



NCC Pediatrics Continuity Clinic Curriculum: Chronic Cough

Goals & Objectives:

To understand the differential diagnosis and management of common causes of pediatric cough:

- List the common etiologies for chronic cough in children, differentiating between specific and non-specific cough and “wet” and “dry” cough.
- Understand the management of chronic, non-specific cough, including trials of therapy for cough-variant asthma and protracted bronchitis.
- Know the current recommendations and rationale behind OTC CCM restrictions.

Pre-Meeting Preparation:

Please read through the following:

- “Cough” (PIR, 2019)
- Cough physiology by Tong
- “Algorithm for the Evaluation of Chronic Cough in Children” (UpToDate, 2020)

Listen to a variety of pediatric coughs via YouTube or other platform

Conference Agenda:

- Review Chronic Cough Quiz
- Complete Chronic Cough Cases
- Round table: Present a case of chronic cough you have managed in clinic
- Share a recording of a pediatric cough and discuss its characteristics with the group

Post-Conference: Board Review Q&A

Extra-Credit:

- [“Managing Chronic Cough. . .CHEST Guideline and Expert Panel Report”](#) (CHEST, 2020)
- ["When the Cough Does Not Improve: A Review on Protracted Bacterial Bronchitis Children"](#) (Frontiers in Pediatrics, 2020)
- ["Otolaryngologic Management of Chronic Cough in School-aged Children"](#) (JAMA ENT, 2020)
- [Habit Cough Syndrome](#) (Miles Weinberger, M.D., University of Iowa SOM, YouTube video)
- ["Chronic Cough Revisited"](#) (J Pediatric Pulmonology, 2022) *2 page synopsis if you are short on time*
- ["Cough Conundrums: A Guide to Chronic Cough in the Pediatric Patient"](#) (PIR, Dec 2022)
- ["History Taking as a Diagnostic Tool in Children with Chronic Cough"](#) (Frontiers in Peds, 2022)
- ["Chronic Cough and Causes in Children"](#) (J. Clin Med, 2023)

Cough

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Practice Gaps

Cough in children is a common chief complaint. It is important to adopt a systematic approach to the evaluation and management of chronic cough and avoid symptomatic treatment. The use of pediatric-specific cough management algorithms improves clinical outcomes.

Objectives After completing this article, readers should be able to:

1. Distinguish between acute and chronic cough in children.
2. Identify cough characteristics and specific cough “pointers” requiring further evaluation.
3. Effectively begin management of nonspecific cough and suspected protracted bacterial bronchitis.
4. Identify children with cough who need evaluation by a specialist.

INTRODUCTION

Cough is a common reason for pediatric outpatient visits. Cough as a manifestation of respiratory disease can range from minor upper respiratory tract infections to serious conditions such as bronchiectasis. Acute cough in children is mostly caused by upper respiratory tract infections (URTIs). Chronic cough, defined as daily cough of at least 4 weeks in duration, (1) can be associated with an underlying serious disorder and, hence, requires systematic and thorough clinical evaluation. There is high-quality evidence that a systematic approach to the management of chronic cough in children using pediatric-specific cough algorithms improves clinical outcomes. (1) Treatment of cough should be based on the etiology. Because cough is a common presenting complaint, pediatricians must become familiar with the initial evaluation and management of children with cough to establish a diagnosis and determine appropriate therapy.

EPIDEMIOLOGY

Cough is one of the most common complaints presented at physician visits and accounts for an estimated 29.5 million annual outpatient visits. (2) The prevalence of chronic cough in children is estimated to be 5% to 10%. (3) In the United States, approximately 2 billion dollars per year is spent on over-the-counter (OTC) cough

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ABBREVIATIONS

BAL	bronchoalveolar lavage
CT	computed tomography
GERD	gastroesophageal reflux disease
ICS	inhaled corticosteroid
OTC	over-the-counter
PBB	protracted bacterial bronchitis
PCD	primary ciliary dyskinesia
URTI	upper respiratory tract infection

products. Additional costs in the management of cough include physician visits, laboratory and radiologic tests, prescription medications, school absence, and parental leave. (4) Chronic cough in children is associated with parental stress, increased physician visits, and disrupted sleep. (5)

PATHOPHYSIOLOGY OF COUGH

Cough is an important airway-protective reflex that involves “a forceful expulsion of air from the lungs that is under both voluntary and involuntary control.” (6)(7) Cough receptors are located in the epithelium of the pharynx, larynx, and tracheobronchial tree. Chemical irritants, mechanical stimuli, and inflammatory mediators stimulate cough receptors. When stimulated, afferent impulses are sent through the vagus nerve to the cough center in the brain stem and pons. The efferent limb includes the vagus, phrenic, and spinal motor nerves to the larynx, diaphragm, and other muscles of expiration.

Cough has three phases: 1) a deep inspiration, 2) closure of the glottis accompanied by relaxation of the diaphragm and contraction of the muscles of expiration, and 3) opening of the glottis. Intrathoracic pressure (up to 300 mm Hg in adults) can be generated during the second phase. Sudden opening of the glottis during the third phase of cough generates high air flow velocity, which helps clear airway debris. (6) In addition, cough improves mucociliary clearance in both healthy individuals and those with lung disease. (4)

An effective cough depends on intact receptors, as well as the afferent and efferent limbs of the cough pathway. Repeated stimulation of the cough receptors can lead to decreased sensitivity of the receptors. This can be seen in children with recurrent aspiration and gastroesophageal reflux (GERD). (6) Respiratory muscle weakness seen in neuromuscular diseases can also lead to inadequate cough, atelectasis, and pneumonia.

CLINICAL APPROACH

When evaluating children with respiratory symptoms, a detailed clinical history and thorough physical examination will guide diagnosis and management. Essential aspects in the history of a child presenting with cough include the nature of the cough, duration, aggravating and relieving factors, diurnal variation, and associated symptoms. Certain cough characteristics may point to the etiology of cough in children. A “brassy” or “barking” cough could suggest croup, tracheomalacia, or habit cough. “Paroxysmal” cough, especially with an inspiratory whoop, generally suggests *Bordetella pertussis* infection. It can also be caused by

Bordetella parapertussis, adenovirus, parainfluenza, respiratory syncytial virus, and mycoplasma. (8) “Staccato” cough in infants suggests infection with chlamydia. “Honking” cough can be seen in psychogenic cough. Cough productive of airway casts suggests plastic bronchitis. Plastic bronchitis is a rare condition in which bronchial casts lead to airway obstruction and respiratory distress in children with cardiac and respiratory diseases. The pathogenesis of airway cast formation remains unclear, and it has been attributed to abnormal pulmonary lymphatic vessels and drainage in children with cardiac disease or lymphatic anomalies. (6)

Pediatric cough can be classified in several ways based on 1) duration of symptoms (acute or chronic), 2) cough character (dry or wet), and 3) likelihood of identifying an etiology for cough (specific or nonspecific).

Based on duration of symptoms, cough can be classified as acute or chronic (lasting >4 weeks). (9) Young children rarely expectorate sputum, so it is important to determine whether the cough is dry or wet. Characterizing the cough as dry or wet aids in following pediatric-specific cough algorithms for evaluation and management. Specific cough is associated with clinical features suggestive of an underlying etiology, whereas nonspecific cough is not associated with any identifiable respiratory disease or known etiology after a thorough clinical assessment. (8)(9)

A thorough physical examination should be performed in children with cough. Height and weight should be recorded to assess for failure to thrive. Inspection of the nose and throat may reveal signs of allergic rhinitis or postnasal drip. The ears should be examined because impacted wax or foreign bodies in the external auditory meatus can be associated with chronic cough in some children via stimulation of the Arnold nerve (a branch of vagus nerve) reflex. (6)(7) The chest wall should be inspected for any deformity. The chest should be auscultated to assess the nature, quality, and symmetry of air entry along with any abnormal breath sounds, such as wheezes or crackles. The fingers should be examined for the presence of clubbing. If the child coughs during the examination or is capable of coughing on request, the character of cough should be assessed, and the chest wall should be palpated for vibrations due to retained airway secretions. (7)(10) Neurologic examination with assessment of muscle tone can help identify children with neurologic impairment or neuromuscular disease who are at risk for developing aspiration lung disease.

ACUTE COUGH

Acute cough has been defined as cough of less than 2 weeks in duration. (8) Viral URTIs are the most common cause of

acute cough in children. (10) However, children with acute cough should be assessed for signs and symptoms of a more serious pathologic condition, such as **inhaled foreign body or lower respiratory tract infection.** (8)(10) **Lower respiratory tract infection should be suspected in children with acute cough, fever, tachypnea, or crackles.** Acute cough can be the initial manifestation of a chronic respiratory disease. Hence, children with acute cough should be evaluated for failure to thrive, digital clubbing, or chest deformity suggesting an underlying chronic respiratory disease. (11) A typical history of aspirating a foreign body may not be evident in all cases, thus **sudden onset of cough or dyspnea** should prompt the clinician to **consider foreign body aspiration.** (10) **A normal chest radiograph does not exclude foreign body aspiration; hence, bronchoscopy is indicated when there is a suspicion for an aspirated foreign body.** (11)

Healthy children experience URTIs several times a year. (9)(10) Cough caused by **URTI** generally resolves within 1 to 3 weeks in children. A prospective cohort study of acute cough in preschool-aged children presenting to primary care showed that **50% of children had recovered in 10 days** but that **10% of children were symptomatic with cough at 25 days.** (12) In most children, acute cough caused by viral URTIs is self-limiting and requires only supportive treatment, such as antipyretics for fever (to comfort the child), and adequate intake of liquids. **A recent Cochrane review reports no good evidence for the effectiveness of OTC medicines in acute cough.** (13) Clinicians should counsel parents about the **potential harm of using OTC** cough medications in children. **Antibiotics are not beneficial** in acute cough due to viral URTIs, and **bronchodilators confer no benefit in acute cough in children without asthma.** (8)(11) Parents must be **counseled about the natural history** of cough due to URTIs and **warning signs (eg, tachypnea, persistent fever, progressive cough) requiring further evaluation** to avoid subsequent office visits for a subsiding cough. (11)

In recent years, there has been an increased interest in using honey for the treatment of acute cough in children. A **Cochrane review** evaluated the effectiveness of honey for acute cough in children and reported that **honey may be better than no treatment**, diphenhydramine, and placebo for the symptomatic relief of cough. The authors concluded that **“there is no strong evidence for or against using honey.”** (14) Clinicians should caution parents about the use of honey in **infants** due to the **risk of botulism.** (15)

Some **indications for performing a chest radiograph** in a child with acute cough are 1) uncertain diagnosis of lower respiratory tract infection in a child with persistent fever, tachypnea, or crackles; 2) suspected foreign body aspiration;

and 3) an atypical clinical course with progressively worsening cough or hemoptysis. (11)

CHRONIC COUGH

In children 14 years and younger, “chronic cough is defined as the presence of daily cough for at least 4 weeks in duration.” (1)(9) This definition is based on the natural history of resolution of cough after URTI in children. Cough lasting for at least 4 weeks warrants careful assessment because it **may suggest a serious underlying condition** in which early diagnosis (eg, airway foreign body leading to bronchiectasis) would improve outcomes. (1)(9) There is high-quality evidence that using pediatric-specific chronic cough algorithms improves clinical outcomes in children. (1)(16)(17)(18) In evaluating children (age ≤ 14 years) with chronic cough, we encourage readers to refer to the **American College of Chest Physicians’ evidence-based clinical practice guidelines** (9) and the CHEST Guideline and Expert Panel Report on the use of management algorithms, (1) which guide the discussion herein. **The evaluation of children with chronic cough should include a thorough history, physical examination, chest radiography, and, when age-appropriate, spirometry.** Collectively, cough “pointers” are diagnostic clues that may identify an underlying etiology for a chronic cough (Table 1). The presence of these pointers classifies chronic cough as specific (likely to have an identifiable etiology) or nonspecific (unlikely to have an identifiable etiology) and guides evaluation and management.

SPECIFIC COUGH

In children with chronic cough, clinicians should assess for symptoms and signs that are suggestive of an underlying disease (whether respiratory or systemic), termed *specific cough pointers* (Table 1). Specific cough pointers suggest that cough is due to an underlying disorder, and further diagnostic evaluation is indicated, often in conjunction with a pediatric pulmonologist. (8)(9)(19) **Some specific cough pointers include chest pain, dyspnea, digital clubbing, feeding problems, failure to thrive, and abnormal pulmonary auscultation.** Diagnoses such as structural airway abnormalities, aspiration lung disease, bronchiectasis, and interstitial lung disease are associated with chronic specific cough (Table 2).

The cough characteristics should be elicited from parents because this may point to the etiology of cough. **A wet or productive cough indicates the presence of excessive airway mucus.** Even when sputum is present, young children rarely expectorate airway secretions. (20) Daily wet cough is a useful clinical marker in predicting a specific cause of

TABLE 1. Specific Cough Pointers (1)(8)(9)

HISTORY	EXAMINATION
Abnormal cough characteristics (eg, brassy, barking, staccato, paroxysmal cough)	Abnormal breath sounds
Cardiac abnormalities	Abnormal cardiac examination
Chest pain	Chest wall deformity
Cyanosis	Digital clubbing
Daily wet or productive cough	Failure to thrive
Dyspnea, including exertional dyspnea	Hypoxemia
Feeding problems	Tachypnea
Fever	TESTS
Foreign body aspiration	Abnormal chest radiograph
Hemoptysis	Abnormal spirometry
History of previous lung disease	
Immune deficiency	
Medication (angiotensin-converting enzyme inhibitors) or illicit drug use	
Neurodevelopmental problems	
Pertussis or tuberculosis exposure, or risk factors	
Recurrent pneumonia	

cough. (19) A daily wet cough can be seen in suppurative lung disease from a variety of etiologies, including cystic fibrosis, primary ciliary dyskinesia (PCD), or other causes of bronchiectasis.

Evaluation of chronic cough should include a discussion about the presence of dyspnea. If there is no report of dyspnea at rest, the parent/child should also be asked about exertional dyspnea. Exercise is a common trigger for cough and wheezing in children with hyperactive airways. (6) Although exertional dyspnea can be associated with asthma, it may also suggest airway or parenchymal lung disease requiring further evaluation. If there is associated chest pain, further details regarding the characteristics of the chest pain should be obtained. If the child has ever had hemoptysis, the clinician should evaluate for tuberculosis, an inhaled foreign body, suppurative lung disease, or vascular abnormalities. A history of cardiac abnormalities can be important, as congenital heart disease can be associated with structural airway abnormalities (eg, airway malacia) and anatomical compression. (21) Children with congenital heart disease can develop cough from congestive cardiac failure with pulmonary edema or from respiratory ciliary dysfunction due to underlying PCD. Expectoration of airway

casts in a child with congenital heart disease suggests plastic bronchitis that requires evaluation by a pediatric cardiologist and pulmonologist. Recurrent pneumonia can be due to immunodeficiency, suppurative lung disease, congenital lung abnormalities, tracheoesophageal fistula, and other conditions. A detailed feeding history should be obtained in children with chronic cough. An episode of choking or acute onset of cough in a child should raise concern for an inhaled foreign body. Cough or choking during feeding should alert the physician to possible recurrent, small-volume pulmonary aspiration. The neurodevelopmental history should be reviewed because aspiration lung disease can be seen in children with developmental delays. In the birth history, prematurity and prolonged oxygen requirement suggest bronchopulmonary dysplasia, which can cause persistent respiratory symptoms in children. A diagnosis of PCD must be considered when there is a history of neonatal respiratory distress, tachypnea, or a supplemental oxygen requirement in a term infant. (22) Family history should be reviewed for asthma and other chronic respiratory conditions, such as cystic fibrosis or PCD. The social history should assess for environmental factors that can cause cough, such as tobacco smoke exposure, indoor pollutants,

TABLE 2. Causes of Cough in Children (6)(9)(11)

Acute (<2 wk)
Upper and lower respiratory tract infections
Viruses
Mycoplasma
Other bacteria
Foreign body aspiration
Chronic (≥4 wk)
Pulmonary causes ^a
Asthma
Bronchiectasis, chronic suppurative lung disease
Cystic fibrosis
Eosinophilic lung disease
Foreign body aspiration
Illicit drugs
Immunodeficiency (with recurrent infection)
Interstitial lung disease
Irritative/noninfective bronchitis (eg, smoke, pollution)
Pertussis
Primary ciliary dyskinesia
Protracted bacterial bronchitis
Recurrent aspiration (laryngeal cleft, tracheoesophageal fistula, swallowing dysfunction)
Structural airway abnormalities
Tuberculosis and other chronic infections
Extrapulmonary causes
Cardiac disease
Habit cough
Gastroesophageal reflux (controversial)
Mediastinal mass
Medications (eg, angiotensin-converting enzyme inhibitors)
Otogenic cough

^aThis is not a comprehensive list because almost any airway or parenchymal lung disease can cause chronic cough.

or allergens. The medication history should be reviewed because children taking angiotensin-converting enzyme inhibitors can develop chronic cough as an adverse effect. Tuberculosis is a common cause of chronic cough in children from countries where tuberculosis is endemic. Hence,

the history should include recent travel or immigration from endemic countries, exposure to individuals with tuberculosis, and other risk factors. Failure to thrive or digital clubbing in a child with chronic cough can be due to cystic fibrosis or other chronic pulmonary diseases. Abnormal auscultatory findings such as wheezing or crackles suggest specific causes of cough. Wheezing may indicate asthma or intrathoracic airway lesions (eg, tracheomalacia), and crackles can be heard in suppurative lung disease or interstitial lung disease. Monophonic wheezing can be auscultated in large airway obstruction from an aspirated foreign body, airway malacia, or compression (eg, enlarged lymph node).

Even if the child is fully immunized, pertussis should be suspected in a child with spasmodic cough, with posttussive emesis, or when there has been contact with an individual with pertussis infection. The appropriate diagnostic test in a child with suspected pertussis depends on the child's age and duration of symptoms. (1) Readers are referred to the American Academy of Pediatrics' Red Book for additional guidance regarding testing and management of pertussis. (23)

Although cough can be a symptom of asthma, most children with isolated cough do not have asthma. (9) Children with asthma generally have recurrent (and variable) symptoms, airflow obstruction with bronchial hyperresponsiveness, and airway inflammation. Readers are referred to the National Heart, Lung, and Blood Institute guidelines for the diagnosis and management of asthma. (24)

Children with specific cough pointers require further evaluation, often in conjunction with a pediatric pulmonologist. Children with chronic wet cough should be promptly evaluated, and early consultation with a pediatric pulmonologist should be considered. (19) Evaluations conducted by pediatric pulmonologists in children with chronic wet cough to identify the etiology often include chest imaging, comprehensive pulmonary function tests, bronchoscopy, sweat chloride testing for cystic fibrosis, a videofluoroscopic swallow study, a ciliary biopsy with electron microscopy (for PCD), and immunologic function tests. (9) In summary, the diagnostic evaluation of chronic specific cough is guided by the clinical findings identified from the specific cough pointers (Table 1). The particulars of these evaluations are not discussed in this review.

NONSPECIFIC COUGH

Nonspecific cough is chronic cough in the absence of specific cough pointers, with normal findings on spirometry (if age-appropriate) and chest radiography. Nonspecific

TABLE 3. Approach to Chronic Cough in Children 14 Years and Younger (1)(9)

1. Is cough present daily for ≥ 4 weeks?
2. A. Thorough history and physical examination, particularly focusing on:
- Cough characteristics (eg, brassy, barking, staccato, paroxysmal cough)
- Specific cough pointers (Table 1)
- Effect of cough on the child and the family
2. B. Spirometry (for patients aged >3 –6 y) and chest radiography
3. If specific cough pointers are present, proceed with appropriate evaluation (eg, pertussis testing when suspected) or referral to a pediatric pulmonologist
4. Nonspecific cough with normal spirometry (when feasible) and normal chest radiograph:
- Evaluate exposures (eg, smoke, pollutants) and intervene (eg, tobacco cessation)
- Watchful waiting for 2 weeks
- If persistent, consider an empirical trial of therapy based on presumed diagnosis (eg, inhaled corticosteroids for dry cough or antibiotics for suspected protracted bacterial bronchitis)
- Follow up in 2–4 weeks to assess response, discontinue therapy to confirm/refute presumed diagnosis, and refer to a pediatric pulmonologist if persistent/recurrent

cough is typically a dry cough for which no underlying etiology is identifiable after a thorough assessment. In most children, nonspecific cough is due to a viral respiratory infection (postviral cough) that resolves spontaneously with time and is not due to a serious etiology. (9) Some children can have a slow recovery of the airway epithelial mucosal cells and hypersensitivity of the cough receptors after a respiratory infection causing prolonged cough. (7)

For most children with nonspecific cough, the initial recommended step is a period of watchful waiting for 1 to 2 weeks (Table 3). The parents can be reassured, and the child can be reevaluated in 2 weeks. At follow-up, the child must be assessed for persistent cough and evaluated for emergence of any specific cough pointers. (9)

If cough persists at follow-up, clinicians can discuss the options with parents: 1) continued watchful waiting and reassessment in 2 weeks or 2) a trial of therapy. If the parents opt for watchful waiting, children must be evaluated in the subsequent 2 weeks for resolution of cough, and a trial of therapy should be considered if cough persists. At this point, it is important to distinguish between nonspecific dry cough and wet cough.

For nonspecific dry cough, asthma can be a cause, particularly if the child has other atopic features (eczema, allergic rhinitis) and a family history of asthma. Some children with asthma can have cough as the predominant symptom. (7) However, unless wheezing and dyspnea are also present, few children with isolated nonspecific cough

have asthma. (10) An empirical trial of a bronchodilator (short-acting β_2 agonist) and a low-dose inhaled corticosteroid (ICS) can be administered when asthma is suspected. (1)(9) It can be difficult to exclude asthma as a cause of chronic dry cough in young children who are unable to perform reliable spirometry, and it may be challenging to identify exertional dyspnea and chest discomfort in young children. A randomized, placebo-controlled trial of inhaled albuterol and ICSs in children with isolated cough showed no benefit of these therapies compared with placebo. (25) Therefore, it is important that trials of asthma therapy are effectively administered (using a spacer with a metered-dose inhaler), are given over a predefined time frame (2–4 weeks), and have concrete therapy end points. (9)(11) If an empirical trial of therapy is pursued, the child should be reassessed in 2 to 4 weeks. If the cough does not improve with a daily low-dose ICS in 2 to 4 weeks, the dose should not be increased, and the medication should be stopped. At follow-up, if cough resolved with an empirical trial of asthma therapies, this can suggest underlying asthma or spontaneous resolution of cough (the period effect). Hence, to confirm the diagnosis, a trial off the medication should be performed. If cough recurs, the asthma therapies should be resumed. At each follow-up visit, the clinician should review specific cough pointers, as well as evaluate tobacco smoke exposure, other pollutant exposure, parental expectations, and evidence of any underlying illness. When the clinical diagnosis of asthma in young children is

challenging, or if there is uncertainty in the diagnosis of asthma, consider evaluation by a pediatric pulmonologist. (10)

For nonspecific isolated wet cough, a diagnosis of protracted bacterial bronchitis (PBB) should be considered if there are no other symptoms and signs. PBB is a common cause of isolated chronic wet cough in children, and it is often misdiagnosed as asthma. (26) Bronchitis refers to inflammation of the bronchus or bronchi. (6) PBB-like conditions were reported in the past few decades; however, its existence was initially controversial. In the early 1980s, a single-center retrospective review of 20 children who underwent bronchoscopy and were diagnosed as having chronic bronchitis showed that these children had bronchoscopic features of airway inflammation, purulent airway secretions, mainly *Haemophilus influenzae* on bacterial culture, and most had clinical improvement after treatment with antibiotics. (27) In the early 2000s, a prospective cohort study of children with chronic cough showed that most of the children had wet cough, increased neutrophils in the bronchoalveolar lavage (BAL) fluid, and a positive BAL bacterial culture and that the cough resolved after treatment with antibiotics. In this study, PBB was the most common diagnosis for chronic cough in children. (28) PBB is recognized as a common cause of chronic wet cough in children and has been incorporated into several pediatric chronic cough management guidelines. (9)(11)(26)(29)(30)

PBB can be diagnosed clinically when all 3 of the following criteria are met: 1) the presence of chronic (>4 weeks) wet or productive cough, 2) the absence of specific cough pointers (ie, symptoms or signs that could suggest other causes of wet or productive cough), and 3) resolution of cough after a 2- to 4-week course of an appropriate oral antibiotic (usually amoxicillin-clavulanate). (26)(29) PBB can be seen in infants, young children, and adolescents. Children with PBB generally appear well, have normal growth, and do not have adventitious breath sounds, digital clubbing, or other signs of suppurative lung disease. Auscultation of the lungs may reveal a rattling sound suggestive of airway secretions. (20) The chest radiograph is normal or may show peribronchial changes, and spirometry (when feasible) is normal. (29) PBB is associated with a persistent bacterial infection and neutrophilic inflammation in the airways that leads to increased mucus production, airway inflammation, and chronic cough. PBB has been speculated as a potential prebronchiectasis state in some children with chronic wet cough. (20) If the child can expectorate, a sputum culture should be performed. If flexible bronchoscopy and BAL are performed, mucopurulent secretions are

noted in the airways, and airway malacia (tracheobronchomalacia) can be seen. (29) Bacteria commonly identified from the BAL or sputum in children with PBB are *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*. There is high-quality evidence in children with chronic wet/productive cough (without specific cough pointers) that using appropriate oral antibiotics improves cough resolution. (30) PBB is treated with a prolonged (2-week) course of antibiotics, typically amoxicillin-clavulanate. Amoxicillin-clavulanate is widely used because it is effective against common pathogens identified in PBB. Other antibiotics, such as oral cephalosporins, trimethoprim-sulfamethoxazole, or macrolides, may be used. (29) If the wet cough persists despite 2 weeks of antibiotics, an additional 2 weeks of antibiotics can be prescribed to complete a total of 4 weeks of therapy. Biofilms produced by bacteria are speculated to be a reason for prolonged antibiotic courses in the treatment of PBB. (26) A study reported increased likelihood of bronchiectasis on chest computed tomographic (CT) scan in children with chronic wet cough that failed to resolve despite 4 weeks of oral antibiotic therapy. (31) Recurrent PBB has been suggested as a risk factor for developing chronic suppurative lung disease (clinical symptoms of bronchiectasis without CT findings of bronchiectasis) or bronchiectasis. (26) Therefore, if chronic wet cough fails to respond to or recurs despite 4 weeks of antibiotic therapy, clinicians should refer the child to a pediatric pulmonologist for evaluation.

Habit cough is characterized by loud, repetitive cough, often described as having a honking or barking quality. Habit cough can occur in both children and adolescents, can last from weeks to months, and is commonly misdiagnosed as asthma. (32) Cough is characteristically absent during sleep. (33) Physical examination findings are normal other than cough, and no organic cause is identified after investigations are performed. A preceding viral respiratory infection is often suggested as an inciting factor. (32) Before arriving at a diagnosis of habit cough, many children may have received medications such as bronchodilators, ICSs, antibiotics, montelukast, or reflux medicines. Tic disorders must be considered when children have vocal (cough tics) and motor tics. Suggestion therapy, generally using a distractor such as sipping warm water along with resisting the urge to cough, has been successful in treating habit cough. (32) Hypnosis has also been used to treat habit cough in children. Children with habit cough may need evaluation by a psychologist or psychiatrist if symptoms do not resolve with suggestion therapy. (34)

Gastroesophageal reflux disease is a common cause of chronic cough in adults; however, pediatric data have not

established GERD to be the sole etiology of nonspecific chronic cough in children. (9) The relationship between GERD and cough is complex in children, as either can precipitate the other. (35) Because cough is common in children, and respiratory symptoms may exacerbate underlying GERD, it may be challenging to distinguish cause and effect in children. (9) Infants frequently regurgitate, yet cough is not a common association in healthy infants with these episodes. An empirical trial of reflux medications in children with nonspecific isolated chronic cough is not recommended unless children have other symptoms suggestive of reflux. (1)(11)

Upper airway cough syndrome and postnasal drip are common causes of chronic cough in adults but are controversial as causes of chronic nonspecific cough in children. (7)(9) There is insufficient evidence that postnasal drip, resulting from allergic rhinitis and sinusitis, is associated with chronic cough in children. Sinusitis has been associated with allergic rhinitis in children, but it is not associated with cough once existent atopy or allergic rhinitis are controlled. Children with allergic rhinitis can have a throat-clearing type of cough. In children with signs of allergic rhinitis, allergen avoidance and a trial of therapy (oral antihistamine or intranasal corticosteroids) is indicated. (11) Although atopy increases the likelihood of having asthma, it is neither sensitive nor specific for asthma. Hence, routine allergy testing is not indicated in the evaluation of children with nonspecific dry cough. (1) Current guidelines for pediatric chronic cough recommend against an empirical approach toward the treatment of upper airway cough syndrome in children with nonspecific isolated dry cough. (1)(11)

Exposure to environmental tobacco smoke causes adverse respiratory health outcomes and has been associated with increased coughing in children. Exposure to other pollutants, such as particulate matter and indoor biomass combustion, is also associated with increased coughing illnesses in children. (9)(11) Current pediatric chronic cough guidelines recommend that in all children with cough, tobacco smoke exposure should be evaluated, and families should be offered interventional options for the cessation of exposure. (9) Readers are encouraged to refer to the American Academy of Pediatrics' clinical practice policy to protect children from tobacco, nicotine, and tobacco smoke. (36)

INVESTIGATIONS

Spirometry (if age-appropriate) and chest radiography should be performed as initial evaluations in children with chronic cough. An abnormal chest radiograph

suggests a specific cause of cough, but a normal chest radiograph does not exclude respiratory disease (eg, bronchiectasis). Findings on the chest radiograph may help guide further evaluations for chronic cough. Bilateral pulmonary hyperinflation is commonly seen in asthma but can also be seen in other chronic respiratory diseases. Unilateral hyperinflation or collapse of the lung can suggest an aspirated foreign body or intraluminal pathology that would require further imaging and bronchoscopy. A right-sided aortic arch may be a normal variant or can be associated with a vascular ring. (6) Organ laterality defects, such as situs inversus totalis, detected on routine imaging in a child with chronic otitis-pulmonary disease should prompt further evaluation for PCD. (22)

Spirometry is a useful clinical test to screen for lung function abnormalities in children with chronic cough. Pulmonary function tests are used to 1) assist in the diagnosis of lung disease by describing and quantifying the impairment in physiologic function, 2) monitor the course of respiratory disease in patients, and 3) assess response to therapy. Spirometry requires good patient effort and cooperation to provide reliable results. Most children can perform valid spirometry by age 6 years. In experienced pediatric pulmonary function laboratories, spirometry results can be obtained in children as young as 3 years. (37) Abnormalities in spirometry findings suggest a specific cause of cough, but normal spirometry results do not exclude respiratory disease. An obstructive pattern detected on spirometry implies asthma or other obstructive airway diseases. In children with obstructive airway disease, spirometry should be performed before and after administration of a bronchodilator. Improvement in airway obstruction after inhalation of a bronchodilator usually indicates a diagnosis of asthma. However, some children with asthma can have normal spirometry results. (1) For a detailed review of spirometry interpretation, readers are referred to a *Pediatrics in Review* article by Kaslovsky and Sadof. (38)

Additional tests to aid in the diagnosis of respiratory disease in a child with chronic cough depend on the history, physical examination findings, presence of specific cough pointers, and clinical suspicion of a particular etiology. Tests include chest CT scans, flexible bronchoscopy with BAL, ciliary biopsy with electron microscopy (for PCD), and genetic studies for cystic fibrosis and PCD. Most of these evaluations are undertaken by pediatric pulmonologists. Pediatric chronic cough management guidelines recommend against routinely performing additional tests such as allergy testing, bronchoscopy,

and chest CT. These tests should be individualized and performed based on the child's clinical symptoms and signs. (1)

MEDICATIONS

Management of cough in children should be directed at identifying the etiology of cough and arriving at an accurate diagnosis. Treatment should be based on the underlying etiology and not targeted toward suppression of cough. There is no good evidence for the effectiveness of OTC cough medications in treating acute cough in children, and these medications can cause serious harm. For a review of OTC cough and cold medications, readers are referred to a *Pediatrics in Review* article by Lowry and Leeder. (39)

There is good evidence that in children with nonspecific chronic cough, an empirical approach targeted toward upper airway cough syndrome, GERD, or asthma should not be used unless there are other clinical features consistent with these diagnoses. (1) In some instances of nonspecific dry cough in young children, an empirical trial of inhaled bronchodilators and ICSs is used when asthma is suspected. As described previously, if an empirical trial of asthma medications is used, a definite period should be set (2–4 weeks), and the child should be reassessed for resolution of cough to confirm or refute the suspected diagnosis. If there is no response to asthma therapies, the medications should be stopped because asthma is unlikely. (11) If the cough did not respond to treatment with ICSs, children should not be treated with increased doses of ICSs. (9) Antibiotics are used when a diagnosis of PBB is suspected in a child with chronic nonspecific isolated wet cough. A systematic approach to the management of chronic cough by using pediatric cough management algorithms improves clinical outcomes. (1)(16)(18)

Summary

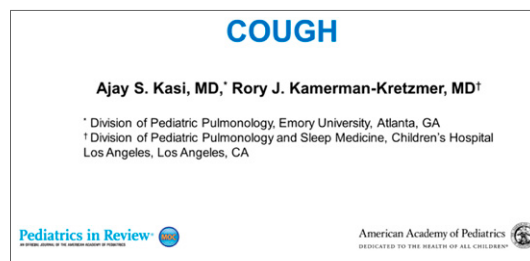
- Acute cough in children is usually caused by viral upper respiratory tract infections, which are self-limiting. There is no good evidence of effectiveness of over-the-counter cough medicines in acute cough, and they can cause serious harm in children. (13)

- Based on consensus, in children 14 years and younger, chronic cough is defined as the presence of daily cough for at least 4 weeks. (1)
- Strong evidence supports using a systematic approach, including a detailed history, thorough physical examination, and assessment of specific cough pointers, to guide the diagnosis, testing, and management of children with chronic cough. (1)
- Protracted bacterial bronchitis can be diagnosed in children with chronic wet cough without signs of an alternative cause who have resolution of cough after 2 to 4 weeks of treatment with an appropriate oral antibiotic. (30)
- In children with chronic cough, management must be based on the etiology of the cough. Based on strong research evidence, the use of pediatric-specific cough management algorithms improves clinical outcomes. (18)

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To view teaching slides that accompany this article, visit <http://pedsinreview.aappublications.org/content/40/4/157.supplemental>.



References for this article are at <http://pedsinreview.aappublications.org/content/40/4/157>.

APPROACH TO A CHILD WITH A COUGH

General Presentation

Background

Cough is a common indication of respiratory illness and is one of the more common symptoms of children seeking medical attention. Not only does it cause discomfort for the child, cough also elicits stress and sleepless nights for their parents. Before we dive into the clinical approach to cough, let us review the respiratory physiology of cough.

Physiology

Mechanics of coughing - three phases:

1. **Inspiratory phase:** air inhalation lengthens the expiratory muscles (favourable length-tension relationship).
2. **Compressive phase:** contraction of expiratory muscles against a closed glottis leads to an increase in intrathoracic pressure.
3. **Expiratory phase:** opening of the glottis results in high expiratory flow and audible coughs. During this phase, the airway undergoes dynamic compression and the expulsion of air facilitates airway debris and secretions clearance.

Cough pathway

Each cough is elicited by the stimulation of the cough reflex arc. Cough receptors, which are afferent endings of the vagus nerve (cranial nerve X), are scattered in the airway mucosa and submucosa. Some of these receptors are mechanosensitive and some are chemosensitive. Mechanoreceptors are sensitive to touch or displacement and are located mainly in the proximal airway such as larynx and trachea. Chemoreceptors are sensitive to acid, heat, and capsaicin derivatives through the activation of type 1 vanilloid receptor (TRPV1) and are located mainly in the distal airways. The receptor locations are represented by red dots in Figure 1.

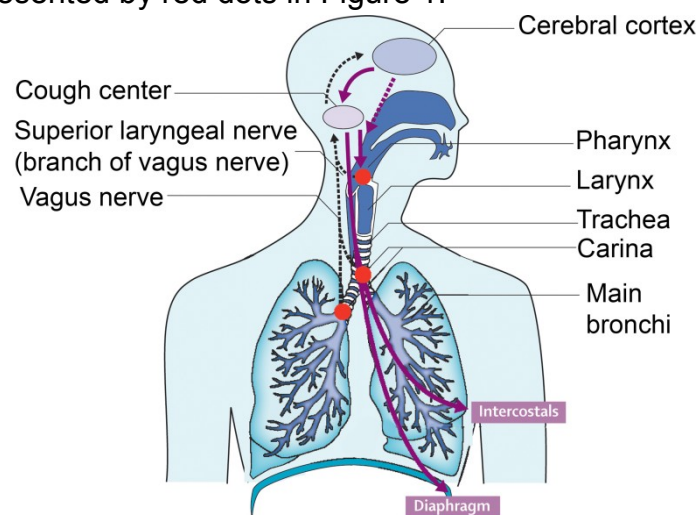
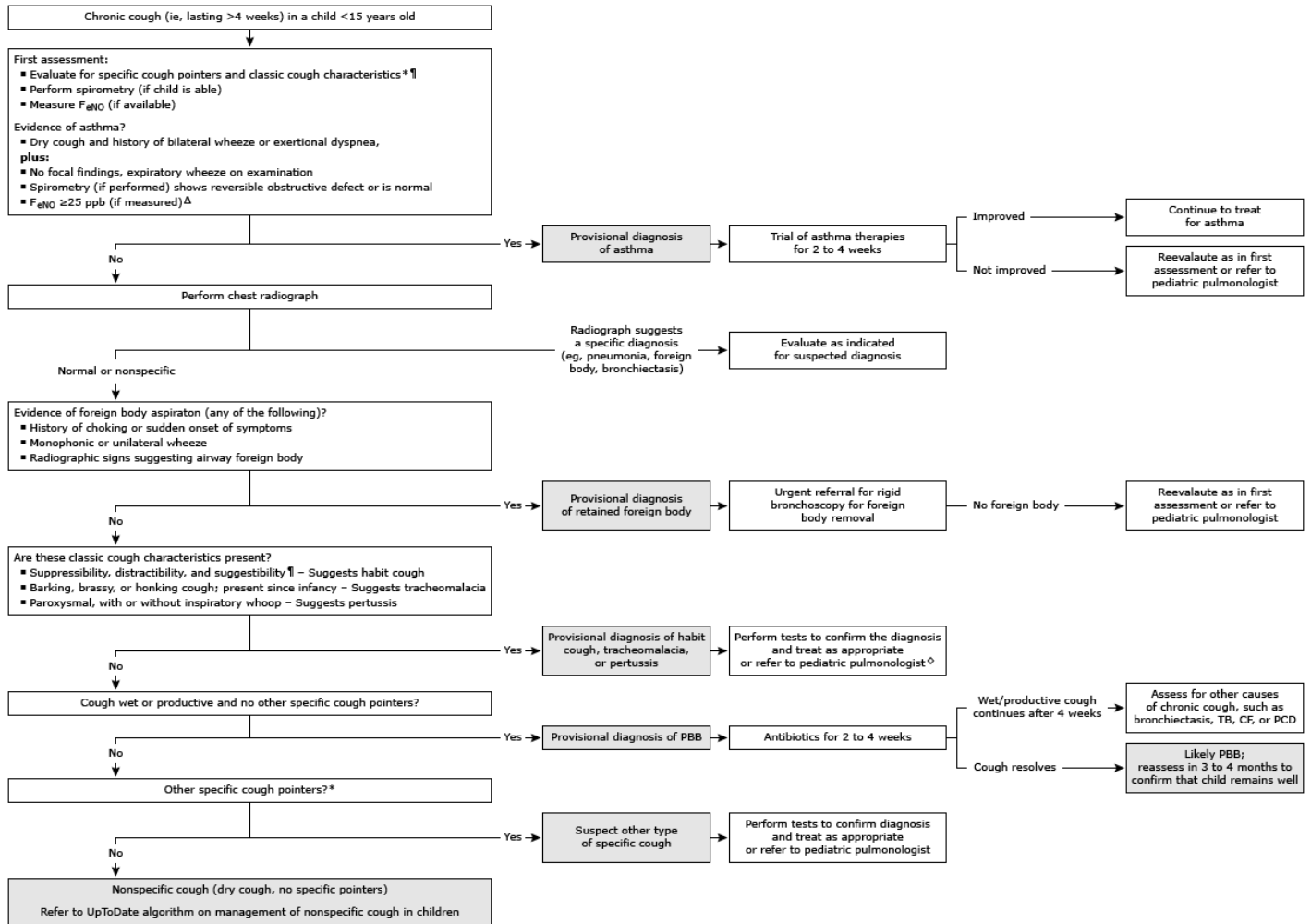


Figure 1 – Cough reflex anatomy: Red dots represent the locations of the cough receptors. Black arrows represent the afferent pathway and purple arrows represent the efferent pathway. (modified from Chung KF, Pavord ID. Prevalence, pathogenesis, and causes of chronic cough. Lancet. Apr 19 2008;371(9621):1364-74)

Via the vagus nerve, impulses from the cough receptors are propagated to the cough center in the medulla and nucleus tractus solitarius. Efferent impulses are generated from the cough centre and are propagated via the spinal motor (to expiratory muscles), phrenic (to the diaphragm), and vagus (to the larynx, trachea, and bronchi) nerves to the expiratory organs to produce cough (see Figure 1).

Algorithm for the evaluation of chronic cough in children



FeNO: exhaled nitric oxide fraction; PBB: protracted bacterial bronchitis; TB: tuberculosis; CF: cystic fibrosis; PCD: primary ciliary dyskinesia.

* Specific cough pointers include^[1]:

- Symptoms – Chronic wet/productive cough, chest pain, history suggestive of inhaled foreign body, dyspnea, exertional dyspnea, hemoptysis, failure to thrive, feeding difficulties (including choking/vomiting), cardiac or neurodevelopmental abnormalities, recurrent sinopulmonary infections, immunodeficiency, or epidemiologic risk factors for exposure to TB
- Signs – Respiratory distress, digital clubbing, chest wall deformity, or auscultatory crackles
- Tests – Chest radiographic changes (other than perihilar changes) or lung function abnormalities

Refer to UpToDate content on chronic cough in children.

¶ Habit cough (also known as tic cough) is typically absent at night or when distracted and may be honking or short/dry^[2].

Δ FeNO value ≥25 ppb with asthma symptoms supports a diagnosis of asthma^[3].

◇ For diagnostic evaluation, refer to UpToDate content on pertussis and tracheomalacia. Tic (habit) cough is diagnosed based on characteristic symptoms.

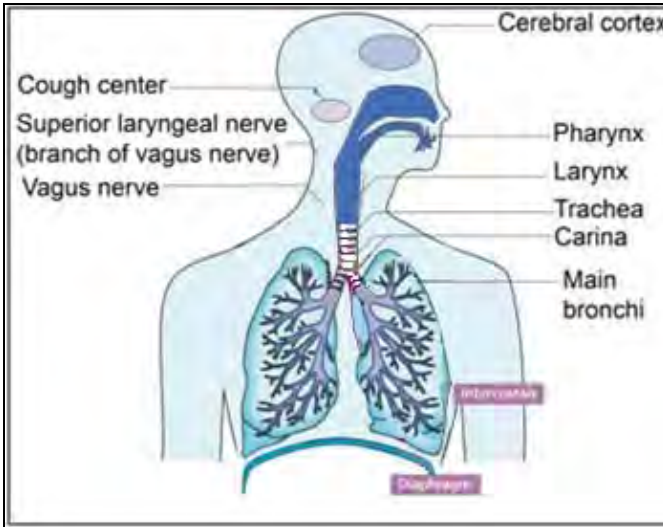
References:

1. Kantar A, Chang AB, Shields MD, et al. ERS statement on protracted bacterial bronchitis in children. *Eur Respir J* 2017; 50: 1602139.
2. Weinberger M, Hoegger M. The cough without a cause: Habit cough syndrome. *J Allergy Clin Immunol* 2016; 137:930.
3. Gaillard EA, Kuehni CE, Turner S, et al. European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5-16 years. *Eur Respir J* 2021; 58:2004173.

Chronic Cough Quiz

1. What is the role of cough?

2. Complete this diagram of the cough reflex. What conditions can cause \uparrow or \downarrow CRS?



(1) Afferent pathway:

Draw arrows and include cough receptors

(2) Efferent pathway:

Draw arrows

(3) CNS cortical modulation:

Draw arrows

- \uparrow CRS: _____
- \downarrow CRS: _____

3. Fill in the following numbers related to chronic cough:

- Percent of school-kids still coughing 10 days s/p common cold: _____
- Number of cough episodes per day in a “normal” child: _____
- Length of acute vs. subacute vs. chronic cough: _____
- Frequency of viral infections in toddlers starting daycare: _____

4. According to both review articles, which of the following is/are not recommended for a trial of therapy for chronic nonspecific cough?

Antibiotics, β_2 agonist, anticholinergics, inhaled corticosteroids, oral steroids, antihistamines, dextromethorphan, H2 antagonist, PPI.

5. What is “specific cough”? Complete the table for *specific* etiologies of chronic cough:

Additional History	Physical Exam	Differential Diagnosis	Work-up
Vomiting/spitting up; Worse lying down; irritable after feeds.			
Snoring, PND			
Wet cough, FTT, recurrent infections			
Early onset of sxs; choking on feeds; recurrent bronchiolitis (± “dying spells”)			

Chronic Cough Cases

Case 1: 5 year-old AJ presents to clinic in late February because his mother is concerned about a cough that seems to be getting worse. He has a PMHx of seasonal allergies that have responded to Zyrtec, and is otherwise healthy. There is also a family history of atopy.

What other historical information would you like to know?

AJ's mother reports that the cough is dry and occurs regularly throughout the winter months, probably since her son started daycare at age 2. The frequency is now 3-4 nights/week. Occasionally, he will cough when he’s playing outside. He had mild rhinorrhea and cold-like symptoms in November and December when the symptoms began this year, but is currently without rhinorrhea, fever, emesis, or sore throat. He does not snore. His mother has never heard him wheeze or show any increased work-of-breathing, and he has never been treated with a bronchodilator.

Is your patient's cough acute, sub-acute, or chronic? How can you distinguish from recurrent viral infections?

Based on this history, what is your differential diagnosis? What questions can you ask to narrow down the differential?

AJ's mother reports that her son has not been free of cough since the initial 2 colds in this fall/winter, and she feels as if the cough is becoming more frequent and "deeper". He has no history of reflux, and his cough is not associated with mealtimes or only when lying down.

On exam, VS are normal, with wt and ht curves tracking at 75%. HEENT exam is remarkable for an erythematous posterior oropharynx. There is no visualized post-nasal drip, sinus tenderness, allergic shiners, or nasal crease. His lung exam shows no tachypnea, flaring, or grunting. He is well-aerated in all fields, without wheezing, rales, or rhonchi. There is no prolonged expiratory phase. He does not have clubbing or cyanosis, and the remainder of his PE is unremarkable.

Based on his history & physical exam, is this cough specific or non-specific?

How will you manage AJ? What labs or radiographic studies, if any, will you obtain? What treatments, if any, will you prescribe? When will you follow-up?

Bonus: What is the difference in physiology between children who cough with viral colds and children who cough due to asthma?

Case 2: 3 yo Lulu presents with parental concern for prolonged cough x 10 days. Father describes the cough as “junky” or “wet-sounding”. The cough occurs throughout the day (“at least 20 times”) and also wakes her up at night (“at least 2 times”). Dad reports that his daughter is “wheezing” and he can feel her chest “rattling” when he hugs her. Lulu has mild rhinorrhea, improving since the start of the cough; no ear-tugging and no sore throat. Subjective fevers noted at home, decreased appetite, and lack of energy. Parents have been treating with Tylenol, Motrin, and [PediaCare “Multi-symptom Cold”](#) Daytime and Nighttime versions (Dad says “because she’s *almost* 4”). Lulu was also prescribed an Albuterol inhaler at an ER visit after the 1st week of cough, but parents stopped after 2-3 days because they saw no response. There is no prior history of RAD, and the patient is otherwise healthy. There is also no FamHx of asthma.

On physical exam, VS are normal and weight and height are tracking at the 50-75th %iles. The patient is somewhat tired-appearing, but alert and well-hydrated. HEENT exam is remarkable for clear rhinorrhea, with erythematous nasal passages and PND visualized in an otherwise normal oropharynx. No increased work-of-breathing, and lung exam reveals transmitted upper airway sounds and rhonchi, but no wheezing or rales. Remainder of exam is normal.

How accurate are parent reports about cough? If dad’s description is accurate, is this cough acute, sub-acute, or chronic? Specific or non-specific? What is your Ddx?

Using the algorithm, what will you recommend? Any other suggestions?

Lulu returns 2 wks later, having followed your home-care advice, and dad reports that his daughter’s energy and appetite have improved, but the junky cough and chest rattle have not abated. He also admits that they returned to the ER again last weekend: a CXR was performed which showed “peri-bronchial cuffing”, but no hyperinflation. The ER recommended Albuterol again, but parents have not continued because they saw no improvement and it made Lulu hyper.

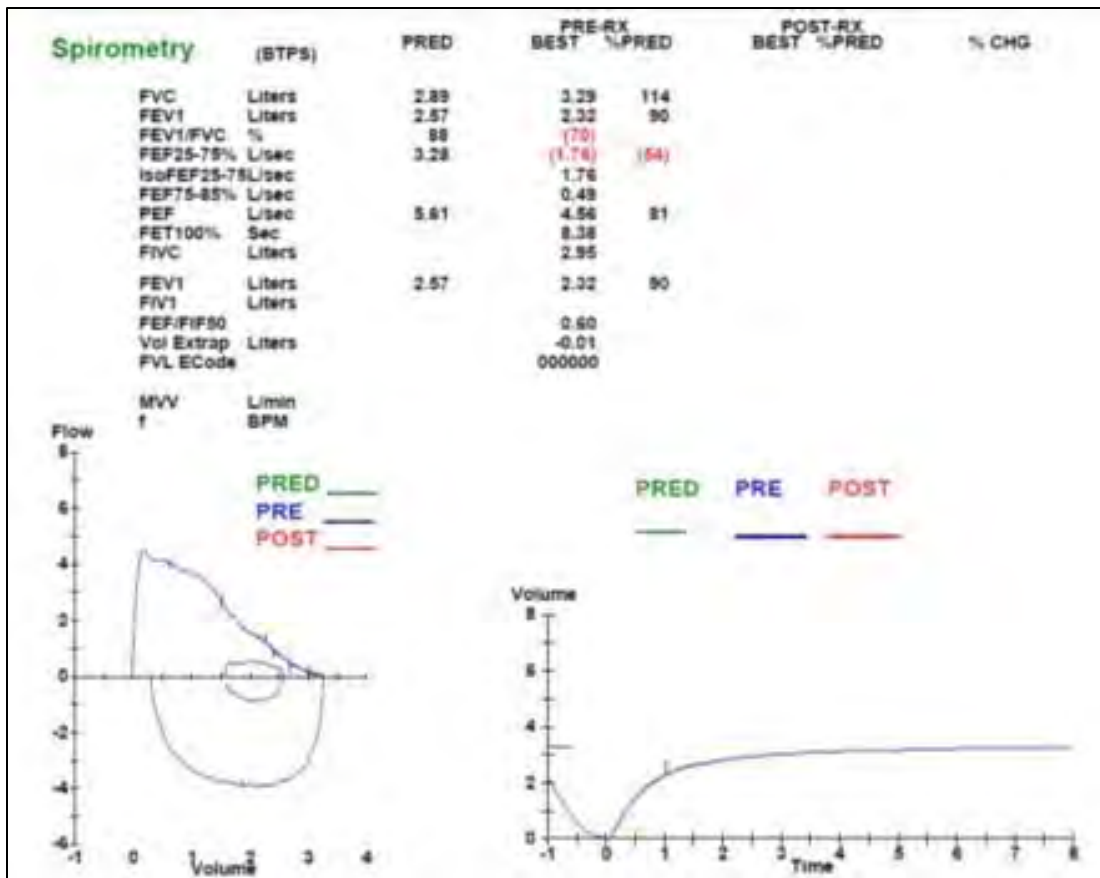
What is your working diagnosis? Which diagnostic category does this patient fit?

Using the algorithm, what will you recommend now? Any labs or other studies?

Bonus Case 3: 7 year old Reya presents complaining of recurrent facial pain associated with nasal congestion, productive cough, and post-nasal drip. Her symptoms have been present on and off for the majority of her life. Usually the rhinorrhea is of varying shades of yellow. Multiple courses of antibiotics have been used in the past, and generally she has been symptom-free for at most 1-2 months. She has also tried an Albuterol MDI and inhaled steroid in the past without much relief. The remainder of her PMHx is unremarkable.

What is your differential diagnosis? What PE findings would help differentiate this list?

The patient's VS were normal with weight and height tracking at 10-25th %ile. Exam was remarkable only for single nasal polyp in right nare and PND; no sinus tenderness. PFTs are below. Prior testing *did not* reveal bronchodilator reversibility.



What is your working diagnosis? Is this a typical presentation?

What is your next step?

Chronic Cough Board Review

1. An 18-month-old boy presents to the emergency department with a 2-day history of cough, posttussive emesis, and diminished food intake, although he has been taking liquids. The coughing began after eating some popcorn. His mother explains that he has had no fever or rhinorrhea. He had an episode of bronchiolitis at 3 months of age but has no other history of respiratory illness, chronic cough, or other health concerns. He is the youngest of four children cared for at home. On physical examination, his vital signs are normal, his height and weight are at the 50th percentile for age, and the boy is mouth-breathing with mild nasal flaring. Oxygen saturation is 94% on room air. Auscultation of the chest reveals diffuse rhonchi and wheezes that are markedly louder on the left side of the chest.

Of the following, the MOST likely diagnosis is

- A. bronchiolitis
- B. community-acquired bacterial pneumonia
- C. cystic fibrosis
- D. foreign body aspiration
- E. reactive airway disease

2. A 10-year-old boy presents with a 2-month history of chronic cough. His parents are unsure of a specific preceding trigger. They are concerned because the school nurse has called on multiple occasions requesting that the boy be taken home due to his persistent cough. The boy denies any chest pain, dyspnea, or syncope. Use of a sedating antihistamine and over-the-counter cold and cough liquid has not alleviated his symptoms. On physical examination, the boy has vital signs within the normal range and appears healthy. A thorough examination reveals no abnormalities. During the encounter, the boy repeatedly exhibits a harsh, "barky" cough that resolves when you leave the examination room, only to recur when you return. You suspect he has a psychogenic cough.

Of the following, the MOST accurate statement regarding psychogenic cough is that

- A. most cases are associated with underlying psychological illness
- B. most cases are preceded by an upper respiratory tract infection
- C. resolution of the cough often is followed by recurrent wheezing
- D. symptoms persist during the day and while the child is asleep
- E. the cough noise often is dramatically different from the postnasal drip syndrome cough

3. A 16-year-old girl who has moderate persistent asthma presents to the emergency department with coughing, wheezing, and increasing dyspnea. She states that she was feeling fine until she was exposed to cologne that one of her classmates was wearing. An ambulance was called after her symptoms did not improve following administration of two puffs of her beta-2 agonist inhaler. On physical examination, the teenager has a respiratory rate of 30 breaths/min, heart rate of 90 beats/min, and pulse oximetry of 98% on room air. She has difficulty completing a sentence and points to her neck, saying it is "hard to get air in." Her lungs are clear to auscultation, and rhinolaryngoscopy demonstrates adduction of one of the vocal cords during inspiration with a posterior glottic "chink." Pulmonary function testing shows a blunted inspiratory loop.

Of the following, the MOST likely cause for this patient's symptoms is

- A. asthma exacerbation
- B. subglottic stenosis
- C. vocal cord dysfunction
- D. vocal cord nodule
- E. vocal cord paralysis

4. The parents of a 6-month-old boy call you in the middle of the night because he is coughing and has nasal congestion. You had diagnosed a viral upper respiratory tract infection when you saw him earlier today. The parents are frustrated that the cough is persistent and request medicine for their boy so they can sleep.

Of the following, the MOST appropriate recommendation is

- A. chlorpheniramine/pseudoephedrine combination
- B. codeine
- C. dextromethorphan
- D. guaifenesin
- E. saline nasal drops