Review article
Infections of the airway

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Summary

Infections of the airway in children may present to the anesthetist as an emergency in several locations: the Emergency Department, the Operating Department or on Intensive Care. In all of these locations, relevant and up to date knowledge of presentations, diagnoses, potential complications and clinical management will help the anesthetist and the surgical team, not only with the performance of their interventions, but also in buying time before these are undertaken, avoiding complications and altering the eventual outcome for the child. Diseases such as epiglottitis and diphtheria may show diminished incidence but they have not gone away and their clinical features and essential management remain unchanged. Paradoxically, perhaps, some conditions such as Lemierre's syndrome appear to be making a comeback. In these instances, clinicians need to be alert to these less common conditions, not only in regard to the disease itself but also to potentially serious complications. This article describes those infections of the airway that are most likely to present to the anesthetist, their attendant complications and recommendations for treatment.

Keywords: pediatric; airway; infection; Lemierre; abscess; laryngotracheitis

Introduction

Given that both viral and bacterial infections may produce disorders of similar presentation and sometimes may do this concurrently, it is more logical to examine these disorders by the site and nature of their condition rather than by their infective origin.

Oro-pharynx

In a 6-year series of head and neck infections in children, it was noted that 49% affected the

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peritonsillar space, 22% the retropharyngeal and 2% para-pharyngeal (1).

Tonsillitis, peritonsillar abscess, retro- or para-pharyngeal abscesses may compromise the airway and so these will be described in turn, together with rarer but important conditions and their complications.

Tonsillitis, peritonsillar abscess & infectious mononucleosis

Bacterial tonsillitis & peritonsillar abscess (Quinsy).
Bacterial tonsillitis can cause airway compromise without extension into surrounding tissue (Figure 1), although this is unusual and more likely in mononucleosis (see below).

Figure 1
Tonsillitis affecting the airway.

Figure 2
Tonsillitis caused by infectious mononucleosis.

The lingual tonsil has also been implicated in airway compromise (2). The typical flora associated with tonsillitis comprises aerobes; *Streptococcus pyogenes*, *Staphylococcus aureus* and *pneumococci*, and anaerobes; *Fusobacterium spp.*, *Prevotella spp.*, *Porphyromonas spp.* and *Actinomyces spp*. Aerobes predominate in the acute primary infection, whereas anaerobes are associated with abscess formation or extension across tissues that form deeper infections through fascial planes (3). Penicillin resistance in beta-lactamase forming organisms is common and third generation cephalosporins or amoxicillin–clavulanate should be used, in part, because they allow growth of 'nonpathogenic interfering bacteria' which compete with the pathogens (3).

Where the infection has extended outside of the tonsil itself, antibiotics effective against anaerobes should be used; metronidazole, carbapenems or beta-lactamase resistant penicillins (e.g. amoxicillin–clavulanate, piperacillin–tazobactam). If the patient is toxic, then clindamycin or linezolid should be added for their ability to prevent bacterial exotoxin release (4).

There is some controversy whether surgical removal of tonsils that have caused airway compromise should be undertaken early because of possible excessive bleeding (5).

When pus has formed, surgical drainage is usually indicated to prevent spontaneous rupture and the serious risks of aspiration, extension into the mediastinum or laterally causing erosion of blood vessels (6).

Infectious mononucleosis.
Infectious mononucleosis (IM) can cause compromise of the airway (Figure 2) and this has been reported in as many as 25–60% of children presenting with IM (7–9).

Although most authors since the 1960s have advocated the use of glucocorticoids to avert the need for surgical intervention, several series note that, despite steroids, 40–88% of patients with airway obstruction required tonsillectomy (7,9). In these reports, no cases of excessive hemorrhage were noted.

The use of glucocorticoids does reduce duration of fever, pharyngitis and abnormal hematological findings and does not appear to be associated with a predilection for development of peritonsillar abscess (10).

Retro- and para-pharyngeal abscess

The bacterial organisms involved in these infections are identical to those producing peri-tonsillar abscesses and can be considered together from the point of view of their microbiology and clinical management as 'deep neck infections' (11,12). The retropharyngeal space contains loose connective tissue and lymph nodes that drain the nasopharynx, paranasal sinuses, middle ear, teeth and adjacent bones. Retropharyngeal abscesses are more common in young children and this may be because lymph tissue in this area involutes and atrophies in older patients (13). Most studies give a male to female ratio of nearly 2 : 1 (11,14) and a median age of 32.5–36 months (15,16).
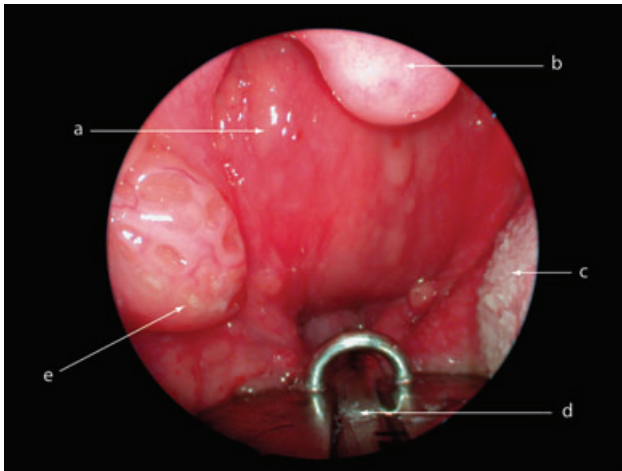
Figure 3
Retropharyngeal abscess: a, abscess bulge; b, uvula; c, tongue; d, laryngoscope blade; e, tonsil.

The incidence of this condition appears to be markedly on the rise (15). In a recent series covering 11 years (1995–2006) and 162 children with retropharyngeal abscesses, Page (11) noted a linearly rising incidence over the study period. Computed tomography was performed in 94% and had an accuracy of 68%. The principal symptoms were fever, sore throat, torticollis and neck pain. There was obstruction of the airway in only 8%. The commonest clinical signs were lymphadenopathy, local tenderness and limited range of movement. However, more specific findings were somewhat less common, e.g. pharyngeal bulge in 23% (Figure 3), tonsillar deviation in 12% and drooling in 10%.

At drainage, 80% of cases showed cloudy fluid or frank pus. A single organism was grown in 25% and polymicrobial in 79%; organisms include group A β-hemolytic Streptococci, *Streptococci*, *Staph. aureus*, of which 30% were methicillin-resistant, *Moraxella*, *Haemophilus* and other mixed oropharyngeal flora.

Features associated with surgical drainage were symptoms for 2 days or more, prior administration of antibiotics and fluid on computed tomography scan with a cross-sectional area of >2 cm^2. There was a trend indicating pharyngeal bulge as a factor but not significant ($P = 0.051$). Some authors disagree with the primacy of surgery as the treatment of choice (16,17) particularly where clindamycin was used in all cases and combined with cefuroxime in most (17).

Airway compromise may be more frequent in those below 1-year-old group (18).The anesthetic management of airways obstructed by such abscesses can be challenging. The airway must be secured without rupturing the abscess and soiling the airway with pus. Inflammation may also have extended to adjacent tissues and the glottis may be hard to visualize and even to locate (19). Where there is stridor a cautious inhalational induction with an otolaryngologist present is appropriate, either in the OR or in the ICU. The use of a cuffed endotracheal tube will be useful to prevent soiling of the lungs from either spontaneous rupture or surgical drainage of the abscess. The use of cuffed tubes, even in young children, has been shown to be safe (20–22). Administration of glucocorticoids does not feature in the large series quoted here and there is no evidence of benefit (11,16).

More than two-thirds of deep neck abscess contain beta-lactamase producing organisms and most abscesses contain anaerobes (6). Antibiotic treatment must take these features into account.

Complications of these abscesses are descending mediastinitis and Lemierre's syndrome. Mediastinitis following retropharyngeal abscess (see Figure 4) may be more common in younger patents and those with methicillin-resistant *Staph. aureus* (MRSA) infections (15).

Mediastinitis has been associated with a high mortality ranging from 16.5 to 50% and the place of surgery to drain the areas affected a subject of debate
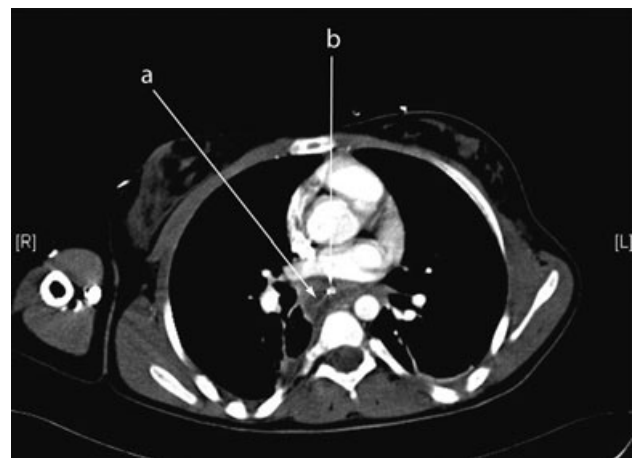
Figure 4
CT with contrast – retropharyngeal abscess with descending mediastinitis: a, abscess; b, nasogastric tube.

but should probably depend on response to maximal antibiotic therapy and monitoring of both clinical infective markers and radiological appearances (23).

Lemierre's syndrome

This is a relatively rare but possibly increasingly seen complication of pharyngo-tonsillar infections (24,25); 'the forgotten disease' (24). In 1936, Lemierre described a condition of 'anaerobic postanginal septicæmias' associated with '*Bacillus funduliformis*' – now known as *Fusobacterium necrophorum* – and '*B. symbiophiles*' (26). This paper described an evolving condition beginning with suppuration at the local site, followed by thrombophlebitis with septic emboli a later feature. No specificity was attributed to *F. necrophorum* but rather a recognition that the picture may be caused by normally saprophytic anaerobes, possibly working in synergy (26), and indeed its growth may be promoted by coexisting aerobes (27). The septicemic phase typically occurs 4–5 days after the onset of a sore throat or tonsillitis and is characterized by a rise in temperature and rigors, whereas the original pharyngeal/tonsillar condition may have improved (28). The infection has local effects, classically causing thrombosis in the ipsilateral internal jugular vein (IJV), and more distant spread with suppuration most commonly affecting the lungs, but also causing septic arthritis and osteomyelitis, meningitis and liver, renal and skin abscesses ('necrobacillosis') (28).

Lemierre's syndrome is normally associated with previously healthy adolescents and young adults. Mortality in the preantibiotic era was 90% and still runs at 4–12% depending on promptness of detection (29) and where fulminant, cavitating suppuration can still be seen (30). However, the full syndrome has been reported in a 3-year old child (31). Additionally, IJV thrombosis has been reported in a 5-month old with mastoiditis infected with *F. necrophorum* (32) and in a 3-month-old female infant with a retropharyngeal abscess infected with MRSA (33).

Examples of both thrombosis of the IJVs and thrombosis in the pulmonary artery are shown in Figures 5 and 6 in a patient presenting with a retropharyngeal abscess complicated by descending mediastinitis (seen above in Figure 4) where *Streptococcus milleri* was the organism isolated from blood and abscess.
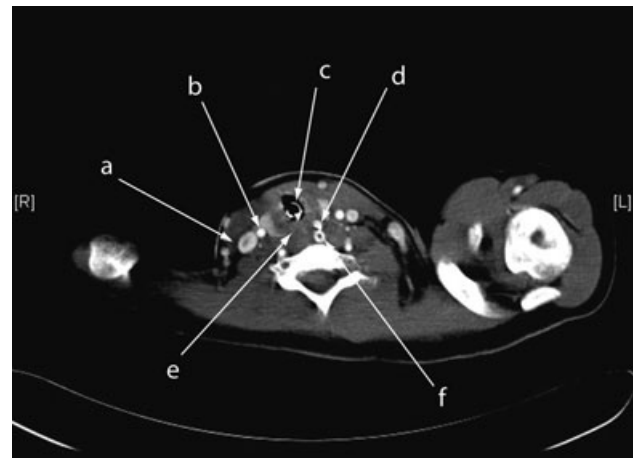
Figure 5
CT with contrast – retropharyngeal abscess with thrombophlebitis: a, right internal jugular vein with intraluminal thrombosis (also seen on Left); b, internal carotid artery; c, trachea with endotracheal tube; d, nasogastric tube; e, descending retropharyngeal abscess; f, Replogle tube placed into abscess cavity.
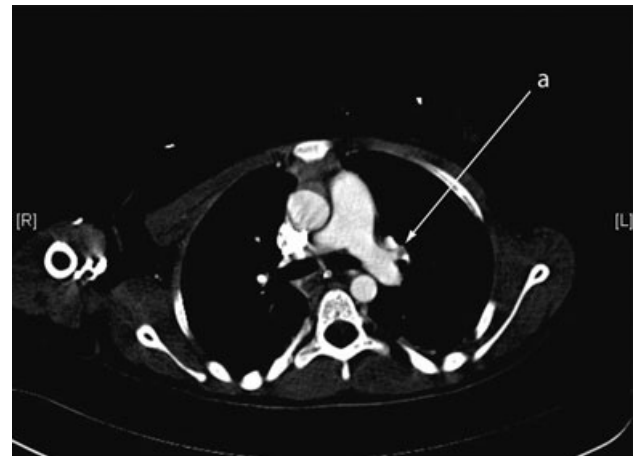
Figure 6
CT scan with contrast – thrombus sitting within branch of left pulmonary artery (same patient as Figure 5).

The incidence of this condition is rising. Whether this is due to better forms of detecting the anaerobic bacteria involved is doubtful, as this is a condition with a distinct clinical presentation (25,26,30). Another theory is that the move away from treating pharyngitis and tonsillitis with antibiotics in primary care has allowed bacterial infections to cause the conditions in which these anaerobic saprophytes can cause opportunistic, but disastrous, infections (25,27,28). Additionally, there may be a genetic explanation why some individuals develop a serious infection from a normally harmless saprophyte (34).

Treatment should be intravenous to start with, using high-dose penicillin with metronidazole or monotherapy with clindamycin. In penicillin allergy, clindamycin should be used because *F. necrophorum* can show resistance to macrolides. A total duration of 2–6 weeks is recommended as viable bacteria can be found in necrotic abscess formations for some weeks (27).

The clinical case for or against anticoagulation is not clear; however, in cases of propagating thrombosis or embolization, heparin administration is advisable (27).

Septic presentations in young people, even when these seem to affect distal sites such as the lungs or the liver should be accompanied by examination of the head, neck and throat to exclude a rare but classic disease (27,30).

Ludwig's angina

Initially described in 1836, this is a diffuse infection of the submandibular and sublingual spaces. Symptoms of severe pain, fever, malaise and dysphagia occur with swelling that can be large enough to cause airway compromise. Normally associated with dental caries, sickle cell disease, immunodeficiency and trauma, it can occur *de novo* in children (35,36). In one series from India, the proportion of children was 24% (35). It has been described in a 4-month-old infant (37).

Bacterial isolates are variable; *staphylococci*, *α-haemolytic streptococci* and anaerobes such as *bacteroides*, *peptococci* and *peptostreptococci* (36).

Antibiotic treatment covering these organisms should include metronidazole, penicillin, flucloxacillin or penicillin–betalactam inhibitor combinations: ticarcillin–clavulanate, amoxicillin–clavulanate or piperacillin–tazobactam. Where penicillin allergy occurs, clindamycin is effective (36). Reduction of edema with glucocorticoids has been proposed (38) but there are no controlled studies to support this. Surgical drainage is sometimes indicated where there is accumulation of pus (35).

Larynx

Papillomatosis

Recurrent respiratory papillomatosis (RRP) is caused by the human papilloma virus (HPV),

Figure 7
Laryngeal papillomatosis.

usually types 6 and 11; the same types seen in more than 90% of genital condylomata and has a prevalence varyingly reported as 3–5 per 100 000 population (39,40). It usually affects the larynx and typical lesions are shown in Figure 7. The squamous–columnar junction is the most frequently affected area (39) but this can extend distally to the larger airways in as much as 29% of patients and intrapulmonary in 7% (41).

The obstruction is of slow onset and the presenting symptom usually hoarseness but if the diagnosis is delayed respiratory obstruction may supervene (39), especially with concomitant acute respiratory infection (40). A more aggressive course is seen in the younger the age of first presentation and in those infected with type 11 (40). Possibly, 25% of all childbearing women worldwide harbor HPV in the genital tract. Although cesarean section possibly reduces transmission, it is thought that transmission may occur *in utero* (42).

The papillomata are treated with laser (CO_2 or KTP) or endoscopic micro-debridement. Surgical access to these lesions is most often achieved using a suspension laryngoscope and anesthesia achieved with either spontaneous ventilation with insufflation of gases into the hypopharynx or by jet ventilation. The latter can be used either supra- or infra-glottically by rigid cannulae fixed to the laryngoscope (43). In either case, an antisialogogue is administered and topical lidocaine sprayed onto the larynx (max. 6 mg·kg^{-1}) (44,45). Disadvantages of jet ventilation, particularly supra-glottically, are the potential dispersion of papillomatous matter distally and the

need for muscle relaxation and, if used sub-glottic-ally, one must ensure adequate escape of gases to prevent barotrauma. However, contamination of the field and the OR with vapors are then avoided (46). Advantages of spontaneous ventilation are the preservation of the patient's respiratory drive, a potential safety factor, and the relative containment of debrided material. Additionally, total intravenous anesthesia can reduce or supplant the need for vapors (44–46). Tracheostomy is generally avoided as this is associated with increased distal spread (41).

Attention has been increasingly paid to 'adjuvant therapies' such as: interferon – given subcutaneously for 6 months, ribavirin and acyclovir. More recently intra-lesional injections of cidofovir have become the most common adjuvant in resistant cases and it has been given systemically for intrapulmonary lesions with some success. However, there is an association with carcinogenicity in animals and so it needs to be used selectively.

Recently, a quadrivalent vaccine has been developed against types 6, 11, 16 and 18, the major causes of RRP, and it is hoped that this will reduce the exposure of infants to this vertically transmissible disease (40).

Epiglottitis

Historically, epiglottitis has been associated primarily with *Haemophilus influenzae* infections, typically occurring in children aged 3 months to 5 years, with a peak incidence between 1 and 3 years, and characterized by a rapid onset of fever, drooling and stridor (47). *Haemophilus influenzae* is a gram-negative coccobacillus that affects only humans. Serious infections are usually caused by the capsulated forms, serotypes a to f. However, type b (Hib) was responsible for approximately 85% of invasive disease in children prior to immunization against this type (48) and epiglottitis accounted for about 12% of Hib infections (49). For those nations who undertook widespread immunization in the late 1980s and early 1990s, the incidence of Hib-related infections dropped dramatically. The adult form seems different; a slower onset of symptoms where dysphagia and sore throat precede stridor (47), a more diffuse anatomic involvement, justifying the term supraglottitis (50), and half the need for airway intervention (47).

In the UK, there was a resurgence in 2003 with over 260 cases of Hib infections, causing a booster program to be launched (51). The UK vaccine is now thought to be only 57% effective (52). This may be due to its acellular composition. Where whole cell vaccines are utilized, effectiveness rates of 95–100% have been demonstrated in California and the Gambia (53).

In the postvaccination era, epiglottis is more likely to be an infection with a 'vaccination breakthrough' type b, or infection with any of the other organisms associated with this condition; *H. parainfluenzae*, group A S*treptococci*, *Pneumococci* or S*taphylococci* (54–56). In immuno-compromised patients, this can also include *Candida spp.*, *Herpes simplex* type 1, *Varicella zoster* and *Parainfluenza*. Vaccination failure is thought to be due either insufficient antibody level (57,58) or to a defect in immunological priming and a decrease in avidity of anticapsular antibodies (59).

The child will be pyrexial and possibly toxic, dysphagic, possibly drooling, anxious and will often adopt a characteristic posture, sitting forward with the head extended; the so-called sniffing position (60).

This situation requires skilled airway management with inhalational induction, the presence of an otolaryngologist prepared to undertake emergency tracheostomy (58) and administration of broad spectrum antibiotics (54,55,61).

Practice varies considerably regarding imaging prior to securing the airway. Either computed tomography or lateral neck radiographs (looking for the 'thumb sign') are still frequently undertaken in some centers; 84% of cases in one US series (55).

Stridor is a late feature and imaging should not delay securing the airway (45,50) and consequently is very often not performed at all, where the priority is seen to be clinical diagnosis and the securing of the airway with confirmation of diagnosis at laryngoscopy (58). The child can be re-intubated nasally and then managed on the Pediatric Intensive Care Unit (PICU). Practice varies between keeping the child sedated and possibly ventilated, or allowing the child to wake and breath spontaneously. If the child is awake, some form of physical restraint is frequently used to prevent accidental extubation and a heat and moisture exchanger attached to the endotracheal tube to prevent drying of secretions.

The choice of antibiotics will vary depending on local flora but should always include an agent with beta-lactamase resistance; a third generation cephalosporin or a penicillin-derived drug combined with a beta-lactamase inhibitor (55,58,62). Some authors recommend administration of steroids (50,55) but this practice is not universal and does not alter outcomes with respect to intubation, duration of intubation, ICU stay or hospitalization (47). In a more recent series from Denmark, the use of steroids was associated with longer hospital stay. This may have been because those receiving steroids were more severely compromised patients but, again, no evidence of benefit was demonstrated (63).

Extubation is usually possible after 48 h (45). Inhalational anesthesia can be employed so that the airway can be reassessed and extubation then performed under controlled conditions.

Trachea

Croup (acute viral laryngo-tracheitis)

This is a fairly common childhood disease characterized by a distinctive barky, hoarse cough progressing to stridor. This is initially associated with inspiratory subcostal recession and then, as the condition worsens, sternal recession and expiratory stridor. These symptoms are often preceded by a nonspecific upper respiratory tract infection for 12–48 h. Denny *et al.* carried out an 11-year study showing that croup occurs between 6 months and 3 years of age, with a peak incidence during the second year. The *Parainfluenza* viruses accounted for 74.2% of all isolates with 65% *Parainfluenza* type1 (64). Respiratory syncytial virus (RSV), influenza viruses A and B, and *Mycoplasma pneumoniae* were the only other agents isolated in appreciable numbers. RSV caused croup in children less than 5 years of age whereas the influenza viruses and *M. pneumoniae* were significant causes of croup only in children more than 5–6 years old (64).

An increasing variety of viruses are now associated with croup, undoubtedly because of improving methods of detection. In 2004, Human *Metapneumovirus* was demonstrated 20% of previously virus-negative samples, a fifth of these had presented with croup (65). *Coronavirus* was first described in German children in 2005 (66) and *Bocavirus* recently in Korea, with less predominance of *Parainfluenza* 1 (67).

Parainfluenza virus has specific effects on the ion transport of respiratory epithelium, which causes more airway secretions and exacerbates the effects of tissue edema (68).

Mortality is relatively rare and an extensive review of the literature estimates overall mortality at 1 in 30 000 cases (60). Although the diagnosis is usually clear, the differential should include foreign body aspiration, epiglottitis, bacterial tracheitis, tonsillitis and peri-tonsillar and retropharyngeal abscesses, tracheobronchiomalacia or vascular rings. Mediastinal masses can also present with 'croup' in all age groups (69). On a worldwide basis, laryngeal diphtheria still occurs and also presents at any age (see below).

The presentation is usually with acute onset of a barky, coarse cough, hoarseness and respiratory distress with stridor (Figure 8).

	Croup (64, 91)	Epiglottitis (47)	Bacterial Tracheitis (91)
Age Range (peak years)	6mo – 3yrs (1.5)	3mo – 5 (2.5)	8mo – 14 years (3.75)
Cough	+++ (Barky & non-productive)	Minimal	+++ (Productive)
Stridor Timing	Early	Late	Early
Stridor Onset	Gradual	Sudden +++	Sudden +
Toxic	No, mild pyrexia	Yes	Yes
Dysphagia	Minimal	Pronounced	Minimal
Drooling	No	Yes	No

Figure 8
Principal clinical features of croup, epiglottitis and bacterial tracheitis.

Pyrexia is usually present but the child should not drool nor appear toxic. Laboratory and radiologic tests are not needed to confirm the diagnosis. Indeed, such unnecessary disturbance may make the situation worse. Only where the diagnosis remains uncertain in the absence of clinical features either for or against the diagnosis of croup should imaging take place. Simple antero-posterior and lateral neck and chest radiographs may then indicate the presence of one of the differential diagnoses. It is clearly safer for the radiography to be performed in the ED, OR or ICU, rather than the child travel to the Radiology Department for such investigations (60).

The management consists of minimal disturbance, making a clinical assessment of the degree of severity and administering glucocorticoids, nebulized epinephrine, antipyretics. The use of humidified gases, although a traditional therapy, has been shown not to have any benefit on outcome (70).

Most studies employ the 'Westley Score' of assessing the severity of the condition (71) but this has not found its way into general clinical practice because of reported inter-observer variance (60).

A meta-analysis of studies showed that treatment with glucocorticoids was associated with nearly a fivefold reduction on the rate of intubation (72). If intubated, the duration of intubation and the rate of reintubation are reduced (73), although a meta-analysis was repeated in 1999, selecting only for randomized controlled studies, which found that while there was general benefit on administering glucocorticoids, no effect on intubation rates was demonstrated (74). Although the inhaled route is of benefit, the best routes to give glucocorticoids are intramuscular or oral (75). It appears dexamethasone at 150 $\mu g \cdot kg^{-1}$ is superior to prednisolone 1 $mg \cdot kg^{-1}$ (76). It has been observed that the duration of the anti-inflammatory effect of one dose of dexamethasone is 2–4 days and the natural history of croup last approximately 72 h, thus making subsequent doses superfluous (60). Regarding the exact dose of dexamethasone required, two recent studies suggest that 150 $\mu g \cdot kg^{-1}$ is as effective as 600 $\mu g \cdot kg^{-1}$ (77,78).

Should the clinical condition be severe on presentation or deteriorate despite steroids, value of nebulized epinephrine has long been established (71,79,80). These effects have a duration of less than 2 h but there does not appear to be a 'rebound' in deterioration (71). Although the first studies were done using racemic epinephrine, the more commonly available 'L-epinephrine' is just as effective (81). A systematic review of dosage concluded that use of 3–5 ml of 'neat' 1 : 1000 L-epinephrine was safe and effective (82). Paradoxically perhaps, the only report of ventricular tachycardia and a myocardial infarction in an otherwise healthy 11-year old with normal echocardiography and coronary anatomy was associated with the use of diluted racemic epinephrine (83).

Should the above measures fail, then consideration can be given to the administration of a helium–oxygen mixture ('Heliox'), which is examined in a separate section. Otherwise, the child should be intubated in a controlled manner with the most skilled anesthetic practitioner available. The usual provisos apply: a full range of airway instrumentation and the presence of an otolaryngologist prepared to undertake tracheostomy should intubation fail. Preservation of spontaneous ventilation till the airway is secured is still recommended, especially when there may be co-existing problems such as underlying tracheal stenosis or compression (69,84) and best achieved with nonirritant inhalational vapors such as sevoflurane and halothane. Typical appearances of the larynx on intubation are shown in Figure 9.

Endotracheal tubes of at least one whole size smaller than predicted by age should be available and so it is unrealistic to expect a leak round the endotracheal tube once the airway is secured. The
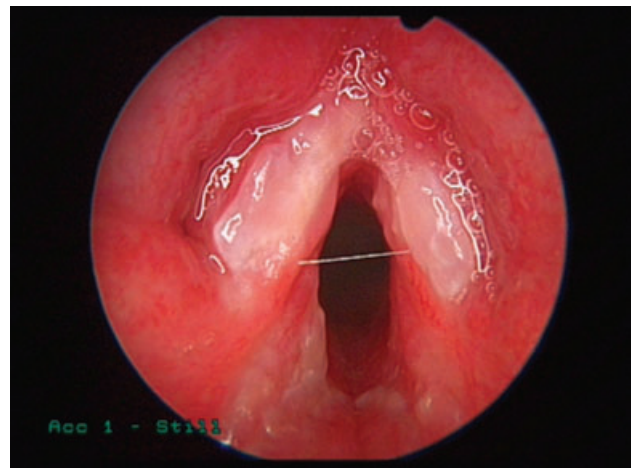
Figure 9
Croup – diffuse acute laryngotracheitis.

child should be cared for in the intensive care unit and the size of the tube may well dictate whether the child should be managed spontaneously ventilating (and possibly awake) or remaining sedated and ventilated. The tube is left in place until there is a clear leak indicating resolution of the edema. If the clinical course extends beyond 48 h further dosing of steroids should be considered (60,73). Normally this condition resolves within a week. If this does not occur then other diagnoses, mentioned above, should be considered. Some clinicians prefer to extubate with the child re-anesthetized but spontaneously ventilating to assess the adequacy of the airway. If there is any suspicion of bacterial secondary infection, then treatment for bacterial tracheitis should be commenced (see appropriate section below).

Diphtheria

From a world viewpoint, diphtheria is still very much with us. It is caused by *Cornyebacterium diphtheriae* and *Cornyebacterium ulcerans*. It is a condition commencing with a croup-like illness, cough and sore throat, but often progressing to death through sepsis (disseminated intravascular coagulation and renal failure), suffocation by the 'pseudomembranes' of serocellular exudate forming in the respiratory tract, and direct effects of the powerful exotoxin that has affinity for neural endings (paralysis), cardiac muscle (heart block and myocardial failure) and the adrenal glands (hypotension with endocrine failure) (85). Electrocardiogram abnormalities can occur in the first week; the overall incidence of cardiomyopathy is 10–20% and this has a mortality of about 50% (86).

Immunization was commenced in the UK in 1942 and the incidence of deaths plummeted, so that by 1952 it was extremely rare (87). The last child deaths from diphtheria infection in the UK were in 1994, in an immigrant child infected in Pakistan, and then in May 2008, in a child that was not immunized and had moved from Europe to the UK in late 2007. Swabs from family and hospital contacts proved negative (88).

Sporadic cases occur in countries with developed immunization programs as a result of immigration (89). Unless there is a high index of suspicion, it is a diagnosis easily missed. Even if correct management

is instituted early, there is an appreciable mortality of 8–10% (86,89). Presence of pseudomembranes and 'bull neck' are predictive of development of cardiomyopathy (86).

A breakdown in primary immunization and booster programs led to the major outbreak in former Soviet States 1990–1995, where nearly 50 000 cases occurred (90).

In a large series of 154 children in 1 year in Vietnam, treatment consisted of specific antitoxin, high-dose penicillin (or erythromycin if allergic) and intravenous hydrocortisone for severe neck edema. If edema or laryngeal pseudomembranes were causing obstruction, tracheotomy was performed (86).
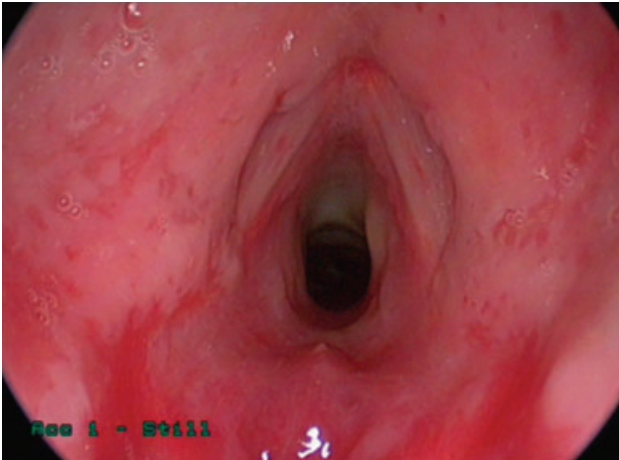
Bacterial tracheitis

It is possible that this condition is becoming relatively more common. Over a 10-year period in Vermont, USA, of the airway infections causing PICU admissions, tracheitis was the most common. Whereas only 17% of viral croup admissions were intubated, 83% of those with tracheitis were. Only 6% of PICU admissions in this period had epiglottitis (91).

Immunizations against *Haemophilus* type b and the efficacy of glucocorticoids in viral croup may have changed the spectrum of PICU admissions. The clinical presentation often follows a prodrome of viral upper respiratory infection, but with sudden progression of cough, stridor and pyrexia with a toxic element (92) (see Figure 8).

The endoscopic features are erythema, edema and thick purulent secretions (91) – see Figure 10; sometimes these have the appearance of pseudomembranes (93).

The microbiology is mixed; predominantly *Staph. aureus* – the most frequent according to most authors (91,93,94), *Streptococcus pneumoniae*, Lancefield Group A *Streptococci*, *Moraxella catarrhalis* and *Haemophilus spp.* (92,93). The presence of *Moraxella* was associated with a higher intubation rate (93). These bacterial infections may occur in the presence of influenza virus A or B (91) but the presence of viruses did not relate to the intubation rate (93).

The therapy consists primarily of antibiotics; these should cover the likely flora and so include third generation cephalosporins with anti-staphylococcal agents, e.g. cefotaxime and flucloxacillin.

Figure 10
Bacterial tracheitis: erythema and mucosal edema with copious purulent secretions.

Glucocorticoids are not thought to have any beneficial effect on the course of the disease, which may develop into full blown sepsis with pneumonia and acute respiratory distress syndrome (91,94). Salamone reported a 10-year series of 94 cases and described a subset of patients that have exudative pseudomembranes that required repeat debridement by bronchoscope and termed this 'exudative tracheitis' (93).

With increasing respiratory distress intubation is necessary. If the diagnosis is in doubt then inhalation induction should be considered and the presence of an otolaryngologist is recommended especially where tenacious secretions may require immediate bronchoscopy and bronchial toilet (93).

Miscellany

Negative pressure edema

Respiratory difficulties observed with obstructed airways may not be due simply the proximal obstruction itself. Increasing respiratory effort is capable of quite large decreases in intrapleural pressure. This will increase the pressure gradient across the pulmonary capillary and override the Starling equilibrium. The resulting transudation of fluid will cause acute pulmonary edema (95). Hypoxia itself will cause failure of the integrity of the alveolar–capillary membrane and exacerbate the transudative leak. The result is decreased pulmonary

compliance which then, in turn, exacerbates the child's dyspnea and respiratory compromise (95,96).

Heliox

Two gas physics equations provide the rationale for substituting helium for the nitrogen in air where there is airway compromise. The Poiseuille equation applies to laminar flow:

$$Q = \Delta P \pi r^4 / 8 \eta l$$

(ΔP is pressure gradient, r is radius, η is viscosity, l is length of airway).

Here, helium has nothing to offer; its viscosity (188 micropoises) approximates to those of nitrogen and oxygen (167 and 192, respectively). However, with a narrowed airway segment, as in many of the conditions referred to above, turbulent flow is more likely to occur. To maintain flow across a restricted cross-sectional area, gas velocity must increase. In these circumstances, turbulent flow is associated with a 'Reynolds number' greater than 2000 (no units) as given by the following:

$$N_r = 2r\rho V / \eta$$

(ρ is density and V average velocity).

Here, helium has a density 0.18 g·l^{-1}, whereas nitrogen and oxygen densities are 1.25 and 1.43, respectively. A helium–oxygen mixture of 79 : 21 has a density of 0.43 g·l^{-1}; this means that, for a given velocity, the Reynolds number will drop by three times and the propensity for turbulent flow drops accordingly (97).

'Heliox' refers to mixtures of helium and oxygen. Potentially this could be in any ratio as found in the bespoke mixtures utilized in sub-aqua diving. However, medically, it is commonly provided as 79 : 21%. This can be added to an oxygen blender and the output monitored, thus providing a variable FiO$_2$ as needed (97,98). In patients that are already hypoxic, the introduction of Heliox should be done incrementally. As the viscosity of the inspired gases drops, any benefit or deterioration in oxgenation should be monitored carefully. When used in croup, heliox has been shown to procure improvements in croup scores similar to nebulized epinephrine (99). Reviews of the available evidence to support the use of heliox in this situation have demonstrated a need for further studies in this area

(97,98,100). Helium has high thermal conductivity and so care needs to be taken with respect to humidification and avoidance of patient hypothermia (101,102) and it should not be used in nebulizers as these depend on the generation of turbulence to deliver the drug (102).

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Conflicts of interest

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