Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Chapter **24**

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Laryngitis, epiglottitis and pharyngitis

Laryngitis

Croup is a common respiratory tract infection of infants and children younger than 6 years of age, with a peak incidence between 7 and 36 months.[1,2] It is characterized by varying degrees of inspiratory stridor (noisy breathing on inspiration), barking cough, and hoarseness as a result of laryngeal and/or tracheal obstruction. Before the advent of treatment with corticosteroids and racemic adrenaline (epinephrine) for severe croup, intubation, tracheotomy and death were typical outcomes. Nowadays, mortality from croup has become a rarity in developed countries. Most children can be managed in the primary care setting.

EPIDEMIOLOGY

Croup is the most common cause of stridor in children and accounts for up to 15% of emergency department and primary care visits for respiratory infections in the USA.[3] The disease mainly affects those aged between 6 months and 3 years, with a peak annual incidence in the second year of life of nearly 5%. However, croup does occur in babies as young as 3 months old and in adolescents.[1] There is a slight male preponderance (male:female ratio, 3:2). Although croup is observed throughout the year, the majority of cases occur with parainfluenza viral infections, typically in the autumn. Those with the respiratory syncytial virus present mainly in the winter. There is often a smaller spring peak. The generalization of treatment with oral corticosteroids and nebulized adrenaline during the 1990s reduced the rate of hospitalization. Nowadays, most cases of croup are managed in the primary care or emergency room setting, with 1.5–31% of patients requiring admission[4] and less than 5% requiring endotracheal intubation.[5]

PATHOGENESIS AND PATHOLOGY

Parainfluenza is the etiologic agent in 50–70% of patients who are hospitalized for croup.[6] Other pathogens causing croup include influenza virus, respiratory syncytial virus, metapneumovirus, adenovirus, rhinovirus, enterovirus and, rarely, measles virus and herpes simplex virus. When croup is caused by influenza virus, the clinical picture is usually more severe than that caused by a parainfluenza virus.[7]

A strong association has been described between both human metapneumovirus and coronavirus HCoV-NL63 infection and croup in children.[8,9] However, a likely possibility is that the increasing number of viruses seen in association with croup is merely a reflection of improvements in methods of detection.

Laryngeal diphtheria is now very rare in immunized populations. However, outbreaks have been reported in case series from Russia and India. Measles remains an important cause of croup in nonimmunized children. Treatment with vitamin A has been reported to be effective for prevention of secondary infections, especially croup, in children with severe measles.

In acute laryngotracheitis, there is erythema and swelling of the lateral walls of the trachea, just below the vocal cords. Histologically, the involved area is edematous, with cellular infiltration in the lamina propria, submucosa and adventitia. The infiltrate contains histiocytes, lymphocytes, plasma cells and neutrophils. In bacterial croup – laryngotracheobronchitis and laryngotracheobronchopneumonitis – the tracheal wall is infiltrated with inflammatory cells; in addition, ulceration, pseudomembranes and microabscesses are present. There is thick pus within the lumen of the trachea and the lower air passages. In spasmodic croup, there is non-inflammatory edema in the subglottic region.[3]

PREVENTION

Prevention of disease depends mainly on good hand washing and preventing the spread of oral secretions. Masks and handkerchiefs inoculated with antiviral drugs have been used in experimental trials; however, after several minutes of breathing, when the mask becomes wet, the protection seems to diminish.

Vaccines are available to prevent some of these diseases. Effective measles vaccines have been used for approximately 30 years, so the disease has decreased dramatically in most countries. Certain adenoviral vaccines have been used with some degree of success, mostly in military personnel. Vaccines against parainfluenza viruses would have the most impact in preventing laryngitis and croup; however, these are still experimental. The ability of influenza vaccine to prevent laryngitis has not been studied.

CLINICAL FEATURES

Croup usually begins with nonspecific respiratory symptoms, including rhinorrhea, sore throat and cough. Fever is generally low grade (38–39°C) but can exceed 40°C. Within 1–2 days, the characteristic signs of hoarseness, barking cough and inspiratory stridor develop, often suddenly, along with a variable degree of respiratory distress. Symptoms may fluctuate depending on whether the child is calm or agitated. They are perceived as worsening at night and most emergency department visits occur at night between 10 pm and 4 am. Croup symptoms are generally short lived, with about 60% of children showing resolution of their barky cough within 48 hours. However, a few

children continue to have symptoms for up to 1 week. Spasmodic croup typically presents at night with the sudden onset of 'croupy' cough and stridor. The child may have mild upper respiratory complaints but more often appears completely well prior to the onset of symptoms.

The diagnosis of croup should be made clinically. The child's symptoms may range from minimal inspiratory stridor to severe respiratory failure secondary to airway obstruction. In mild cases, respiratory sounds at rest are normal; however, mild expiratory wheezing may be heard. Children with more severe infection have inspiratory and expiratory stridor at rest with suprasternal, intercostal and subcostal retractions. Air entry may be poor. Lethargy and agitation may be a result of hypoxemia. Warning signs of severe respiratory disease include tachypnea, tachycardia out of proportion to fever and hypotonia. Children may be unable to maintain adequate oral intake, which results in dehydration. Cyanosis is often a late ominous sign.

Determination of disease severity relies on clinical assessment. The most commonly used scoring system has been that of Westley *et al.*[10] (Table 24.1), which evaluates the severity of croup by assessing five factors: level of consciousness, cyanosis, stridor, air entry and retractions. This system has been extremely valuable in treatment trials but has little use in the routine clinical setting. However, the Alberta Clinical Practice Guideline Working Group has developed another clinically useful severity assessment table. Using this classification scheme, 85% of children in 21 general emergency departments in Alberta, Canada,[11] were determined to have mild croup and less than 1% had severe croup. The assessment is as follows:

- mild croup: occasional barking cough, no audible rest stridor, and either mild or no suprasternal or intercostal retractions;
- moderate croup: frequent barking cough, easily audible rest stridor, and suprasternal and sternal retractions at rest, with little or no agitation;
- severe croup: frequent barking cough, prominent inspiratory and, occasionally, expiratory stridor, marked sternal retractions, agitation and distress; and
- impending respiratory failure: barking cough (often not prominent), audible rest stridor, sternal retractions may not be marked, lethargy or decreased vigilance, and often dusky appearance with no supplemental oxygen.

Table 24.1 Westley croup score[10]

Symptom	Descriptor	Score
Stridor	None When agitated At rest	0 1 2
Retractions	None Mild Moderate Severe	0 1 2 3
Air entry	Normal Decreased Markedly decreased	0 1 2
Cyanosis in room air	None With agitation At rest	0 4 5
Level of consciousness	Normal Disoriented	0 5
Total score		0–17

Mild croup: scores 1–2; moderate croup: scores 3–8; severe croup: scores >8.

DIAGNOSIS

Radiologic studies are not recommended in a child who has a typical history of croup and who responds appropriately to treatment. Plain films of the airway and a chest radiograph may be obtained to rule out findings suggestive of another etiology. Anteroposterior films may demonstrate symmetric subglottic narrowing ('steeple sign') (Fig. 24.1),[12] although this may be absent in up to 50% of cases and may be present in the absence of croup. If radiographs are justified by an atypical clinical picture, the child must be closely monitored during imaging by skilled personnel with appropriate airway management equipment, as airway obstruction can worsen rapidly.

Cardiorespiratory monitoring, including continuous pulse oximetry, is indicated in children with severe croup but it is not necessary in mild cases. Oxygen saturation may be near normal in severe croup and yet significantly lowered in some children with mild to moderate disease.[10] This apparent discrepancy may relate to the degree of lower airway disease present.

MANAGEMENT

Over the past 50 years, there has been considerable controversy regarding many therapies for croup, including the role of humidified air and the optimal type (warm versus cold) and the roles of corticosteroids and racemic adrenaline (epinephrine).[3] However, the marked success of corticosteroids in the outpatient management of croup and the effectiveness of nebulized adrenaline (epinephrine) in more severe cases have led to the resolution of many of the controversies. The general consensus is that children with croup should be made as comfortable as possible, and clinicians should take special care during assessment and treatment not to frighten or upset them because agitation causes substantial worsening of symptoms. Sitting the child comfortably in the lap of a parent or caregiver is usually the best way to lessen agitation.

Oxygen is the immediate treatment of choice for children with severe viral croup who have considerable upper airway obstruction with significant oxygen desaturation (SaO_2 <90%). This therapy has not been subjected to a randomized controlled trial and is unlikely ever to be. It is the initial treatment before the administration of pharmacologic treatment in the hospital setting.

During much of the 20th century, treatment with humidified air (mist therapy) was the cornerstone of the management of croup.[3]

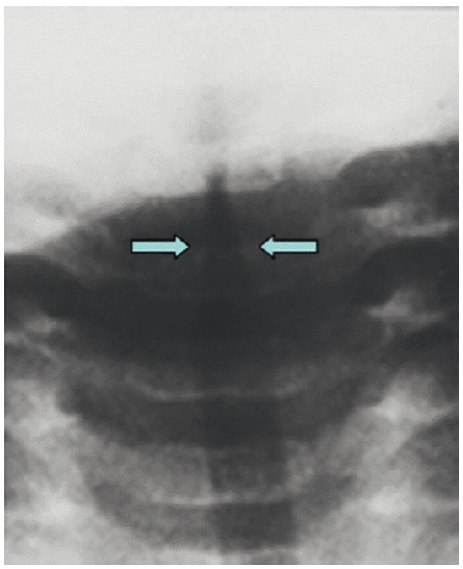

Fig. 24.1 Anteroposterior neck film demonstrating steeple sign (arrows) in a case of croup.

More recently, however, the effectiveness of mist therapy has been questioned. In a recent trial[13] comparing the effects of high humidity (100%), low humidity (40%), and blow-by humidity (in which a plastic hose is held near the child's nose and mouth) in children with mild croup, there were no significant differences in the croup score responses among the three groups; each group had significant improvement (about 33%) over baseline in the croup score 60 minutes after administration. In two other small trials, control subjects who received nebulized saline also had improvement in their croup scores over baseline values.[10] Since none of these studies included an untreated control group, it is not possible to determine whether or not the improvements were due to the moist air. A recent Cochrane Review of data from three other studies concluded that there was no evidence that inhalation of humidified air in children with mild-to-moderate croup resulted in a substantial improvement in the croup score.[14]

Corticosteroid therapy is now routinely recommended by all experts. In a cotton-rat laryngotracheitis model,[15] corticosteroids reduced the degree of inflammation and cell damage; although the viral load was increased, the duration of shedding was not prolonged. Meta-analyses of randomized trials[16] have consistently demonstrated significant improvement in patients treated with corticosteroids as compared with controls. For example, in a meta-analysis of 37 trials, patients who were given corticosteroids had significantly lower croup scores at 6 hours, a decrease in return visits and a decrease in time spent in emergency rooms or hospitals.[16]

Trials of corticosteroids in croup have involved a variety of drugs, dosages and routes of administration. The regimens studied most frequently have been single-dose dexamethasone (0.6 mg/kg of body weight given orally or intramuscularly) and nebulized budesonide (2 mg in 4 ml of water); some studies have involved additional doses (up to four doses of dexamethasone or nebulized budesonide given over a period of 2 days). No studies have directly compared the outcomes of single-dose therapy with the outcomes of 2-day treatment schedules. The 1992 recommendation by the Canadian Paediatric Society to use dexamethasone for treatment was followed by a marked decrease in hospitalizations for croup in Ontario, providing further support for the use of corticosteroids.[2] Similar findings were noted in Perth, Australia.

A potential concern with corticosteroids, however, is their immunosuppressive effects, which might predispose the patient to infectious complications. Trials have not been powered to assess these risks, but such complications would be expected to be rare with standard (single-dose) therapy.

Nebulized adrenaline (epinephrine) has been extensively studied for the treatment of croup. Early controlled trials demonstrated that the administration of 2.25% racemic adrenaline (epinephrine) (0.5 ml in 2.5 ml of saline) by intermittent positive-pressure breathing resulted in a significant reduction in the croup severity score,[10,17] but this benefit lasted for less than 2 hours. Later trials also showed that nebulized L-epinephrine diluted in 5 ml of saline at a ratio of 1:1000 was as effective as racemic adrenaline (epinephrine) in the treatment of croup.[18] In severe croup, repeated treatments with adrenaline (epinephrine) have been used and have often decreased the need for intubation.

GUIDELINES

The American Academy of Pediatrics has no guidelines for the management of croup. The Infectious Diseases and Immunization Committee of the Canadian Paediatric Society published a brief statement in 1992, recommending corticosteroid therapy for children admitted to the hospital with croup. The Alberta Medical Association published a guideline for the diagnosis and management of croup in 2004, which was updated in 2007.[11] An algorithm for the management of croup in the outpatient setting is shown in Figure 24.2.

Epiglottitis

Epiglottitis is an acute inflammation of the epiglottis or supraglottis that may lead to the rapid onset of life-threatening airway obstruction and is considered an otolaryngologic emergency. Since the widespread implementation of a conjugate vaccine for *Haemophilus influenzae* type b (Hib) nearly 2 decades ago, the incidence of epiglottitis has significantly declined in children. Securing the airway should be accomplished immediately in a controlled setting. Coordinated communication between the otolaryngologist, anesthesiologist, and intensive care physician is vital to the care provided to these critically ill patients.

PATHOGENESIS AND PATHOLOGY

Haemophilus influenzae type b (Hib) can colonize the pharynges of otherwise healthy children through respiratory transmission from intimate contact. These bacteria may penetrate the mucosal barrier, invading the bloodstream and causing bacteremia and seeding of the epiglottis and surrounding tissues. Bacteremia may also lead to infection of the meninges, skin, lungs, ears and joints.

Hib infection of the epiglottis leads to acute onset of inflammatory edema, beginning on the lingual surface of the epiglottis where the submucosa is loosely attached. Swelling significantly reduces the airway aperture. Edema rapidly progresses to involve the aryepiglottic folds, the arytenoids and the entire supraglottic larynx. The tightly bound epithelium on the vocal cords halts edema spread at this level. Aspiration of oropharyngeal secretions or mucous plugging can cause respiratory arrest.

Despite the dramatic decrease of Hib-related infections after the introduction of the vaccine, recent reports have shown that Hib may still cause epiglottitis despite adequate vaccination.[19,20] It should be noted, however, that vaccination failure may have prevailed with use of the older, purified polysaccharide vaccine.[19] Infectious agents in the postvaccination era associated with epiglottitis include group A *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Haemophilus parainfluenzae* and β-hemolytic streptococci.

EPIDEMIOLOGY

Traditionally, epiglottitis was most commonly caused by Hib and primarily reported in children aged 2–7 years. The introduction of the Hib conjugate vaccine in 1988 dramatically changed the epidemiology of acute epiglottis. At the Children's Hospital of Buffalo, a rate of 3.5 cases of epiglottis per 10 000 admissions in 1969–1977 decreased to 0.3 cases per 10 000 admissions in 1995–2003. Hib was the causative organism identified in 84% of the cases in the earlier years, but was completely absent in the later segment of the study.[21] A 5-year retrospective review of the incidence of epiglottitis at the Children's Hospital of Philadelphia indicated a frequency of 10.9 per 10 000 admissions before 1990. Only 1.8 episodes per 10 000 admissions were noted 5 years after introduction of the vaccine.[22] A Finnish study also demonstrated a decreased prevaccination era incidence of 50 and 60 cases annually in 1985 and 1986, respectively, to only two cases in 1992 after widespread administration of the Hib vaccine.[23] In a Swedish study, the incidence of epiglottitis also decreased substantially from 20.9 in 1987 to 0.9 in 1996 for children younger than 5 years.[24]

There is a male preponderance of acute epiglottitis, with male-to-female ratios ranging from 1.2:1 to 4:1. Most studies have not demonstrated a seasonal variation in the incidence of acute epiglottitis.

Mortality rates have decreased considerably since the introduction of the Hib vaccine and the consequent shift in disease from young children to adults. Death rates are now less than 1% for children but approach 7% for adults. When deaths have occurred, a large percentage transpired due to delay in diagnosis or shortly after arrival at a medical facility for appropriate care.[25]

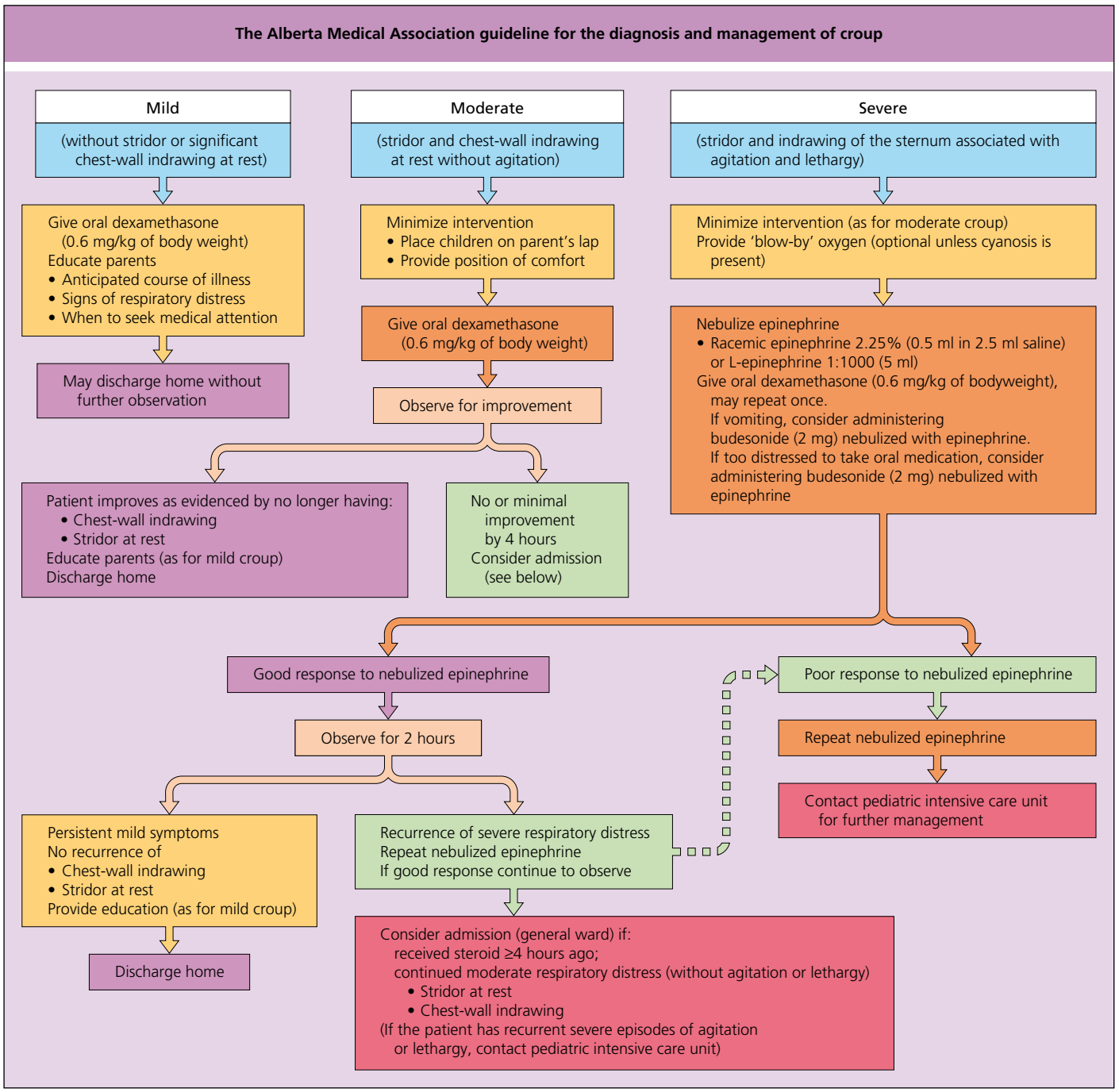

Fig. 24.2 The Alberta Medical Association guideline for the diagnosis and management of croup.[11]

PREVENTION

In the only study to date seeking specific risk factors for epiglottitis, day-care attendance was the strongest predictor for disease but the association was modified by whether the subject had had an upper respiratory illness in the previous 4 weeks. There was also the suggestion that northern European ancestry was a risk factor as well. Fortunately, the incidence of epiglottitis (and meningitis) has decreased markedly since the advent of the Hib vaccination. Whether the incidence of Hib disease in adults may change in the future is unknown, because long-term immunity from vaccination may prove to be either more or less effective than that due to natural infection.

CLINICAL FEATURES

Patients with epiglottitis often have an underlying illness, presumed to be viral. They then have sudden onset of fever, with the neck extended forward, drooling and air hunger. Affected children are anxious and lean forward to open their airway. The diagnosis is easily made by viewing the epiglottitis, which is swollen and red (Fig. 24.3). Intubation is often required. Culturing swabs from the epiglottis in children almost always obtains *Haemophilus influenzae* type b. Some children have been discharged without intubation after receiving only one dose of ceftriaxone when the epiglottis did not appear reddened, but subsequent epiglottic and blood cultures have been positive for Hib. They were

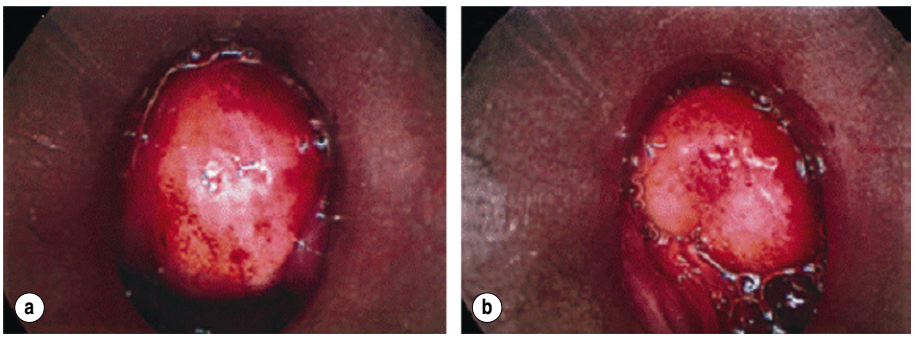

Fig. 24.3 Acute epiglottitis with views of the cherry red epiglottis on direct laryngoscopy.

cured completely. The duration of hospital treatment averages 3 days. Intubation is needed for less than 24 hours in most cases.[26]

In adults other pathogens may be obtained.[27] In most adults the disease is less severe and of slower onset. The airway obstruction occurs because of a progressive cellulitis of the supraglottic area. Thus at presentation, antibiotic treatment and intubation at the first sign of increasing respiratory compromise may avert the need for tracheotomy. The use of steroids to reduce inflammation and decrease the need for tracheotomy is appealing but unproven.

DIAGNOSIS

Visualization of the posterior pharynx is the best way to confirm the diagnosis of epiglottitis. Because airway obstruction is the most feared complication of this disease, this examination should be done in a manner and place where immediate intubation can be performed if necessary.

Lateral neck radiographs may demonstrate the classic thumb sign (Fig. 24.4). It is actually a rounded mass shadow of the normal leaf-like epiglottis resulting from the thickening and edema of the inflamed epiglottic tissue. Another radiologic feature of acute epiglottitis is the 'vallecula sign', which is the result of partial or complete obliteration of a well-defined air pocket bounding the base of the tongue and the epiglottis. The poor sensitivity (38%) and specificity (78%) of plain films limits the utility of this radiographic modality in the current age of technologic advances, whereby the larynx can be safely and accurately visualized with flexible laryngoscopy.[28]

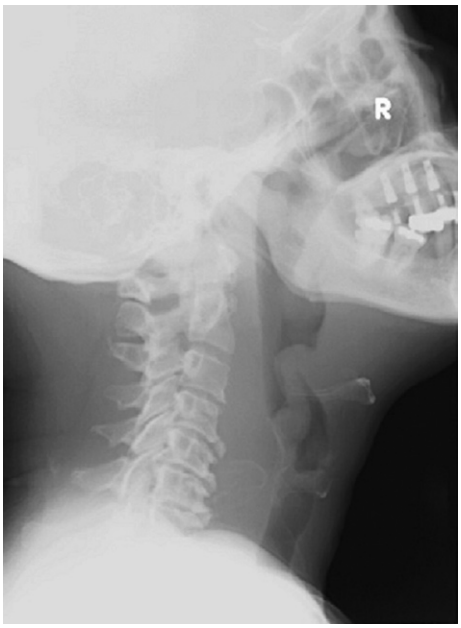

Fig. 24.4 Lateral neck film demonstrating thumb sign with edema of the epiglottis.

A complete blood cell count with differential, blood cultures and epiglottic cultures (when an artificial airway has been placed) are obtained after the airway is secure and the patient is stable. Elevated white blood cell counts are frequently present, but positive blood culture results are extremely variable (6–15%).

MANAGEMENT

Securing the airway is the initial step in the management of epiglottitis. Various studies have been performed to identify predictive factors for the need for airway intervention. A combination of features such as stridor, drooling, acute onset or rapid progression, hoarseness, respiratory distress, dyspnea, chest wall retractions and upright position have been associated with the need for airway intervention.[29]

Appropriate antibiotics include ceftriaxone, cefotaxime and cefuroxime (for non-meningitic infections). Ampicillin should not be used due to the high frequency of ampicillin-resistant strains of Hib. Steroids are commonly employed to decrease mucosal edema of the epiglottis, but no data exist in the literature to prove any benefit from their use.

Most children can be successfully extubated after 24 hours of antibiotic therapy and some extubate themselves before that time has expired. Family members and day-care contacts should receive rifampin prophylaxis (300 mg q12h for 2 days) to avoid secondary infection.

Pharyngitis

Pharyngitis is a very common inflammatory condition of the pharynx accompanied by a sore throat and occasionally difficulty in swallowing. It is usually viral but may be caused by bacterial or fungal infection. Gastroesophageal reflux disease (GERD) or particularly extraesophageal reflux (EER) can also cause an acid pharyngitis in adults and children. Serious complications of pharyngitis may include peritonsillar abscess or retropharyngeal abscess.

EPIDEMIOLOGY

Pharyngitis can be separated into one group of illnesses with associated nasal symptoms (which are most commonly viral in origin) and another that causes only pharyngitis. It is important to distinguish between these infections because rheumatic fever and acute glomerulonephritis may complicate untreated group A β-hemolytic streptococcal infections, but they can usually be prevented by appropriate antibiotic treatment.

Adenoviruses, rhinoviruses, coronaviruses, enteroviruses and parainfluenza viruses most frequently cause self-limiting viral infections. Other viral infections, such as respiratory syncytial virus (RSV) and Epstein–Barr virus (EBV), are less common but still frequently

occur. Bacterial causes of upper respiratory infections are led by group A β-hemolytic streptococci (GAS) but can also be caused by *Haemophilus influenzae*, *Bordetella pertussis*, *Chlamydia pneumoniae*, *Corynebacterium haemolyticum*, *Mycoplasma pneumoniae* and *Yersinia enterocolitica* among others.

These upper respiratory infections are often difficult to differentiate and hence difficult to diagnose, frequently leading to futile overtreatment in many cases. Further complicating the issue is the fact that primary viral infections are often succeeded by secondary 'opportunistic' bacterial infections, making undertreatment a problem in a significant minority of infections. Additionally, individuals with allergies are sometimes more prone to secondary bacterial infections. The clinician is therefore challenged to weigh multiple factors involved in deciding whether an infection is viral or bacterial in origin, and whether antibiotic treatment is warranted.

Viral upper respiratory infections frequently occur in mini-epidemics (RSV, parainfluenza, influenza, varicella, measles). They are more common in the winter except for those caused by enteroviruses, which are more common in the summer.[30] Some viral infections occur year round, with no seasonal pattern (adenoviruses). Group A β-hemolytic streptococcal infections are more common in the winter, but many other nonviral respiratory infections do not appear to be seasonally linked (*Chlamydia* and *Mycoplasma* spp.). Some bacterial infections appear to be linked to preceding viral infections and hence occur more commonly in the winter. Pharyngeal colonization may occur throughout the year.

Influenza infections vary significantly from year to year. In the USA one subtype was predominant each year until about 1990, since which time both H3N2 and H1N1 strains have been circulating simultaneously. When there is a major shift in antigen type, significant excess morbidity occurs as the new strain infects the community. Increasing air travel has accelerated the rate at which the influenza viruses travel around the world and has perhaps been responsible for the increasing frequency with which the viruses are detected. The shifted strain outbreaks have most affected the elderly and children with congenital heart and lung disease. Minor influenza drifts have occurred also, but cause less disease. There has also been a recent decrease in the average age at which children acquire upper respiratory diseases because of the increasing use of day care for children. Although the long-term effect of this is unknown, in the short term it appears that it has been responsible for a significant increase in the number of ear infections in children less than 2 years old.[31]

Rheumatic fever, a complication of group A β-hemolytic streptococcal pharyngitis, has waxed and waned in importance.[32] After a century of prominence, the disease was in considerable decline in developed countries for 40 years. Recently, clusters of rheumatic fever cases have occurred, for example in Salt Lake City, Utah, USA, where it is hypothesized that the re-emergence of certain M types has been responsible.

PATHOGENESIS AND PATHOLOGY

The pathogenesis of the sore throat due to pharyngitis is poorly understood. Volunteers given rhinoviral infections produce bradykinin and lysylbradykinin, which are known inflammatory mediators that can excite nerve endings in the pharynx to cause pain.[33] There is also suggestive evidence from laboratory animals that adenovirus, RSV and other viral infections directly invade the pharyngeal cells and produce an inflammatory response. This leads to the well-described 'red, sore throat'. Additionally, adenovirus and EBV often produce lymphoid hyperplasia and tonsillar exudation. Herpes simplex virus (HSV) and coxsackievirus infections frequently lead to ulcerations of the oral mucosa. Herpes simplex virus ulcers are more common in the anterior part of the mouth and coxsackievirus ulcers occur more frequently in the posterior part of the pharynx, but this is only a guide and both viruses can cause ulcers in any part of the oropharynx. Herpes simplex often produces a significant gingivitis as well.

Streptococcal pharyngitis often involves the posterior pharynx, with petechiae on the uvula and soft palate.[34] When one sees this clinical sign, GAS is often isolated by throat culture. A confusing factor is that up to 10% of patients who have EBV infections will have a secondary group A β-hemolytic streptococcal pharyngitis during their illness. *Corynebacterium diphtheriae* can also cause pharyngitis, producing a characteristic gray membrane across the structures of the posterior pharynx. This is seldom seen today except in a few geographic areas where diphtheria outbreaks have occurred recently, such as Russia. There are also noninfectious causes of pharyngitis, such as Behçet's syndrome, Kawasaki disease, Marshall's syndrome and Stevens–Johnson syndrome.

PREVENTION

Preventing pharyngitis is desirable but difficult to achieve. Mostly aerosolized oral secretions, hand-to-mouth contact with multiple individuals and the use of common utensils, glassware, etc. spread viral pharyngitis. Certain viruses are known to be particularly resilient; RSV has been cultured from tabletops hours after being inoculated.[35] Measles has been known to be contracted from the air in a physician's waiting room, as long as 1 hour after the child with measles had left the room. Other viruses may be less durable and less contagious, but close contact is obviously not necessary to transmit many of these agents. Prevention of disease depends mainly on good hand washing and preventing the spread of oral secretions. Masks and handkerchiefs inoculated with antiviral drugs have been used in experimental trials, but after several minutes of breathing, when the mask becomes wet, the benefit seems to diminish.

There are vaccines available to prevent some of these diseases. Effective measles vaccines have been used for approximately 30 years, so the disease has decreased dramatically in most countries. Certain adenoviral vaccines have been used with some degree of success, mostly in military personnel. Vaccines for RSV and parainfluenza viruses are currently under development. These vaccines could have a significant effect on the population's health, particularly on that of the youngest children.

Transmission of streptococcal pharyngitis seems to require closer contact than for most viruses. Studies performed in the military during the Second World War showed that soldiers in barracks sleeping on either side of the index case were more likely to have disease than those further away.

To date, there are no immunizations available to prevent streptococcal disease, although trials evaluating group B and group A vaccines are under way. For patients who have had prior group A disease and subsequent rheumatic fever, penicillin prophylaxis is recommended. Most patients receive intramuscular benzathine penicillin, 1.2 million units, once per month; although oral regimens are acceptable, they have poorer compliance rates.

CLINICAL FEATURES

Pharyngitis is a ubiquitous infection. A 'sore throat' affects most people at least once every year. Most cases of viral pharyngitis are associated with an upper respiratory infection (nasopharyngitis). Generally nasopharyngitis has a prodrome that may include malaise, diaphoresis, fever, headache and general aches and/or pains. Coryza and sore throat then begin. Many infections will progress to produce a cough and/or laryngitis. Some viral infections produce predominantly coryza, others more pharyngitis, and others more cough or laryngitis. Coxsackieviruses often cause ulcers in the posterior pharynx along with a sore throat. Measles can cause a severe pharyngitis, but the associated symptoms of conjunctivitis, rash and Koplik's spots make the disease easily diagnosable. Parainfluenza and influenza viruses can give a particularly painful pharyngitis, with frequently associated symptoms of cough and laryngitis.

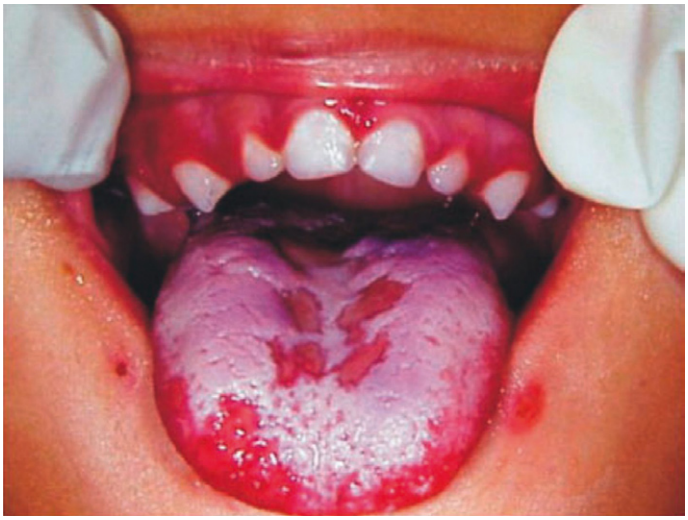

Fig. 24.5 Primary infection of HSV-1

The DNA viruses EBV, adenovirus, cytomegalovirus and HSV can produce significant pharyngitis. They also tend to last longer than the other viral causes of pharyngitis. These viruses produce other upper respiratory symptoms such as nontender cervical adenopathy of, in the case of HSV, tongue and mouth ulcers. Herpes simplex virus pharyngitis has been described as a disease in which 'the gums swell up and swallow the teeth' (Fig. 24.5). Rhinoviruses and RSV infections give upper respiratory symptoms as well as pharyngitis in infants.

The syndrome of acute HIV infection ('seroconversion illness') is well described and may cause symptoms in up to 50% of patients. It is a mononucleosis-like illness in which pharyngitis is a prominent feature. Patients will also have fever, lymphadenopathy, rash and myalgias. The symptoms are nonspecific.

It is important to diagnose bacterial causes of pharyngitis because, unlike viral causes, many can be treated specifically with antibiotics. Proper treatment can avoid significant morbidity and/or mortality. Pharyngitis caused by GAS is the most common infection causing significant pharyngeal edema, frequently with petechiae on the soft palate and uvula (Fig. 24.6). Tender cervical nodes are common. Small children may complain of abdominal pain, which may be due to mesenteric adenitis. Headache and raised temperature are also common. Some patients who have a streptococcal sore throat have a characteristic red 'scarlet fever' rash that begins in the groin and axillary areas and spreads over the body (Fig. 24.7). The rash is sandpaper-like and may itch. A strawberry tongue is also often present. Other patients have a characteristic rash on the face. Without treatment the illness usually resolves over 3 or 4 days, but rheumatic fever may ensue.

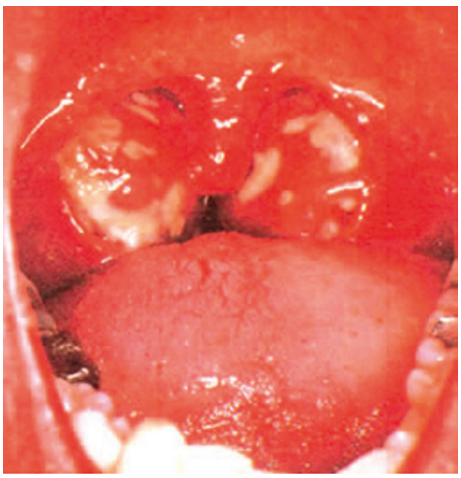

Fig. 24.6 GAS tonsillitis.

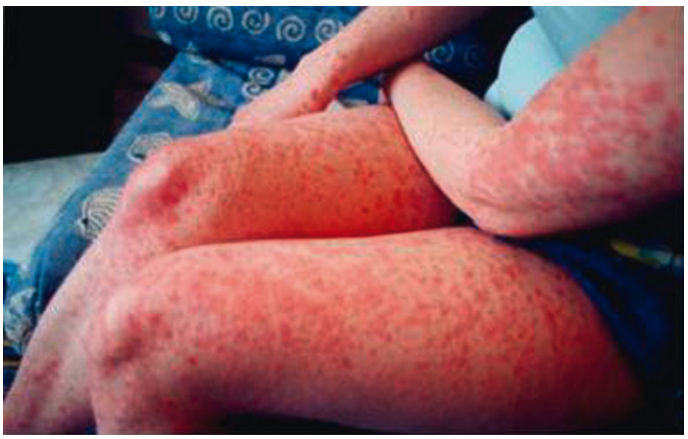

Fig. 24.7 Scarlatine rash.

The recommended treatment is penicillin, or clindamycin, erythromycin or azithromycin for those allergic to penicillin. There is concern about the recurrence rate of streptococcal pharyngitis in adequately treated patients but there is no evidence for microbiologic resistance to therapy. It is more likely that the organism is reacquired or sequestered in a sanctuary site and simply re-emerges after therapy is discontinued. Some have used rifampin at the end of therapy in an attempt to alleviate this possibility. While all therapies have similar response profiles, azithromycin has a higher culture-positive recurrence rate.

The risk of rheumatic fever without antibiotic treatment is difficult to assess. Wannamaker and colleagues documented rates as high as 3% in 1952;[36] however, more typical rates of 0.4% were found in a pediatric population in 1961.[37] Certainly M protein type, genetic susceptibility and previous infection play a part in this diversity of recurrence rates. Other β-hemolytic streptococcal infections (groups C, G and B) can cause pharyngitis but not rheumatic fever. For these, antibiotic treatment may provide symptomatic relief.

Occasionally, pharyngitis can be secondary to an abscess in the peritonsillar area. This is usually easily diagnosed by an asymmetry of the tonsillar pillars. The affected side is asymmetrically enlarged and protrudes anteriorly into the mouth. *Haemophilus influenzae* (nontypeable and types a–f) can cause pharyngitis and type b can also cause epiglottitis or meningitis. Many individuals are carriers but are not ill.

Corynebacterium diphtheriae causes diphtheria, which is easily diagnosed because of the gray pseudomembrane in the posterior pharynx along with pharyngitis (Fig. 24.8). The disease has recently become endemic in parts of the former Soviet Union. *Arcanobacterium* (previously *Corynebacterium*) *haemolyticum* is a common cause of pharyngitis and can also cause a scarlatiniform rash. It is the cause of many non-GAS throat infections.[38] *Neisseria gonorrhoeae* can also cause pharyngitis. The appearance of the pharyngitis is nondiagnostic, so a heightened awareness is required to make this diagnosis.[39] *Chlamydia*

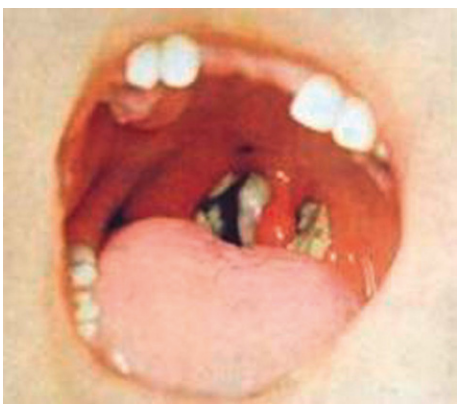

Fig. 24.8 Diphtheria pharyngitis with gray pseudomembranes in the posterior pharynx.

pneumoniae and *Mycoplasma pneumoniae* can cause pharyngitis, but generally will go on to cause cough also, often with wheezing and pneumonia.[40,41] *Candida albicans* can cause pharyngitis but normally only in the immunocompromised host. The pharyngitis is hyperemic, with white plaques on the buccal mucosa.

Aphthous stomatitis is a common feature of mouth ulcers. The etiology is unclear. Small painful ulcers appear on the buccal mucosa, but can also appear in the posterior pharynx. The ulcers are usually stress related and last approximately 1 week. Very extensive aphthous ulceration can also be seen as a complication of HIV infection. Behçet's syndrome may cause aphthous stomatitis. Kawasaki disease, most common in young children, can cause significant redness of the oral mucosa. Most children with Kawasaki disease also have fever, a strawberry tongue and, importantly, conjunctivitis. This condition is frequently confused with streptococcal disease. Stevens–Johnson syndrome can result in pharyngitis, stomatitis and perioral swelling and ulcerations. Marshall's syndrome or PFAPA (periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis) syndrome is a pediatric periodic disease characterized by recurrent febrile episodes associated with head and neck symptoms.[42]

DIAGNOSIS

Prevalence of group A β-hemolytic streptococcus (GABHS) during school outbreaks of pharyngitis is between 15% and 50% in healthy school-age children. Since toddlers with GABHS respiratory tract infection may not present with classic symptoms, the diagnosis of GABHS pharyngitis among children should be based on laboratory tests in conjunction with the clinical findings. Culture isolation of GABHS from the pharynx is the gold standard, but 2 days are needed for it to be informative. On the other hand, the rapid antigen detection test (RADT) detects the presence of GABHS within a few minutes and has high sensitivity and specificity.

Rapid testing has many additional benefits: early treatment within 48 hours provides symptomatic relief for the child and limits spreading of the organism. In addition, it allows the practitioner to treat only those cases with GABHS, thus avoiding prescribing antibiotics for viral infections. Group B, C and G streptococci can also cause significant morbidity, but only group A leads to rheumatic fever, so the reason for treatment is not only to eliminate the pharyngitis but also to prevent the subsequent rheumatic disease. Viral causes of pharyngitis do not normally require specific diagnosis, but serologic tests are available for mononucleosis (EBV) and cytomegalovirus. Adenoviruses, RSV and parainfluenza viruses can be diagnosed using rapid antigen tests, which are available but rarely used in uncomplicated community-acquired infections.

MANAGEMENT

For group A streptococcal pharyngitis the recommended therapy is 6–10 days of oral penicillin or amoxicillin. Erythromycin and clindamycin are acceptable alternatives. There have been studies showing that one dose of ceftriaxone intramuscularly or oral azithromycin or cefaclor for 5 days is equally effective at eliminating carriage of GAS, but recurrent pharyngeal colonization occurs with all treatment regimens. Viral causes of pharyngitis can be most suitably treated with supportive measures: gargles, lozenges, etc. *Mycoplasma* and *Chlamydia* spp. infections can be treated with erythromycin or tetracycline (depending on age). Diphtheria and *Arcanobacterium* spp. infections should be treated with erythromycin or penicillin. *Legionella* spp. infections should be treated with tetracycline. *Haemophilus influenzae* type b and *Yersinia enterocolitica* infections should be treated with a third-generation cephalosporin.

REFERENCES

References for this chapter can be found online at http://www.expertconsult.com