead to iatrogenic damage to the cornea if not performed properly (125). For patients who are not expected to have any meaningful facial nerve recovery, a gold weight can be placed in the upper eyelid to help promote adequate closure (126). ■

References

1 Domino KB, Posner KL, Caplan RA, Cheney FW. Airway injury during anesthesia: a closed claims analysis. *Anesthesiology* 1999;91: 1703–1711.

2 Tadié JM, Behm E, Lecuyer L, Benhmamed R, Hans S, Brasnu D, *et al*. Post-intubation laryngeal injuries and extubation failure: a fiberoptic endoscopic study. *Intensive Care Med* 2010;36:991–998.

3 Girard TD, Alhazzani W, Kress JP, Ouellette DR, Schmidt GA, Truwit JD, *et al*.; ATS/CHEST Ad Hoc Committee on Liberation from Mechanical Ventilation in Adults. An Official American Thoracic Society/American College of Chest Physicians Clinical Practice guideline: liberation from mechanical ventilation in critically ill adults. Rehabilitation protocols, ventilator liberation protocols, and cuff leak tests. *Am J Respir Crit Care Med* 2017;195: 120–133.

4 Mort TC. Continuous airway access for the difficult extubation: the efficacy of the airway exchange catheter. *Anesth Analg* 2007;105: 1357–1362.

5 Duggan LV, Law JA, Murphy MF. Brief review: supplementing oxygen through an airway exchange catheter: efficacy, complications, and recommendations. *Can J Anaesth* 2011;58:560–568.

6 McLean S, Lanam CR, Benedict W, Kirkpatrick N, Kheterpal S, Ramachandran SK. Airway exchange failure and complications with the use of the Cook Airway Exchange Catheter®: a single center cohort study of 1177 patients. *Anesth Analg* 2013;117: 1325–1327.

7 Kikura M, Suzuki K, Itagaki T, Takada T, Sato S. Age and comorbidity as risk factors for vocal cord paralysis associated with tracheal intubation. *Br J Anaesth* 2007;98:524–530.

8 Hagberg CA, Connis RT. Difficult Airway Society 2015 guidelines for the management of unanticipated difficult intubation in adults: not just another algorithm. *Br J Anaesth* 2015;115:812–814. [Published erratum appears in *Br J Anaesth* 2016;116:309.]

9 Langvad S, Hyldmo PK, Nakstad AR, Vist GE, Sandberg M. Emergency cricothyrotomy – a systematic review. *Scand J Trauma Resusc Emerg Med* 2013;21:43.

10 Gillespie MB, Eisele DW. Outcomes of emergency surgical airway procedures in a hospital-wide setting. *Laryngoscope* 1999;109: 1766–1769.

11 Higgins KM, Punthakee X. Meta-analysis comparison of open versus percutaneous tracheostomy. *Laryngoscope* 2007;117:447–454.

12 De Leyn P, Bedert L, Delcroix M, Depuydt P, Lauwers G, Sokolov Y, *et al*.; Belgian Association of Pneumology and Belgian Association of Cardiothoracic Surgery. Tracheotomy: clinical review and guidelines. *Eur J Cardiothorac Surg* 2007;32:412–421.

13 el-Kilany SM. Complications of tracheostomy. *Ear Nose Throat J* 1980; 59:123–129.

14 Walsh TJ, Anaissie EJ, Denning DW, Herbrecht R, Kontoyiannis DP, Marr KA, *et al*.; Infectious Diseases Society of America. Treatment of aspergillosis: clinical practice guidelines of the Infectious Diseases Society of America. *Clin Infect Dis* 2008;46:327–360.

15 Kumar T, Epstein M, Markovskaya Y, Narasimhan M, Rosen M, Talwar A. Bronchoscopy and endobronchial disease in patients with human immunodeficiency virus infection. *Indian J Chest Dis Allied Sci* 2011;53:99–105.

16 Miller RF, Tomlinson MC, Cottrill CP, Donald JJ, Spittle MF, Semple SJ. Bronchopulmonary Kaposi's sarcoma in patients with AIDS. *Thorax* 1992;47:721–725.

17 Imoto EM, Stein RM, Shellito JE, Curtis JL. Central airway obstruction due to cytomegalovirus-induced necrotizing tracheitis in a patient with AIDS. *Am Rev Respir Dis* 1990;142:884–886.

18 Baras L, Farber CM, Van Vooren JP, Parent D. Herpes simplex virus tracheitis in a patient with the acquired immunodeficiency syndrome. *Eur Respir J* 1994;7:2091–2093.

19 Nseir S, Di Pompeo C, Pronnier P, Beague S, Onimus T, Saulnier F, *et al*. Nosocomial tracheobronchitis in mechanically ventilated patients: incidence, aetiology and outcome. *Eur Respir J* 2002;20: 1483–1489.

20 Henley SJ, Richards TB, Underwood JM, Eheman CR, Plescia M, McAfee TA; Centers for Disease Control and Prevention (CDC). Lung cancer incidence trends among men and women – United States, 2005–2009. *MMWR Morb Mortal Wkly Rep* 2014;63:1–5. [Published erratum appears in *MMWR Morb Mortal Wkly Rep* 2014;63:45.]

21 Kwong JS, Adler BD, Padley SP, Müller NL. Diagnosis of diseases of the trachea and main bronchi: chest radiography vs CT. *AJR Am J Roentgenol* 1993;161:519–522.

22 Wu CC, Shepard JAO. Tracheal and airway neoplasms. *Semin Roentgenol* 2013;48:354–364.

23 Gaissert HA, Grillo HC, Shadmehr MB, Wright CD, Gokhale M, Wain JC, *et al*. Long-term survival after resection of primary adenoid cystic and squamous cell carcinoma of the trachea and carina. *Ann Thorac Surg* 2004;78:1889–1896, discussion 1896–1897.

24 Bhattacharyya N. Contemporary staging and prognosis for primary tracheal malignancies: a population-based analysis. *Otolaryngol Head Neck Surg* 2004;131:639–642.

25 Webb BD, Walsh GL, Roberts DB, Sturgis EM. Primary tracheal malignant neoplasms: the University of Texas MD Anderson Cancer Center experience. *J Am Coll Surg* 2006;202:237–246.

26 Anand VK, Alemar G, Warren ET. Surgical considerations in tracheal stenosis. *Laryngoscope* 1992;102:237–243.

27 Streitz JM Jr, Shapshay SM. Airway injury after tracheotomy and endotracheal intubation. *Surg Clin North Am* 1991;71:1211–1230.

28 Al-Qadi MO, Artenstein AW, Braman SS. The "forgotten zone": acquired disorders of the trachea in adults. *Respir Med* 2013;107: 1301–1313.

29 D'Andrilli A, Venuta F, Rendina EA. Subglottic tracheal stenosis. *J Thorac Dis* 2016;8(Suppl 2):S140–S147.

30 Muniappan A, Wain JC, Wright CD, Donahue DM, Gaissert H, Lanuti M, *et al*. Surgical treatment of nonmalignant tracheoesophageal fistula: a thirty-five year experience. *Ann Thorac Surg* 2013;95: 1141–1146.

31 Ke M, Wu X, Zeng J. The treatment strategy for tracheoesophageal fistula. *J Thorac Dis* 2015;7(Suppl 4):S389–S397.

32 Moellman JJ, Bernstein JA, Lindsell C, Banerji A, Busse PJ, Camargo CA Jr, *et al*.; American College of Allergy, Asthma & Immunology (ACAAI); Society for Academic Emergency Medicine (SAEM). A consensus parameter for the evaluation and management of angioedema in the emergency department. *Acad Emerg Med* 2014; 21:469–484.

33 Ishoo E, Shah UK, Grillone GA, Stram JR, Fuleihan NS. Predicting airway risk in angioedema: staging system based on presentation. *Otolaryngol Head Neck Surg* 1999;121:263–268.

34 Simons FER, Ardusso LRF, Bilò MB, Dimov V, Ebisawa M, El-Gamal YM, *et al*.; World Allergy Organization. 2012 update: World Allergy Organization guidelines for the assessment and management of anaphylaxis. *Curr Opin Allergy Clin Immunol* 2012; 12:389–399.

35 Kemp SF, Lockey RF. Anaphylaxis: a review of causes and mechanisms. *J Allergy Clin Immunol* 2002;110:341–348.

36 Driver BE, McGill JW. Emergency department airway management of severe angioedema: a video review of 45 intubations. *Ann Emerg Med* 2017;69:635–639.

37 Müllner M, Urbanek B, Havel C, Losert H, Waechter F, Gamper G. Vasopressors for shock. *Cochrane Database Syst Rev* 2004;(3): CD003709.

38 Kemp SF, Lockey RF, Simons FER; World Allergy Organization ad hoc Committee on Epinephrine in Anaphylaxis. Epinephrine: the drug of choice for anaphylaxis. A statement of the World Allergy Organization. *Allergy* 2008;63:1061–1070.

39 Ring J, Grosber M, Möhrenschlager M, Brockow K. Anaphylaxis: acute treatment and management. *Chem Immunol Allergy* 2010;95: 201–210.

40 Craig TJ, Bernstein JA, Farkas H, Bouillet L, Boccon-Gibod I. Diagnosis and treatment of bradykinin-mediated angioedema: outcomes from an angioedema expert consensus meeting. *Int Arch Allergy Immunol* 2014;165:119–127.

41 Stauber T, Confino-Cohen R, Goldberg A. Life-threatening angioedema induced by angiotensin-converting enzyme inhibitors: characteristics and risk factors. *Am J Rhinol Allergy* 2014;28:54–58.

42 Kostis JB, Kim HJ, Rusnak J, Casale T, Kaplan A, Corren J, *et al*. Incidence and characteristics of angioedema associated with enalapril. *Arch Intern Med* 2005;165:1637–1642.

43 Hassen GW, Kalantari H, Parraga M, Chirurgi R, Meletiche C, Chan C, *et al*. Fresh frozen plasma for progressive and refractory angiotensin-converting enzyme inhibitor-induced angioedema. *J Emerg Med* 2013;44:764–772.

44 Sabroe RA, Black AK. Angiotensin-converting enzyme (ACE) inhibitors and angio-oedema. *Br J Dermatol* 1997;136:153–158.

45 Malde B, Regalado J, Greenberger PA. Investigation of angioedema associated with the use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. *Ann Allergy Asthma Immunol* 2007;98:57–63.

46 Baş M, Greve J, Stelter K, Havel M, Strassen U, Rotter N, *et al*. A randomized trial of icatibant in ACE-inhibitor-induced angioedema. *N Engl J Med* 2015;372:418–425.

47 Strassen U, Bas M, Hoffmann TK, Knopf A, Greve J. Treatment of angiotensin receptor blocker-induced angioedema: a case series. *Laryngoscope* 2015;125:1619–1623.

48 Haymore BR, Yoon J, Mikita CP, Klote MM, DeZee KJ. Risk of angioedema with angiotensin receptor blockers in patients with prior angioedema associated with angiotensin-converting enzyme inhibitors: a meta-analysis. *Ann Allergy Asthma Immunol* 2008;101: 495–499.

49 Nzeako UC, Frigas E, Tremaine WJ. Hereditary angioedema as a cause of transient abdominal pain. *J Clin Gastroenterol* 2002;34:57–61.

50 Nzeako UC, Frigas E, Tremaine WJ. Hereditary angioedema: a broad review for clinicians. *Arch Intern Med* 2001;161:2417–2429.

51 Cicardi M, Zanichelli A. Acquired angioedema. *Allergy Asthma Clin Immunol* 2010;6:14.

52 Bowen T, Cicardi M, Farkas H, Bork K, Longhurst HJ, Zuraw B, *et al*. 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. *Allergy Asthma Clin Immunol* 2010;6:24.

53 Longhurst HJ, Carr S, Khair K. C1-inhibitor concentrate home therapy for hereditary angioedema: a viable, effective treatment option. *Clin Exp Immunol* 2007;147:11–17.

54 De Serres J, Gröner A, Lindner J. Safety and efficacy of pasteurized C1 inhibitor concentrate (Berinert P) in hereditary angioedema: a review. *Transfus Apher Sci* 2003;29:247–254.

55 Cicardi M, Banerji A, Bracho F, Malbrán A, Rosenkranz B, Riedl M, *et al*. Icatibant, a new bradykinin-receptor antagonist, in hereditary angioedema. *N Engl J Med* 2010;363:532–541.

56 Cicardi M, Levy RJ, McNeil DL, Li HH, Sheffer AL, Campion M, *et al*. Ecallantide for the treatment of acute attacks in hereditary angioedema. *N Engl J Med* 2010;363:523–531.

57 Agostoni A, Aygören-Pürsün E, Binkley KE, Blanch A, Bork K, Bouillet L, *et al*. Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond. *J Allergy Clin Immunol* 2004;114(3 Suppl): S51–S131.

58 Gelfand JA, Sherins RJ, Alling DW, Frank MM. Treatment of hereditary angioedema with danazol: reversal of clinical and biochemical abnormalities. *N Engl J Med* 1976;295:1444–1448.

59 Blohmé G. Treatment of hereditary angioneurotic oedema with tranexamic acid: a random double-blind cross-over study. *Acta Med Scand* 1972;192:293–298.

60 Longhurst H, Cicardi M, Craig T, Bork K, Grattan C, Baker J, *et al*.; COMPACT Investigators. Prevention of hereditary angioedema attacks with a subcutaneous C1 inhibitor. *N Engl J Med* 2017;376: 1131–1140.

61 Cornpropst M, Collis P, Collier J, Babu YS, Wilson R, Zhang J, *et al*. Safety, pharmacokinetics, and pharmacodynamics of avoralstat, an oral plasma kallikrein inhibitor: phase 1 study. *Allergy* 2016;71: 1676–1683.

62 Schlosser RJ. Epistaxis. *N Engl J Med* 2009;360:784–789.

63 Middleton PM. Epistaxis. *Emerg Med Australas* 2004;16:428–440.

64 Sotello D, Rivas M, Mulkey Z, Nugent K. High-flow nasal cannula oxygen in adult patients: a narrative review. *Am J Med Sci* 2015;349: 179–185.

65 Lim M, Chaudhari M, Devesa PM, Waddell A, Gupta D. Management of upper airway obstruction secondary to warfarin therapy: the conservative approach. *J Laryngol Otol* 2006;120:e12.

66 Sim WS, Chung IS, Chin JU, Park YS, Cha KJ, Lee SC, *et al*. Risk factors for epistaxis during nasotracheal intubation. *Anaesth Intensive Care* 2002;30:449–452.

67 Pacheco-Lopez PC, Berkow LC, Hillel AT, Akst LM. Complications of airway management. *Respir Care* 2014;59:1006–1019, discussion 1019–1021.

68 Mulla O, Prowse S, Sanders T, Nix P. Epistaxis. *BMJ* 2012;344:e1097.

69 Sparacino LL. Epistaxis management: what's new and what's noteworthy. *Lippincotts Prim Care Pract* 2000;4:498–507.

70 Vaghela HM. Using a swimmer's nose clip in the treatment of epistaxis in the A&E department. *Accid Emerg Nurs* 2005;13:261–263.

71 Kamhieh Y, Fox H. Tranexamic acid in epistaxis: a systematic review. *Clin Otolaryngol* 2016;41:771–776.

72 Singer AJ, Blanda M, Cronin K, LoGiudice-Khwaja M, Gulla J, Bradshaw J, *et al*. Comparison of nasal tampons for the treatment of epistaxis in the emergency department: a randomized controlled trial. *Ann Emerg Med* 2005;45:134–139.

73 Awasthi D, Roy TM, Byrd RP Jr. Epistaxis and death by the trigeminocardiac reflex: a cautionary report. A case of trigeminocardiac reflex following nasal packing for epistaxis led to respiratory and cardiac arrest and patient death. *Fed Pract* 2015;32:73–77.

74 DeVries AS, Lesher L, Schlievert PM, Rogers T, Villaume LG, Danila R, *et al*. Staphylococcal toxic shock syndrome 2000–2006: epidemiology, clinical features, and molecular characteristics. *PLoS One* 2011;6: e22997.

75 Lin G, Bleier B. Surgical management of severe epistaxis. *Otolaryngol Clin North Am* 2016;49:627–637.

76 Reyre A, Michel J, Santini L, Dessi P, Vidal V, Bartoli JM, *et al*. Epistaxis: the role of arterial embolization. *Diagn Interv Imaging* 2015;96:757–773.

77 Alherabi AZ. Retropharyngeal hematoma. *Saudi Med J* 2008;29: 1501–1503.

78 Cohen AF, Warman SP. Upper airway obstruction secondary to warfarin-induced sublingual hematoma. *Arch Otolaryngol Head Neck Surg* 1989;115:718–720.

79 Kamming D, Patel A. Emergency anaesthetic strategies for the bleeding upper airway. *Hosp Med* 2005;66:250–251.

80 Khanna S, Dagum AB. A critical review of the literature and an evidence-based approach for life-threatening hemorrhage in maxillofacial surgery. *Ann Plast Surg* 2012;69:474–478.

81 van Zanten ARH, Dixon JM, Nipshagen MD, de Bree R, Girbes ARJ, Polderman KH. Hospital-acquired sinusitis is a common cause of fever of unknown origin in orotracheally intubated critically ill patients. *Crit Care* 2005;9:R583–R590.

82 George DL, Falk PS, Umberto Meduri G, Leeper KV Jr, Wunderink RG, Steere EL, *et al*. Nosocomial sinusitis in patients in the medical intensive care unit: a prospective epidemiological study. *Clin Infect Dis* 1998;27:463–470.

83 Rouby JJ, Laurent P, Gosnach M, Cambau E, Lamas G, Zouaoui A, *et al*. Risk factors and clinical relevance of nosocomial maxillary sinusitis in the critically ill. *Am J Respir Crit Care Med* 1994;150:776–783.

84 Plümer L, Schön G, Klatt J, Hanken H, Schmelzle R, Pohlenz P. Nasal position of nasotracheal tubes: a retrospective analysis of intraoperatively generated three-dimensional X-rays during maxillofacial surgery. *Eur J Med Res* 2014;19:55.

85 Hilbert G, Vargas F, Valentino R, Gruson D, Chene G, Bébéar C, *et al*. Comparison of B-mode ultrasound and computed tomography in the diagnosis of maxillary sinusitis in mechanically ventilated patients. *Crit Care Med* 2001;29:1337–1342.

86 Aaløkken TM, Hagtvedt T, Dalen I, Kolbenstvedt A. Conventional sinus radiography compared with CT in the diagnosis of acute sinusitis. *Dentomaxillofac Radiol* 2003;32:60–62.

87 Pneumatikos I, Konstantonis D, Tsagaris I, Theodorou V, Vretzakis G, Danielides V, *et al*. Prevention of nosocomial maxillary sinusitis in the ICU: the effects of topically applied alpha-adrenergic agonists and corticosteroids. *Intensive Care Med* 2006;32:532–537.

88 DeShazo R, Chapin K, Swain R. Fungal sinusitis. *N Engl J Med* 1997; 254:7–12.

89 Gillespie MB, O'Malley BW Jr, Francis HW. An approach to fulminant invasive fungal rhinosinusitis in the immunocompromised host. *Arch Otolaryngol Head Neck Surg* 1998;124:520–526.

90 Sun HY, Singh N. Mucormycosis: its contemporary face and management strategies. *Lancet Infect Dis* 2011;11:301–311.

91 Lackner M, de Hoog GS, Verweij PE, Najafzadeh MJ, Curfs-Breuker I, Klaassen CH, *et al*. Species-specific antifungal susceptibility patterns of *Scedosporium* and *Pseudallescheria* species. *Antimicrob Agents Chemother* 2012;56:2635–2642.

92 Grodinsky M. Retropharyngeal and lateral pharyngeal abscesses: an anatomic and clinical study. *Ann Surg* 1939;110:177–199.

93 Moreland LW, Corey J, McKenzie R. Ludwig's angina: report of a case and review of the literature. *Arch Intern Med* 1988;148:461–466.

94 Duprey K, Rose J, Fromm C. Ludwig's angina. *Int J Emerg Med* 2010;3: 201–202.

95 Bansal A, Miskoff J, Lis RJ. Otolaryngologic critical care. *Crit Care Clin* 2003;19:55–72.

96 Botha A, Jacobs F, Postma C. Retrospective analysis of etiology and comorbid diseases associated with Ludwig's angina. *Ann Maxillofac Surg* 2015;5:168–173.

97 Boscolo-Rizzo P, Stellin M, Muzzi E, Mantovani M, Fuson R, Lupato V, *et al*. Deep neck infections: a study of 365 cases highlighting recommendations for management and treatment. *Eur Arch Otorhinolaryngol* 2012;269:1241–1249.

98 Woods CR, Cash ED, Smith AM, Smith MJ, Myers JA, Espinosa CM, *et al*. Retropharyngeal and parapharyngeal abscesses among children and adolescents in the United States: epidemiology and management trends, 2003–2012. *J Pediatric Infect Dis Soc* 2016;5:259–268.

99 Elsherif AM, Park AH, Alder SC, Smith ME, Muntz HR, Grimmer F. Indicators of a more complicated clinical course for pediatric patients with retropharyngeal abscess. *Int J Pediatr Otorhinolaryngol* 2010;74:198–201.

100 Adil E, Tarshish Y, Roberson D, Jang J, Licameli G, Kenna M. The public health impact of pediatric deep neck space infections. *Otolaryngol Head Neck Surg* 2015;153:1036–1041.

101 Hasegawa J, Hidaka H, Tateda M, Kudo T, Sagai S, Miyazaki M, *et al*. An analysis of clinical risk factors of deep neck infection. *Auris Nasus Larynx* 2011;38:101–107.

102 Caccamese JF Jr, Coletti DP. Deep neck infections: clinical considerations in aggressive disease. *Oral Maxillofac Surg Clin North Am* 2008;20: 367–380.

103 Nagy M, Backstrom J. Comparison of the sensitivity of lateral neck radiographs and computed tomography scanning in pediatric deep-neck infections. *Laryngoscope* 1999;109:775–779.

104 Bakir S, Tanriverdi MH, Gün R, Yorgancilar AE, Yildirim M, Tekbaş G, *et al*. Deep neck space infections: a retrospective review of 173 cases. *Am J Otolaryngol* 2012;33:56–63.

105 Lee JK, Kim HD, Lim SC. Predisposing factors of complicated deep neck infection: an analysis of 158 cases. *Yonsei Med J* 2007;48: 55–62.

106 Westerhuis B, Bietz MG, Lindemann J. Acute epiglottitis in adults: an under-recognized and life-threatening condition. *S D Med* 2013;66: 309–311, 313.

107 Chroboczek T, Cour M, Hernu R, Baudry T, Bohé J, Piriou V, *et al*. Long-term outcome of critically ill adult patients with acute epiglottitis. *PLoS One* 2015;10:e0125736.

108 Sturgis EM, Cinciripini PM. Trends in head and neck cancer incidence in relation to smoking prevalence: an emerging epidemic of human papillomavirus-associated cancers? *Cancer* 2007;110:1429–1435.

109 Rettig EM, D'Souza G. Epidemiology of head and neck cancer. *Surg Oncol Clin N Am* 2015;24:379–396.

110 Pang G, Edwards MJ, Greenland KB. Vocal cords-carina distance in anaesthetised Caucasian adults and its clinical implications for tracheal intubation. *Anaesth Intensive Care* 2010;38:1029–1033.

111 Grillo HC. Development of tracheal surgery: a historical review. Part 2: Treatment of tracheal diseases. *Ann Thorac Surg* 2003;75: 1039–1047.

112 Wright CD, Grillo HC, Wain JC, Wong DR, Donahue DM, Gaissert HA, *et al*. Anastomotic complications after tracheal resection: prognostic factors and management. *J Thorac Cardiovasc Surg* 2004;128: 731–739.

113 Auchincloss HG, Wright CD. Complications after tracheal resection and reconstruction: prevention and treatment. *J Thorac Dis* 2016;8 (Suppl 2):S160–S167.

114 Cohen J, Rad I. Contemporary management of carotid blowout. *Curr Opin Otolaryngol Head Neck Surg* 2004;12:110–115.

115 Powitzky R, Vasan N, Krempl G, Medina J. Carotid blowout in patients with head and neck cancer. *Ann Otol Rhinol Laryngol* 2010;119: 476–484.

116 Haas RA, Ahn SH. Interventional management of head and neck emergencies: carotid blowout. *Semin Intervent Radiol* 2013;30: 245–248.

117 Bui DT, Cordeiro PG, Hu QY, Disa JJ, Pusic A, Mehrara BJ. Free flap reexploration: indications, treatment, and outcomes in 1193 free flaps. *Plast Reconstr Surg* 2007;119:2092–2100.

118 Smit JM, Acosta R, Zeebregts CJ, Liss AG, Anniko M, Hartman EH. Early reintervention of compromised free flaps improves success rate. *Microsurgery* 2007;27:612–616.

119 Hirigoyen MB, Urken ML, Weinberg H. Free flap monitoring: a review of current practice. *Microsurgery* 1995;16:723–726, discussion 727.

120 Chepeha DB, Nussenbaum B, Bradford CR, Teknos TN. Leech therapy for patients with surgically unsalvageable venous obstruction after revascularized free tissue transfer. *Arch Otolaryngol Head Neck Surg* 2002;128:960–965.

121 Levenson MJ, Desloge RB, Parisier SC. Beta-2 transferrin: limitations of use as a clinical marker for perilymph. *Laryngoscope* 1996;106: 159–161.

122 Seehusen DA, Reeves MM, Fomin DA. Cerebrospinal fluid analysis. *Am Fam Physician* 2003;68:1103–1108.

123 Fishman AJ, Hoffman RA, Roland JT Jr, Lebowitz RA, Cohen NL. Cerebrospinal fluid drainage in the management of CSF leak following acoustic neuroma surgery. *Laryngoscope* 1996;106: 1002–1004.

124 Lacour M. Restoration of vestibular function: basic aspects and practical advances for rehabilitation. *Curr Med Res Opin* 2006;22: 1651–1659.

125 Rahman I, Sadiq SA. Ophthalmic management of facial nerve palsy: a review. *Surv Ophthalmol* 2007;52:121–144.

126 Grusha YO, Fedorov AA, Iskusnykh NS, Bogacheva NV, Kobzova MV, Novikov IA, *et al*. Gold weight implants for lagophthalmos correction in chronic facial nerve paralysis (late results) [in Russian]. *Vestn Oftalmol* 2016;132:26–32.