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21 Respiratory Tract Symptom Complexes

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MUCOPURULENT RHINORRHEA

Mucopurulent rhinorrhea, or purulent nasal discharge, denotes nasal discharge that is thick, opaque, and colored. It occurs at any age, usually as a manifestation of self-limited, uncomplicated viral upper respiratory tract infection (URI). Mucopurulent rhinorrhea is most problematic in children younger than 3 years because of: (1) protracted course and frequent recurrence, especially in those in out-of-home child care;[1] (2) parental concern about and misperception of etiology; and (3) overprescription of antibiotics

TABLE 21-1. Causes of Mucopurulent Rhinorrhea

	Chronic or Recurrent	
Acute	**Underlying Conditions**	**Obstructing Lesions**
Viral nasopharyngitis	Allergy[a]	Polyps
Bacterial sinusitis	Medications[a] (antihypertensives, oral estrogens, aspirin and nonsteroidal anti-inflammatory drugs)	Congenital nasal anomalies (choanal atresia or stenosis, Tornwaldt cyst, deviated septum)
Acute otitis media	Pregnancy[a]	Neuroembryonal mass (dermoid, encephalocele, glioma, teratoma)
Streptococcal nasopharyngitis	Hypothyroidism[a]	Tumor (hemangioma, angiofibroma, neurofibroma, lipoma, craniopharyngioma)
Anaerobic bacterial nasopharyngitis (nasal foreign body)	Rhinitis medicamentosa[a] (α_1-adrenergic agonists)	Neoplasm (lymphoma, rhabdomyosarcoma, nasopharyngeal carcinoma)
Adenoiditis	Immunoglobulin deficiency	
Syphilis	Human immunodeficiency virus infection	
Pertussis	Cystic fibrosis	
	Ciliary dyskinesia	

[a]*Rhinorrhea is characteristically clear, but opaque white discharge is not unusual.*

by healthcare providers.[2–5] Occasionally, this symptom is a clue to diagnosis of a treatable bacterial infection or underlying condition.

Acute, sporadic mucopurulent rhinorrhea has an infectious cause and almost always is the manifestation of the uncomplicated "common cold" due to rhinovirus, coronavirus, or other circulating viruses.[6] When the problem is chronic or recurrent, or persistent and unilateral, broader underlying anatomic, obstructive, immunologic, and allergic disorders are considered (Table 21-1).[7–10] Onset in an infant younger than 3 months heightens suspicion of anatomic anomaly, ciliary dyskinesia, or cystic fibrosis. Accompanying sinusitis, otitis media, or pneumonia raises consideration of an immunologic deficiency (especially immunoglobulin deficiency or dysfunction, as in hypogammaglobulinemia or human immunodeficiency virus (HIV) infection), neutrophil defect, cystic fibrosis, or ciliary dyskinesia. URIs are conspicuously severe in such instances, with recrudescence almost immediately after discontinuation of antibiotic therapy. Unilateral nasal discharge and obstruction should prompt investigation for a foreign body, mass lesion, or unilateral posterior choanal atresia.

Table 21-2 shows differentiating features of important or common causes of acute mucopurulent rhinorrhea; allergic rhinitis is included because it is frequently part of the differential diagnosis in older children and adolescents.

Causes of Acute Mucopurulent Rhinorrhea

Viral Nasopharyngitis

In uncomplicated viral nasopharyngitis or rhinitis, nasal discharge is initially clear but can become white, yellow, or green (related to mucous secretions, dryness, blood, exfoliation of damaged epithelial cells and cilia, and leukocytic inflammatory response). Presence of high fever and persistence of discharge depend on the specific viral cause but are more common in uncomplicated infection than generally perceived.

In a study of hospitalized children, more than 50% of those with uncomplicated adenovirus, influenza, parainfluenza, or respiratory syncytial virus infection had temperatures >39°C, and 12% had temperatures >40°C; height of fever in these children was not different from that in children with serious bacterial infection.[11] Fever persisted for 5 days or longer in 37% of the children in the study; 20% to 30% of those with adenovirus or influenza A infection had fever for 7 days or longer. In another study, nasal discharge or congestion associated with uncomplicated URI persisted for 6.6 days in 1- to 2-year-old children who were in home care and for 8.9 days in children younger than 1 year in out-of-home childcare centers.[1] In this study, 13% of 2- to 3-year-old children in out-of-home childcare had symptoms for more than 15 days.

The bacteriology of nasopharyngeal flora in children with uncomplicated viral respiratory illnesses, mucopurulent rhinorrhea, acute otitis media, and sinusitis has been evaluated and compared with that in normal children.[6,12–23] Viral infection is associated with acquisition of new serotypes of *Streptococcus pneumoniae* and with temporally increased risk of acute otitis media.[21] Quantitative, and some qualitative, differences in nasopharyngeal flora have been found in children with purulent nasopharyngitis (and uncomplicated viral upper respiratory illnesses), with excessive isolation rates reported for *S. pneumoniae* and *Haemophilus influenzae*,[13,18] *Peptostreptococcus* spp., *Fusobacterium* spp., and *Prevotella melaninogenica*.[18,19] The significance of such findings is unclear; isolation of such organisms may reflect exuberant proliferation in virus-induced inflammatory mucus or acquisition of a more robust specimen than is collected in healthy subjects. Furthermore, "high" rates of isolation of *S. pneumoniae* in 25% to 46% of subjects do not exceed those in healthy young children when fastidious technique is used.[22]

Only two systematically performed studies on the course of mucopurulent rhinorrhea have been published. In one study, prospective evaluation showed that there was no difference in duration of illness or complications in children with clear or purulent nasal discharge.[14] In a placebo-controlled, blinded study of 142 children 3 months to 3 years old with mucopurulent rhinorrhea of any duration, antibiotic therapy (cephalexin), systemic use of an antihistamine-decongestant, or both had no effect on the course or complications of mucopurulent rhinorrhea.[12] In a small pilot study of 13 children younger than 2 years whose purulent nasal discharge had persisted for at least 10 days without improvement, amoxicillin-clavulanate (40 mg/kg per day divided into 3 doses for 10 days) was significantly associated with resolution of symptoms in comparison with placebo.[15]

Response to antimicrobial therapy does not necessarily validate an entity of bacterial nasopharyngitis, however; it seems more likely that some children with such responses have an incomplete symptom complex of ethmoid sinusitis. Acute bacterial adenoiditis is postulated to be another cause of purulent nasal discharge when: (1) tympanic membranes are normal; (2) *S. pyogenes* is not found in culture specimens; and (3) radiographs show an enlarged adenoid shadow but no sinus abnormality.[23,24] Critical study has not been performed to validate this entity.

Bacterial Sinusitis

Mucopurulent rhinorrhea or daytime cough (which frequently is worse at night), or both of 10 or more days' duration without improvement (or recrudescence after improvement or new onset of fever) is highly suggestive of paranasal bacterial sinusitis and responsive to antibiotic therapy.[17,25,26] Sinus radiographs show significant abnormalities in nearly 90% of children 2 to 6 years old with uncomplicated upper respiratory tract illness (see Chapter 32, Sinusitis), and thus are nonspecific in this age group, supporting a clinical approach to diagnosis without imaging.

Streptococcal Nasopharyngitis

In children younger than 3 years, *S. pyogenes* has been associated with high fever, toxicity, and clear rhinorrhea or indolent infection with irregular fever and purulent nasal discharge, sometimes with associated excoriation of nares or tender anterior cervical lymphadenitis.[13,18,25] In a streptococcal outbreak studied in a childcare facility for school-aged and young children, 26% of children younger than 3 years were affected, but pharyngitis was predominant, with no case of nasal streptococcosis.[27]

TABLE 21-2. Differentiating Among Causes of Nasal Discharge[a]

	Viral Nasopharyngitis[1,11–15]	Acute Bacterial Sinusitis[16,17,24]	Streptococcal Nasopharyngitis[25]	Foreign Body-Related Rhinitis (Bacterial)[18]	Allergic Rhinitis[10]
HISTORY					
Peak age	Peak in first 2 years after "new recruitment" into childcare or school	Any	<3 years	<3 years	>2 years; peak in adolescence
Onset	Dryness, burning in nose or nasopharynx	Insidious, with cough day and night; occasionally, acute, febrile, toxic	Insidious; occasional acute, febrile, toxic	Insidious	Seasonal; precipitants
Associated symptoms	Nasal congestion, sneezing, malaise	Malodorous breath; head or facial pain, edema		Malodorous breath ± hyponasal voice	Sneezing; nasal or palatal pruritus; tearing; snoring
Fever	Yes/no	No/yes	Low/high	No	No
Duration of discharge	3–8 days	≥10 days	>5 days	Chronic	Chronic, recurrent
PHYSICAL EXAMINATION					
Associated findings	Red, excoriated nares; sometimes, acute otitis media	Periorbital swelling, facial tenderness; mucopurulent postnasal discharge	Anterior cervical lymphadenitis; impetiginous lesions below nose	Mouth-breathing	Transverse nasal or lower eyelid crease; periorbital hyperpigmentation; cobblestone conjunctivae or posterior pharynx
Character of discharge	Clear or colored, watery or thick	Thick, colored	Thick, colored	Unilateral, purulent, putrid bloodstained	Watery, clear, or white
Rhinoscopy	Hyperemic mucosa; dry or glazed early, edematous later; crusted discharge	Normal mucosa; discharge from middle meatus	Normal, hyperemic, or excoriated mucosa	Identifiable object (button, pit, nut), boggy mass (vegetable), or rhinolith	Pale or blue, edematous turbinates
DIAGNOSTIC TESTS	None; nasal smear shows neutrophils and mononuclear cells ± inclusion bodies, pyknotic epithelial cells	None; sinus radiograph (>6 years of age)	Nasopharyngeal culture for streptococcus only	Rhinoscopy	Nasal smear shows goblet cells and eosinophils; skin test or radioallergosorbent test (RAST)
CAUSE	Multiple agents, depending on age and seaso	*Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*	*Streptococcus pyogenes*	Normal nasopharyngeal facultative and anaerobic bacteria	Allergens in predisposed individual
THERAPY	Saline nasal drops, humidification; amoxicillin if acute otitis media	Amoxicillin; amoxicilin-clavulanate (14:1 formulation)	Penicillin V	Removal of obstruction; amoxicillin-clavulanate if tissue or sinus complication	Avoidance; oral antihistamine/ decongestant; or topical corticosteroid; cromolyn

[a]*Superscript numbers indicate references.*

Other Infectious Causes

Bacterial nasopharyngitis associated with nasal foreign body is typified by the young age of the patient and putrid, commonly bloodstained, unilateral nasal discharge. Fever is unusual unless infection has spread to contiguous sinuses or distant sites. *Prevotella, Fusobacterium,* and *Peptostreptococcus* spp. as well as facultative flora are responsible. Nasal discharge can be the first manifestation of congenital syphilis and a later finding in nasal diphtheria, in which discharge is putrid and sanguineous and contains pieces of pseudomembrane.

Allergic Rhinitis

Allergic rhinitis typically begins in the second decade of life, is uncommon before age 3 years, and incidence appears to be increasing in children between these ages. Diagnosis can be suspected because of the season, environmental precipitants, personal and family history of allergy, other associated symptoms and physical findings, and the response to specific interventions of avoidance or pharmacotherapy (see Table 21-2). Nasal secretions usually are clear or whitish. Diagnostic usefulness of nasal cytologic analysis is controversial;[10,28] relative eosinophilia (above 20%) is suggestive but not diagnostic of allergic rhinitis.

Management of Acute Mucopurulent Rhinorrhea

In the vast majority of children with purulent nasal discharge (even if thick and green) of up to 1 week in duration, history and setting of illness, associated symptoms, and physical findings suggest uncomplicated viral URI. Antimicrobial therapy is inappropriate unless acute otitis media or sinusitis is diagnosed from additional findings (see Chapter 32, Sinusitis). Symptomatic therapy with saline nose drops or lavage facilitates expulsion of secretions and provides humidification. Its effectiveness reduces parental pressure to prescribe an antibiotic.[29]

If mucopurulent rhinorrhea persists for more than 5 days, and especially if some findings (e.g., anterior cervical lymphadenitis, scarlatiniform rash, excoriation around nostrils) or the epidemiology heightens the likelihood of group A streptococcal disease, nasopharyngeal specimens should be obtained for culture of *S. pyogenes* only. If culture is positive, penicillin V is given for 10 days. Routine culture for, or recovery of, *S. pneumoniae, H. influenzae, Moraxella catarrhalis,* or *Staphylococcus aureus* has no meaning and is an opportunity for misinterpretation.

If mucopurulent rhinorrhea persists for more than 10 days without diminution, and especially if other symptoms are present, paranasal sinusitis is likely. Nasal mucosa is examined after use of single or second (5 minutes after the first) application of a topical

vasoconstrictor such as oxymetazoline.[15] If purulent secretions flow from the middle meatus, the diagnosis of acute sinusitis is confirmed. Signs of allergic rhinitis also can be confirmed. Radiographs may be helpful in patients older than 6 years to confirm sinusitis (or possibly to suggest adenoiditis). Many clinicians would treat children who have purulent nasal discharge of greater than 10 days' duration as for acute sinusitis, usually with amoxicillin initially. When antimicrobial therapy is effective, substantial improvement of symptoms is expected within 48 to 72 hours. Therapy is continued for 1 week beyond complete resolution of respiratory symptoms.

STRIDOR

Characteristics

Stridor is a rough, crowing sound caused by passage of air through a narrowed upper airway, which includes the extrathoracic trachea, larynx, and hypopharynx. Because the extrathoracic airway normally narrows during the inspiratory phase of respiration, stridor due to upper-airway disease occurs during inspiration (or is more pronounced during inspiration if severe narrowing causes obstruction during inspiration and expiration). Because the intrathoracic trachea normally narrows during expiration, obstruction of the intrathoracic trachea, such as that due to extrinsic compression of vascular ring or intraluminal obstruction of foreign body, inflammation, or tracheomalacia, causes a loud noise, acoustically like stridor, heard during both phases of respiration but is more pronounced on expiration. Extrathoracic obstruction (inspiratory stridor) is associated with prolonged inspiration and underaeration of the chest, whereas intrathoracic obstruction (expiratory stridor or wheezing) is associated with prolonged expiration and overinflated chest. Stridor can be associated with mild tachypnea, but a respiratory rate >50 breaths/minute should not be ascribed to upper-airway obstruction alone.

The timbre of the stridulous sound provides a clue to etiology: for example, (1) the high-pitched, fixed, dry sound of congenital subglottic stenosis; (2) the wet, rhonchal changing sound of inflammatory laryngotracheitis; and (3) the low-pitched, vibratory, positionally variable sound of laryngomalacia. Associated voice changes are useful in specifying disease as well. Vocal cord paralysis causes a weak, dysphonic cry; supraglottic obstruction, a muffled voice; and laryngotracheitis, hoarseness or aphonia, frequently with a barking cough.

Etiology

Categorization of the setting and duration of stridor as acute, persistent, or recurrent or episodic provides a framework for considering likely causes (Table 21-3).[30–34] Infectious agents cause most acute upper-airway obstruction, from intraluminal, epithelial inflammation or by encroachment on the airway by reactive or infected lymphoid tissue in parapharyngeal or paratracheal spaces. Fungal or viral tracheobronchitis must be considered when stridor occurs in an immunocompromised child; odynophagia and dysphagia also are present commonly.[31] Congenital anatomic abnormalities are considered, especially in infants whose persistent stridor began neonatally. Acquired obstruction can have abrupt onset and an obvious cause (such as foreign-body aspiration or necrotizing tracheobronchitis in ventilated neonates) or more insidious onset and inapparent cause (such as expanding laryngotracheal papillomas or hemangioma or an extrinsic compressing mass). The younger the infant, the more likely that sudden obstruction, apnea, or feeding difficulties overshadow a singular complaint of stridor.

TABLE 21-3. Causes of Upper-Airway Obstruction and Stridor[a]

Acute	Persistent[30]
INFECTIOUS	**CONGENITAL**
Viral laryngotracheitis (croup)	Laryngotracheal web, cleft, cyst, hemangioma
Bacterial tracheitis	Tracheal stenosis
Epiglottitis, supraglottitis	Vascular ring
Peritonsillar, retropharyngeal, or parapharyngeal abscess	Laryngotracheal malacia
Tracheobronchitis associated with immunodeficiency[31]	Neuromuscular disorder
	Cystic hygroma
NONINFECTIOUS	**ACQUIRED**
Angioedema	Posttraumatic tracheal stenosis
Foreign body	Foreign-body aspiration
Necrotizing tracheobronchitis in neonates[32,33]	Mediastinal mass (tumor, lymphatic, vascular)
Recurrent/episodic	Papilloma (perinatally acquired)
Spasmodic croup	Posttraumatic spinal cord, vagal or glossopharyngeal nerve, or vocal cord damage
Gastroesophageal reflux[34]	Bulbar neuropathy (infectious, postinfectious, malignant)

[a]*Superscript numbers indicate references.*

Clinical Features of Acute Infectious Causes

Recognition, care to avoid precipitating sudden airway occlusion, and urgent, expert intervention to establish an airway when indicated are paramount to avert disastrous outcomes of acute upper-airway obstruction. Table 21-4 shows characteristic features of infectious causes of stridor and acute airway obstruction.[35–42] Viral laryngotracheitis (infectious croup) or laryngotracheobronchitis due to parainfluenza viruses is by far the most common.[35,36] Influenza viruses, respiratory syncytial virus, adenoviruses, and other viruses typically cause symptomatic disease elsewhere in the respiratory tract, but during epidemic seasons, stridor is the predominant feature in a minority of infected children. Bacterial tracheitis is usually a complication of viral laryngotracheitis (with concordant peak age and season) but can occur at any age or as a complication of oropharyngeal surgery.[43] *Staphylococcus aureus* is the most common cause, followed by *Streptococcus pyogenes;* the role of anaerobic bacteria is less clear.[41,43] With the universal use of *H. influenzae* b vaccine, epiglottitis is a rare cause of stridor; current cases of supraglottitis are more likely to affect the aryepiglottic region and to be caused by streptococci. Parapharyngeal and retropharyngeal infections in young children must also be considered; their incidence is increasing[42,44,45] (see Chapter 28, Infections Related to the Upper and Middle Airways).

The history surrounding the onset of stridor and the patient's age and demeanor are the most helpful clues to the likely site and cause of infection. The child with viral laryngotracheitis usually has had 2 to 3 days of typical upper respiratory tract illness when cough worsens and stridor begins. The child with bacterial tracheitis usually has had a similar background illness and then has sudden high fever, toxicity, and rapid progression of airway obstruction. The young child with retropharyngeal abscess or adolescent with peritonsillar abscess has less stridor but refuses to swallow, has a muffled voice, and a guarded posture to maximize the oropharyngeal airway. Trismus is an expected and useful finding in patients with peritonsillar abscess as well as in some with lateral pharyngeal space infections of odontogenic origin.[38] Epiglottitis and supraglottitis cause the patient to guard anxiously in a sitting posture with arms back, jaw forward, and chin raised ("sniffing dog") to maximize "lift" of the epiglottis away from the airway. In contrast, subglottic, tracheal obstruction cannot be lessened by position; patients with laryngotracheitis or bacterial tracheitis thrash about with the anxiety of suffocation.

The expected course[36,46,47] and sequelae of acute infectious airway obstruction are shown in Table 21-5. Children with viral laryngotracheitis are less prone to sudden complete obstruction; hourly course is predictable by degree of stridor and adequacy of aeration; response to racemic epinephrine and corticosteroid therapy usually averts intubation. Establishment of an artificial airway is urgently required for almost all patients with stridor due to acute supraglottic and bacterial tracheal infection, and for many with retropharyngeal infection. The course of disease in children

TABLE 21-4. Differentiating among Infectious Causes of Upper-Airway Obstruction[a]

	Viral Laryngotracheitis[35–37]	Supraglottitis[38,39]	Bacterial Tracheitis[40,41]	Retropharyngeal Abscess[38,40,42]
HISTORY				
Peak age	1–2 years	3–6 years, any	2–4 years, any	<3 years
Peak season	Late fall, late spring	Any	Late fall, late spring; any	Any
Prodrome	Viral illness	Uncommon	Viral illness	Uncommon
Onset of stridor	Gradual	Abrupt	Abrupt	Abrupt
PHYSICAL EXAMINATION				
Peak temperature (°C)	38–39	>39	>39	>39
Predominant findings	Brassy cough, stridor	Toxicity, stridor	Toxicity, stridor	Toxicity, stridor
Associated findings	Bark, rhinorrhea	Sore throat, odynophagia, dysphagia, anxiety, drooling	Brassy cough, anxiety	Lethargy
Voice	Hoarse, raspy	Normal, muffled, mute	Hoarse, raspy	Muffled, mute
Position	Any; thrashing	"Sniffing dog"; still	Any; thrashing	"Sniffing dog"; still
Airway occlusion	Predictable from degree of stridor	Sudden	Sudden	Sudden
Response to racemic epinephrine?	Yes, with rebound	No	No or partial	No
LABORATORY TESTS				
Peripheral neutrophils	Normal or low	High	Immature	Immature
RADIOGRAPH				
Hypopharynx	Distended	Distended	Distended	Anteriorly displaced
Airway	Subglottic narrowing; edema cords	Swollen epiglottitis, aryepiglottic folds	Subglottic narrowing; irregular trachea ± intraluminal mass	Prevertebral soft-tissue mass with anterior displacement of airway (not valid sign if expiratory film, flexed neck)
Chest	Underaerated ± cardiomegaly	Underaerated ± cardiomegaly	Patchy parenchymal peribronchial infiltrate	Underaerated ± cardiomegaly
ENDOSCOPY	Red, edematous subglottis; crusting pseudomembrane	Red, edematous supraglottic structures	Red, edematous, eroded trachea and bronchi; purulence, pseudomembrane	Bulging mass in posterior pharyngeal wall; purulence
CAUSE	Parainfluenza viruses (epidemic); other viruses (sporadic)	*Streptococcus pyogenes, Streptococcus pneumoniae, Haemophilus influenzae* b	*Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae*	*Streptococcus pyogenes; Staphylococcus aureus;* rare *Streptococcus pneumoniae*

[a]*Superscript numbers indicate references.*

TABLE 21-5. Expected Course and Sequelae of Acute Infectious Upper-Airway Obstruction

	Viral Laryngotracheitis	Supraglottitis, Epiglottitis	Bacterial Tracheitis	Retropharyngeal Abscess
Artificial airway (% of cases)	<20	>90	>75	≥75
Median intubation period	4 days	2 days	6 days	2 days
Airway occlusion after intubation	Rare	No	Yes	No
Death during hospitalization	No	No	Yes	No
Airway sequelae (% of cases)	<3	Rare	<3	No

with bacterial tracheitis can be further complicated, because infection (and obstructive consequences) commonly extends the length of the trachea and below.

COUGH

Characteristics

Cough is a critical protective mechanism to expel particulate matter from the larynx and trachea as well as a cardinal sign of infectious and noninfectious respiratory tract and nonrespiratory tract disorders. Occasional acute life-threatening infectious and noninfectious causes may be overlooked unless the clinician adopts a disciplined approach. Careful assessment of a pathologic cough – its onset, duration, clinical context, and association with other findings as well as its specific timbre, pattern, and productivity – frequently predicts the site of pathophysiology and narrows the differential diagnosis to a limited number of entities. Cough usually is defined as acute (<3 weeks), subacute (3–8 weeks), or chronic (>8 weeks). A "wet" or "moist" cough in children, frequently referred to as *productive* (although young children rarely expectorate), is associated with detectable secretions by bronchoscopy and can be reported accurately by parents and clinicians.[47]

Etiology

A dry cough is expected in allergic rhinitis/sinusitis or asthma while a wet cough is typical in infectious sinusitis, bronchitis, bronchiectasis, and pneumonia. The vast majority of coughs are related to self-limited viral upper respiratory tract illness (URI), with up to 40% of school-aged children still coughing 10 days after onset of a common cold, and 10% of preschool-aged

children coughing 25 days after a URI.[48] Isolated subacute cough (in absence of other symptoms), which usually is dry and follows viral infection, frequently is related to increased cough receptor sensitivity.[49] Chronic cough is pathologic. Differential diagnosis also can be focused by age, history, and clinical findings; algorithm for sequential evaluation and management is specific and sometimes complex[50] – best performed by a pediatric pulmonologist. Most common causes of chronic cough evaluated in older (mean 8–9 years) U.S.[51] and Turkish[52] children were: allergic or nonallergic rhinitis and sinusitis, asthma, protracted bacterial bronchitis, and gastroesophageal reflux disease. An important minority of children have cystic fibrosis, non-CF bronchiectasis, or ciliary dyskinesia syndrome. The focus of management is etiology. No evidence supports the use of medications aimed at symptomatic relief of acute or chronic cough and some data suggest potential harmful effects.

Cough should not be accepted as a sign of self-limited URI in infants younger than 3 months. The mnemonic CRADLE may be useful to call to mind important considerations for such patients:[53] *C,* cystic fibrosis; *R,* respiratory tract infections (especially pneumonia and pertussis); *A,* aspiration (swallowing dysfunction, gastroesophageal reflux, tracheoesophageal fistula); *D,* dyskinesia of cilia; *L,* lung, vascular, or airway malformations; *E,* edema (heart failure, pulmonary lymphangiectasia).

Table 21-6 provides a framework for consideration of cough illnesses. Comments on certain infections follow. There is

TABLE 21-6. Differentiating among Causes of Cough

	Peak Age	Nature of Cough	Cough Dominant Feature?	Anticipated/Associated Findings
INFECTIONS OF THE RESPIRATORY TRACT				
Viral laryngotracheitis	>5 years	Brassy, painful	Yes	Hoarse, raspy voice; viral URI complex[a]
Viral laryngotracheitis/ laryngotracheobronchitis	4 months–3 years	Barking, brassy	Codominant with stridor	Stridor, hoarseness, viral URI complex[a]
Mycoplasmal tracheobronchitis	Adolescent	Hacking, paroxysmal, painful	Yes	Prodromal, fever, headache, myalgia; then gradual worsening cough
Pertussis	Infancy, adolescence	Sudden paroxysm of explosive machine-gun bursts (15–30 per breath)	Yes	Bulging, watering eyes during paroxysm, posttussive emesis; skin and conjunctival hemorrhages; afebrile, without lower respiratory tract symptoms or symptoms between paroxysms
Chlamydia trachomatis pneumonia	1–3 months	Staccato, dry (single cough per breath)	Yes	History can include conjunctivitis; afebrile, tachypnea, rales
Bronchiolitis	4 months–2 years	High-pitched or grunt	No	Wheezing, rhinorrhea, respiratory distress; ± fever
Pneumonia (bacterial or viral)	Any	Wet, productive or nonproductive	Codominant with respiratory distress	Tachypnea, rales, respiratory distress; fever
Pleurodynia	Any	Inspiratory hitch; expiratory grunt	Codominant with chest pain	Chest pain; costochondral tenderness
Sinusitis	Any	Irritative; occurs in day and worsens at night	Sometimes	Mucopurulent rhinorrhea, postnasal discharge; facial pain, swelling, or tenderness; headache; ± fever
Tracheoesophagitis (fungal or viral)	Any	Irritative	No	Odynophagia or dysphagia; immune-compromised host; hoarseness; oropharyngeal lesions
Cystic fibrosis	<2 years; any	Wet, productive; paroxysmal, hacking	Sometimes	Poor growth; persistent and recurrent sinusitis, pneumonia; digital clubbing
Protracted bacterial bronchitis	Any, mean 8–9 years	Wet, productive; >8 weeks	Yes	Bronchoscopy; neutrophils, bacteria, cytokines; response to antibiotic
OTHER CONDITIONS				
Purulent pericarditis	Any	Grunt	Sometimes	Fever, toxicity, respiratory distress/dyspnea; displaced point of maximum impulse; muffled heart sounds
Myocarditis	Any	Grunt	Sometimes	Fatigue, dyspnea, tachypnea; ± fever
Congestive heart failure	Any	Grunt, wet, or brassy	Sometimes	Fatigue, dyspnea, sweating, tachycardia, tachypnea; ± fever; distended neck veins, liver
NONINFECTIOUS AIRWAY ABNORMALITIES				
Gastroesophageal reflux	6 weeks–6 months	High-pitched, dry	Codominant with other symptoms	Stridor, choking, gagging, irritability, arching (Sandifer syndrome) ± regurgitation, pneumonia
Reactive airway, asthma	6 months–adolescence	Irritative dry, repetitive (not paroxysmal); night especially	Sometimes	Atopic, precipitants, seasonal; ± wheezing; response to β-agonist
Congenital vascular rings, pulmonary sling	Infancy	Brassy	No	Stridor; onset of symptoms in first month of life
Compression on airway or glossopharyngeal or phrenic nerve	Any	Irritative, dry	Sometimes initially	Can be positional (tumors, other masses), associated with other neuropathies, stridor, changes in phonation
Habit cough	Adolescence	Vibratory, low-pitched, honking; disappears with sleep	Yes, sole feature	"La belle indifference"; family dynamics and other somatization

[a]*Viral upper respiratory tract infection (URI) complex consists of fever, rhinorrhea, sore throat, conjunctivitis, exanthem, enanthem.*

considerable overlap in symptomatology of cough caused by certain infectious agents, such as *Bordetella pertussis* or *Mycoplasma pneumoniae* in adolescents,[54] because of a common tracheobronchial site of pathophysiology and frequent dual infection by microbes.[55] *B. pertussis* causes a dramatic, debilitating paroxysmal cough without airway or lower tract abnormalities (unless secondary pneumonia occurs, leading to fever and toxicity), whereas *C. trachomatis* causes pneumonia with prominent tachypnea: the cough is only important because it brings the child to medical attention (see Chapter 162, *Bordetella pertussis* (Pertussis) and Other *Bordetella* Species; Chapter 167, *Chlamydia trachomatis*). Diagnosis of pneumonia is based on signs of lower respiratory tract involvement, such as tachypnea and retractions, in addition to cough, and the likely causative agent is determined from the constellation of clinical findings (Tables 21-7 and 21-8).

Protracted bacterial bronchitis is inadequately studied but may be an underdiagnosed cause of chronic wet cough, or misdiagnosed as asthma.[56] Diagnosis rests on clinical bronchoscopy findings, i.e., presence of dense bacteria and neutrophilic acute inflammatory response,[57] normal imaging of the chest, and response to antimicrobial therapy. Commonly implicated organisms are *Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis*. In attempts to avoid bronchoscopy, some pulmonologists prescribe a trial of amoxicillin-clavulanate (14:1 formulation) for 2 weeks in patients with typical isolated episode of chronic cough.

TABLE 21-7. Symptoms and Signs of Pneumonia

Symptoms	Signs	Physical Examinations
Fever	Fever	Rales
Cough	Cough	Wheezes
Rapid breathing	Tachypnea	Diminished breath sounds
Difficulty breathing	Dyspnea	Tubular breath sounds
Vomiting	Retractions	Dullness to percussion
Poor feeding	Nasal flaring	Decreased tactile and vocal fremitus
Irritability	Grunting	Meningismus
Lethargy	Splinting	Ileus
Chest pain	Apnea	Pleural friction rub
Abdominal pain		
Shoulder pain		

TACHYPNEA AND OTHER SIGNS OF LOWER RESPIRATORY TRACT DISORDERS

Tachypnea can be a voluntary or involuntary response to anxiety, fright, or pain; an abnormal breathing pattern related to central nervous system dysfunction; or the physiologic response to increased temperature or metabolic state. It is most usually the response to respiratory acidosis or hypoxemia of acute infection or the attempt to restore pH balance during metabolic acidosis (e.g., diabetes, salicylate poisoning, dehydration). Metabolic causes should not be forgotten, while the clinician pursues the

TABLE 21-8. Clinical Features of Pneumonia in Infants Younger than 3 Months

	Respiratory Syncytial Virus	Other Respiratory Viruses	*Chlamydia trachomatis*	Cytomegalovirus	Pertussis[a]
History					
Season	Winter	Unique to each	Any	Any	Any; peak July–October
Onset	Acute, days	Acute, days	Insidious	Insidious	Progressive, days
Illness in others	URI	URI, "flu," croup	No	No	Cough
Fever	Half of cases	Majority of cases	No	Unusual	No
Cough	Yes	Yes	Yes/staccato	Yes	Yes/paroxysmal
Associated features	Apnea, URI	URI, croup, conjunctivitis	Conjunctivitis (prior or current)	Failure to thrive, hepatosplenomegaly	Apnea, cyanosis, posttussive vomiting
Physical examination					
Predominant feature	Respiratory distress	Respiratory distress	Cough	Failure to thrive	Cough
General appearance	Ill, not toxic	Ill, not toxic	Well, tachypneic	Chronically ill	Well between paroxysms
Degree of illness: respiratory findings	Degree of illness = findings	Degree of illness = findings	Findings > degree of illness	Ill general appearance > respiratory illness	Ill only during cough
Auscultation	Wheezes, coarse crackles	Crackles, wheezes	Diffuse crackles	Crackles, ± wheezes	Clear
Laboratory studies					
Chest radiograph	Hyperaeration, sub-segmental atelectasis	Hyperaeration, ± peribronchial thickening, ± diffuse interstitial infiltrates	Hyperaeration, diffuse alveolar and interstitial infiltrates	Diffuse interstitial infiltrates	Normal or perihilar infiltrate
White blood cell count	Normal or lymphocytosis	Normal, lymphocytosis, neutropenia	Eosinophilia	Normal, eosinophilia, lymphocytosis neutropenia	Lymphocytosis; eosinophilia unusual
Other findings	Hypoxemia		Increases in IgG, IgA, IgM	Increases in IgG, IgA, IgM; thrombocytopenia	
Diagnostic tests	Nasal wash EIA, DFA, PCR, culture	Nasal wash EIA, DFA, PCR, culture	Conjunctival, NP DFA, EIA	Throat, bronchoscopy, lung biopsy, or urine culture	NP DFA, culture, PCR

DFA, direct fluorescent antibody (test); EIA, enzyme immunoassay; Ig, immunoglobulin; NP, nasopharyngeal specimen; PCR, polymerase chain reaction; URI, upper respiratory tract infection.

[a]*Pertussis is included in this table because it should be considered in young infants with cough and respiratory distress, although pneumonia is characteristically absent.*

much more likely primary pulmonary causes. Additionally, tachypnea can result from primary cardiac abnormalities (congestive heart failure, cyanotic congenital heart disease), pulmonary vascular abnormalities (cardiac shunts, capillary dilatation, hemorrhage, obstructed return to the heart, or infarction), impaired lymphatic flow (congenital lymphangiectasia, tumor), or pleural fluid collections (hemorrhagic, purulent, transudative, or lymphatic fluid or a misplaced infusion from a vascular catheter).

Clinical practice guidelines for management of community-associated pneumonia in infants and children have been published from the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America, and include excellent literature review of clinical findings.[58] Table 21-7 shows symptoms and signs of pneumonia in infants and children. Tachypnea is thought to be the best clinical predictor of lower respiratory tract infection in children. The World Health Organization defines pneumonia primarily as cough or difficult breathing and tachypnea, which definition is age-related: respiratory rate (RR) in breaths/minute >60 in infants 0–2 months of age, >50 in infants 2 to 12 months, >40 in children 1 to 5 years, and >20 in children >5 years of age.[59] Tachypnea has sensitivity of 50% to 85% for diagnosis of lower respiratory tract infection with specificity of 70% to 97%.[60,61] The younger the patient under 24 months of age, the less likely that pneumonia is present if tachypnea is absent. In one study, for infants younger than 2 months, respiratory rate of 60 breaths/minute, retractions, or nasal flaring had sensitivity for diagnosis of pneumonia of 91%.[61] Tachypnea also can be a response to fever, dehydration, or metabolic acidosis. In a study from a U.S. emergency department of children younger than 5 years of age who were undergoing chest radiography for possible pneumonia, respiratory rates in those with and without documented pneumonia did not differ significantly. However, 20% of those with WHO-defined tachypnea had pneumonia confirmed compared with 12% in those who did not.[62] Performance of a chest radiograph in febrile infants without an apparent focus of infection to exclude pneumonia "missed" by physical examination has low yield in the absence of tachypnea.[63,64] Cough is a more sensitive but nonspecific symptom of pneumonia. Other symptoms and signs associated with pneumonia, such as nasal flaring, intercostal retractions, and cyanosis, have less sensitivity (25%, 9%, and 9%, respectively) but high specificity (87%, 93%, and 94%, respectively).[60] Although fever, cough, and tachypnea are cardinal features, any or all of them can be overshadowed or overlooked in patients who come to medical attention for pneumonia-associated stiff neck, abdominal pain, or chest pain or for nonspecific symptoms of illness, such as feeding difficulty in infants. While chest radiograph is not necessary routinely in children with any of these complaints, it should be considered if the patient has fever and cough or tachypnea.[65,66] Classic symptoms of pneumonia reported in adolescents and adults are fever, chills, pleuritic chest pain, and cough productive of purulent sputum, with less noticeable tachypnea.[67]

Grunting is an expiratory sound produced in the larynx when vocal cords are adducted to generate positive end-expiratory pressure (self-induced PEEP) and increased resting volume of the lung. Its causes are myriad but never trivial. Grunting can be a sign of surfactant deficiency in the neonate, or of pulmonary edema, foreign-body aspiration, severe pneumonia, mediastinal mass or severe mediastinal shift from any cause, pleuritic or musculoskeletal chest pain, or myopericarditis or other cardiac abnormalities at any age.[68] Retractions (intercostal, subcostal, or suprasternal) and grunting have been associated with severe pneumonia; and nasal flaring and head bobbing with hypoxemia.

Adventitial respiratory sounds usually indicate lower respiratory tract disease, pulmonary edema, or hemorrhage. *Wheezes* are musical continuous sounds present predominantly on expiration and are a sign of airway obstruction. Widespread bronchiolar narrowing, as most commonly occurs with the inflammation of virus-associated lower respiratory tract infection, produces heterophonous high-pitched, sibilant wheezes of variable pitch and presence in different lung fields. Fixed obstruction in a larger airway, as from foreign body or anomaly, produces homophonous, monotonous wheeze. The rate of radiographically confirmed pneumonia among children with wheezing is low, <5% overall, and 2% in the absence of fever.[65] *Rhonchi*, sometimes also termed low-pitched wheezes, or coarse crackles, are nonrepetitive, nonmusical, low-pitched sounds frequently present on early inspiration and expiration; they are usually a sign of turbulent airflow through secretions in large airways. *Fine crackles* (the term preferred by pulmonologists for rales, which has a variety of meanings across languages) are high-pitched, low-amplitude, end-inspiratory, discontinuous popping sounds indicative of the opening of peripheral air–fluid interfaces. Fine crackle is the auscultatory finding suggestive of the diagnosis of pneumonia. Auscultatory abnormalities of crackles and wheezing have disparate diagnostic usefulness among various studies, depending on the categorization of bronchiolitis. Tachypnea is a more sensitive finding than crackles for bacterial pneumonia; wheezing is more sensitive than tachypnea for bronchiolitis.

Diminished or distant breath sounds, dullness to percussion, and decreased vocal fremitus indicate peripheral pulmonary consolidation, pleural mass, or fluid collection. *Tubular breath sounds* (low-pitched sound of similar intensity throughout inspiration and expiration, as normally heard in the intrascapular area), dullness to percussion, and increased vocal fremitus indicate parenchymal consolidation, atelectasis, or the presence of another continuous tissue or fluid density abutting both a bronchus and the chest wall.

Radiographic infiltrates have been reported in 5% to 19% of children with fever in the absence of symptoms or signs of lower respiratory tract infection.[69,70] Rate of pneumonia deemed as occult fell from 15% to 9% after universal vaccination with 7-valent pneumococcal conjugate vaccine (PCV7) in one study.[70] Clinical features associated with occult pneumonia in another study included presence of cough, fever greater than 5 days' duration, high fever (>39 °C) and leukocytosis >20,000 cells/mm^3; only 5% of children without cough had radiographically confirmed pneumonia.[69]

DIFFERENTIATING FEATURES OF PNEUMONIA

Pneumonia in Young Infants

In young infants, acute infection with bacterial and nonbacterial respiratory tract pathogens frequently leads to lower respiratory tract infection. Except in the first few days of life, when pneumonia is due predominantly to bacteria acquired from the mother's genital tract or to organisms acquired transplacentally, nonbacterial pathogens are overwhelmingly predominant.[68] As perinatally acquired agents persist, community exposures increase, and maternally derived antibody protection wanes, the infant between 3 weeks and 3 months old is vulnerable to a unique array of lower respiratory tract pathogens.[71] Clinical setting, specific symptom complex, and severity of illness in proportion to findings on physical examination aid distinction of likely causes and guide the diagnostic and therapeutic approach (see Table 21-8). Although the pathogens listed in Table 21-8 frequently are referred to as causing "afebrile pneumonia," this is a misnomer, because *Bordetella pertussis* infrequently causes lower respiratory tract abnormalities, and respiratory syncytial virus and especially other respiratory viruses frequently cause fever.[11,68,72,73] A causal role for *Ureaplasma urealyticum* is not completely defined, because the situation is confounded by the asymptomatic presence of this organism in women and young infants. Pneumonia due to *Pneumocystis jirovecii* probably is confined to infants with severe debilitation or immune defects.

Pneumonia in Older Infants, Children, and Adolescents

Table 21-9 categorizes the features of acute pneumonia in older infants, children, and adolescents by etiology. No single fact

TABLE 21-9. Clinical Features of Acute Pneumonia in Children and Adolescents

	Bacteria	Virus	Mycoplasma	Tuberculosis
HISTORY				
Age	Any; infants especially	Any	School age	Any; <4 years and 15–19 years especially
Temperature (°C)	Most ≥39	Most <39	Most <39	Most <39 (unless empyema)
Onset	Abrupt	Gradual	Worsening cough	Insidious cough
Others in home ill	No	Yes, concurrent; upper respiratory tract infection, rash, conjunctivitis	Yes, weeks apart; pharyngitis, "flu," cough	Yes, persistent cough
Associated signs, symptoms	Toxicity, rigors	Myalgia, rash, mucous membrane involvement	Headache, sore throat, chills, myalgia, rash, pharyngitis, myringitis	Weight loss, night sweats (late)
Cough	Wet, productive	Nonproductive	Hacking, paroxysmal, usually nonproductive	Irritative or productive
PHYSICAL EXAMINATION				
Predominant feature	Toxicity, respiratory distress	Respiratory distress	Cough	Persistent cough
Degree of illness: respiratory finding	Degree of illness > findings	Degree of illness ≥ findings	Degree of illness < findings	Well → no findings (± cough); ill → findings
Pleuritic chest pain	No/yes	No	No	No/occasional
Auscultation	Unilateral, anatomically confined or no crackles; dullness, diminished or tubular sounds	Diffuse, bilateral crackles, wheezes	Unilateral, anatomically confined crackles; ± wheezes	Most normal; or unilateral crackles ± dullness
LABORATORY STUDIES				
Chest radiograph	Hyperaeration, patchy alveolar infiltrate or consolidation in lobe, segment, subsegment	Hyperaeration, interstitial infiltrate in diffuse or perihilar distribution; "wandering" atelectasis	Patchy alveolar and/or interstitial infiltrate in single or contiguous, usually lower lobe(s), unilaterally; perihilar adenopathy	Patchy alveolar infiltrate in single or contiguous lobes with disproportionate hilar adenopathy; or miliary or lobar consolidation
Pleural fluid	No/yes → large	No/yes → small	No/yes → small	No/yes → small, large
Peripheral white blood cell count (cells per mm^3)	Majority >15,000; neutrophils ± bands	Majority <15,000; lymphocytes	Majority <15,000; neutrophils	Majority <15,000; neutrophils, monocytes
Sedimentation rate >40 mm/hour	Usual	Infrequent	Infrequent	Frequent
Sputum	Copious, purulent; neutrophils, abundant bacteria	Scant mucoid; epithelial, mononuclear cells	Scant mucoid; mixed mononuclear cells/ neutrophils	Scant → copious; neutrophils (if copious)
Diagnostic tests	Sputum Gram stain, culture; blood culture	Nasal wash, throat, bronchoscopy specimen for antigen detection, culture; acute and convalescent serology	Cold agglutinin; acute and convalescent specific serology; throat culture, antigen detection, DNA techniques	Gastric aspirate; sputum stain and culture

in history or finding on examination is unique for any agent, but when they are taken together, a working diagnosis emerges and guides intervention or further diagnostic testing. Chest radiography and laboratory tests usually are reserved for patients who are ill and hospitalized or whose clinical picture is not compelling for a category of etiologic agents. A number of studies using complex diagnostic methodologies have confirmed the specific cause of pneumonia in 45% to 85% of cases.[72–76] Viral etiologies predominate, and, currently, most are amenable to diagnosis.[72] The efficacy trial and postmarketing studies of PCV7 infers *Streptococcus pneumoniae* as a relatively common cause of pneumonia with patchy or consolidative infiltrates.[77,78] Urine antigen detection test in children with lobar pneumonia also supports the important role of *S. pneumoniae;*[79] however, the test is positive in >15% of children with asymptomatic colonization.[80] Testing for *Mycoplasma pneumoniae* using IgM enzyme immunoassay serologic test is problematic because of false-positive tests, and may be best utilized in school-aged children and adolescents with findings consistent with mycoplasma infection in those whose pretest probability is moderate or higher.[58,81] Currently, ascribing a causal role of pneumonia to *Chlamydophila pneumoniae* is confounded by the findings of prolonged asymptomatic carriage and inconsistent serologic results among studies.[82]

HEMOPTYSIS

Hemoptysis, defined as coughing up of blood that originated below the larynx, is uncommon in children; most commonly, supposed episodes are due to a posteriorly draining nosebleed. Mechanisms of hemoptysis include bleeding from: (1) congenital or acquired abnormal bronchial or pulmonary blood flow, venous obstruction, or vascular abnormalities; (2) immune-mediated endothelial damage; or (3) infectious or traumatic erosion of tracheal, bronchial, or bronchiolar epithelium. Hemorrhage can be mild (tracheitis, tracheobronchitis) or massive (congenital malformations, foreign body, bronchiectasis, pulmonary hemosiderosis). Causes of hemoptysis in children are listed in Table 21-10. Infection is

TABLE 21-10. Causes of Hemoptysis in Children

Epithelial Damage	Vascular Abnormality/Damage
Acute infection (bacterial and fungal)	Congenital heart disease or pulmonary vascular anomalies (venous obstruction, arteriovenous fistulae)
Bronchiectasis (cystic fibrosis, non-CF, immunodeficiency, retained foreign body)	Congenital malformation (pulmonary sequestration)
Trauma (airway or chest)	Autoimmune vasculitis (systemic lupus erythematosus, sarcoidosis, Wegener granulomatosis, inflammatory bowel disease, Goodpasture syndrome)
Foreign body	Sickle-cell disease
Tumor (primary airway or pulmonary, metastatic)	Pulmonary hemosiderosis
	Nonspecific endothelial damage (chemical, drug)

the most common cause of mild hemoptysis. Panton–Valentine leukocidin-producing *Staphylococcus aureus* pneumonia is specifically associated with hemoptysis.[83] Epstein–Barr virus was implicated in a single case.[84] For more severe hemoptysis, bronchiectasis associated with cystic fibrosis accounts for as many cases as all other causes combined.[85]

Rigid bronchoscopy, computed tomography, and magnetic resonance imaging are useful diagnostic modalities in most cases of hemoptysis. Digital subtraction angiography and, occasionally, cardiac catheterization or arteriography are required.

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