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28 Infections of the Upper and Middle Airways

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Supraglottic infections comprise peritonsillar abscess, retropharyngeal abscess, parapharyngeal abscess, and epiglottitis. Infections of the middle airways include croup (i.e., laryngotracheitis) and bacterial tracheitis. All of these conditions share the potential for respiratory compromise and airway obstruction. Table 28.1 summarizes the typically affected age groups, common clinical features at presentation, and the most commonly implicated organisms. Differentiation from other airway infections is discussed in Chapter 21 (see Table 21.4).

PERITONSILLAR ABSCESS

Peritonsillar abscess (i.e., quinsy) is the most common deep oropharyngeal infection.[1] Although rare, it usually is a complication of pharyngotonsillitis. The infection primarily affects adolescents and young adults, but it can occur at any age.

Etiologic Agents. *Streptococcus pyogenes* is the most commonly isolated aerobic bacterium in cases with peritonsillar abscess.[2–9] Other streptococci, *Staphylococcus aureus*, and *Haemophilus influenzae* are less frequently implicated. Anaerobic bacteria, including *Prevotella*, *Bacteroides,* and *Peptostreptococcus* species, also are common isolates.[10] Polymicrobial infection occurs in some cases.[10]

Epidemiology and Pathogenesis. The peak incidence of peritonsillar abscess is in adolescence and early adult life.[1,3,7,11–14] However, although uncommon, peritonsillar abscess can occur in very young children, including infants.[15–17] There is no clear sex predilection.

Peritonsillar abscess traditionally has been thought to result from extension of acute exudative pharyngotonsillitis. However, there is some evidence to suggest that this condition also can result from abscess formation within Weber salivary glands located in the supratonsillar fossa.[18]

Clinical Manifestations and Diagnosis. At presentation, the patient usually has a severe sore throat and odynophagia.[7,11,13] Difficulty with swallowing often leads to decreased oral intake, which can result in dehydration.[13] Symptoms may worsen, and the patient may become unable to swallow saliva, causing drooling. Fever is reported in most cases, but it is not universal.[13] Common clinical signs at initial presentation include peritonsillar swelling, muffling of the voice, cervical lymphadenopathy, trismus, and uvular deviation toward the contralateral tonsil.[11,13] Bilateral disease is very rare.[12,19]

Inflammatory markers, including the white blood cell (WBC) count and C-reactive protein (CRP) level, are frequently elevated.[11,13] When there is doubt about the diagnosis, transcutaneous or intraoral ultrasound or computed tomography (CT) can be useful for confirmation.[20–23]

Management. Peritonsillar abscess requires drainage, which can be achieved by needle aspiration, incision and drainage, or tonsillectomy (for quinsy).[13,14] Pus obtained during the procedure should be sent for Gram stain and routine and anaerobic culture. Intervention practices vary widely,[24] and there are no convincing data to suggest that one approach is superior to another.[25–28] Data from a nationwide study of more than 20,000 children with peritonsillar abscess admitted to US hospitals show that approximately half were managed conservatively, whereas incision and drainage was performed in more than one third of cases; fewer than 20% underwent tonsillectomy.[29]

Antibiotic therapy is empiric and should provide sufficient coverage for anaerobic and β-lactamase–producing bacteria. Suggested regimens include penicillin combined with metronidazole, amoxicillin-clavulanate, ampicillin-sulbactam, cefoxitin, and clindamycin.[7,30–34]

The role of adjuvant corticosteroid treatment remains controversial.[11,25,35,36] Data from one randomized, controlled trial (RCT) suggest that corticosteroids may expedite symptomatic improvement in adults.[37] The choice about whether to treat a patient with peritonsillar abscess on an outpatient or inpatient basis should take into account the patient's age, coexisting morbidities, and the need for intravenous hydration, pain control, and airway monitoring.[13]

Complications and Prognosis. A small proportion of patients require intensive care support, usually for management of airway compromise.[11] The course of the illness can be complicated by contiguous extension of infection to the retropharyngeal or parapharyngeal space.[11,12] Other potential complications include aspiration pneumonia and mediastinitis.

The prognosis for appropriately managed peritonsillar abscess is good. A fatal outcome is rare. Relapse or recurrence occurs in approximately 5% to 10% of cases.[11–13,19]

RETROPHARYNGEAL ABSCESS

The retropharyngeal space extends from the base of the skull to the upper thoracic spine. The anterior border of this space is formed by the constrictor muscles of the pharynx, the lateral borders by the carotid sheaths, and the posterior border by the prevertebral fascia.

Etiologic Agents. Polymicrobial infection is common; mixed aerobic and anaerobic infection occurs frequently.[38–43] Commonly implicated aerobic bacteria include *S. pyogenes*, viridans streptococci, *S. aureus,* and *Haemophilus* and *Neisseria* species.[a] Methicillin-resistant *S. aureus* (MRSA) as a cause varies geographically.[41,42] A series from Texas highlighted MRSA as a more frequent cause than methicillin-susceptible *S. aureus* (MSSA).[49] Common anaerobic isolates include *Peptostreptococcus*, *Prevotella*, *Bacteroides,* and *Fusobacterium* species.

Epidemiology and Pathogenesis. Retropharyngeal abscess can occur at any age, but most commonly affects children younger than 5 years of age.[7,38,45,49–52] In most reports, there is some male predominance.[b] The US incidence peaks during the winter and spring months, and the same has been reported in Europe.[45,46,48,53] Some data suggest that the US

[a]References 7, 30, 38, 41, 44–48.
[b]References 38, 41, 42, 45, 49, 50, 52–54.

TABLE 28.1 Clinical Features and Causative Organisms of Infections of the Upper and Middle Airways

Disease	Typical Age Group	Potential Initial Infection	Key Clinical Findings	Typical Organisms
Peritonsillar abscess	Adolescents	Pharyngotonsillitis	Sore throat, odynophagia, dysphagia, peritonsillar swelling, uvular deviation to contralateral side, muffled voice	*Streptococcus pyogenes*
Retropharyngeal abscess	<5 yr	Pharyngitis, tonsillitis, adenitis	Sore throat, odynophagia, dysphagia, neck pain and swelling, limited neck mobility, torticollis	*Streptococcus pyogenes,* viridans streptococci, *Staphylococcus aureus, Haemophilus* and *Neisseria* spp., anaerobic bacteria; often polymicrobial
Parapharyngeal abscess	All age groups	Pharyngitis, tonsillitis, adenitis, otitis media	Sore throat, odynophagia, dysphagia, neck pain and swelling, torticollis, deviation of the lateral wall of the oropharynx to the midline	Same as for retropharyngeal abscess
Lemierre syndrome (primary oropharyngeal infection; septicemia; thrombophlebitis of the internal jugular vein; metastatic infection at distant sites)	Adolescents	Pharyngitis, tonsillitis, adenitis, otitis media, mastoiditis	High-grade fever, neck pain and swelling, dysphagia, nausea and vomiting, hypotension; pulmonary involvement: dyspnea, hemoptysis, pleuritic chest pain	*Fusobacterium necrophorum*
Epiglottitis	In Hib-unimmunized populations: children <4 yr; in Hib-immunized populations: school-age children	—	Unwell looking, high-grade fever, stridor, drooling, muffled voice, tripod position with neck extension	*Haemophilus influenzae* type b
Croup (laryngotracheitis)	6 mo to 2 yr	—	Inspiratory stridor, barking cough, hoarseness; symptoms typically worsen during nighttime	Parainfluenza virus, influenza virus, respiratory syncytial virus
Bacterial tracheitis	2 to 10 yr	—	Moderate- to high-grade fever, cough, stridor, dyspnea, retractions; rapid deterioration is common	*Staphylococcus aureus*

incidence of retropharyngeal abscess has increased over the past decade.[38,41,43,49] Similar observations have been reported from the UK.[55]

Retropharyngeal abscess in children predominately results from infection and suppuration of the retropharyngeal chains of lymph nodes, which drain the nasopharynx, the paranasal sinuses, and the adenoids.[38,40–43,46] Common primary infections include pharyngitis, tonsillitis, adenitis, and less frequently, sinusitis, otitis media, mastoiditis, and dental infections. Unlike in adults, local trauma and foreign body ingestion play a relatively minor role in children.[c]

Clinical Manifestations and Differential Diagnosis. Common presenting features include pyrexia, sore throat, dysphagia, odynophagia, neck pain, neck swelling, limited neck mobility (particularly on extension), and torticollis.[d] Trismus is uncommon, but drooling can occur. Most patients have evidence of pharyngitis or tonsillitis and cervical lymphadenitis on examination.[44,52] In most reports, the proportion of patients with symptoms that indicate airway obstruction, such as difficulty in breathing and stridor, is relatively small.[41,43–46,50,52] Airway obstruction in the context of retropharyngeal abscess predominately occurs in infants and very young children.[41–43]

Peripheral blood leukocytosis is common.[e] The CRP level and erythrocyte sedimentation rate (ESR) usually are elevated.[49,52] In most cases, enlargement of the retropharyngeal space/prevertebral tissue can be seen

[c]References 7, 41, 43, 44, 46, 50.

[d]References 7, 38, 41, 46, 49–52, 54.

[e]References 7, 38, 41, 46, 50, 52.

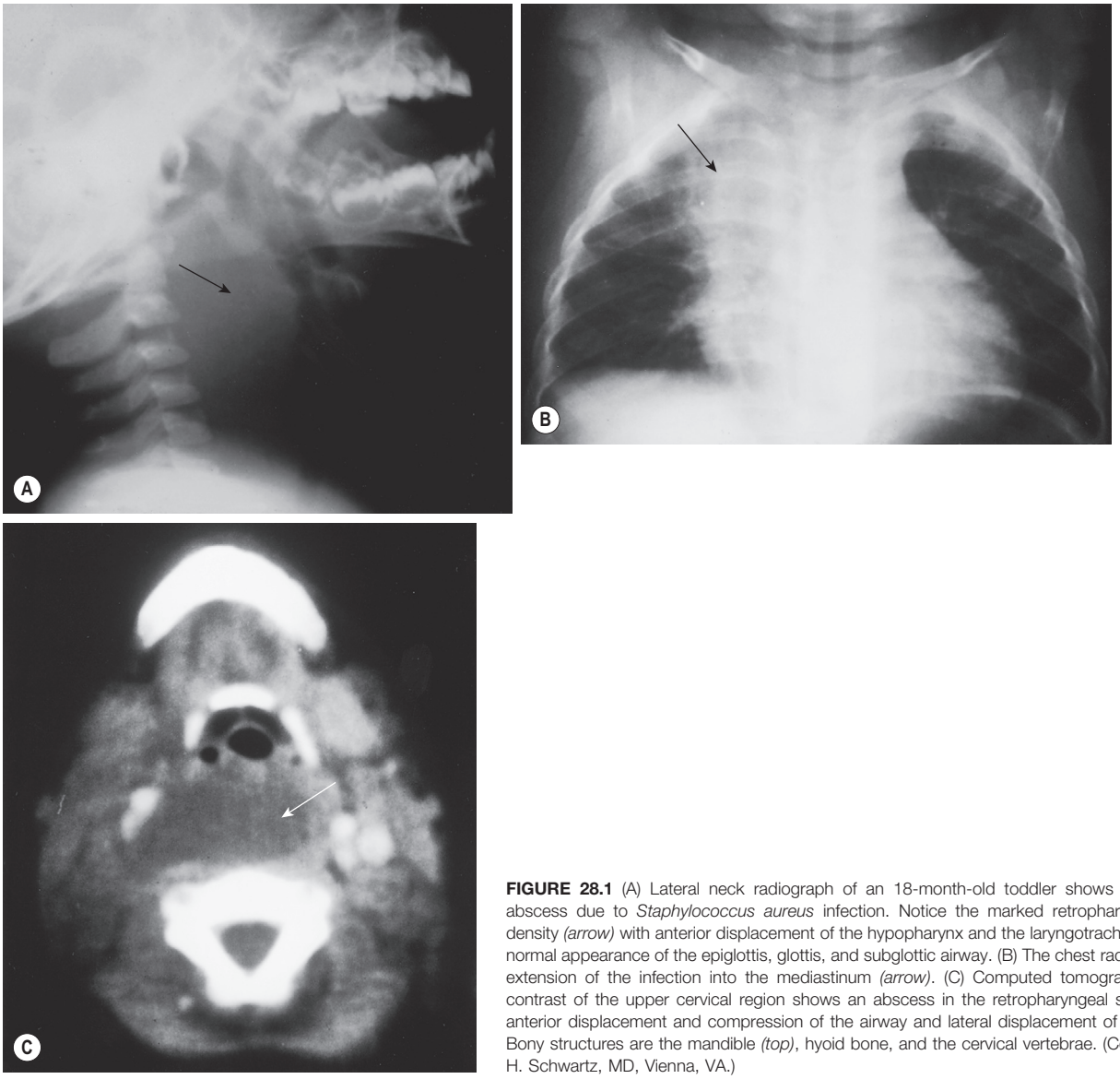

FIGURE 28.1 (A) Lateral neck radiograph of an 18-month-old toddler shows a retropharyngeal abscess due to *Staphylococcus aureus* infection. Notice the marked retropharyngeal soft tissue density *(arrow)* with anterior displacement of the hypopharynx and the laryngotracheal airway and the normal appearance of the epiglottis, glottis, and subglottic airway. (B) The chest radiograph shows an extension of the infection into the mediastinum *(arrow)*. (C) Computed tomography scan without contrast of the upper cervical region shows an abscess in the retropharyngeal space *(arrow)* with anterior displacement and compression of the airway and lateral displacement of the great vessels. Bony structures are the mandible *(top)*, hyoid bone, and the cervical vertebrae. (Courtesy of Richard H. Schwartz, MD, Vienna, VA.)

on plain lateral neck radiographs (Fig. 28.1).[38,43,44,56] However, CT is more sensitive and is the imaging modality of choice.[43,45,50,56–62]

Management. There is no consensus about the optimal empiric antibiotic treatment. Penicillin or ampicillin alone is insufficient because β-lactamase–producing organisms, *S. aureus,* and mixed infections are common. Appropriate empiric antibiotic regimens include a second- or third-generation cephalosporin plus clindamycin or metronidazole, amoxicillin-clavulanate, ampicillin-sulbactam, and piperacillin-tazobactam.[f] Some physicians think that clindamycin alone may be sufficient.[40,54] Local patterns of susceptibility of *S. aureus* and the clinical state of the patient should be taken into account, frequently leading to a combination of antibiotics that includes clindamycin or vancomycin.[49]

The role of surgical drainage remains controversial.[g] Patients with significant respiratory distress require urgent airway management and surgical drainage. However, there is debate about whether a trial of conservative management with intravenous antibiotics for a 24- to 48-hour period in conjunction with close monitoring is appropriate for patients who are stable and have no respiratory distress.[38,44–46,50] The reported success rates with conservative management alone vary considerably between studies, and there have been no randomized trials.[h] Surgical drainage usually is performed using the transoral approach and less commonly using the transcervical route.[i]

Complications and Prognosis. Potential complications include airway obstruction, internal jugular vein thrombosis, mycotic aneurysm of the carotid artery, aspiration pneumonia, mediastinitis, and sepsis, although these are rare overall.[j] Few patients require repeated surgical intervention.[43,45,49] Most patients have an uncomplicated course and can be discharged on oral antibiotics within a few days.[41,42] Fatal outcomes have been rare in recent studies.

PARAPHARYNGEAL ABSCESS

The lateral pharyngeal space (i.e., parapharyngeal space) is shaped like an inverted cone extending from the base of the skull to the hyoid bone. It is bound medially by the superior pharyngeal constrictor muscle and laterally by the internal pterygoid muscle.[69] The lateral pharyngeal space contains the internal carotid artery, the internal jugular vein, cranial nerves IX to XII, the sympathetic chain, and the lymph nodes. This space is separated from the retropharyngeal space by only the alar fascia, which provides little barrier against the spread of infection.[69] Simultaneous infection of both compartments is common, and some investigators

[f]References 38, 45, 46, 60, 63–66.
[g]References 38, 41, 46, 50, 52, 61, 67.
[h]References 38, 44–46, 50, 52, 54, 68.
[i]References 41–43, 45, 46, 49, 54, 60, 61.
[j]References 41–43, 45, 49–51, 68.

think that a distinction between parapharyngeal and retropharyngeal abscess is not meaningful clinically.[46,65,69–71]

Etiologic Agents, Epidemiology, and Pathogenesis. The spectrum and frequency of causative organisms are similar to those reported for retropharyngeal abscess.[30,72] Studies of deep neck space infections in children suggest that parapharyngeal abscesses are less common than retropharyngeal abscesses.[7,31,45,52] Unlike retropharyngeal abscess, parapharyngeal abscess occurs in all age groups without a predilection for younger children.[51,73] Parapharyngeal abscess is thought to result primarily from infection and subsequent suppuration of lymph nodes in the lateral pharyngeal space, which are part of the lymphatic drainage of the nasopharynx and middle ear.[73–76] In many cases, there is a history of preceding pharyngitis or tonsillitis.

Clinical Manifestations and Differential Diagnosis. The clinical features of parapharyngeal abscess closely resemble those associated with retropharyngeal abscess.[69] Fever and neck swelling are common; patients also can have dysphagia, odynophagia, torticollis, or trismus.[k] A common feature distinguishing parapharyngeal abscess from retropharyngeal abscess is deviation of the lateral wall of the oropharynx to the midline on oral inspection.[73,77–79]

Peripheral blood leukocytosis and an elevated CRP level are common.[66,74] Contrast-enhanced CT is the imaging modality of choice for investigating suspected cases.[l] Plain lateral neck radiographs are not useful.[45]

Management, Complications, and Prognosis. Management of parapharyngeal abscess is similar to that for retropharyngeal abscess. There is ongoing controversy among experts about whether surgery is mandatory in all patients.[m] Traditionally, an external cervical approach has been used for the drainage of parapharyngeal abscesses,[7,60,81] but transoral drainage has been reported to be safe and effective in selected cases with abscess location medial to the great vessels.[69,71,76,77,81] The transoral approach has cosmetic advantages, and the intraoperative time usually is shorter.[81]

Potential complications comprise internal jugular vein thrombosis, erosion of the carotid artery, airway obstruction, aspiration pneumonia, pleural empyema, mediastinitis, pericarditis, and septic shock.[n] Fatal outcomes and long-term sequelae are rare.[31,70,73]

LEMIERRE SYNDROME

The first description of Lemierre syndrome was published in 1900 by Courmont and Cade,[84] followed by a report by Schottmüller in 1918.[85] The clinical syndrome, also referred to as *necrobacillosis*, is named in honor of André Lemierre, who described a series of 20 cases of "postanginal septicemia" in 1920.[86] Lemierre syndrome is characterized by primary infection of the oropharynx, blood culture–confirmed septicemia, evidence of thrombophlebitis of the internal jugular vein, and metastatic infection at one or more distant sites.[87]

Etiologic Agents. *Fusobacterium necrophorum* is by far the most commonly implicated etiologic agent in cases of Lemierre syndrome.[87–90] *F. necrophorum* is an obligate anaerobic, gram-negative bacillus that is part of the normal flora of the oral cavity and the gastrointestinal and female genital tract. Most strains are susceptible to second- and third-generation cephalosporins, clindamycin, and metronidazole; a significant proportion of clinical isolates produce β-lactamase.[91–93]

Other causative bacteria associated with Lemierre syndrome include other *Fusobacterium* species, *Bacteroides* species, *Prevotella* species, streptococci (mainly non–group A), and infrequently staphylococci.[87,88,90,94–96] Mixed infections also occur.[89,95]

Epidemiology and Pathogenesis. Despite the absence of solid epidemiologic data, most experts agree that the incidence of the disease declined considerably during the antibiotic era. Lemierre syndrome currently is uncommon, with an estimated annual incidence of approximately 1 case per 1 million people.[97] However, some data suggest that the incidence has increased in recent years.[98] The disease typically affects teenagers and young adults,[o] although a few cases in infancy have been described.[91,100] There appears to be male predominance.[87,101] Most cases have no predisposing illness.

In most cases, the disease process begins with a primary focus of infection in the oropharynx (e.g., palatine tonsils, peritonsillar tissue). Other infections in the head and neck area, including sinusitis, otitis, mastoiditis, parotitis, and odontogenic infections, are less common sources.[p] The infection subsequently spreads to the lateral pharyngeal space or parapharyngeal space. Further progression results in infectious thrombophlebitis of the internal jugular vein, which causes septic pulmonary emboli and metastatic infection at other distant sites. The lungs are the most commonly involved secondary site, followed by joint and soft tissue infections,[87,88,95,101] Other manifestations, such as skin infection, osteomyelitis, liver abscess, splenic abscess, and meningitis, are rare.[87,91,101,104–107]

Clinical Manifestations and Differential Diagnosis. The presenting features of Lemierre syndrome depend partly on the primary site of infection. Most cases are diagnosed within 7 days of onset of the primary infection.[87] In patients with an oropharyngeal source, inspection may reveal exudative tonsillitis, hyperemia, or grayish pseudomembranes. An unremarkable oropharyngeal appearance at the time of septicemia does not rule out Lemierre syndrome.[87,108] Patients with otitis media or mastoiditis as the primary focus can have otorrhea or postauricular fluctuation.[91,109] Most patients have high-grade pyrexia (>39.5°C) at presentation, although fever can be absent. Neck swelling and tenderness is seen in most cases.

Other symptoms and signs include trismus, dysphagia, dyspnea, hemoptysis, pleuritic chest pain, nausea and vomiting, jaundice, hepatomegaly, and hypotension. Severe shock and renal failure are uncommon despite the septicemic state.[87,94] Auscultation and percussion of the chest may reveal crepitations and evidence of pleural effusions in cases with pulmonary involvement.

The WBC count, CRP, and ESR often are markedly elevated.[q] Thrombocytopenia occurs in approximately a quarter of patients.[110] Levels of liver enzymes and bilirubin are sometimes not elevated.[87,95] Blood cultures typically are positive, but they may be sterile in patients who have taken antibiotics before samples were collected for culture.

Contrast-enhanced CT of the neck is the most useful investigation. Possible CT findings include distended neck veins, intraluminal filling defects, and soft tissue swelling.[95,100,111,113,114] Doppler ultrasonography and magnetic resonance imaging are also useful in this setting. The chest radiograph and chest CT may reveal pulmonary infiltrates, pulmonary cavitation, or pleural effusions (Fig. 28.2).

Management. Antibiotic treatment is the mainstay of therapy. Common empiric regimens include high-dose penicillin with metronidazole, clindamycin, ticarcillin-clavulanate, and ampicillin-sulbactam.[r] Due to the endovascular nature of the infection, intravenous therapy is required for several weeks.

Surgical debridement of necrotic tissues and drainage of abscess or empyema often are required in conjunction with medical therapy. Ligation or resection of the internal jugular vein was a common therapeutic intervention in the preantibiotic era. However, this is rarely necessary and should be restricted to unstable patients who fail to respond to conservative therapy.[98,110,111,116] The role of routine anticoagulation therapy in Lemierre syndrome continues to be controversial.[s]

Complications and Prognosis. Metastatic infections can cause complications depending on their location. Pleural effusions, empyema, lung abscesses, and pulmonary cavitation can occur in patients with Lemierre syndrome. Pneumatocele and pneumothorax can occur. Septic pyogenic arthritis typically affects larger joints, such as the shoulder, elbow, and hip joints (see Fig. 28.2).[87,101] Renal involvement can be associated with proteinuria or hematuria.

In the preantibiotic era, the prognosis was poor, with fatality rates as high as 90% in some historical reports.[86,102] Recent reviews of the literature suggest that fatal outcomes are uncommon, typically between 5% and 10%.[87,88]

[k]References 51, 65, 66, 69, 71–73, 75–78.
[l]References 45, 51, 52, 65, 69, 70, 77, 80.
[m]References 46, 52, 65, 70, 71, 73, 75, 76, 78.
[n]References 7, 51, 70, 72, 73, 76, 82, 83.
[o]References 87, 88, 94, 95, 98, 99.
[p]References 87, 91, 94, 95, 97, 100–103.
[q]References 88, 95, 98, 100, 101, 110–113.
[r]References 90, 95, 98, 108, 110–112, 115.
[s]References 89, 94, 95, 98, 109, 110, 116, 117.

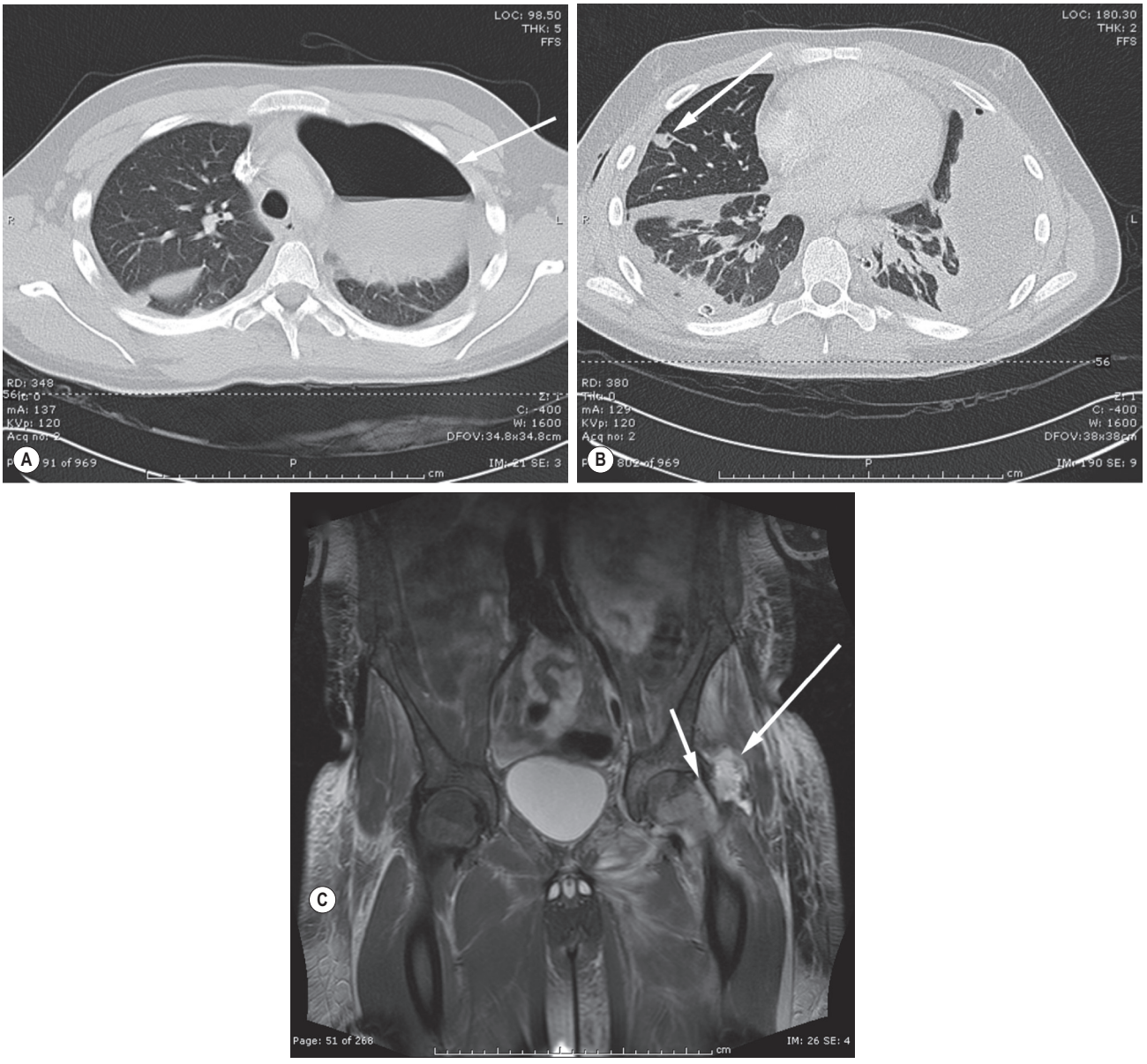

FIGURE 28.2 (A) Chest computed tomography scan of a 16-year-old patient with Lemierre syndrome with marked pulmonary involvement shows a large, left-sided pneumothorax *(arrow)* and adjacent empyema. (B) Chest computed tomography scan of the same patient shows widespread bilateral pulmonary consolidation and nodular foci. The central cavitation in the lesion is marked by an *arrow*. (C) Coronal magnetic resonance image shows the hip region in the same patient, who also developed septic arthritis of the left hip joint and abscess formation in the adjacent muscles. Notice the synovial enhancement *(small arrow)* and the fluid collection *(large arrow)*, which extended anteriorly between the iliopsoas, the rectus femoris medially, and the gluteus muscles laterally.

ACUTE EPIGLOTTITIS

The incidence of invasive *Haemophilus influenzae* type b (Hib) disease decreased dramatically, and epiglottitis (i.e., supraglottitis) has become a rare disease in countries where Hib vaccines are used routinely.[118–129] Data from England and Wales show that the incidence of invasive Hib disease after 2 decades of routine immunization fell to 0.02 cases per 100,000 inhabitants.[130] Necrotizing epiglottitis is a rare variant, which has been reported predominately among immunocompromised patients.[131]

Etiologic Agents. Hib infection accounted for approximately 75% to 90% of epiglottitis cases in the pre-Hib vaccination era.[119,126,132] Currently, only rare cases due to vaccination failure are reported.[t] Other organisms implicated in epiglottitis are *S. pyogenes*, *S. pneumoniae*, *S. aureus*, nontypeable *H. influenzae*, *H. parainfluenzae*, *Pseudomonas* species, *Klebsiella* species, and *Moraxella catarrhalis*.[119,126,132,137–140]

Epidemiology and Pathogenesis. In the pre-Hib vaccination era, the incidence of epiglottitis peaked in early childhood, typically affecting children younger than 4 years of age.[132,137,141] After institution of universal Hib vaccination, the peak incidence shifted toward an older age group, with a simultaneous increase in the proportion of adult cases.[u] Many studies show no sex predominance, while others report some male predominance.[122,132,143–145] There is little seasonal variation in incidence in temperate climates.[129,143–146]

Acute epiglottitis is a localized, invasive bacterial infection of the supraglottic area, comprising the epiglottis, arytenoid cartilages, aryepiglottic folds, and false vocal chords. Inflammation results in airway edema and narrowing, which leads to airway obstruction manifesting as stridor and respiratory distress. The localized infection can evolve into phlegmon and abscess formation. Bacteremia is common in cases caused by Hib, but dissemination to distant sites (e.g., causing septic arthritis or meningitis) is rare.

[t]References 119, 122, 126, 130, 132–136.

[u]References 119, 125, 129, 130, 136, 137, 140, 142, 143.

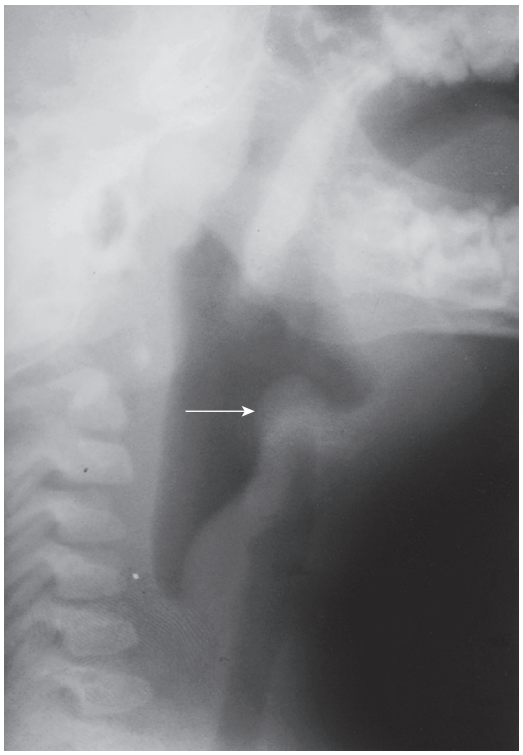

FIGURE 28.3 Lateral neck radiograph of a 4-year-old child with acute epiglottitis shows the characteristically distended hypopharynx and "thumbprint" edematous epiglottis and aryepiglottic folds *(arrow)*. (Courtesy of Richard H. Schwartz, MD, Vienna, VA.)

Clinical Manifestations and Diagnosis. Children with epiglottitis typically look systemically unwell and have high-grade fever and stridor.[122,137,145] Aphonia, hoarseness, and a muffled, "hot potato" voice are common features.[129,137] Odynophagia is common, and drooling frequently is observed. Most patients assume an upright tripod position with forward leaning and extension of the neck.[147] Cervical lymphadenopathy also is a common feature.[137]

Peripheral blood leukocytosis is present in most cases.[129,137,140,146] Lateral neck radiographs demonstrate epiglottic enlargement with a distended hypopharynx, a classic thumb sign that has high sensitivity (Fig. 28.3). However, this should be attempted only for a stable, cooperative patient in a safe environment because performing radiography in the lateral position can precipitate respiratory arrest from complete airway obstruction, especially if the child's neck is repositioned for optimal results.[133,137]

Management. Effective airway management is critical. Upsetting the child during attempts to inspect the oropharynx can result in complete airway obstruction. Nebulized epinephrine (i.e., adrenaline) can provide some transient improvement in respiratory distress but also can cause agitation and precipitate airway obstruction. Unstable patients should be urgently intubated by direct laryngoscopy or bronchoscopy in a controlled setting (i.e., operating room or intensive care unit). Although rarely required, facilities to perform a tracheostomy must be available in case attempts to intubate fail.[122,129,137,143] There continues to be controversy about whether cases at the mild end of the disease spectrum without significant respiratory distress can be managed safely without intubation while being closely monitored.[129,137,148]

Blood cultures and throat or epiglottic swabs (in intubated cases) should be obtained for culture and susceptibility testing. Empiric antibiotic therapy, such as a third-generation cephalosporin or ampicillin-sulbactam, should be commenced promptly.[v] The routine use of corticosteroids, which is intended to reduce airway edema, remains controversial, and no RCT has addressed this question.[120,140,148] However, previous, uncontrolled studies have not shown a clear benefit regarding the need for intubation, duration of ventilation, or duration of hospital stay.[137,140,146]

In cases with confirmed Hib epiglottitis, prophylaxis with rifampin should be considered for household contacts according to American Academy of Pediatrics recommendations.[150] The latest UK guidelines also recommend the use of rifampin and suggest ciprofloxacin or azithromycin as an alternative for people who cannot tolerate rifampin or in whom rifampin can interfere with other drugs.[151]

Complications and Prognosis. Potential complications include complete airway obstruction and cardiac arrest, epiglottic abscess, deep neck infection, pneumonia, and seizures.[122,129,132,137] Most patients require only a short period of intubation and ventilation and can be extubated in 24 to 72 hours.[122,129,132,145] The mortality rate is less than 5% in settings where good intensive care support is available.[129,132,137,141,143]

CROUP

Viral croup (i.e., laryngotracheitis) is the most common cause of infectious upper airway obstruction in young children. Some physicians prefer to divide croup into spasmodic croup and laryngotracheitis, also referred to as laryngotracheobronchitis.[152] However, in the clinical setting, this distinction is not particularly meaningful, and *croup* is therefore used in this chapter.

Etiologic Agents and Epidemiology. Parainfluenza virus types 1, 2, and 3 are the most common causative agents of croup, accounting for 50% to 80% of cases, followed by influenza A, influenza B, and respiratory syncytial virus.[153–159] Less common etiologic agents include adenoviruses, rhinoviruses, coxsackieviruses, and echoviruses.[153,154,158,160] Studies have associated human metapneumovirus, human bocavirus, and human coronavirus NL63 with croup.[160–167] Some data suggest that the clinical course of croup caused by influenza virus is more severe than croup caused by parainfluenza virus.[153]

Epidemiology and Pathogenesis. Croup is common. One study from Seattle estimated the annual incidence to be as high as 7 cases per 1000 children younger than 6 years of age.[158] The incidence of croup is highest among children between the ages of 6 months and 2 years.[154,156–158] Typical croup symptoms are rarely observed in children older than 6 years of age, likely because of the increase in airway diameter.[157] The incidence is higher among boys.[152–154,156,168] In temperate climates, the incidence typically peaks in late autumn and winter.[154,156,158,168,169]

Inflammatory edema and mucus production result in airway narrowing in the subglottic region, resulting in stridor.[147,152,170,171] Inflammation of the vocal chords results in hoarseness and sometimes in aphonia.

Clinical Manifestations and Differential Diagnosis.

The typical features of croup are inspiratory stridor, a barking cough, and hoarseness. Symptoms often start abruptly and typically worsen during the night.[172] Nonspecific coryzal symptoms frequently precede the illness. Most patients have low-grade or moderate-grade fever.[155,156] Less than 3% of cases in a primary care setting require hospitalization.[155,156]

Infectious and noninfectious causes and clinical features of upper airway obstruction, including croup, are delineated in Chapter 21 (see Tables 21.3–21.5). The noninfectious differential diagnosis includes foreign body aspiration, vocal chord dysfunction, laryngeal webs, allergic or hypocalcemic laryngospasm, subglottic stenosis (e.g., after prolonged intubation), tracheomalacia, H-type tracheoesophageal fistula, gastroesophageal reflux, and vascular ring.[153,172–175] Laryngeal diphtheria, now a rare but potentially life-threatening infection, can begin as severe croup.[172,176,177]

The diagnosis of croup is made primarily on clinical grounds. Airway or chest radiographs are not indicated in cases with uncomplicated croup.[172,178,179] However, a radiograph showing narrowing of the subglottic airway can be useful if an alternative diagnosis is suspected. Respiratory viral panel testing by PCR can confirm a typical agent but frequently does not aid management.[172]

Management. Treatment with mist or humidified air has been a key component of croup management for much of the 20th century,[152] although only a few published RCTs have investigated the effectiveness of humidified air in hospitalized patients.[180–183] There are no published data on the effectiveness of warm, humidified air in the home environment—a measure frequently recommended to parents.[184] A

[v]References 119, 122, 132, 135, 148, 149.

Cochrane review that included pooled data from three RCTs found that there was a modest, statistically not significant improvement in the croup severity score of patients receiving humidified air compared with untreated patients during the first hour of treatment; there was no difference between treatment groups for other outcome measures.[184]

Treatment with corticosteroids is routinely indicated.[152] A Cochrane review that included 31 RCTs showed that corticosteroid treatment was associated with significant improvement in the croup severity score at 6 and 12 hours compared with placebo.[185] Corticosteroid treatment was associated with a shorter duration of stay in the emergency department or hospital, fewer admissions, and fewer return visits. However, a range of different corticosteroids (e.g., dexamethasone, budesonide, methylprednisolone, fluticasone), different routes of administration (e.g., oral, intramuscular, inhalation), and doses were used in the trials. Most experts recommend the use of oral or intramuscular dexamethasone (0.6 mg/kg) or nebulized budesonide (2 mg).[152,178,186–188] It remains unclear whether repeated doses over the first 48 hours improve outcome.[189]

Many studies have shown that nebulized epinephrine is effective for achieving symptomatic improvement in children with moderate to severe croup.[190–195] Some data suggest that the use of nebulized epinephrine results in a considerable reduction in the need for intubation or tracheostomy.[196] The drug can be administered as racemic epinephrine (2.25%; 0.5 mL in 2.5 mL of saline) or L-epinephrine (1:1000 solution; 5 mL). A 2013 Cochrane review concluded that the two drugs were equally effective.[197] The treatment is safe, and side effects such as pallor and tachycardia usually are mild and transient.[198]

For children with moderate croup (i.e., stridor and chest wall indrawing at rest) who fail to improve sufficiently within 4 to 6 hours of administration of a corticosteroid, hospitalization should be considered. Children with severe croup should receive a dose of a corticosteroid and be treated with nebulized epinephrine; repeated administration of nebulized epinephrine may be necessary. Intensive care support should be considered if there is an insufficient response. The effect of nebulized epinephrine lasts for only 1 to 2 hours.[190] After that, clinical symptoms can return to baseline or become more severe (i.e., rebound effect).[186]

Children with oxygen saturation below 92% on room air should be given supplemental oxygen. Several reports have described the use of heliox in treating croup with some promising results.[199–201] However, two Cochrane reviews concluded that there was insufficient evidence to support its use in this setting.[202,203]

The use of antitussive and decongestant agents is not recommended.[152,186] Treatment with antibiotics is not indicated unless clinical features or laboratory test results indicate a secondary bacterial infection.[152,173,186] In cases of severe croup caused by influenza A or B virus, treatment with neuraminidase inhibitors should be considered, although there are insufficient efficacy data for this approach in this setting.[152,202–206]

Complications and Prognosis. Few patients with croup require intubation and ventilation.[153,154] Contiguous spread of the viral infection can occur and can cause otitis media, bronchiolitis, or pneumonia. Bacterial superinfection can lead to bacterial tracheitis (discussed later) or bronchopneumonia.

The prognosis for uncomplicated croup is very good. Symptoms largely resolve within 48 to 72 hours in most patients.[172] A fatal outcome is very rare.

ACUTE LARYNGITIS

Isolated, acute laryngitis is primarily a disease described in adolescents and adults.

Etiologic Agents. Acute laryngitis is caused most commonly by viruses; the spectrum of causative agents is similar to that for croup.[207–211] Bacteria implicated in acute laryngitis include *S. pneumoniae*, *H. influenzae,* and *M. catarrhalis*.[212–214]

Clinical Manifestations and Management

The key features of acute laryngitis are a change in the normal pitch of the voice and hoarseness, which typically last for 3 to 7 days. Coexistence of nonspecific upper respiratory tract infection symptoms, such as coryza, sore throat, and cough, is common.

Acute laryngitis in previously healthy people usually is a self-limited viral disease. Treatment with antibiotics is not routinely indicated. A Cochrane review on this topic, which included two RCTs evaluating penicillin V and erythromycin versus placebo, concluded that routine antibiotic treatment has no proven benefit.[215]

BACTERIAL TRACHEITIS

The term *bacterial tracheitis* was first used in a publication by Jones and colleagues in 1979.[216] Earlier reports describe cases of *laryngotracheobronchitis* that closely resemble descriptions of bacterial tracheitis, suggesting that this entity was recognized previously.[217,218]

Etiologic Agents. *S. aureus* is by far the most common causative organism.[125,219–221] Other bacteria commonly implicated in bacterial tracheitis are *S. pyogenes*, *S. pneumoniae*, *H. influenzae,* and *M. catarrhalis*. Cases attributed to a variety of other bacteria, including *Pseudomonas aeruginosa*, *Bacillus cereus*, *Escherichia coli*, *Prevotella* species, and *Bacteroides* species also have been reported, although they appear to be uncommon.[219–226]

Epidemiology and Pathogenesis. Bacterial tracheitis is rare, with an estimated annual incidence below 0.1 case per 100,000 children in the United Kingdom and Australia.[220] Incidence data have not been published for other countries. Some data suggest that the incidence peaks during autumn and winter.[220] Bacterial tracheitis predominately affects young children, although a few adult cases have been described.[227–229]

The pathogenesis of bacterial tracheitis remains unclear. It has been postulated that viral infection of the upper respiratory tract may facilitate secondary bacterial infection and invasion of the airways, resulting in inflammation and edema, which ultimately leads to narrowing of the trachea.[219] The peak incidence of bacterial tracheitis coincides with the peak season for viral respiratory pathogens, suggesting synergy. In one large case series, coinfection with influenza virus was identified in almost one third of the cases.[221] Coinfection with parainfluenza virus, respiratory syncytial virus, or adenovirus has been described in other reports.[125,220,223,230]

Clinical Manifestations and Differential Diagnosis. Most patients with bacterial tracheitis report prodromal symptoms suggestive of a minor upper respiratory tract infection, which typically began 2 to 5 days before the onset of stridor.[219,220] After stridor and dyspnea develop, patients often deteriorate rapidly, frequently requiring intubation within the first 24 hours to overcome increasing upper airway obstruction.[216,220,231–233] Other common features at presentation include fever (often moderate to high grade), hoarse voice or aphonia, cough, and intercostal and subcostal recessions. Drooling is uncommon. Most cases show little or no response to nebulized epinephrine.[234]

The main differential diagnoses are epiglottis and viral croup. Unlike cases of bacterial tracheitis, children with epiglottitis typically refuse to speak, have drooling, and adopt an upright position with extension of the neck. Children with croup typically have only low-grade pyrexia, do not appear toxic, and usually respond to nebulized epinephrine.

An inflammatory response, including an elevated CRP level and WBC count, is seen in most patients at presentation.[220,234] The radiograph may demonstrate narrowing of the tracheal air shadow and intraluminal tracheal membranes, although these are not universal findings (Fig. 28.4).[223,230] Coexisting pulmonary changes, including infiltrates and atelectases, are common.[220,234–237] Direct visualization of the airways reveals an unremarkable or only mildly inflamed epiglottis but shows marked subglottic inflammation, edema of the tracheal mucosa, and copious purulent endotracheal secretions.[216,234] Endotracheal aspirates should be obtained and sent for bacterial culture and susceptibility testing. Blood cultures are rarely helpful, as bacteremia is relatively uncommon in these patients.

Management. Proactive airway management is critical in managing bacterial tracheitis to prevent complete airway obstruction and consequent respiratory arrest. In most of the larger published case series, 80% to 100% of patients required intubation or tracheostomy and mechanical ventilation. Intubation usually is challenging and requires the use of an endotracheal tube of considerably smaller diameter than would be expected based on the patient's age. The personnel and equipment for a tracheostomy must be readily available in case conventional intubation fails.

Appropriate empiric antibiotic treatment must include effective antistaphylococcal coverage. A combination of a third-generation

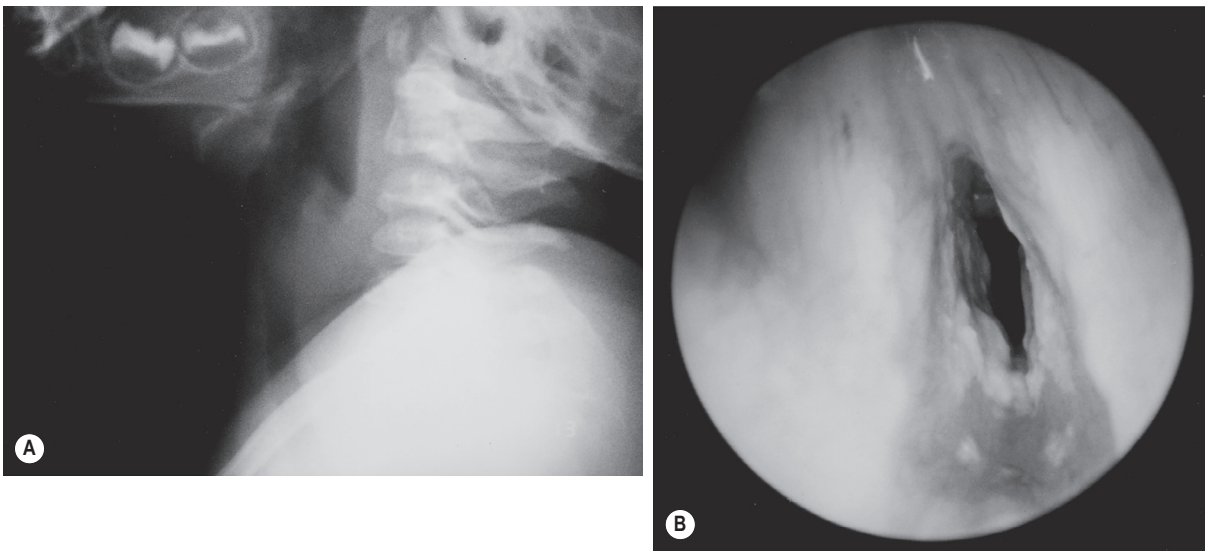

FIGURE 28.4 (A) Lateral neck radiograph of a 22-month-old boy with bacterial tracheitis caused by *Staphylococcus aureus* shows subglottic haziness (similar to croup). (B) Endoscopic view of the trachea shows mucosal denudation, intraluminal debris, and purulent laryngotracheal secretions. (Courtesy of Richard H. Schwartz, MD, Vienna, VA.)

cephalosporin (e.g., ceftriaxone, cefotaxime) and a penicillinase-resistant penicillin (e.g., cloxacillin, nafcillin) given intravenously is a suitable choice in areas where community-acquired MRSA infections are unlikely. Otherwise, vancomycin should replace the latter component. Good-quality evidence is lacking, but many centers use systemic corticosteroids in the first few days of the illness with the intention to reduce airway edema.

Most patients require ventilatory support for only 2 to 5 days unless complications occur. The optimal duration of antibiotic treatment is unknown, but most experts recommend a minimum of 10 days of treatment.

Complications and Prognosis. Complications of bacterial tracheitis include pneumothorax, pneumomediastinum, pulmonary edema, acute respiratory distress syndrome, hypotension, and cardiorespiratory arrest.[230,223,234,238] Cases with concurrent toxic shock syndrome have been described.[230,232,239] Neurologic sequelae are common in patients who experience cardiorespiratory arrest. Subglottic stenosis and subglottic polyps are rare long-term sequelae.[230,240]

Bacterial tracheitis is a potentially life-threatening condition, with some early publications reporting case fatalities in excess of 20%.[230,238] Fatal outcomes have been uncommon in the past decade, likely reflecting improvements in intensive care support.[125,220,221]

ACUTE BRONCHITIS

Acute bronchitis predominately occurs in adolescents and adults. Data from the US National Health Interview Survey suggest that approximately 5% of all adults experience one or more episodes of bronchitis per year.[241] The incidence peaks in autumn and winter.[242]

Etiologic Agents. Most cases of bronchitis are nonbacterial in nature, although no causative organism can be identified in many patients. Viral infections appear to account for most cases.[243,244] Viruses commonly implicated in acute bronchitis include influenza virus, parainfluenza virus, respiratory syncytial virus, rhinovirus, adenovirus, and human metapneumovirus.[243–248] Infection due to bacterial organisms, including *Bordetella pertussis*, *Chlamydophila pneumoniae,* and *Mycoplasma pneumoniae*, is less common.[243–245]

Clinical Manifestations and Management. Illness typically begins with nonspecific upper respiratory tract infection symptoms, which usually last for a few days. This is followed by a second phase characterized by persistent cough, frequently with sputum production or wheezing, which typically lasts for 1 to 3 weeks.[242,243]

Antibiotic therapy is not routinely indicated for previously healthy people with acute bronchitis.[242,249] A Cochrane review that included nine RCTs showed that antibiotic treatment on average reduced the duration of cough by less than 1 day compared with placebo; adverse effects were significantly more common in the antibiotic-treated patients.[250] The update of this review, which included 17 RCTs, concluded that the benefits of antibiotic treatment in bronchitis were marginal.[251,252] Guidelines for treating acute bronchitis by the American College of Physicians and the American College of Chest Physicians have discouraged the routine use of antibiotics, inhaled bronchodilators, or mucolytic agents.[253,254] However, patients diagnosed with pertussis should receive azithromycin, primarily to limit transmission.[242]

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All references are available online at www.expertconsult.com.

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