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# Common Pediatric Respiratory Emergencies

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**KEYWORDS**

• Pediatric • Asthma • Bronchiolitis • Croup • Pneumonia

Acute respiratory distress is one of the most common reasons why parents bring their children to the emergency department (ED). Severity can range from mild, self-limiting illness to life-threatening disease. This article reviews the 4 most common of these conditions, namely asthma, croup, bronchiolitis, and pneumonia, to update the reader on the current state of evidence in the assessment and treatment of these conditions.

## ASTHMA IN CHILDREN

Asthma is a chronic inflammatory condition of the airways leading to episodic wheezing, coughing, chest tightness, and shortness of breath. It is a common condition, with the highest prevalence occurring between the ages of 5 and 17 years. Asthma afflicted 7.0 million children in this age group in the United States in 2008.[1] It led to 1.7 million ED visits in 2006, and children younger than 15 years accounted for 33% of those with a discharge diagnosis of asthma while this age group only represents 20% of the general population.[1]

Asthma is the most activity-limiting condition in children and accounts for 14.4 million lost school days. It is an expensive disease, with an annual burden of $15.6 billion in direct health care costs and $5.1 billion in indirect health care costs and lost productivity, for a total annual sum of $20.7 billion.[1]

### *Pathophysiology*

Asthma is a chronic disease of the lower airways punctuated with episodic acute exacerbations. The clinical manifestations are caused by airway hyperresponsiveness to stimuli that are generally innocuous, leading to constriction of bronchial smooth

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muscle (bronchospasm), the major cause of wheezing during an asthma exacerbation. Airway inflammation and edema in response to these stimuli further narrows the airway and restricts ventilation.[2,3]

These physiologic changes on the cellular level can occur through IgE-mediated pathways (allergen-triggered asthma)[4] and non–IgE-mediated pathways (asthma in response to nonsteroidal anti-inflammatory drugs,[5] certain other drugs, exercise, and cold temperatures).[3] Both pathways lead to a release of various cytokines and chemokines from inflammatory cells, which promote further migration and activation of inflammatory cells in the lower airways, thus perpetuating the cycle.[3]

### *Diagnosis*

The diagnosis of asthma is particularly challenging in the pediatric population. Young children usually cannot be cooperative enough to undergo formal pulmonary function testing, which is the gold standard in the diagnosis of asthma. Thus they often must be diagnosed clinically.

Many first-time wheezers also present to the ED. Most instances of wheezing in young children presenting to the ED are solely related to upper respiratory infections (URI) causing inflammation of the lower airways rather than true asthma.[6] The majority of early wheezers do not go on to develop asthma in later childhood or adulthood.[6,7] This distinction is an important one, as it can affect the efficacy of certain therapeutic options.[8] Clues that increase the likelihood that the wheezing is due to asthma include the frequency of episodes (more than once a month), triggers (exercise, allergens, tobacco smoke), prolonged respiratory symptoms in the setting of URI (symptoms lasting more than 10 days suggest a viral trigger of asthma), personal or family history of atopy or asthma, and a history of a good and rapid response to bronchodilator therapy.[3,6,9]

Other historical features of the patient that may aid in predicting the severity of the asthma exacerbation include the frequency and compliance in using asthma medications at home, previous hospital visits for asthma exacerbations (requiring admission to the ward or intensive care unit [ICU]), and severity of asthma exacerbations (requiring intubation). Social attributes of the patient and caregivers, such as the ability to purchase medications and comply to their use, a household environment free of known or suspected asthma triggers, and ability to obtain follow-up and access medical services in the event of another exacerbation, have important discharge planning implications and should be elicited early.[2,3,7,9]

The physical examination may reveal any combination of the classic constellation of symptoms in the acute asthma exacerbation, which includes wheezing, cough, chest tightness, tachypnea, respiratory distress, intercostal indrawing, and accessory muscle use.[3,7,9] Of interest, the use of the scalene muscles and suprasternal retractions have the highest interrater reliability and correlation with asthma severity.[10] Clinical asthma assessment tools, such as the Pediatric Respiratory Assessment Measure (PRAM; **Table 1**)[10,11] and the Pediatric Asthma Severity Score (PASS),[12] have been independently shown to be predictive in discriminating a patient's length of stay in the hospital and admission.[10,12] The strength of these two scales is that they include preschool-aged children, in comparison with older severity scales such as the Pulmonary Index and the Pulmonary Score, which are only validated in older, school-aged children.[10–12] A recent head-to-head comparison of the two scores showed very similar performance in their ability to predict a prolonged stay (>6 hours) and/or admission when taken at triage.[13] However, a repeat score taken 90 minutes after treatment showed that the PRAM score was more responsive and predictive

**Table 1**
**The Pediatric Respiratory Assessment Measure (PRAM) score**

| Signs | 0 | 1 | 2 | 3 |
|---|---|---|---|---|
| Suprasternal indrawing | Absent | | Present | |
| Scalene use | Absent | | Present | |
| Wheezing | Absent | Expiratory only | Inspiratory and expiratory | Audible without stethoscope or minimal air entry/silent chest |
| Air entry | Normal | Decreased at bases | Widespread decrease | Minimal air entry/silent chest |
| Pulse oximetry on room air | >95% | 92%–94% | <91% | |

*Data from* Ducharme F, Chalut D, Plotnick L, et al. The Pediatric Respiratory Assessment Measure: a valid clinical score for assessing acute asthma severity from toddlers to teenagers. J Pediatr 2008;152(4):476–80, 480.e471.

(area under the receiver-operator characteristic curve 0.82 vs 0.72).[13] These tools can be particularly useful when integrated into protocolized treatment regimens.[2,9,14]

Investigations should include measurement of oxygen saturation, with more severe exacerbations deserving continuous monitoring. A blood gas sample may be useful in severe exacerbations in addition to clinical signs to determine respiratory function and responsiveness to therapy. In particular, normocarbia or hypercarbia in a patient after a round of standard treatment is a worrisome sign.[3,9]

Peak expiratory flow (PEF) is an objective method of assessing the degree of airway obstruction. However, it is often exceedingly difficult (if not impossible) to obtain these measurements in children younger than 6 years, and even with a cooperative child the measurements may not be reliable in an acute exacerbation.[15,16] If PEF values are obtained, suggested categories include mild (PEF >80% predicted), moderate (PEF 60%–80% predicted), or severe (PEF <60%),[2] though different governing bodies have varying values.[3,9]

Additional blood work and imaging only aid in excluding complications or other diagnoses based on clinical suspicion,[3,9] and are not routinely recommended.

### *First-Line Treatment*

Children with acute exacerbations should be rapidly assessed and triaged to a location in the ED where observation and frequent reassessment can be performed by medical and nursing staff. Reassessment of patients after each round of treatment is by far the most important aspect in the management of acute asthma exacerbations. Children, and especially infants, are particularly at risk for respiratory failure. Hypoxemia develops more rapidly in children than in adults; therefore monitoring of oxygen saturation is necessary.[3,9] Oxygen should be administered only to maintain a saturation of greater than 92%–94%,[3,9] as indiscriminate high-flow oxygen despite good saturations can lead to poorer outcomes.[17]

Short-acting β-agonist (SABA) treatment is the most effective method of relieving bronchospasm, and should be given to all patients with asthma exacerbations.[3,9] SABA can be administered as either intermittent therapy spaced 15 to 20 minutes apart via wet nebulizer or metered-dose inhaler (MDI) with a holding chamber, or as continuous therapy via a nebulizer.[18,19] In mild to moderate asthma, an MDI has been shown to be at least equivalent if not better in efficacy than a nebulizer in infants, children, and adults,[20–23] and is more cost effective.[24] Factors that influence the choice of MDI

versus nebulizer include patient cooperation, response to treatment via MDI, and severity of the exacerbation. Salbutamol (albuterol, Ventolin) 2 to 4 puffs, can be given every 15 minutes via MDI with chamber, waiting 5 tidal volume breaths between puffs.[3,9] More puffs can be administered (up to 10) in more resistant exacerbations. Salbutamol can also be given at 0.15 to 0.3 mg/kg via nebulizer, with a minimum of 2.5 mg and maximum of 5 mg per nebulized mask. This volume is then diluted with normal saline for a total of 5 mL of fluid per nebulized mask. The most severe exacerbations may benefit from continuous therapy[19] with a nebulizer driven by oxygen if hypoxia is also present.[3,9,17] With continuous nebulization, salbutamol is recommended to be given at 0.5 mg/kg/h with the hourly dose not exceeding 10 to 15 mg/h.[3]

Levosalbutamol ((*R*)-salbutamol, also known as levalbuterol) is the pure (*R*)-enantiomer of the salbutamol molecule. In a typical salbutamol preparation, there is a 50:50 mixture of the (*S*)- and (*R*)-enantiomers, and it is the (*R*)-enantiomer that provides the vast majority of the bronchodilating effects, due to its 100-fold higher affinity for the β2-adrenergic receptor. The selectivity of levosalbutamol theoretically maximizes the bronchodilating effects while minimizing systemic side effects such as tachycardia[25] and hypokalemia.[26] Small trials have shown mixed results, with some trials showing benefit in pulmonary function,[27,28] reduction in hospital admission rates,[29] and reduced side effects[26,30]; whereas other studies have shown no difference.[30,31] Levosalbutamol is considerably more expensive than the conventional racemic mixture, and current guidelines do not recommend using one over the other. The dose of levosalbutamol is half that of salbutamol.

Ipratropium bromide (Atrovent) has been shown to be an effective adjunct in moderate to severe asthma in addition to inhaled β-agonists.[32,33] It is a muscarinic acetylcholine receptor blocker, which produces bronchodilation via smooth muscle relaxation. Ipratropium bromide can be given via MDI (4–8 puffs every 15–20 minutes) or nebulizer (0.25–0.5 mg, combined in the same nebulizer as the β-agonist).[3,9] Treatment can be tapered as the patient improves clinically.

Systemic corticosteroids (SCS) have been shown to decrease the need for hospital admission from the ED when given early[34,35] and to decrease the length of stay.[36] SCS should be considered in all but the mildest exacerbations.[3,9,34] However, there is evidence that shows administration of steroids to children with wheezing triggered by a URI and with no other history suggesting asthma provides no benefit in time to discharge, admission rate, morbidity, or mortality.[8] The efficacy of oral versus intravenous (IV) SCS has been shown to be equivalent in pediatric asthma exacerbations.[37,38] Parenteral SCS should be reserved for those who cannot tolerate oral steroids or have intestinal issues that would affect its absorption.[3,9] Oral prednisone or prednisolone, 1 to 2 mg/kg, should be given once daily, with a maximum dose of 60 mg/d for 3 to 5 days.[2,3] Studies suggest that a 2-day course of oral dexamethasone (dosed at 0.6 mg/kg daily, maximum of 16 mg) is as effective (measured by symptoms scores, admission rates, and 10-day relapse rate) and well tolerated (rates of nausea and vomiting) as a 5-day course of oral prednisone in adults[39] and children.[40,41] Another study even suggests that a single dose is non-inferior to a 5-day course of prednisone.[42] Intramuscular (IM) injection of depot steroids, such as dexamethasone acetate, has also been shown in small studies to be as effective as a 5-day course of prednisone.[43,44] IV steroids can be given as methylprednisolone, 2 mg/kg/d in two divided doses.[3] Inhaled corticosteroids (ICS) are not currently recommended as a replacement for SCS for the treatment of acute asthma exacerbations presenting to the ED,[3,9] because of the lack of efficacy when used alone.[34,35,45–48] Recent evidence suggests that the addition of inhaled budesonide to standard therapy including SCS does not improve outcomes.[49]

### *Second-Line Treatments*

In children with severe or life-threatening asthma, the aforementioned therapies may not be sufficient. It is crucial to recognize refractory asthma and to treat it aggressively.

Magnesium sulfate is a safe drug with few side effects, which has been shown to have bronchodilating effects.[50–52] Its use has not been shown to be beneficial in mild to moderate asthma, but has demonstrated a reduction in admission rates for severe asthma, with minimal side effects.[53,54] A single IV dose of 25 to 75 mg/kg (not exceeding 2 g) can be given over 2 hours.[3,9] Inhaled magnesium sulfate has been shown in small studies to improve expiratory flow measures when used in addition to inhaled β-agonists in severe asthma exacerbations,[55,56] but confers no benefit in mild to moderate episodes.[57] A Cochrane review showed that nebulized magnesium sulfate provided significant improvement in pulmonary function tests and a nonsignificant trend to decreased hospital admission rates in severe asthma exacerbations, but no statistically significant difference when included in all severities of asthma attacks.[58] Inhaled magnesium sulfate is given as the diluent in place of normal saline (usually 2.5 mL of a 250 mmol/L solution) combined with salbutamol and ipratropium bromide in the same nebulized mask.

Oral leukotriene receptor antagonists (LTRA) such as montelukast (Singulair) have been shown to decrease symptoms of mild to moderate asthma exacerbations,[59,60] but their role in severe asthma is unknown because of their slow onset of action.[61] In moderate to severe asthma there is some evidence in the adult literature that IV administration may be effective,[62] but there are no corresponding studies done in children. The oral dosage of montelukast in children is 4 to 10 mg orally once per day.

Heliox is a blend of helium and oxygen, the use of which is based on the principle of increased ventilation into the lower airspaces in asthma, due to its low viscosity.[63] Some studies have shown modest benefit[63–65] whereas others show no benefit.[66] It has a level D recommendation as the driver of nebulized salbutamol in severe asthma,[3] mainly because of its lack of side effects.

Routine antibiotics are not recommended unless there is a suspicion of pneumonia (fever, purulent sputum) or bacterial sinusitis.[2,3,9] Mucolytics and sedation are not recommended.[2,3,9]

### *Status Asthmaticus and Imminent Respiratory Failure*

One of the most terrifying prospects for an emergency physician is the sight of a child with asthma not responding to treatment and heading toward respiratory failure. Signs include increasing somnolence, tiring of breathing muscles, cyanosis, and a silent chest. Heralds of impending cardiac arrest are bradycardia, severe hypoxia, and hypercapnia.

If not already performed, IV access should be obtained and any hypovolemia should be corrected. This action is also taken to prevent hypotension that the induction drugs may cause during rapid sequence intubation and positive ventilation.

IV β-agonists have not been shown to be beneficial in severe exacerbations, and carry significant side effects.[3,67] Likewise, aminophylline has not been recommended, due to its considerable toxicity and lack of clear benefit,[68] though a study has shown some effect in children with life-threatening asthma already receiving maximum doses of conventional therapy.[69] However, in the setting of a status asthmaticus in extremis with no response to other therapies, guidelines still endorse consideration of their use as a last resort.[2,3,9]

Temporizing measures can include a trial of noninvasive positive-pressure ventilation (NPPV). There are small studies analyzing the ability of NPPV to avoid intubation

and improve outcomes in children with status asthmaticus,[70–75] and a Cochrane review showed a trend toward benefit.[76] If the patient is unable to tolerate NPPV and continues to deteriorate, endotracheal intubation with mechanical ventilation is necessary.[3,9] Once the decision has been made, the most experienced physician should make the attempt, as asthmatic patients are often difficult to intubate and desaturate quickly. Traditionally the induction agent of choice is ketamine (1–2 mg/kg IV) because of its mild bronchodilating properties,[77] though the clinical significance of this bronchodilation is questionable,[77,78] and several trials using ketamine infusion as an adjunct in status asthmaticus have shown no benefit.[78,79] Ketamine can also increase oral and airway secretions[80] and trigger laryngospasm, and should be used in conjunction with a paralytic agent to counteract this possibility.[81] Other choices for induction include etomidate (0.3 mg/kg IV) and propofol (1.5–3 mg/kg IV). The paralytic agent of choice depends on patient characteristics, the presence of contraindications to particular agents, and physician preference and experience.

A ventilator strategy that has shown benefit is one of permissive hypercapnea.[3,82–86] With this strategy, $P_{CO_2}$ is allowed to reach up to 70 mm Hg, providing high $F_{IO_2}$ concentrations to maintain saturations greater than 92%, and manipulating ventilator settings (such as the prolonging the expiratory time to allow for complete exhalation) to minimize pressures and avoid barotrauma and other complications. Bicarbonate can be given to correct severe acidosis.[87]

### *Disposition*

The decision to hospitalize children with severe asthma depends on the severity of the exacerbation and its response to ED therapy. Those who present with PEF less than 25%, or have a PEF less than 40% or significant symptoms after therapy, should be admitted for continued treatment and observation.[2,3] Unstable home situations or predicted poor compliance and follow-up are also indications for admission.[2,3,9]

Children receiving treatment in the ED should be monitored for at least 1 hour after their last round of treatment to ensure resolution of symptoms.[2,3,9] In those able to provide PEF measures, a general value of greater than 70% to 80% of expected value is acceptable for discharge. Those with a PEF of 40% to 69% with minimal symptoms can also be discharged if they have good follow-up and demonstrate good compliance, and if medical attention is readily accessible.[2,3]

Follow-up with a primary care provider or asthma specialist should be arranged within a month of discharge from the ED to reassess medications and treatment plans,[2,3] as this has been shown to improve outcomes and decrease ED visits.[88,89] The appointment should be scheduled before discharge from the ED, as this has been shown to increase compliance.[90,91]

Medications to be continued after discharge include inhaled salbutamol and oral steroids as already described, with no need for a tapering dose.[2,3,9] Current guidelines state that the initiation of ICS should be considered in those with moderate to severe exacerbations who were not previously on ICS.[2,3,9] Patients should be given a 1- to 2-month supply, as this has been shown to reduce the number of exacerbations and ED visits.[46,92,93] ICS should be continued if previously prescribed. Ipratropium bromide has not been shown to be of benefit after discharge from the ED.

Discharge home with a peak flow meter is also recommended for children older than 5 years,[3] especially in those who do not perceive mild symptoms well or have recurrent severe exacerbations.[94]

Children to be discharged should be provided a written action plan (WAP) that delineates clearly discharge medications, instructions in proper inhaler and peak flow

meter technique, follow-up appointments, and warning signs that indicate a need to return to the ED.[2,3]

## CROUP

Croup is a common cause of stridor in the young child. Croup is characterized by a harsh inspiratory stridor and a hoarse cough that is often described as barky or resembling a seal, secondary to upper airway inflammation and edema. Although usually benign and self-limiting, it can cause significant respiratory distress requiring intubation.

Croup is the most common cause of stridor in young children older than 6 months. It peaks between 6 and 36 months of life. At 2 years of age, 5% of all children will have had croup.[95] In a 14-year observational study in Ontario, Canada, its incidence seems to have a biennial mid-autumn peak and an annual summer trough, with boys being affected 1.5 times as often as girls.[96]

### *Pathophysiology*

There has been much confusion in the use of the term croup. It has been used to describe different disease entities in which stridor and hoarse cough are the predominant symptoms,[95] such as spasmodic croup, laryngotracheobronchitis (LTB), laryngotracheobronchopneumonia (LTBP), bacterial tracheitis, and diphtheria. In this review croup specifically refers to laryngotracheitis, as the other entities have different presentations, treatment options, and prognoses.

Croup is commonly caused by parainfluenza virus (PIV)-1.[97] PIV-2 and PIV-3 are also implicated in croup, with type 2 causing a milder form and type 3 causing a more severe form. Other viruses that can lead to croup include influenza, respiratory syncytial virus (RSV), rhinoviruses, enteroviruses, and measles, among others.[95]

Viral infection often starts via inoculation of the nares and pharynx, which leads to typical URI symptoms of low-grade fever, coryza, and rhinorrhea. The infection then spreads down to the larynx and subglottic area, causing cough and inflammation and edema of the upper airway and leading to varying degrees of obstruction. According to Poiseuille's equation, resistance to flow is inversely proportional to radius to the fourth power. Therefore even slight decreases in diameter can cause significant resistance, especially in the already tiny airways of the young child. The lower airways are usually not affected in PIV-associated croup, though RSV and influenza can cause lower respiratory symptoms.

### *Diagnosis*

The constellation of a barky cough, hoarseness, and stridor is common in many diseases, and differentiation between them is of utmost importance, as treatment and potential complications vary widely.

The onset and progression of symptoms leading to the ED visit should be explored. The history of a preceding URI in the last day or two is often elicited. In addition to cough and stridor, the child is often febrile. Combined with other features of the history, a suddenly stridorous child without fever or URI should raise a suspicion of foreign body aspiration or angioneurotic edema. An immunization and travel history should be elicited, since an unimmunized child is at higher risk of developing laryngeal diphtheria from *Corynebacterium diphtheriae* infection. Pharyngitis and dysphagia are features that are uncommon with croup, and may suggest retropharyngeal abscess, peritonsillar abscess, epiglottitis, or diphtheria. Finally, caution is required when diagnosing croup in a stridorous child younger than 6 months, due to the important

differential diagnosis in this age group. The differential includes laryngomalacia (the most common cause, and a self-limited condition that 90% grow out of by 12–18 months),[98] vocal cord paralysis,[99] papillomatosis,[100] congenital causes (such as hemangiomas,[101] laryngeal webs,[100] and neurofibromas[102]), and iatrogenic causes (such as subglottic stenosis following intubation for prematurity,[103] or vocal cord paralysis caused by laryngeal nerve damage from thoracic or cardiac procedures[104]).

The child should otherwise appear well; a toxic-looking child should be investigated for alternative diagnoses such as bacterial tracheitis (which can be a complication of croup), LTB, LTBP, or epiglottitis. There should be no signs of lower airway involvement such as wheezing or crackles, which may suggest an alternative diagnosis. If hemangiomas are noted on the child, especially above the clavicles, a subglottic hemangioma should be considered along with historical features such as a lack of URI symptoms. A throat examination should identify pharyngeal causes of stridor easily, though caution should be exercised if the presentation is suspicious for epiglottitis. The epiglottis, if visualized, should be normal.

The diagnosis of croup remains a clinical one, with additional testing being useful in ruling out other differential diagnoses. Complete blood cell counts (CBC) may show a mildly elevated white cell count in croup, whereas it is usually markedly elevated or depressed in bacterial infections of the upper airway with increased neutrophils and band forms. Posterior-anterior neck radiographs in croup may show subglottic narrowing (steeple sign) with a smooth tracheal contour. Irregularity of this contour suggests bacterial tracheitis and other diagnoses.[95] Lower respiratory symptoms should be investigated with a chest radiograph (CXR) to assess for a possible pneumonia. A lateral neck radiograph showing a thickened mass at the level of the epiglottis (thumbprint sign) suggests epiglottitis.[105] Foreign bodies may appear on plain films, depending on the object.

### *Classification*

Different classification scales based on physical examination findings have been devised. The Westley Croup Score[106] is the most widely known and used, although it is used more commonly in research protocols and less frequently in clinical practice.[107] Key criteria used in this score include level of consciousness, stridor, air entry, cyanosis, and chest wall retractions.[95,106,107]

A simplified classification, based from the original Westley Croup Score, has been suggested by several investigators.[95,107] Mild croup is defined by an absence of stridor at rest, minimal respiratory distress, and occasional cough. Moderate croup has stridor at rest and increased amount of respiratory distress, but behavior and mental status are normal. Severe croup has significant respiratory distress and mental status changes, with increasing somnolence and decreasing air entry signifying impending respiratory failure.

### *Treatment*

As with all patients, the ABCs (Airway, Breathing, Circulation) must be prioritized. Patients with signs of impending respiratory failure should be intubated with an endotracheal tube 0.5 to 1 mm smaller than the expected size. Oxygen should be delivered to maintain oxygen saturation greater than 92% to 94%. Where possible, the child should be kept calm to decrease respiratory distress and improve airway dynamics.

The mainstays of pharmacotherapy in the ED management of croup are corticosteroids and nebulized epinephrine. Dexamethasone remains the corticosteroid of choice over prednisolone through its ability to decrease return visits and admissions.[108] In

a recent Cochrane review, dexamethasone was shown to reduce symptoms in the ED, decrease length of stay, and result in fewer return visits.[109] Dexamethasone is given as a single dose of 0.6 mg/kg by mouth/IM/IV (oral is preferred, though parenteral routes have been shown to be equally effective[110]) to a maximum of 10 mg. There are several studies that show lower doses of dexamethasone (0.15–0.3 mg/kg) may be equally effective.[111–113] Inhaled budesonide can be used if available (2 mg via nebulizer) and has been shown to be similar in efficacy to dexamethasone,[109,114,115] though availability, cost, and convenience makes dexamethasone a more attractive option. There does not appear to be any additional benefit from combining oral and inhaled steroids in the setting of croup.[116] Corticosteroids should be considered in all severities of croup.

Nebulized epinephrine is used in moderate to severe croup, and has been shown to be highly efficacious in reducing symptom scores at 30 minutes after treatment and time spent in the ED.[117] However, the natural history of the disease is unchanged, and thus it is important to monitor children after epinephrine treatment for rebound reactions.[106,118] Despite the theoretical benefits of L-epinephrine over racemic epinephrine, studies did not show a benefit of choosing one over the other.[117] L-Epinephrine is given as 5 mL of a 1:1000 solution (racemic epinephrine is given as 0.5 mL of a 2.25% solution in 2.5 mL of normal saline) delivered via nebulizer every 15 minutes to effect. Although serious cardiac complications from epinephrine treatment are exceedingly rare, it is prudent to put children requiring multiple treatments on continuous cardiac monitoring.

Although cold, humid air anecdotally has been thought to improve croup symptoms, recent trials did not show this benefit in the ED setting.[119–121] A study evaluating the use of Heliox showed that it may be as effective as nebulized racemic epinephrine in moderate to severe croup.[122] Heliox also demonstrated a nonstatistically significant trend toward improvement in croup scores when combined with epinephrine and steroids.[123] However, a Cochrane review showed no significant difference in croup scores when Heliox was added to conventional therapy, and therefore did not routinely recommend its use at this time.[124] Antibiotics should be saved for suspected bacterial complications such as bacterial tracheitis or LTBP. Sedatives and antitussives are not indicated.[95,107]

### *Disposition*

Most cases of croup are mild to moderate and respond well to steroid with or without nebulized epinephrine therapy, and the vast majority of patients are discharged home. Children with mild symptoms (ie, no stridor at rest) can be safely sent home. Patients receiving epinephrine should be observed for 4 hours to watch for any rebound phenomenon. Children who require multiple epinephrine doses should be admitted for observation. ICU admission may be required in cases of severe croup that fail to respond to treatment. On discharge, it is prudent to inform the parents that symptoms of croup usually peak between days 2 to 3.

## BRONCHIOLITIS

Bronchiolitis is the most common lower respiratory tract condition in children younger than 2 years, and is the leading cause of hospitalization of infants. Its most common cause, RSV, is ubiquitous worldwide, affecting nearly all children by the age of 2, often causing dyspnea in its tiniest of victims with the potential to cause respiratory failure and death. Significant literature and practice guidelines have been published to guide practitioners. Active research in the field is ongoing, and even small improvements in therapy or resource use can make a major impact given the burden of disease.

### *Definition and Epidemiology*

Bronchiolitis is typically caused by viral infection, characterized by bronchiolar inflammation in children usually younger than 2 years. Children from age 2 to 5 years with similar symptoms rarely have bronchiolitis, as asthma, recurrent viral wheeze, or pneumonia are more likely diagnoses. Wheezing is the hallmark of the American definition of bronchiolitis, where British and Australian definitions include inspiratory crackles as part of the diagnosis.[125,126] Most studies and guidelines define bronchiolitis as the first episode of wheezing or crackles. As the presentations of bronchiolitis, viral-associated wheeze, and asthma may appear similar, attention to the features of patients becomes very important given differing pathophysiology and responses to treatment.[125]

RSV continues to be the most common cause, responsible for approximately 50% to 80% of cases. The epidemiology of bronchiolitis follows closely that of RSV. A strongly seasonal virus, RSV causes outbreaks most commonly between November and March in the northern hemisphere and between May and September in the southern hemisphere. Up to half of infected children younger than 2 years will have lower respiratory tract symptoms, whereas older children and adults are more likely to have upper tract disease only. Peak age for bronchiolitis is 2 to 6 months old, with most cases occurring before age 9 months. Reinfection with RSV is common, given poor postinfection immunity.

Recent studies demonstrate an increasing role and frequency of other viruses causing bronchiolitis, including human metapneumovirus (10%–20%), human bocavirus, rhinovirus, parainfluenza, adenovirus, influenza, and coronavirus.[127–129] Although rhinovirus and human metapneumovirus infection has been shown to be generally less severe than RSV (Group A strains causing more severe disease than Group B strains), etiologic diagnosis is often not known in the ED and does not currently affect ED management.[127,130]

Bronchiolitis-associated hospitalizations have more than doubled over recent decades, likely attributable to several factors including increased spread of viral illnesses from daycare exposures, greater awareness of hospitalization criteria, routine oximetry use, and marginally larger numbers of higher-risk children afflicted because of higher survival rates of at-risk populations.[131] Associated mortalities for the condition fortunately have fallen from an alarming 4500 annually in the United States in 1985 to 390 in 1999.[132] Although a significant portion of the decrease in mortality is likely attributable to proper recognition and admission of high-risk infants and improvements in supportive care, a continuing challenge for emergency room providers remains predicting those children in true need of hospitalization as opposed to those requiring appropriate supportive outpatient care.

### *Clinical Presentation and Course*

Nasopharyngeal viral invasion usually causes rhinorrhea and coryza. As infection spreads via inhalation and direct spread of the virus toward the lower respiratory tract, a dry wheezy cough develops. Low-grade fever (<39°C) may often occur. A high (>40°C) or prolonged fever is unusual, and should prompt consideration for coexistent infection. Lower respiratory symptoms typically start on the second to third day of symptoms and peak within the third to fifth day. Viral invasion proceeds distally, leading to the classic changes of bronchiolar inflammation, edema, increased mucus production, bronchospasm, and necrosis and sloughing of epithelial cells.[125,126] This process leads to bronchiolar airway obstruction, atelectasis,

and hyperinflation. Tachypnea, increased respiratory effort, and wheezing become common reasons for ED presentation. Patients may or may not have audible crackles on examination.

The peak in symptom severity may be an important consideration with respect to ED disposition decisions and parental education. Although symptoms may improve substantially after 7 days, it is not uncommon for postbronchiolitic symptoms such as dry cough and wheeze to continue on to the second and third week for almost half of children, with up to 9% extending beyond 4 weeks.[133,134] This aspect is important to address with respect to parental anticipatory guidance and management of parental expectations. Education on duration may potentially affect the frequency of otherwise unwarranted return ED visits.[133,134]

The differential diagnosis of wheeze in the infant and young child must be considered, which includes asthma, episodic viral wheeze, bronchitis, pneumonia, congestive heart failure, gastroesophageal reflux, and foreign body aspiration. Patients not matching the traditional features of acute viral bronchiolitis may require diagnostic testing and management appropriate for the presumptive diagnosis.

For most patients, bronchiolitis will be a mild self-limited disease and will resolve without notable sequelae. Significant complications may occur in up to 10% to 20% of patients and may include dehydration, hypoxemia, coinfection, apneic periods, and respiratory failure. Rates of admission for bronchiolitis cases assessed in the ED range between 19% and 45% in some studies.[127] The duration of hospitalization is usually between 2 and 4 days for the average patient. Children more severely afflicted manifest with markedly increased respiratory effort, and rarely with altered mental status, sepsis syndrome, and cyanosis. Feeding difficulties and sleeping disturbances may occur secondary to the respiratory symptoms or occult hypoxemia, and are thus important additional markers of severity that should be inquired about in the ED.[130] It is crucial to recognize significant feeding difficulties, which may be harbingers of early respiratory failure. Approximately 3% of hospital admissions will require ICU admission[135] and as many as 1.5% may require assisted ventilation.[136] Although the mortality rate has recently remained stable, the potential lethality of the illness will always remain a key concern.

A common question of both parents and clinicians concerns future risk of asthma in children and infants presenting with bronchiolitis. Literature and expert opinion suggest that viral lower respiratory tract infections do not cause asthma, but that children affected remain at higher risk of future episodes of non-atopic wheezing as well as asthma exacerbations.[137–139]

### *Assessment and Management*

The diagnosis of bronchiolitis can be made clinically in most children with classic signs and symptoms. Given that a very significant proportion of bronchiolitis cases are mild, they resolve with supportive care alone. Routine diagnostic tests such as CXR, viral cultures, and blood tests have rarely been shown to have an impact on the clinical course, and often add unnecessary and unjustified expense.

Multiple studies and guidelines have illustrated the low yield of CXR in the setting of bronchiolitis, particularly in the mildly ill child without risk factors. Moreover, routine CXR has been shown to increase the rate of unnecessary antibiotic prescription without improving outcomes.[140] Schuh and colleagues[141] reported on 265 cases of children with a clinical diagnosis of likely bronchiolitis who underwent CXR. Of these, 92.8% showed airway disease and another 6.9% showed airway and airspace disease, both patterns consistent with viral bronchiolitis. In only 0.75% of cases did CXR reveal lobar consolidation warranting antibiotics. This study concluded that the

risk of airspace disease was particularly low in patients with $O_2$ saturation greater than 92% and only mild to moderate respiratory distress, and that CXR was unwarranted in this patient subgroup. Another study of 270 children found that the subset of patients with focal findings on CXR were more likely to present with fever, have temperature higher than 38.4°C in the ED, and were 4 times more likely to present with focal crackles on examination.[142] Settings whereby CXR has been shown to be more likely of value include prolonged or unusually high fevers, significant hypoxemia (<90%), previous cardiopulmonary disease, need for ICU admission or mechanical ventilation, and atypical cases.

Although rapid RSV identification is available in many centers and offers sensitivities up to of 90%, the added value over clinical diagnosis for patients well enough for discharge remains questionable, and therefore should not be routinely ordered. For those patients requiring admission, nasopharyngeal fluid testing may be of value. In some situations, testing of febrile young infants for RSV may decrease the extent of septic workup that would otherwise be undertaken. Rapid influenza testing may be warranted if treatment of a positive result would be indicated.

A CBC is not routinely recommended in the setting of bronchiolitis. Although often taken in patients being admitted, the use of an elevated white blood cell count (WBC) to predict bacterial superinfection in this setting has been shown to be unreliable. A study of 1920 patients with confirmed RSV infection showed that the WBC was unable to distinguish between those with and without serious bacterial infection.[143] WBC can also be significantly elevated in the setting of adenovirus infections.[144]

Coinfection should be considered in cases with unexpectedly high or prolonged fevers. Otitis media has been reported to be the most common coinfection with RSV, in the range of 53% to 62%.[130] Although the possibility of RSV etiology is possible in individual cases, bacterial isolation has been shown to be extremely common in this scenario and should be treated as such. The literature has also addressed the issue of the extent of workup necessary in infants 1 to 90 days old with a clinical diagnosis of bronchiolitis. It has been shown that the incidence of serious bacterial illness (SBI) is lower compared with controls without the diagnosis of bronchiolitis,[145] though a full septic workup is still recommended for patients younger than 1 month. In two case series of 42 and 187 children having blood, urine, and cerebrospinal fluid cultures sent despite the diagnosis of bronchiolitis, no cases of septicemia or meningitis were found and the incidence of urinary tract infection (UTI) in the latter study was 2%. One study of 282 infants younger than 60 days with bronchiolitis showed a 1.5% incidence of SBI including 3 UTI, 1 pneumococcal bacteremia, and 1 meningitis; however, the clinical presentations included shock, apnea/cyanosis, hypothermia, and resolving pneumonia.[146] These studies together suggest that the yield of a full septic workup in this scenario is very low, including the yield of urine culture, and that antibiotics should be used sparingly and with clear indications.[147] One notable caveat to this is that several studies have documented significantly higher rates of bacterial coinfection (mainly bacterial pneumonia) in bronchiolitic patients ill enough to require admission to the ICU,[148,149] so further testing in this population is likely warranted.

### *Treatment*

Despite several studies and Cochrane reviews on the possible interventions to treat bronchiolitis, there has been little impact on the overall course and outcome in patients presenting to the ED.[150–156] Supportive care measures such as suctioning, supplemental oxygen, hydration, and respiratory monitoring remain the current cornerstones

of treatment. Nasal suctioning is an easy, useful adjunctive treatment that may improve respiratory status, given the significant secretions in many younger infants who are obligate nose breathers; it is recommended before feeds.[157] No evidence currently exists to support deeper airway suctioning. Oxygen should be administered for saturation less than 90% according to American Academy of Pediatrics Guidelines,[130] and is an option in those with saturations of 90% to 94% and moderate signs of respiratory distress.[157,158] Non-invasive positive-pressure ventilation or intubation is indicated for those rare cases presenting with respiratory failure. IV hydration is necessary for those with dehydration and feeding difficulty. Attention to the risk of syndrome of inappropriate antidiuretic hormone secretion (SIADH) is necessary. Chest physiotherapy has been well studied in the inpatient setting and has not been shown to improve short-term clinical scores or hospital course, and is therefore discouraged.[130,157–159]

The benefit of bronchodilators such as epinephrine and salbutamol is controversial. A recent Cochrane review of more than 1912 infants showed no significant effect of bronchodilators on $O_2$ saturation, hospital admission rate, length of stay, and disease duration.[160] There was a small improvement in clinical scores in the outpatient studies; however, the clinical significance of this is questionable. Another systematic review included 48 trials using bronchodilators (and/or steroids).[151] Only epinephrine use was found to decrease hospital admissions on day 1 by 33% compared with placebo (relative risk [RR] of 0.67 with 95% confidence interval [CI] of 0.50–0.89). This figure translates into a number needed to treat of 15 for epinephrine to avoid 1 hospitalization (95% CI 10–45). However, a 2004 Cochrane review found the benefit of nebulized epinephrine in inpatients to be unproven.[150] Future studies will likely clarify the role of nebulized epinephrine ED treatments.

One cost estimate of bronchodilator use in 2003 in the United States for admitted patients was $37.5 million,[160] suggesting overutilization of these often temporizing treatments. Side effects such as tachycardia, agitation, hyperactivity, flushing, prolonged cough and tremor, and decreased oxygen saturation[160] are reported, although significant morbidity from their use is rare. As a result, routine use of bronchodilators in the setting of clear bronchiolitis is discouraged in all guidelines.[130,157–159]

However, because of the challenges in distinguishing bronchiolitis from asthma and episodic viral wheeze, an initial trial of bronchodilators remains an option.[130,158,159] Up to 25% of patients may respond to bronchodilators,[130] although the positive placebo response has been estimated at up to 43%.[161] Clinical scores such as the Respiratory Distress Assessment Index or Respiratory Assessment Change Score[130,162] before and after bronchodilator treatment is recommended.

Anticholinergics such as ipratropium bromide have been studied, often in conjunction with β-agonists, and have been shown not to add any benefit in the setting of bronchiolitis.[153]

In examining the role of steroids in the management of bronchiolitis, a 2010 Cochrane systematic review[154] of 17 controlled studies concluded no effect of systemic or inhaled glucocorticoids on the rate of admissions or length of hospitalization. Furthermore, a large, multicenter, randomized controlled trial of 600 patients in the United States showed no benefit from steroid treatment, including subgroup analysis of those with a personal or family history of atopy or asthma.[163] This finding refutes the theory proposed by some that a small asthmatic subgroup may benefit.

In a much debated study, the Pediatric Emergency Research Canada (PERC) group published a multicenter ED study of a series of 800 patients who were treated with nebulized epinephrine, dexamethasone, neither, or both, and outcome measures

such as risk of hospitalization at 1 week were documented.[164] Unexpectedly, the combined treatment of inhaled epinephrine and dexamethasone demonstrated a significantly reduced admission rate versus placebo at day 7 (RR 0.65, 95% CI 0.44–0.95). Improvements in breathing and feeding were noted on subsequent days, without harmful outcomes. However, given the high doses of dexamethasone used (1 mg/kg day 1, 0.6 mg/kg days 2–6) and its potential side effects, lack of efficacy of dexamethasone alone, and the lack of other supporting studies, this treatment option needs further validation. Evidence for treatment synergy as well as rationale for potential efficacy via targeting various aspects of the pathophysiology of the disease exists.[126]

Nebulized hypertonic (3%) saline has emerged over the last decade as a potentially promising inpatient therapy for bronchiolitis. Given its proposed actions on improving clearance of mucus and cellular debris, initial studies in the setting of cystic fibrosis showed some benefit.[165] Multiple studies and a 2010 Cochrane review[155] have revealed that nebulized hypertonic saline consistently improves post-inhalation clinical scores and decreases length of stay in hospital by approximately 25% or 0.94 days.[166] In contrast to the inpatient data whereby nebulized hypertonic saline is given at intervals of every 8 hours or less over several days, ED studies using 1 to 3 consecutive doses with a bronchodilator have not to date shown statistically significant improvement in short-term clinical scores, nor decreased hospitalization rates (although trends to these outcomes are suggested and decreased severity is found at 24–72 hours).[135,151,155,162,166,167] Nebulized hypertonic saline may need to be given at adequate intervals, dose, and duration for a significant treatment benefit to be seen. It may also be possible that ED initiation followed by continuation of treatment may lead to later benefits in hospital. Further research is currently under way to better establish and clarify the roles of nebulized hypertonic saline in both the outpatient and inpatient settings.

Small studies looking at the effect of Heliox have demonstrated some benefits in improving short-term respiratory distress scores, but without clear reductions in the need for intubation or length of ICU stay.[156,168] The use of ventilatory support with positive-pressure ventilation has also been examined in small studies showing improved carbon dioxide clearance and clinical scores, but without a clear decrease in the need for intubation.[135,161]

Given that bacterial superinfection is rare in bronchiolitis, antibiotics should only be administered in the setting of proven or highly likely bacterial illness or in suspected sepsis in the unusual toxic child with bronchiolitis. Although pertussis and atypical pneumonias such as *Mycoplasma* and *Chlamydophila* may mimic bronchiolitis, significant suspicion for these entities should exist before empiric treatment is considered.

Use of ribavirin should be restricted to immunodeficient children with severe illness, given the lack of evidence in other scenarios.[130,158,159] Surfactant treatment may play a role in young infants requiring ICU care or intubation, although its current role in the ED is not clearly defined.[135]

Given the highly contagious nature of RSV through direct contact and contact with fomites, the importance of hand washing with soap or alcohol-based solutions must be observed by ED personnel and must be stressed to parents. Exposure to second-hand smoke has been found to be a risk factor RSV infection, whereas breastfeeding has been shown to be protective. Palivizumab (Synagis), a monoclonal antibody against RSV given preventatively in 5 monthly doses at the start of the RSV season, may be prescribed for infants at high risk. However, cost effectiveness compared with isolation strategies for those infants at high risk of severe disease has not been well studied, and calls its routine use into question.

### *Disposition*

Admission ideally should be reserved for those at high risk of morbidity and mortality or in whom admission allows for (1) necessary physical observation in the likelihood of serious deterioration requiring immediate medical interventions, and (2) provision of medical interventions and treatment that are not available or practical in the outpatient setting.

Many attempts to define admission criteria are present in the literature. Because bronchiolitis typically worsens and peaks after 3 to 5 days, the natural history of the disease should be taken into account in determining disposition.

Mansbach and colleagues[169] published in 2008 a multicenter cohort study to identify factors associated with safe discharge from the ED in order to create a low-risk model. These factors include:

1. Age $\geq$2 months
2. No history of intubation
3. Eczema
4. Respiratory rate less than normal for age
5. Mild retractions
6. Initial $O_2$ saturation $\geq$94%
7. Few treatments with $\beta$-agonists or epinephrine in the first hour
8. Adequate fluid intake.

Infants at high risk of apnea are currently considered a high-risk group and require admission for monitoring. Willwerth and colleagues[170] reviewed admitted bronchiolitis infants over a 5-year period and retrospectively identified a set of risk criteria that predicted the occurrence of apnea in all of the 19 of 691 (2.7%) infants who developed apnea in hospital. These criteria were: (1) born at full term but chronologic age less than 1 month; (2) born preterm at less than 37 weeks but chronologic age less than 48 weeks post conception; or (3) witnessed prior apnea event by parents or a clinician before admission.

In an attempt to identify predictors of bounce-back visits for worsening bronchiolitis within 2 weeks of ED discharge, Norwood and colleagues[171] reviewed 121 of 717 patients with unscheduled return visits, and identified age younger than 2 months, male sex, and history of previous hospitalization as risk factors. Identifying patients at higher risk of return visits or deterioration may be useful to stratify those patients and families in need of the highest level of discharge counseling and instruction, and follow-up with a primary care provider in the following days.

Assessment of physical signs is required to determine need for admission. However, it must be noted that no single physical examination parameter (except perhaps oxygen saturation) has been found to be strongly predictive of severe disease. Studies have instead emphasized constellations of signs and symptoms.

A study in 2011 identified 5 predictors of admission. These factors were then assimilated into a clinical scoring system in which each was equally weighted with 1 point[172]:

1. Duration of symptoms less than 5 days
2. Respiratory rate 50 breaths/min or more
3. Heart rate 155 beats/min or more
4. Oxygen saturation less than 97%
5. Age less than 18 weeks.

The study suggests that patients with scores of 3 or more may require admission or careful monitoring, and scores could be used in conjunction with assessment

of other high-risk factors. This study, while providing promising conclusions, has yet to be validated.

## PNEUMONIA IN CHILDREN

Pediatric pneumonia is the number one cause of mortality in children worldwide, with an annual incidence of more than 150 million cases per year. More children die of pneumonia than of diarrheal illnesses, malaria, and AIDS,[173] making it a significant global health care concern. In developed countries pneumonia in children, although significantly less likely to cause mortality, remains a common ED presentation.

### *Assessment*

The assessment of a child for pneumonia can be challenging for numerous reasons:

1. Significant overlap in presentation may occur with other common respiratory conditions such as bronchiolitis, asthma, and bronchitis, among others
2. Significant overlap in the presentation between viral, bacterial, and atypical pathogens makes definitive diagnosis challenging given lack of readily available, precise, rapid, noninvasive etiologic testing in the ED setting
3. The extent to which diagnostic testing may truly aid and change the clinical course is often not known
4. An important minority of cases may be caused by atypical pathogens requiring specific testing and treatment beyond standard empiric treatments.

### *Clinical Presentation*

Although the classic presenting symptoms of fever, productive cough, dyspnea and chest pain can assist the ED practitioner in recognizing pneumonia, children may have less typical presentations that require a higher level of suspicion and discernment. Neonates and infants may simply present with lethargy, poor feeding, or irritability. Atypical pneumonias may present with predominantly upper respiratory tract or systemic symptoms such as malaise, headache, vomiting, or rash. Neck pain and, rarely, meningismus may be a manifestation of an upper lobe consolidative process. Abdominal pain is a not uncommon presenting symptom of pneumonia in children, although usually cough, fever, or other symptoms of a URI are present.[174] Fever without a localizable source may be a less common presentation, but is well described.

The World Health Organization guidelines advocate measurement of respiratory rate as an important initial guide to suspecting pneumonia. These guidelines suggest thresholds of RR greater than 60 in infants younger than 2 months, RR greater than 50 in infants 2 to 12 months old, RR greater than 40 in children 1 to 5 years old, and RR greater than 30 in children older than 5 years[175,176] as a simple tool that may help detect as many as 50% to 80% of pneumonias. Respiratory rates should be counted for a full minute when the child is calm. However, studies show the specificity of tachypnea in developed countries is reportedly low in infants under 6 months (39%) compared with older children up to age 5 years (67%).[177] Tachypnea beyond age-specific limits was found in 61% of children under 2 years old and in 26% of those patients older than 2 years in another study of radiographically confirmed pneumonia,[178] underscoring the limits of using tachypnea alone to predict pneumonia.

Other physical findings associated with pneumonia in infants and younger children include nasal flaring, grunting, and retractions, although their specificity for pneumonia is low in infants and younger children, who are more likely to have bronchiolitis. The prevalence of classic pneumonia signs such as crackles (49%), decreased breath sounds (58%), and fever (88%) were documented in a 2008 study of 101 cases of

community-acquired pneumonia (CAP).[178] Wheeze may occasionally occur in typical bacterial pneumonia (reported in the literature at 4.9%), but is more likely associated with viral lower respiratory tract infection and *Mycoplasma* (atypical) pneumonia (up to 30%).[179] Absence of all respiratory findings, especially without fever or cough, makes pneumonia highly unlikely, though occult pneumonia (defined as pneumonia in the absence of any noted respiratory and auscultatory findings on examination) has an incidence of 5% to 6%,[176] with absence of auscultatory findings in up to 30%.[180]

For the emergency physician, a careful assessment of presenting signs is crucial to determine the likelihood of diagnosis as well as appropriate treatment and disposition. These signs include hypoxemia, abnormal respiratory rates (respiratory rate >70 or apnea in infants under 2 months, or respiratory rate >50 in children ages 1–4), signs of significantly increased work of breathing, inability to maintain oral hydration, clinical signs of dehydration, signs of sepsis/shock/toxicity, and high fever.[181] Significantly decreased breath sounds or dullness at a lung base may suggest a dense consolidation or effusion/empyema. Features associated with empyema described in a Finnish study included pain on abdominal palpation and tachypnea with greater duration of fever before admission.[182] In contrast to the adult literature, severity scores and indices (eg, CURB-65 score, Pneumonia Severity Index, and so forth) have not to date been validated for use in pediatric pneumonia.

### *Etiology*

Most pediatric pneumonia seen in the ED is caused by respiratory viruses, typical bacterial agents (primarily *Streptococcus pneumoniae*), or atypical bacterial agents (*Mycoplasma* and *Chlamydophila*). Awareness and knowledge of rare but "critically causal" agents is important to properly diagnose and treat these unusual causes, which include tuberculosis, pertussis, *Legionella*, coronavirus/severe acute respiratory syndrome (SARS), H1N1 influenza, hantavirus, varicella, measles, fungi, and potential bioterrorist agents such as anthrax and plague. Workup and treatment beyond the standard empiric approach would be required and is beyond the scope of this review.

The single most important predictor of the causative agent for pneumonia is age. Neonatal pneumonia (<1 month) is unique, as it has a significant incidence of maternally transmitted organisms such as group B *Streptococcus*, gram-negative organisms (*Escherichia coli*, *Haemophilus influenzae*), *Listeria monocytogenes*, anaerobes, and occasionally herpes simplex virus and cytomegalovirus. In the age group between 2 and 12 weeks an organism unique to this age range is *Chlamydophila trachomatis*, which causes an afebrile pneumonitis syndrome characterized by a well-appearing child presenting with cough, tachypnea, and interstitial infiltrates on CXR. The incidence of this disease has declined significantly with prenatal screening for this vertically transmitted organism from mothers. Other bacteria commonly seen in the first 3 to 4 months include *H influenzae* (nontypable or Type B), *Moraxella catarrhalis*, *Streptococcus pyogenes*, *Staphylococcus aureus* and, rarely, *Bordetella pertussis*.

In younger children, especially under the age of 2 years, viral causes predominate. RSV is the most common, followed by parainfluenza, adenovirus, rhinovirus, human metapneumovirus, and influenza viruses. Bacterial causes, mainly *S pneumoniae*, is common, especially in children who require hospitalization. Between the age of 2 and 5 years, the incidence of pneumococcal and atypical organisms rises. In school-aged children, there is a greater increase in the incidence of *Mycoplasma* and *Chlamydophila* pneumonia, while *S pneumoniae* remains the most common bacterial cause. Viral agents remain an important cause in this age group. Tuberculosis accounts for a very small percentage of pediatric CAP.

Classic pneumococcal pneumonia presents with sudden onset of high fever and rigors with a productive cough, focal pleuritic chest pain, mild to moderate systemic toxicity (lethargy, malaise, nausea, vomiting), and focal chest findings on examination. Unfortunately, only a small minority of patients who have a confirmed pneumococcal pneumonia present with these findings. Initial ED presentations may be subtle or atypical. WBC and C-reactive protein (CRP) may be helpful in more severe disease but are nonspecific for milder cases.[144] CXR is significantly limited given that pneumococcus may present as a bronchopneumonia instead of lobar infiltrate.

Features that may be more common in pneumonia caused by *Mycoplasma* or *Chlamydophila* include a more insidious onset with constitutional symptoms of malaise, myalgias, pharyngitis, headache, low-grade fever, and a dry cough that progressively worsens. Bullous myringitis and rashes such as erythema nodosum or a generalized maculopapular eruption occasionally occur with *Mycoplasma* infection.

Viral pneumonias are most common in those younger than 5 years, often presenting in the fall or winter, and usually associated with a viral prodrome such as coryza, pharyngitis, low-grade fever, and dry cough. Viral pneumonias account for the majority of pneumonias in children younger than 2 years in North America. Radiographically, perihilar predominance with peribronchial thickening, hyperinflation, and interstitial involvement is most often seen; however, lobar infiltrates can also be seen.[183] Coinfection with viral and bacterial agents is fairly common, especially in those under the age of 5 years, often ranging from 20% to 35% in many studies.[178,184]

Staphylococcal pneumonia is rare but is associated with more severe illness, especially in the setting of viral coinfection. Reports suggest a rising incidence with the increased prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in the community and in hospital settings.[185] Risk factors for staphylococcal pneumonia include younger age (<1 year old), complicated CXR appearance (effusion/empyema, cavitating or necrotizing infiltrate, lung abscess), toxic appearance, known MRSA contacts or history of community-acquired MRSA, and viral coinfection (notably influenza A).[186,187] Presentation in the ED with hemoptysis, hypotension, and leukopenia should also heighten suspicion for the organism.[186]

### *Investigations and Workup*

Well-appearing children with a clinical diagnosis of pneumonia require no specific workup, as outcome with empiric therapy is very favorable. Circumstances that warrant more rigorous efforts to identify a specific etiologic agent include:

1. The ill child requiring intensive care (ie, those with evidence of hypotension, sepsis, shock, hypoxemia <92%, hypovolemia, respiratory distress, altered mental status) or age <3 months (at higher risk of hypoxemia, apnea, and mortality than older children)[175,188]
2. Significant comorbidities including immunocompromise, underlying cardiopulmonary disease (eg, cystic fibrosis) or neuromuscular/neurologic impairment
3. Evidence of complicated pneumonia on CXR (significant effusion/empyema, pneumatocele, lung abscess)
4. Patients failing treatment, having persistent fever or prolonged clinical courses, or showing clinical deterioration[189]
5. Suspected resistant microbes or rare etiologies (eg, varicella, SARS, fungi, tuberculosis)[189]
6. Unexplained community outbreaks caused by an unclear organism.

Knowledge of local epidemiologic data is important to recognize the possibility of community outbreaks or rising antibiotic resistance patterns. The recent outbreaks of SARS in 2002 to 2003 and of H1N1 in 2008 to 2009 serve as poignant reminders that vigilance is key, and stringent infection control precautions are crucial to minimizing the spread of disease. Appropriate contact, droplet, and airborne precautions must be used. Household contact counseling, testing and treatment may be indicated in outbreaks of serious respiratory infections.

Clinical diagnosis of pneumonia in children is challenging, and physician judgment based on physical findings alone has been shown to have limited predictive power. In a study of 2071 children undergoing CXR in a pediatric ED for suspicion of pneumonia, 7% showed definite pneumonia while 15% showed definite or probable pneumonia.[190] Among the group judged by clinicians to have a high likelihood of pneumonia (>75%), CXR revealed definite consolidation in 30.6% and definite or probable consolidation in 52.8%. In the low-likelihood (<5% clinician suspicion) category, 4.3% showed definite and 10.0% showed definite or probable pneumonia. Another study in 2007 showed a prevalence rate of only 41.2% of positive or equivocal pneumonia in patients with clinical signs of pneumonia.[176] Although not addressing the issue of sensitivity of CXR to the diagnosis, these studies highlight the potential limitations of diagnosis and treatment decisions based on purely clinical grounds.

Many studies use radiographic criteria as the gold standard in the diagnosis of pneumonia, but evidence suggests that CXR lacks sensitivity in making the diagnosis, and lacks specificity in differentiating potential causes.[191] CXR has been shown to have limited specificity in differentiating typical bacterial from atypical bacterial and viral pneumonias. Although lobar consolidation and effusion are more commonly seen with typical bacterial causes, atypical agents such as *Mycoplasma* may present with lobar infiltrates as well as the more classic interstitial pattern and hilar adenopathy.[181] In 2002, Virkki and colleagues[183] evaluated 254 cases of CAP in which etiology was determined in 85%, and compared with CXR findings. Although the classic alveolar/lobar pattern was significantly correlated with a bacterial cause in 78% ($P<.001$), the interstitial pattern traditionally associated with atypical bacteria and viral infections was less specific, with 50% caused by bacteria (typical and atypical) and 50% caused by viruses. Variability among guidelines regarding the necessity of CXR exists. It has been shown that antimicrobial choice as well as overall outcome is not affected with the use of CXR in children 2 months to 5 years of age with mild disease.[140] As a result, they should not be considered mandatory in these cases.

Although CXR is often ordered in the large number of children with wheezing seen in EDs, the incidence of radiographic pneumonia is very low (3.7%–4.9%) unless fever (>38°C), abdominal pain, or significant hypoxemia (<92%) is present.[179] Moreover, atelectasis may often mimic early consolidation. In those under the age of 2 years with wheezing and crackles, viral bronchiolitis is the most likely diagnosis, with bacterial superinfection being very rare in mild cases.

Ultrasonography has recently emerged as a valuable tool in the diagnosis of pneumonia. Most studies in the adult literature on lung ultrasonography suggest higher sensitivity than CXR, better delineation of complications (such as loculated effusion, empyema, abscess, necrosis, and pneumatocele), and rapid performance times (usually less than 5 minutes).[192,193] Ultrasonography in children has compared very favorably with computed tomography (CT) scanning with respect to diagnosis, complications, and guidance of thoracocentesis, without radiation exposure and risk.[194] Furthermore, ultrasonography is less likely to require patient sedation in comparison with CT scanning. Given these advantages, ED clinicians should be aware of its evolving role.

CBC and differential can sometimes be helpful in suggesting a bacterial cause of pneumonia. A European study reported that *S pneumoniae* pneumonia was more commonly associated with WBC of greater than 15,000 to 20,000/mm$^3$, and a mean of 25,000/mm$^3$ if there was also a concomitant bacteremia.[144] However, invasive viral disease such as adenovirus or even influenza may cause similar WBC elevations, so interpretation should be done with caution in consideration of the overall clinical picture. Acute phase reactants such as erythrocyte sedimentation rate and CRP have shown suboptimal utility as sole determinants to distinguish bacterial from viral causes, due to limited specificities.[181,194] Although a procalcitonin level greater than 1.0 ng/mL was helpful in distinguishing bacterial from viral CAP in a recent study,[178] it was unable to distinguish pneumococcal from atypical bacterial pneumonia.

Blood cultures can be highly specific for the etiologic organism and can identify antimicrobial sensitivity patterns important to later care, but play little to no role in initial ED management. Two ED-based studies have shown that bacteremia occurs in only 2% to 3% of patients with radiographic CAP.[195,196] Shah and colleagues[195] reported higher yields of up to 13% in a subset of patients with complicated pneumonia. Due to the overall low yield, the use of blood cultures should be individualized to patients with suspected bacteremia, more ill patients, or patients with complications.

Bacterial serology from serum or urine samples is currently neither widely available nor practical in most EDs. Sensitivity and specificity is low, therefore testing is not recommended by most recent guidelines.[175,181,189,194,197] Cold agglutinin testing, although easy to perform, was shown to have a positive predictive value of only 70%.[181] *Mycoplasma* IgM detection via enzyme-linked immunosorbent assay is sensitive and may be considered in children older than 2 years.[189] Urine for pneumococcal antigen has been shown to lack high specificity in children. *Legionella* antigen testing in the urine may be considered for more severe cases requiring admission to the ICU or when clinical suspicion is high. Nasopharyngeal testing for pertussis and skin testing for tuberculosis should be done when these entities are suspected. Further testing should be based on clinical suspicion.

Rapid viral testing is now available in many settings, and can allow early diagnosis of influenza and RSV. Early identification allows treatment decisions with antivirals (which are rarely indicated), infectious precaution advice, and isolation as inpatients. Disadvantages include cost and low benefit/expense ratio in cases where clinical diagnosis is already clear and the necessity of obtaining specific etiologic diagnosis is low. The overall utility is generally low and should not be routine.[198] Testing may be considered in those with severe illness warranting hospitalization.

Sputum for Gram stain and culture may be feasible for older school-aged children capable of producing more reliable sputum specimens, and may be done for those requiring hospitalization for severe disease.[194,199] Limitations include frequent poor-quality specimens (especially in younger children) and difficulties in culturing organisms such as *Mycoplasma*, *Chlamydophila*, *Legionella*, *Moraxella*, and tuberculosis. Nasopharyngeal and throat cultures have poor reliability in predicting the etiology of pneumonia and are not recommended.

### *Treatment*

Treatment regimens in suspected bacterial CAP take into account the age of the child, treatment setting, severity, special circumstances in each case, and local patterns of organisms and antibiotic susceptibilities.[175,181,189,194,197,199] Consideration for withholding antibiotics should be given for those non-ill children with clinical presentations

**Table 2**
**Empiric antibiotic therapy for suspected bacterial community-acquired pneumonia**

| Age | Outpatient Treatment | Inpatient Treatment |
|---|---|---|
| Neonate | Not recommended > Admit | Ampicillin 50–200 mg/kg/d IV div q 6–12 h plus<br>Cefotaxime 150–200 mg/kg/d IV div q 6 h–q 8 h<br><br>If ill, add gentamycin 7.5 mg/kg/d IV div q 8 h<br><br>If HSV likely, add acyclovir 500 mg/$m^2$/dose IV q 8 h |
| 1–4 months | If afebrile pneumonitis<br>Clarithromycin 15 mg/kg/d PO div BID[a] or<br>Erythromycin 40 mg/kg/d PO div q 6 h<br><br>Amoxicillin 90 mg/kg/d PO div BID–TID[b,c]<br><br>If febrile or hypoxic > Admit | If afebrile pneumonitis<br>Clarithromycin 15 mg/kg/d PO/IV div BID[a] or<br>Erythromycin 40 mg/kg/d PO or 20 mg/kg/d IV div q 6 h<br><br>If febrile, cefotaxime 150–200 mg/kg/d IV div q 8 h<br>or cefuroxime IV 150 mg/kg/d IV div q 8 h<br><br>If ill or MRSA suspected,<br>add vancomycin 40–60 mg/kg/d IV div q 6–8 h or<br>clindamycin 40 mg/kg/d IV div q 6–8 h<br><br>If MSSA suspected,<br>cloxacillin 150–200 mg/kg/d IV div q 6 h |
| 4 months to 5 years | Amoxicillin 90 mg/kg/d PO div BID–TID[b,c]<br><br>If atypical suspected add Macrolide PO (doses as above)<br><br>Second-line alternatives:<br>Amoxicillin-clavulanic acid 90 mg/kg/d PO div BID or TID[b,c]<br>Cefuroxime axetil 30 mg/kg/d PO div BID | Ceftriaxone 50–100 mg/kg/d IV div q 12–24 h or<br>Cefotaxime 150–200 mg/kg/d IV div q 8 h or<br>Cefuroxime 150 mg/kg/d IV div q 8 h<br><br>If *Streptococcus pneumoniae* likely,<br>Ampicillin 150–200 mg/kg/d IV div q 8 h–q 6 h<br><br>If severely ill,<br>add vancomycin 40–60 mg/kg/d IV div q 6–8 h or<br>cloxacillin 150–200 mg/kg/d IV div q 6 h<br>or if pleural effusion,<br>clindamycin 40 mg/kg/d IV div q 6–8 h<br><br>If atypical suspected: Macrolide IV or PO (doses as above)[a] |

(*continued on next page*)

**Table 2**
**(*continued*)**

| Age | Outpatient Treatment | Inpatient Treatment |
|---|---|---|
| 5–18 years | Azithromycin 10 mg/kg/d, Day 1 + 5 mg/kg/d, Days 2–5 or<br>Clarithromycin 15 mg/kg/d div BID or<br>Erythromycin 40 mg/kg/d div q 6 h<br><br>If *S pneumoniae* likely<br>Amoxicillin 90 mg/kg/d PO div BID[b,c]<br><br>Alternatives:<br>Doxycycline[d] 2–4 mg/kg/d PO div BID<br>Amoxicillin-clavulanic acid 90 mg/kg/d PO div BID or TID[b,c]<br>Cefuroxime axetil 30 mg/kg/d PO div BID<br>Levofloxacin[e] 500 mg PO daily or<br>Moxifloxacin[e] 400 mg PO daily | Ceftriaxone 50 mg/kg/d IV div q 12 h or q 24 h (max 2 g/d) or<br>Cefuroxime 150 mg/kg/d IV div q 8 h (max 1.5 g/d) or<br><br>If *S pneumoniae* likely,<br>Ampicillin 150–200 mg/kg/d IV div q 8 h–q 6 h<br><br>If atypicals suspected<br>Macrolide IV or PO (doses as above)<br><br>If severely ill,<br>add vancomycin 40–60 mg/kg/d IV div q 6–8 h or<br>cloxacillin 150–200 mg/kg/d IV div q 6 h, or<br><br>If pleural effusion,<br>clindamycin 40 mg/kg/d IV div q 6–8 h |

*Abbreviations:* BID, twice daily; div, divided (for dosages based on a daily dose, which needs to be then divided into intervals); HSV, herpes simplex virus; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; PO, by mouth; q, every; TID, 3 times daily.

[a] Azithromycin: Safety and effectiveness not fully established in infants under 6 months of age. Not approved by US Food and Drug Administration in this age group.

[b] Higher-dose amoxicillin recommended especially if in day-care attendance, recently on antibiotics, or hospitalized in last 3 months, age under 2 years, or area with *S pneumoniae* penicillin resistance greater than 2.0 μg/mL.

[c] Lower-dose amoxicillin 45 mg/kg/d potentially effective in absence of risk factors for resistant *S pneumoniae*.

[d] Avoid if younger than 8 years, because of effects on dentition.

[e] Use only if growth plates are closed.

*Data from* Refs.[175,181,189,194,199]

consistent with viral illness, given the association between inappropriate antibiotic use and increase in resistant organisms. Suggested empiric antibiotic treatments for CAP are listed in **Table 2**.

Anaerobic coverage should be considered if aspiration is suspected. Antiviral therapy for influenza-related pneumonia should be initiated in high-risk populations within 48 hours of symptom onset. The anti-RSV treatment ribavirin should be limited to high-risk patients as per American Academy of Pediatrics Guidelines.[130]

A large multicenter trial (the PIVOT trial) in 2007, of 246 cases of pediatric CAP comparing oral amoxicillin to IV penicillin followed by oral amoxicillin demonstrated similar outcomes, suggesting IV treatment may not always be necessary for admitted patients with milder cases, thereby saving hospital costs and avoiding IV cannulation.[200] Examining the duration of antibiotic therapy, a 2008 Cochrane systematic review concluded equal efficacy of 3-day versus 5-day treatment regimens in mild CAP in otherwise healthy children 2 months to 5 years of age.[201]

### *Adjunctive Treatments*

Standard supportive care includes oxygen for hypoxemia less than 92%, suctioning of younger infants, and bronchodilators as necessary. IV fluids should be given when necessary but with caution, given the association of SIADH with more severe pneumonias. IV fluid regimens started in the ED may require adjustment in the presence of hyponatremia. Chest physiotherapy has been found to be of no added value and is not routinely recommended. Steroids have no role currently in the treatment of the pneumonia. Noninvasive ventilator support with continuous positive airway pressure or bilevel positive airway pressure may be necessary for those with respiratory failure. Intubation is rarely indicated.

### *Complications*

Complications of pneumonia may include sepsis, respiratory failure, effusion, empyema, abscess, pneumatocele, and infectious spread such as, meningitis, septic arthritis, or osteomyelitis.[175,181] Small free-flowing parapneumonic effusions suspected to be transudative may be given a trial of antibiotics and reassessed for pleurocentesis as necessary. Moderate and large effusions, especially if in respiratory distress, should be considered for prompt pleurocentesis before starting antibiotics, as this may affect culture results.[175] Proven empyemas should be drained and further treatment decisions should be made in consultation with thoracic surgery. Pulmonary

**Table 3**
**Suggested admission criteria for pediatric community-acquired pneumonia**

| | |
|---|---|
| Definite admission | Age <1 month<br>Oxygen saturation $\leq$92%<br>Signs of significant respiratory distress (tachypnea/apnea, significant work of breathing)<br>Signs of sepsis or toxic appearance<br>Complicated pneumonia on chest radiograph (effusion/empyema, pneumatocele, necrosis, or lung abscess) |
| Probable admission | Age 1–3 months<br>Oxygen saturation 93%–94%<br>Significant comorbidity (chronic lung disease, congenital heart disease, cystic fibrosis, etc)<br>Significant burden of disease (multilobar or complete lobar consolidation)<br>Immunocompromise (sickle cell disease, human immunodeficiency virus, post-splenectomy, malignancy/recent chemotherapy)<br>Unresolving or worsening illness<br>Significant dehydration/vomiting<br>Inability of parents/caregivers to ensure adequate observation or follow-up |
| Consider admission | Age 3–6 months<br>Failure of outpatient treatment, especially if any clinical deterioration<br>Larger infiltrate or significant atelectasis on chest radiograph |
| Outpatient therapy | Non-ill or minimally ill child<br>Uncomplicated mild pneumonia<br>Adequate oxygenation<br>Tolerating feeds well<br>Reliable parents for observation and follow-up |

*Data from* Refs.[175,181,189,194,199]

and infectious disease specialist involvement may be warranted for cases of unresolving infiltrates, abscesses, pneumatoceles, or effusions.

### *Admission Criteria/Predictors of Poor Outcome*

Worldwide, significantly at-risk groups include neonates, human immunodeficiency virus (HIV)-related pneumonia (3–8 times higher case fatality rates compared with non-HIV infected), and severely malnourished children.[188] Significant hypoxemia is also associated with a 2- to 5-fold increase in risk of death.[202] Predictors of antibiotic treatment failure include young age, immunocompromised state (eg, HIV or malnutrition), presence of empyema, prior antibiotic use, poor adherence to treatment, and antibiotic resistance.[188]

Admission criteria based on published guidelines and literature reviews have been proposed, though they have not been vigorously studied. Such criteria should be used with clinical judgment while taking into account modifying factors. Suggested admission criteria are listed in **Table 3**.

Other options for less ill or complicated patients include admission to a short-stay or observation unit for children in whom rapid clinical response is expected, or once-daily IV or IM antibiotics such as ceftriaxone with daily follow-up by an intensive ambulatory care service, as exists in some major hospitals.

### *Follow-Up*

Forty-eight-hour follow-up is strongly recommended for all children diagnosed with pneumonia,[174] especially if any signs of deterioration occur. The World Health Organization definition of clinical improvement requires "slower breathing, less fever, eating better."[202] In children with clinical improvement, follow-up radiography is suggested in cases of complicated pneumonia, round pneumonia, congenital abnormalities, lobar collapse, complicated courses, or persistent clinical abnormalities.[181,189] A recent radiographic follow-up study demonstrated that residual or new changes on CXR could be seen in 30% of cases after 3 to 7 weeks but did not affect management.[203]

## SUMMARY

Common respiratory illnesses including asthma, croup, bronchiolitis, and pneumonia will undoubtedly continue to make up the bulk of pediatric respiratory problems presenting to EDs. Given their potential to cause life-threatening illness, emergency clinicians will need to continue to maintain and update their knowledge on current recommendations for these illnesses. Underuse of some key therapies and overutilization of unproven therapies and low-utility diagnostic tests are several important areas that can be improved through improved education and knowledge of published clinical practice guidelines.

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