

# Update in Nonpulmonary Critical Care

## An Update on Otolaryngology in Critical Care

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Otolaryngologic disorders present several peculiarities that pose a formidable challenge to the practicing intensivist. The proximity of sensitive anatomic structures in a relatively narrow space predisposes patients to serious complications from infectious and neoplastic diseases, yet the critical care literature addressing otolaryngologic problems is conspicuously lacking. Although a thorough discussion of this topic is beyond the scope of this article, we have provided an update on nosocomial bacterial rhinosinusitis, upper airway complications, and otic disorders from a critical care perspective. The now widely used technique of percutaneous dilatational tracheostomy in intensive care units (ICUs) has been described extensively in the recent literature (1, 2) and is not addressed in this review.

### NOSOCOMIAL SINUSITIS

According to the National Nosocomial Infection Survey System, infections of the ear, eyes, nose, or throat account for 4% of all nosocomial infections (3). Sinusitis represented 64% of these infections alone. Epidemiologic surveys have linked both nasotracheal and nasogastric intubation to the occurrence of nosocomial sinusitis (4, 5). In a prospective study of 162 patients, Rouby and colleagues (4) demonstrated that after 7 days of nasotracheal intubation and nasogastric tube placement, 95% of patients had evidence of radiologic pansinusitis compared with 25% with orotracheal and orogastric intubation. The principal mechanism responsible for the development of sinusitis in these patients is impaired drainage of the paranasal sinuses as a result of physical irritation and mechanical obstruction of the ostia, which lead to an overgrowth of bacterial flora in the sinuses. Other contributory factors have included nasal colonization with enteric gram-negative bacilli, sedation, use of high-dose corticosteroid therapy, and a Glasgow coma score of 7 or more (6), although none have been proven to be causative.

There is an ongoing debate on whether nosocomial sinusitis can be the source of ventilator-associated pneumonia. In three studies of patients requiring mechanical ventilation (7–9), the incidence of ventilator-associated pneumonia ranged from 29–67% among patients with sinusitis, compared with 5–43% without sinusitis. Similarities between organisms isolated from the lower respiratory tract and the sinuses occurred in 38–56%.

The diagnosis of nosocomial sinusitis involves typically radiographic evaluation. Plain bedside radiography is of little value in the ICU setting because adequate radiographic examination

will require at least five views to achieve a confidence level of 88% (10). B-mode ultrasonography has been suggested as a rapid and innocuous tool for the daily monitoring of maxillary sinusitis in critically ill patients with a sensitivity of 50–100% and a specificity of 87–100% when compared with computer tomography scan or standard radiography (11–13). Its accuracy, however, is questionable in suspected ethmoid, frontal, or sphenoid involvement (14). A computer tomography scan remains the most reliable noninvasive diagnostic modality for those deemed stable to be transferred to the radiology suite. The presence of an air fluid level or opacification is considered the hallmark for the diagnosis of radiographic sinusitis. In these cases, the yield of positive cultures on aspiration has ranged from 40–70% (15, 16). When the presence of purulence in the middle meatus on endoscopic examination was combined with radiographic evidence of sinusitis, positive antral lavage increased to 92% (17).

Antral lavage is considered the standard diagnostic and therapeutic procedure among ICU patients with rhinosinusitis (18). The technique is performed either transnasally via the inferior meatus or transorally through the canine fossa. Both methods carry the risk of contamination with the local bacterial flora (19). Even with thorough disinfection of the nasal cavity with povidone-iodine, only 50% of septum swab samples were free of bacteria (4). To avoid contact with the oral mucosa, Westergren and colleagues attempted antral penetration by preparing a free bone area for trocar insertion (20) reducing the rate of contamination to 5% (95% confidence interval, 0–23%). Using 16S ribosomal RNA polymerase chain reaction followed by sequencing, the same group of investigators suggested that induction of maxillary sinus infection could take place within the mucosa and is not necessarily a direct propagation from the antrum (21). Not uncommonly, the diagnostic value of sinus aspirates in patients who are receiving antibiotics is put to question as prior antibiotic therapy may preclude the recovery of organisms in sinus aspirate cultures (6). However, in a prospective study of 24 mechanically ventilated patients with radiographic evidence of sinusitis, Souweine and colleagues were able to isolate at least one etiologic organism in 63% of the cases while receiving antibiotic treatment (22).

Limiting aspiration to the maxillary sinuses might miss the source of infection if located in the other sinuses. The potential importance of this observation is supported by the lack of improvement of 12% of patients who underwent maxillary sinus drainage with no other source of infection other than opacification of the accompanying ethmoid and sphenoid sinuses on computer tomography scan (4).

The choice of antibiotics must consider the local hospital flora and the antibiogram of drug-resistant pathogens such as methicillin-resistant *Staphylococcus aureus*, extended spectrum  $\beta$ -lactamase-positive enterobacteriaceae, and quinolone-resistant *Pseudomonas aeruginosa*. Anaerobic coverage should be entertained as anaerobic bacteria have been cultured in up to 60% of the cases (23).

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Antibiotics should be adjusted according to the susceptibility of antral cultures. In retrospective study of 42 critically ill patients, Ramadan and colleagues showed that 83% of these patients had a resolution of fever when their antibiotic were changed to match the antibiogram of pathogens recovered from antral lavage (18). The optimal duration of therapy is not well defined, although a minimum of 7 days of systemic antibiotics is recommended (24). Failure to respond should prompt the insertion of a drainage catheter. Nasal decongestants are often prescribed, but their efficacy remains unclear in the absence of randomized controlled studies.

## AIRWAY DISORDERS

### Upper Airway Obstruction

Supraglottitis was predominantly a disease of children, but the widespread use of the *Haemophilus influenzae* type B vaccination in children in the late 1980s has reduced its incidence to 0.6 per 100,000 according to the most recent survey (25). By comparison, the mean annual incidence of supraglottitis in adults has risen from 0.8 to 3.1 per 100,000 in the years spanning 1986–2000 (26). The case fatality rate remained constant, however, with reports ranging from 0–7.1% (27, 28).

Throat culture is positive in 45–61% of the cases (29), whereas bacteremia occurs in 12–26%, with *H. influenzae* type B accounting for the majority of isolates (30). Other agents occasionally implicated are pneumococci, staphylococci, streptococci, and *Candida albicans*. Although herpes simplex has been reported in a number of cases (31), the role of viruses in acute epiglottitis has not been well established. Noninfectious etiologies have included both chemical and thermal injuries sustained during the ingestion of caustic material (32) and the inhalation of hot objects while smoking illicit drugs (33).

Over 90% of those afflicted with the disease present with severe sore throat and odynophagia (31). Stridor, drooling, and sitting erect have been reported in less than 50% of the cases. Physical examination may reveal tenderness of anterior neck and cervical adenopathy. The diagnosis could be easily mistaken for a case of pharyngitis unless a high index of suspicion is maintained. Once suspected, it is recommended that oral examination be conducted in the presence of an anesthesiologist or an otolaryngologist because of the risk of sudden airway occlusion. A radiograph of the lateral neck may show thickening of the epiglottis, prevertebral soft tissue swelling, and an emphysematous epiglottitis. However, there are reports of a normal-appearing epiglottis on radiographic examination (34). To account for the wide variability in size of the soft tissue structures in the supraglottic region, Nemzek and coworkers proposed that the ratio of the width of the epiglottis to the anteroposterior width of the C-4 vertebral body should not be greater than 0.33 (35). When tested on 27 adult patients with epiglottitis, the sensitivity and specificity were determined at 96% and 100%, respectively. In cases of normal-appearing epiglottis on lateral neck radiography, careful nasopharyngeal fiberoptic examination may be attempted. Typically, there is diffuse swelling of the aryepiglottic structures unlike the classic cherry red epiglottis in the pediatric age group.

For those presenting with symptoms suggestive of airway compromise, an examination in the operating room with placement of an artificial airway is recommended. In less severe cases, the timing of elective intubation before signs of airway obstruction is unclear because of the lack of reliable criteria for discriminating at presentation between patients who may sustain a sudden airway obstruction (36) from those whose course may be benign. It has been suggested that adults who present within 8 hours of symptoms onset are more likely to develop respiratory distress requir-

ing an artificial airway than those who present later and thus may not progress (31).

Orotracheal intubation or tracheostomy may be performed under local anesthesia, but both are potentially stimulating procedures that may precipitate a sudden loss of the airway. Bag and mask ventilation can simply worsen or complete the airway obstruction and should be avoided. Friedman and colleagues recommended a rapid sequence induction with the facility to perform a cricothyroid puncture if intubation proves difficult (37).

Treatment should begin promptly with an intravenous antibiotic active against  $\beta$  lactamase-producing *H. influenzae*. A delay in recovery or deterioration in clinical condition should prompt the search for a coexisting epiglottic abscess. Epinephrine, either nebulized or intramuscular, has not shown to alter the need for placement of artificial airways, decrease ICU stay, or length of hospitalization (28). The indication for glucocorticoids use has been based on reducing the inflammatory edema. Many practitioners use them empirically, although no conclusive evidence for their benefits has been shown.

### Ludwig's Angina

Ludwig's angina is a rapidly spreading cellulitis of the floor of the mouth involving the sublingual, submandibular, and submental spaces. It is characterized by a brawny, hard induration of the floor of the oral cavity with tongue elevation and airway compromise. The infection has usually an odontogenic cause pointing to a decayed mandibular molar tooth. Other less common causes include submandibular sialoadenitis, mandibular fractures, or trauma resulting from intubation or after bronchoscopy (38, 39).

Ludwig's angina has been reported in patients with history of alcoholism, diabetes mellitus, aplastic anemia, and immunodeficiency disorders, although the majority of those presenting with the disease have no prior comorbid conditions (40). A mixed flora of aerobic and anaerobic microbes, including streptococcal species, *S. aureus*, *Borrelia vincentii*, *Fusobacterium*, and *Bacteroides* species, is implicated in most cases. *Eikenella corrodens* is becoming a more frequently cultured pathogen with significant clinical implication because this organism tends to be resistant to clindamycin (41).

Management is directed toward securing a patent airway, providing systemic antibiotic therapy, and instituting early surgical decompression of the sublingual, submental, and submandibular spaces. Thirty-five percent will require an airway control in the form of either endotracheal intubation or tracheotomy (42). Stridor, drooling, and cyanosis are late signs of impeding airway obstruction and signal the need for an immediate artificial airway. Blind nasotracheal intubation is contraindicated, and rapid sequence induction for orotracheal intubation is controversial given the potential difficulties in obtaining adequate laryngoscopic visualization. Cricothyroidotomy is considered the preferred method in the acute period given that low tracheostomy carries the potential risk of spreading the infection to the mediastinum.

Medical management involves the administration of an immediate dose of 10 to 20 mg of dexamethasone on arrival to the emergency department followed by 4 to 6 mg every 6 hours for 48 hours (43). Dexamethasone treatment provides initial chemical decompression by decreasing edema and cellulitis, thus allowing improved penetration of antibiotics in the area. Antibiotic therapy consists of a combination of  $\beta$ -lactamase-resistant penicillin in combination with metronidazole. For those patients allergic to penicillin, a quinolone can be used instead. If indicated, surgical decompression and drainage are performed with removal of all offending teeth in the first 24 to 48 hours (39). Mortality ranges from 0–8.5% and occurs secondary to pneumonia, sepsis, empyema, and respiratory obstruction.

## Angioedema

Currently, angiotensin-converting enzyme inhibitors (ACEIs) account for more than 50% of the cases of angioedema in the United States (44). The edema is usually mild and regresses spontaneously with discontinuation of therapy. However, in 20% of the patients, symptoms progress rapidly to life-threatening airway obstruction. The majority of reactions occur in the first week of treatment, but delayed cases even after several years of therapy have been reported (45). The risk of angioedema with ACEIs is higher in blacks and appears not to be related to dose, specific ACEIs, or concomitant medications (46). The mechanism of ACEI-associated angioedema is not completely understood, although it is thought to be related to an altered metabolism of the kallikrein–kinin pathway. One hypothesis postulates that bradykinin, which is normally degraded by kininase II/angiotensin-converting enzyme, accumulates in the tissues causing vasodilation, increased vascular permeability, and histamine release (47). Low plasma levels of aminopeptidase P and dipeptidyl peptidase IV have been recently associated with ACEI-induced angioedema (48), although no skin or blood test is currently available to identify patients at risk for this complication.

Shortly after the release of angiotensin II receptor antagonists, similar reports of angioedema have been described in patients not having received previously ACEIs (49, 50). Because of the potential cross-reactivity, albeit small, the use of this class of drugs is not recommended for those patients who have experienced previously angioedema with an ACEI.

Apart from securing the airway, treatment includes antihistamines, subcutaneous epinephrine, and intravenous corticosteroids. However, the efficacy of these agents has not been proven in controlled trials, and the administration of these therapeutic measures does not appear to shorten the recovery period, although they may modify the progression of the disease (51). Recently, fresh-frozen plasma has been shown to substantially improve ACEI-related angioedema (52). Detailed documentation of the episode and adequate instruction of patients regarding the nature of the adverse event are crucial to prevent recurrences.

## Upper Airway Hemorrhage

Posterior epistaxis accounts for 20% of nosebleeds (53) and requires admission to an ICU in up to 13% of the cases (54). It is reported more commonly in older adults, especially men in the fifth decade of life with a history of hypertension and arteriosclerosis.

The traditional approach to control posterior bleeding relies on anterior–posterior nasal packing using commercial balloons, a Foley catheter, or specialized nasal packs (55, 56). However, these measures can be extremely uncomfortable and have been associated with serious complications such as septicemia, cerebral ischemia, myocardial infarction, and even death (57). Moreover, the failure rate for this approach can range from 0–52% (58, 59). A new paradigm advocating surgical intervention as a primary treatment for posterior epistaxis has been favored by shorter hospital stay (3.2 days), higher success rate (90%), and a cost savings of \$1,846 per patient for those undergoing arterial ligation over traditional packing (60). Alternatively, arterial embolization is advocated for bleeding sites that are difficult to reach surgically, for those with systemic bleeding disorders, and for patients who are compromised hemodynamically to undergo a surgical intervention. In experienced hands, the embolization success rate surpasses 90% with long-term morbidity rate of less than 1% (61).

Among the other causes of upper airway hemorrhage, tracheoinnominate fistula after tracheostomy placement represents an uncommon but a life-threatening complication, with a peak incidence between the first and second week (62). Approxi-

mately 50% of patients present with a massive hemorrhage, whereas the other half may report a small “herald” bleed (63). Although the most frequent site of fistula formation is at the level of the endotracheal cuff, approximately one-third results from pressure necrosis from the elbow or the tip of the cannula. Other predisposing factors include the presence of an anomalous innominate artery, infection, and the use of steroids.

Overinflation of the tracheostomy is the first maneuver that should be attempted in the face of a bedside massive hemorrhage. This technique can be successful in 85% of the cases (63). Otherwise, a cuffed endotracheal tube should be inserted under direct laryngoscopy into the glottis and beyond the tracheoinnominate fistula. Finger pressure is then applied on the innominate artery through the stomal opening after removal of the tracheostomy tube (64).

For those patients presenting with sentinel bleed, preparation should be made for transfer to the operating room and emergency chest exploration. A diagnostic flexible bronchoscopy might be attempted first, but a rigid bronchoscopy is recommended for a better visualization and superior ability to suction blood clots. The rigid bronchoscope allows the operator also to stop the bleeding by applying the tube firmly against the innominate artery. The postoperative death is relatively high, as only 25% of those who survive the surgery are discharged alive (65).

## OTIC DISORDERS

Hearing loss is a potentially debilitating complication of critical illness, yet the critical care literature has been lacking in addressing the problems of the auditory system in the ICU. Causes of hearing loss in critically ill patients encompass both the conductive and the sensorineural pathways. Classically, aminoglycosides have been implicated in hearing loss in critically ill patients. The ototoxicity manifests as an increase in the threshold of the highest frequencies (4000–8000 Hz) with a progressive rise in threshold across lower frequencies (66). The incidence of auditory toxicity is similar for gentamicin, tobramycin, and amikacin (6–13%), with netilmicin having the lowest incidence of cochlear toxicity (2.4%) (67). The risk of cochlear toxicity is increased with the duration of aminoglycoside therapy, the total dosage, the use of concomitant ototoxic medications, and the presence of hepatic or renal dysfunction (68). Recently, a genetic predisposition in a subpopulation of patients with alteration in the 12S subunit of the mitochondrial DNA has been linked to increased aminoglycoside toxicity. Fischel-Ghodsian and colleagues reported that this mutation was found in 17.1% who had aminoglycoside ototoxicity compared with none of the 400 controls who did not (69). Patients with this mutation can experience significant hearing loss after one or two doses.

Symptoms of ototoxicity can be delayed for as long as 6 weeks after completion of aminoglycoside treatment (70); however, up to 50% will recover between 1 week to 6 months after therapy is discontinued. Many studies have been conducted with the aim of finding a mechanism to protect the inner ear from aminoglycosides. Rigorous maintenance of peak and trough levels is no guarantee that a patient will not experience ototoxicity. Iron chelators, glial cell line–derived neurotrophic factor, *N*-methyl-D-aspartate antagonists, and fosfomycin have shown promising results in animal models, but further studies are needed to assess clinical utility (71).

Ototoxicity from macrolides, including the newer generation (clarithromycin and azithromycin), has been widely reported. Erythromycin appears to affect the auditory system when the dose equals or exceeds 4 g/day (72). Clarithromycin and azithromycin ototoxicity has been described in cases of prolonged treat-

ment of *Mycobacterium avium* complex infections (73, 74), but there are no reports to our knowledge implicating these agents in auditory impairment when administered in critical care settings. In contrast to aminoglycosides, the hearing loss from macrolides affects those frequencies used for everyday communication as well as those of higher frequencies. Albeit reversible in the majority of cases, there are reports of permanent ototoxicity (75).

Loop diuretics have been implicated in cochlear toxicity in both clinical reports and experimental studies. Otic injury is most likely to occur in patients with underlying renal disease, hypoalbuminemia, or those receiving other ototoxic drugs. The hearing loss occur typically within minutes of administration and resolves spontaneously within 24 hours. In the case of furosemide, ototoxicity usually occurs with total daily doses ranging from 40 mg to 21.6 g (76). More troublesome than the usually reversible cochlear toxicity associated with loop diuretics is the synergistic ototoxic effects of loop diuretics with aminoglycosides. Animal studies indicate that after a dose of an aminoglycoside, loop diuretics can cause outer hair cell loss in the cochlea up to 8 hours after treatment. The synergism does not occur, however, when the diuretic is given before aminoglycoside infusion (77).

Vancomycin is generally believed to be ototoxic, but reports of vancomycin-induced ototoxicity have been flawed as other potentially ototoxic agents were used concomitantly. In experimental animal studies to which large doses were given, there was no convincing evidence of ototoxicity from vancomycin use (78).

Besides pharmaceutical-induced ototoxicity, there are other ICU-related therapies that have been linked to otic disorders. Middle ear effusion has been reported to occur in 29–80% of patients with endotracheal intubation (79, 80). The majority of the effusions are sterile but infectious etiology as documented in up to 30% of patients receiving ventilatory support (79). The isolation of nosocomial gram-negative organisms, such as *P. aeruginosa*, *Enterobacter cloacae*, and *Klebsiella oxytoca* suggests a reflux of these bacteria into the eustachian tube with contiguous spread into the middle ear cavity (79).

Invasive positive pressure ventilation has not been linked, to our knowledge, with hearing loss; however, there are reports of tympanic injury sustained during resuscitation from respiratory arrest when positive pressures were delivered by mask ventilation (81). With the widespread use of noninvasive positive pressure ventilation, a more accurate assessment of auditory impairment is worthwhile to investigate in future research trials.

A high incidence of middle ear complications from hyperbaric oxygen therapy has been described in patients with artificial airways. In a retrospective study of 267 patients, 94% of intubated patients developed middle ear complications after hyperbaric oxygen treatment (serous otitis media, hemotympanum, and tympanic membrane rupture), with 61% requiring placement of tympanostomy tubes (82). The use of nasal decongestants has not been proven efficacious.

Periodic assessment of ICU noise ought to be undertaken, although a risk assessment for hearing impairment as a result of ICU noise pollution is unavailable at the present. The cost-utility of conducting surveillance for hearing loss in the ICU is limited by the inherent constraints of the portable testing devices available and the overriding therapeutic life-saving measures.

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