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 & **compare** the following 2 reviews on chronic cough:*

- "Cough in the Pediatric Population" *(The Journal of Pediatrics, 2010)*
- "Paediatric Problems of Cough" *(Pediatric Pharmacology & Therapeutics, 2002)*

*Please review the following editorial on **OTC meds** and complete the homework:*

- "Investigating OTC CCM: Why did it take so long?" *(Contemp Peds, 2008)*
- **Choose one of the following OTC meds** *(or another from your experience)* and determine its generic name, class of medicine/use, and potential side-effects:
  - Dimetapp®, Pediacare®, Triaminic®, Robitussin®, Mucinex®, Sudafed®

Conference Agenda:

- *Review* Chronic Cough Quiz
- Complete Chronic Cough Cases
- Round table: Present your selected OTC cough & cold medicine to the group, focusing on its intended use and potential side-effects.

Post-Conference: *Board Review Q&A*

Extra-Credit:

- "Guidelines for Evaluating Chronic Cough in Pediatrics" *(ACCP- Chest, 2006)*
- "Chronic Wet Cough: Protracted Bronchitis . . .& Bronchiectasis" *(Ped Pulm, 2008)*
- OTC Meds: FDA Advisory (2008); AAP Position *(with links to **parent handouts**)*

Reviewed by COL Andy Lipton and MAJ Christine Gould.

Cough in the Pediatric Population

Alan B. Goldsobel, MD, FAAP, FAAAAI and Bradley E. Chipps, MD, FAAP, FAAAAI, FCCP

Cough is the most common presenting symptom for medical office visits in the United States. Cough in children is usually related to viral respiratory tract infection and typically resolves spontaneously. Between 35% and 40% of school-age children still cough 10 days after the onset of a common cold, and 10% of preschool children have cough 25 days after respiratory tract infection.[1] In children, cough has been associated with environmental factors, such as outdoor and indoor air pollution, including particulate matter, irritant gases, environmental tobacco smoke exposure, and dampness in the home.[2] The frequent presentation of cough in children is further complicated by studies documenting that parental reporting of cough in children correlates poorly with objective measurement of frequency, duration, or intensity of cough.[3] Cough in children disrupts both the parent's and the child's daily activities and can be associated with impaired quality of life in the child and significant stress in parents that improves with cough resolution.[4] It is extremely common for parents to treat children with over-the-counter (OTC) cough and cold medications (CCMs) before seeing a health care provider. In a recent survey, approximately 10% of US children were found to be receiving an OTC CCM in any given week. Although OTC CCMs receive Food and Drug Administration (FDA) approval for adults, testing for efficacy and safety in young children has not been adequate,[5] and inappropriate use of CCMs in children has been documented.[6] Adverse events associated with use of OTC CCMs do occur and rare infant deaths have been reported. In January 2008, the FDA issued a public health advisory regarding OTC CCM use in children questioning safety and efficacy and whether the clinical benefits justify potential risks;[7] it now recommends avoiding these medications in children under age 2 years. The FDA also has supported the recent recommendation by the Consumer Health Product Association to avoid OTC CCM use in children under age 4 years. An American Academy of Pediatrics (AAP) position statement questions the efficacy and safety of these medications in children under age 6 years.

AAP	American Academy of Pediatrics
ACCP	American College of Chest Physicians
BAL	Bronchoalveolar lavage
CCM	Cough and cold medications
CF	Cystic fibrosis
CRS	Cough reflex sensitivity
CT	Computed tomography
FDA	Food and Drug Administration
FeNO	Fraction of exhaled nitric oxide
GERD	Gastroesophageal reflux disease
ICS	Inhaled corticosteroids
OTC	Over the counter
PBB	Protracted bacterial bronchitis
UACS	Upper airway cough syndrome

The Cough Reflex

Cough is a protective reflex, a component of normal respiratory physiology that enhances mucociliary function and clears excessive secretions and airway debris from the respiratory tract, as well as a very common symptom of respiratory disease. Cough receptors are located in the respiratory tract from the larynx to the segmental bronchi.[8] The cough reflex has vagal afferent input, brain stem centralization with cortical modulation, and motor efferent activity involving respiratory muscles. Cough reflex sensitivity (CRS) can be modulated either by disease or pharmacologically. Up-regulation of CRS causes triggering of cough from a relatively nonspecific provocation. Heightened CRS has been demonstrated following viral respiratory tract infections[9] (postviral or postinfectious cough), as well as in asthma, gastroesophageal reflux disease (GERD), and angiotensin-converting enzyme inhibitor therapy. The prevalence of CRS is similar in prepubertal and early pubertal girls and boys but significantly higher in postpubertal girls and adult women. Using mechanical stimulation, cough can be elicited in 10% of 27-week gestational age preterm infants and up to 90% of full-term infants.[10]

Defining Cough in Children

Children cough differently from adults in terms of duration, presentation, and underlying causes. The classification of cough in children reflects these differences.

Normal or Expected Cough

"Normal" children cough. According to objective measurements, healthy school-age children (mean age, 10 years; no respiratory illness in the 4 weeks before the study) typically experience 10 or 11 (and as many as 34) cough episodes/

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day.[11] Sometimes these "normal" cough episodes are prolonged or nocturnal, triggering parental concerns about discomfort and disturbed sleep. Recurrent viral respiratory infections are common in children, particularly in the fall and winter. These may appear to cause persistent cough, but usually the child experiences short breaks between illnesses. Postinfectious cough in normal children may have multiple causes, including heightened CRS. Less than 5% of coughs persisting >8 weeks are believed to be postinfectious (other than pertussis syndromes).[12]

Abnormal Cough

Abnormal cough in children includes cough associated with underlying disease states, as well as ineffective cough from underlying neuromuscular weakness or structural airway abnormalities. Abnormal cough in children can be classified by duration (acute vs chronic); character, quality, and timing (eg, dry vs wet, day vs night); age of child; and etiology (specific vs nonspecific). Overlap among the different categories can make classifying abnormal pediatric cough confusing. To aid in the diagnosis and treatment of the coughing child, the following questions may be helpful:

1. How long has the child coughed? Most adult studies and consensus guidelines define cough as acute (<3 weeks), subacute (3 to 8 weeks) or chronic (>8 weeks).[13] Most acute and subacute coughs in adults and children are associated with viral upper respiratory tract infection and do not require specific diagnostic evaluation. The definition of chronic or persistent cough in children varies, ranging from 3 to 12 weeks depending on the study or guideline.[14,15]
2. What is the character of the cough? The character or quality of chronic cough in adults has been shown to be not helpful in predicting specific etiology, and the 2006 American College of Chest Physicians (ACCP) guidelines recommend it not be used in determining etiology in adults.[13] In contrast, the character or quality of cough in some children is recognizable and reproducible, and may suggest a specific etiology (Table I).
3. Is the cough wet or dry? A moist or wet cough in children is associated with secretions detected on bronchoscopy and can be accurately reported by clinicians and parents.[16] The descriptor "wet" or "moist" cough may be used interchangeably with "productive" cough, even though young children rarely expectorate despite excessive secretions. A recent cross-sectional survey of more than 2000 children age 11 to 15 years found a 7.2% prevalence of chronic productive cough.[17] Chronic productive cough was strongly associated with reports of current asthma symptoms and with environmental tobacco smoke exposure, although specific causes were not investigated.[17] A recent review of chronic wet cough in children without cystic fibrosis (CF) found that the majority of the children had an endobronchial bacterial infection.[18] Chronic wet cough is very rare in children with uncomplicated asthma. Sinusitis with or without asthma also may cause a wet cough that is responsive to antibiotic therapy. Chronic cough with purulent sputum in children is always pathological, calling for specific assessment for such conditions as CF, non-CF bronchiectasis, and ciliary dysmotility syndromes.
4. Is the cough nocturnal? Nocturnal cough is often cited a hallmark of asthma; however, most objective studies have not confirmed this finding, and parental reporting of nocturnal cough is unreliable compared with objective measurements.[3,19] As such, other causes of cough should be considered as well. Cough generally is suppressed by sleep, and habit cough most characteristically ceases at night.[20]
5. How old is the child? Age at onset of cough is important diagnostically; in infants and younger children, greater consideration must be given to anatomic abnormalities of the upper and lower respiratory tracts and the gastrointestinal (GI) tract, as well as possible foreign body aspiration (Table I).

Table I. Traditional recognizable cough characteristics at various ages

Cough characteristic	Possible etiology
Infancy	
Barking or brassy	Croup, tracheomalacia/other anatomic abnormalities of respiratory or GI tract
Dry, staccato	Chlamydophilia
Wet	PBB, sinusitis
Childhood	
Barking or brassy	Croup
Spasmodic/paroxysmal (with or without whoop)	Pertussis-like syndrome
Wet (with or without produced sputum)	PBB/sinusitis
Adolescence	
Barking/honking	Habit/psychogenic
Spasmodic/paroxysmal (with or without whoop)	Pertussis-like syndrome
Wet (with or without produced sputum)	Pneumonia/PBB/sinusitis

Modified with permission.[13]

In children, as in adults, cough is subject to psychological influences.[13] Habit cough is more commonly recognized in children.[20] Age also may play a role in the etiology of chronic cough in children. Studies with younger children demonstrate different causes of chronic cough compared with those with predominately older children and teens, who have similar causes as adults.[21-23]

Etiology of Abnormal Pediatric Cough

A previously proposed diagnostic paradigm of specific versus nonspecific cough in children forms the basis of the approach to evaluation and treatment in the 2006 ACCP guidelines.[13,24] Specific cough is associated with underlying respiratory or systemic disease, and the need for further investigation is typically evident from coexisting symptoms

and signs, radiographs, and laboratory results (Table II; available at www.jpeds.com). A frequent (daily) wet cough is the best clinical marker of the presence of a specific cough. Chronic dyspnea and hemoptysis are also historical predictors of specific cough, as are abnormal chest x-ray and auscultation findings.

Nonspecific cough is defined as cough in the absence of other signs and symptoms (Table II). Nonspecific cough is "isolated" cough; that is, cough is the sole or predominant symptom and typically is dry. In many cases, nonspecific cough is related to postviral infection and increased cough receptor sensitivity.[25] Resolution is spontaneous in the majority of children.[26]

Specific and nonspecific coughs may have various overlapping causes. In adults, prospective studies have shown that >90% of chronic (>8 weeks) nonspecific coughs can be attributed to 3 predominant causes: upper airway cough syndrome (UACS, previously referred to as postnasal drip syndrome), asthma or eosinophilic bronchitis, and GERD.[13] Similar data in children are limited. A prospective study in highly selected young children (median age, 2.6 years) referred to a tertiary pediatric respiratory center indicated that UACS, asthma, and GERD accounted for <10% of persistent cough, although 50% of the children had received a diagnosis of asthma before referral.[21] Wet cough was present in 89% of the children, with a median duration of 6 months. Onset in the first year of life occurred in 62%; environmental tobacco smoke exposure was identified in 43%. The primary cause of cough in this cohort was protracted bacterial bronchitis (PBB), diagnosed in 40%.[21] The results based on this young tertiary referral population may not be representative of the general pediatric population, however.

A retrospective observational report on chronic cough in young children (mean age, 3 years, 9 months) referred to a European respiratory center also documented PBB as the most common diagnosis.[27] A recent prospective study from the United States in older children (mean age, 9.2 years) with chronic cough (persisting for >8 weeks) with no cigarette smoke exposure found similar diagnoses as reported in adult studies: UACS (23%), GERD (28%), asthma (13%) and multiple etiologies (20%).[22] A specific cause was found in 90% of cases. Another recent study of similar-aged children (mean age, 8.4 years) presenting to a children's hospital in Turkey found that the most common causes of cough persisting for >8 weeks were asthma (25%), PBB (23%), UACS (20%), and GERD (5%).[23] The differences in results may reflect differences in patient age as well as in the study populations (Table III; available at www.jpeds.com).

Protracted Bacterial Bronchitis

Defined as chronic wet cough, positive bronchoalveolar lavage (BAL), and resolution with antibiotic therapy, PBB is poorly characterized, and data suggest that it is underdiagnosed and often misdiagnosed as asthma.[27] Bronchoscopy typically reveals an intense neutrophilic airway inflammatory response.[28] The most common organisms implicated are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. A reasonable alternative approach to avoid invasive bronchoscopy is a trial of antibiotics (eg, amoxicillin and clavulanate for 2 weeks),[21] but this may not allow for a definitive diagnosis. Adaptive immune function is normal in these children, but preliminary data have shown a marked inflammatory mediator response in BAL fluid and innate immune system activation.[28] Further studies of immune system abnormalities in these children are needed.

Gastroesophageal Reflux Disease

GERD is common in infants and children, and aspiration with swallowing in the absence of GERD also may cause cough and other respiratory symptoms in infants.[29] Although a high percentage of children with respiratory symptoms have GERD detectable by abnormal esophageal pH, symptoms may be subtle, especially in young children,[30] and the specific association between GERD and cough remains controversial.[31] A positive response to empiric therapy with thickened feedings in infants and an acid-suppressive regimen may be used to support a presumed diagnosis of GERD,[32] but lack of cough resolution can be seen with nonacid reflux detectable by impedance measurement.[33] The diagnoses of GERD or asthma are not mutually exclusive, particularly in older children.[30,34] As many as half of children with asthma and abnormal esophageal pH exhibit few or no obvious symptoms of GERD (eg, heartburn, regurgitation).[30]

Habit Cough Syndrome

Recognizing habit cough and other functional respiratory disorders, such as vocal cord dysfunction and hyperventilation/sighing dyspnea, is important in pediatric patients. Habit cough, also known as "psychogenic cough," may be mistaken for asthma, UACS, or another cause of chronic cough. Weinberger et al[34] used the term "pseudoasthma" to describe this and other organic and nonorganic disorders misdiagnosed as asthma. The usual presentation of habit cough is a harsh, dry, often honking repetitive cough occurring intermittently throughout the day, often with great frequency. Even though the cough sounds annoying, the child is usually unperturbed ("la belle indifference"). Yet the cough is often very disturbing to parents, teachers, and other caregivers and may lead to school and social disruption. Characteristically, there is significant improvement with distraction and absence when asleep. The cough is generally reproducible on request.

Habit cough may evolve following upper respiratory tract infection, with an initial brief, wet cough developing into the more characteristic dry, barking cough. The reported frequency of psychosomatic or psychological problems in these patients varies widely; most pediatric patients do not exhibit severe psychopathology. Habit cough occasionally may be difficult to differentiate from tic disorders, even though the vocalization characteristic of Tourette syndrome is usually not present.

Evaluating Chronic Cough in Children

There are no historical features of cough that provide a clear diagnosis in most cases of pediatric chronic, nonspecific cough. Rather than applying a comprehensive battery of tests for chronic cough in all children, most clinicians use clinical pointers in the history and physical examination to target the investigation.

The recommended evaluation of chronic cough is outlined in Figure 1. A trial of pharmacotherapy is often used as a diagnostic modality, although spontaneous resolution of cough can necessitate multiple trials to pinpoint the etiology. Recommendations are based primarily on expert opinion, due to the lack of controlled pediatric studies. Thus, the duration of pharmacotherapy trials is empiric, but premature discontinuation can lead to lack of resolution. Children with a prolonged moist cough should be treated initially with an antibiotic for possible PBB or chronic sinus disease. Recurring wet cough after initial clearing with antibiotic treatment is often seen in inadequately treated sinusitis. For children with dry cough, a trial of inhaled corticosteroids (ICS) will address the possible diagnosis of asthma. Certain focused diagnostic tests may be helpful in patients in whom the diagnosis is not secured by history and physical examination, as well as in patients with specific chronic cough (Figure 2). Referral to an allergy or pulmonary specialist also is recommended, as shown in Figure 2.

A chest x-ray should be obtained in all children with chronic cough. A chest computed tomography (CT) scan without contrast is requisite to support a diagnosis of bronchiectasis or interstitial lung disease. In patients with concomitant persistent upper airway symptoms, a limited CT scan of the sinuses is most helpful when normal to rule out intrinsic sinus disease.[35] The results must be interpreted carefully, because abnormal sinus scans are not uncommon in asymptomatic children.[36]

Spirometry can be performed in most children age >6 years and in some age >3 years with training.[13] Spirometry with a bronchodilator demonstrating reversible airway obstruction (>12% improvement in forced expiratory volume in 1 second) is helpful in suggesting a diagnosis of asthma. When spirometry is normal, more advanced tests are needed to aid diagnosis. Measurements of airway hyperreactivity, such as the methacholine challenge test, are most helpful when negative; however, a positive airway hyperreactivity test does not necessarily confirm asthma or predict response to therapy. In patients with abnormal pulmonary function who do not respond to a bronchodilator or ICS, bronchiectasis, aspiration, interstitial lung disease, chronic infection, structural airway abnormalities, and cardiac etiologies should be considered.

Measurement of airway inflammation is most reliably performed with induced sputum samples. The findings of >2% eosinophils per high-power field is helpful in supporting a diagnosis of asthma and predicting a response to ICS.[37] The measurement of exhaled nitric oxide (FeNO) is helpful when normal. Kostikas et al[38] recently reported FeNO values

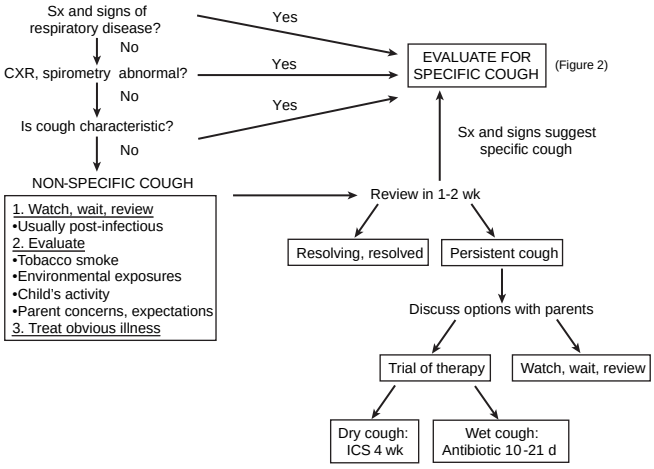

Figure 1. Algorithm for evaluating chronic cough in children. Modified with permission.[13]

>19 ppb in young adults as a cutoff point to support a diagnosis of asthma. Similar results have been reported in children. FeNO has been shown to predict response to ICS in adults with chronic cough.[39] Chronic cough in children with no history of wheezing, reversible airflow obstruction, or elevated markers of airway inflammation does not support a diagnosis of asthma.

Laboratory studies for chronic cough in children are supportive and can be used to help rule out an infectious

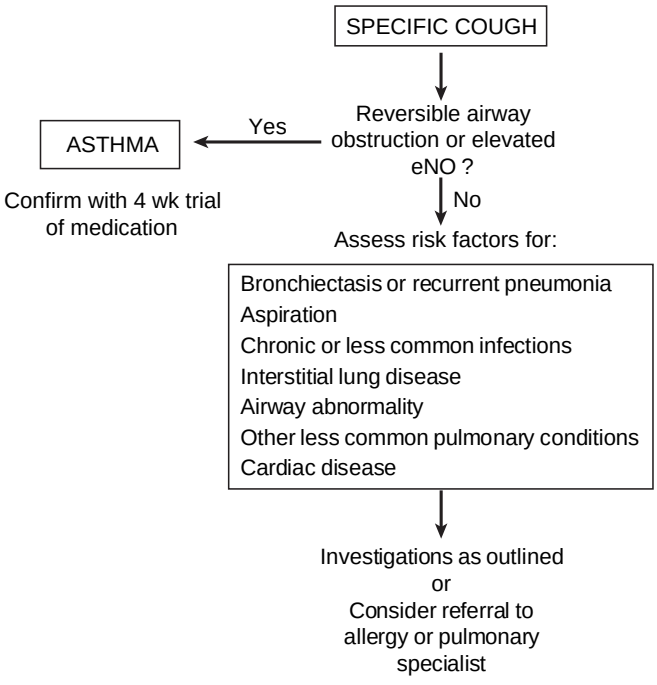

Figure 2. Algorithm for evaluating specific chronic cough in children. Modified with permission.[13]

etiology, CF, and immunodeficiency. Quantitative immunoglobulins should be measured in all children with persistent cough secondary to recurrent bacterial infections. Flexible bronchoscopy may be used to detect the presence of airway abnormalities, chronic infection, or aspiration with or without retained foreign body; however, bronchoscopy has not been shown to be useful in adults with chronic cough.[40] A pH probe study to diagnose GER with or without aspiration may be helpful; impedance studies to assess nonacid reflux are increasingly recommended.[33]

Treating Pediatric Cough

Children with chronic cough need a different management protocol than adults. Cough in children should be treated according to etiology; however, for chronic nonspecific cough, empiric trials of therapy are frequently used. There is little evidence to support the use of medications for symptomatic relief only in acute cough.[13]

OTC Cough Medications

The published data indicate that OTC cough medications have little, if any, clinical benefit beyond the placebo effect for symptom relief in children.[41] The AAP has advised against using dextromethorphan (as well as codeine) for treating any type of cough.[42] These medications have been associated with significant morbidity and rarely mortality related to intentional and unintentional ingestion.[5,6]

Asthma Therapy

Therapy for cough associated with asthma is similar to routine guideline therapy for asthma based on age.[43] It is important that the diagnosis of asthma be established, because there are no data to support the empiric use of beta-adrenergic bronchodilators, anticholinergics, theophylline, or leukotriene modifiers for chronic, nonspecific cough in children.[13]

An empiric trial of ICS is recommended in children with an isolated, dry cough for possible asthma. A moderate dose of ICS (200 to 400 μg/day fluticasone, 400 to 800 μg/day budesonide or equivalent) is recommended; the use of spacers or nebulizers depends on the patient's age and ability. Recommendations for the duration of therapeutic trials vary from 2 to 12 weeks. Most patients will respond within 4 weeks if proper inhalation technique is used. The presence of more than one cause of cough may delay the response to therapy if all causes are not treated appropriately. It is important to periodically reassess therapy and discontinue it in patients who do not respond. By itself, a response to ICS does not confirm a diagnosis of asthma. Anticholinergic bronchodilators with or without beta agonist have shown limited benefit in patients with cough, and may have some benefit in postinfectious cough.[44]

Therapy for UACS

UACS includes various types of rhinosinus diseases that can induce cough, particularly allergic or nonallergic rhinitis and sinusitis. Tonsillar hypertrophy, causing tissue impingement on the epiglottis, also has been reported to cause chronic cough in children.[34] Unlike in adults, in children antihistamines (administered alone or in combination with decongestants, dextromethorphan, or codeine) have little or no effect on the duration or intensity of acute cough and do not appear to relieve acute nocturnal cough or sleep disturbance associated with nocturnal cough.[45] ACCP adult cough guidelines recommend first-generation antihistamine therapy as first-line empiric treatment for UACS-related cough, noting that studies have not demonstrated efficacy for newer second-generation antihistamines. Significant improvements in cough in children with allergic rhinitis from treatment with oral cetirizine, terfenadine, and mometasone nasal spray have been reported. [46-48] Cough resolution from UACS can take up to 2 to 4 weeks of therapy, depending on the cause (adult data).[13]

GERD Therapy

Data are inconclusive regarding the efficacy of treating chronic nonspecific cough in children with empiric GERD therapy. Meta-analyses have not demonstrated the efficacy of GERD therapy in chronic nonspecific cough in children or adults.[31] Useful therapies for GERD in children include proton pump inhibitors, prokinetic agents, and H_2 antagonists.[32] In adult studies, the response of cough and other extraesophageal manifestations of GERD to therapy can take up to 8 to 12 weeks.[13] There is increasing recognition of nonacid reflux that does not respond to acid-suppressive therapies.

Antimicrobials

Antibiotic agents appear to have no effect during the short duration of viral upper respiratory tract infections.[49] In cases with convincing physical evidence of persistent purulent rhinosinusitis or radiographic evidence of paranasal sinus infection with symptom duration >10 days, a course of antibiotics may demonstrate a small benefit in decreasing the duration of cough.[50] PBB, seen in some young children with chronic cough, is amenable to antibiotic therapy.

Treating Habit Cough Syndrome

Various treatment modalities for habit cough syndrome have been recommended, including self-hypnosis, biofeedback, and suggestion therapy, which has been reported to result in complete cessation of symptoms within 15 minutes.[51-53] Suggestion therapy can be conducted by the general pediatrician, but the sessions require much dedicated time with the child.

Conclusion

Cough in children is common, and the majority of cases reflect respiratory infections. Cough is rarely associated with a serious disorder; all children with cough persisting for >8 weeks should be evaluated. A careful history, physical examination, chest x-ray, and spirometry (in an able child) are recommended for all children with chronic cough. If a diagnosis is not evident ("nonspecific" cough), then an approach based

on characterizing the cough as "wet" or "dry" may be helpful. In each case, specific etiology-based treatment is recommended when possible; otherwise, a therapeutic trial is indicated, with ICS for children with dry cough (for possible asthma) and antibiotics for wet cough (for possible PBB or sinusitis). If a trial of medication is used, the treatment should be reviewed within the specified time frame for normal response. If no effect is obvious, the treatment should be stopped and alternative diagnoses considered. Multiple etiologies may need to be treated concomitantly. The treatment of persistent cough in children focuses on etiology; every effort should be made to identify the underlying cause. There is no evidence supporting the use of medications for symptomatic relief of acute or chronic cough in children; some data suggests potentially harmful effects. ■

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References

1. Hay AD, Wilson A, Fahey T, Peters TJ. The duration of acute cough in preschool children presenting to primary care: a prospective cohort study. Fam Pract 2003;20:696-705.
2. Fuentes-Leonarte V, Tenias JM, Ballester F. Levels of pollutants in indoor air and respiratory health in preschool children: a systematic review. Pediatr Pulmonol 2009;44:231-3.
3. Archer LNJ, Simpson H. Night cough counts and diary cough scores in asthma. Arch Dis Child 1985;60:473-4.
4. Marchant JM, Newcombe PA, Juniper EF, Sheffield JK, Stathis SL, Chang AB. What is the burden of chronic cough for families? Chest 2008;134:303-9.
5. Lokker N, Sanders L, Perrin EM, Kumar D, Finkle J, Franco V, et al. Parental misinterpretations of over-the-counter pediatric cough and cold medication labels. Pediatrics 2009;123:1464-71.
6. Schaefer MK, Shehab N, Cohen AL, Budnitz DS. Adverse events from cough and cold medications in children. Pediatrics 2008;121:783-7.
7. US Food and Drug Administration Nonprescription Drug Advisory Committee. Cold, cough, allergy, bronchodilator, antiasthmatic drug products for over-the-counter human use, October 18 and 19, 2007. Available from: www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-02-FDA.pdf. Accessed September 21, 2008.
8. Chang AB. Cough, cough receptors, and asthma in children. Pediatr Pulmonol 1999;28:59-70.
9. O'Connell F, Thomas VE, Studham JM, Pride NB, Fuller RW. Capsaicin cough sensitivity increases during upper respiratory infection. Respir Med 1996;90:279-86.
10. Chang AB, Widdicombe JG. Cough throughout life: children, adults and the senile. Pulm Pharmacol Ther 2007;20:371-82.
11. Munyard P, Bush A. How much coughing is normal? Arch Dis Child 1996;74:531-4.
12. Kwon NH, Oh MJ, Min TH, Lee BJ, Choi DC. Causes and clinical features of subacute cough. Chest 2006;129:1142-7.
13. Irwin RS, Baumann MH, Bolser DC, Boulet LP, Braman SS, Brightling CE, et al. Diagnosis and management of cough: ACCP evidence-based clinical practice guidelines. Chest 2006;129(Suppl 1): 1S-292S.
14. Shields MD, Bush A, Everard ML, McKenzie SA, Primhak R. British Thoracic Society Guidelines: recommendations for the assessment and management of cough in children. Thorax 2008;63(suppl III). iii1-15.
15. Chang AB, Landau LI, Van Asperen PP, Glasgow MJ, Robertson CF, Marchant JM, et al. Cough in children: definitions and clinical evaluation. Med J Aust 2006;184:398-403.
16. Chang AB, Eastburn MM, Gaffney J, Faoagali J, Cox NC, Masters IB. Cough quality in children: a comparison of subjective vs bronchoscopic findings. Respir Res 2005;6:1-8.
17. Carter E, Debley J, Redding G. Chronic productive cough in school children: prevalence and associations with asthma and environmental tobacco smoke exposure. Cough 2006;2:11-8.
18. Chang AB, Redding GJ, Everard ML. Chronic wet cough: protracted bronchitis, chronic suppurative lung disease and bronchiectasis. Pediatr Pulmonol 2003;36:73-5.
19. Li AM, Lex C, Zacharasiewicz A, Wong E, Erin E, Hansel T, et al. Cough frequency in children with stable asthma: correlation with lung function, exhaled nitric oxide, and sputum eosinophil count. Thorax 2003;58:974-8.
20. McGarvey L, Warke T, McNiff C, Heaney L, MacMahon J. Psychogenic cough in a schoolboy: evaluation using an ambulatory cough recorder. Pediatr Pulmonol 2003;36:73-5.
21. Marchant J, Masters IB, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. Chest 2006;129(1 Suppl):1132S-41.
22. Khoshoo V, Edell D, Mohnot S, Haydel R, Saturno E, Kobernick A. Associated factors in children with chronic cough. Chest 2009;136:811-5.
23. Asilsoy S, Bayram E, Agin H, Apa H, Can D, Gulle S, et al. Evaluation of chronic cough in children. Chest 2008;134:1122-8.
24. Marchant JM, Masters IB, Taylor SM, Chang AB. Utility of signs and symptoms of chronic cough in predicting specific cause in children. Thorax 2006;61:694-8.
25. Chang AB, Phelan PD, Sawyer SM, Robertson CF. Airway hyperresponsiveness and cough-receptor sensitivity in children with recurrent cough. Am J Respir Crit Care Med 1997;155:1935-9.
26. Brooke AM, Lambert PC, Burton PR, Clarke C, Luyt DK, Simpson H. Recurrent cough: natural history and significance in infancy and early childhood. Pediatr Pulmonol 1998;26:256-61.
27. Donnelly D, Critchlow A, Everard ML. Outcomes in children treated for persistent bacterial bronchitis. Thorax 2007;62:80-4.
28. Marchant JM, Gibson PG, Grissell TV, Timmins NL, Masters IB, Chang AB. Prospective assessment of protracted bacterial bronchitis: airway inflammation and innate immune activation. Pediatr Pulmonol 2008;43:1092-9.
29. Sheikh S, Allen E, Shell R, Hruschak J, Iram D, Castile R, et al. Chronic aspiration without gastroesophageal reflux as a cause of chronic respiratory symptoms in neurologically normal infants. Chest 2001;120:1190-5.
30. Eid NS. Gastroesophageal reflux is a major cause of lung disease: pro. Pediatr Pulmonol 2004;(Suppl 26):194-6.
31. Chang AB, Lasserson TJ, Kiljander TO, Connor FL, Gaffney JT, Garske LA. Systematic review and meta-analysis of randomized controlled trials of gastro-oesophageal reflux interventions for chronic cough associated with gastro-oesophageal reflux. BMJ 2006;332:11-7.
32. Rudolph CD, Mazur LJ, Liptak GS, Baker RD, Boyle JT, Colletti RB, et al. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr 2001;(32 Suppl):S1-31.
33. Mattioli G, Pini-Prato A, Gentilino V, Caponcelli E, Avanzini S, Parodi S, et al. Esophageal impedance/pH monitoring in pediatric patients: preliminary experience with 50 cases. Dig Dis Sci 2006;51:2341-7.
34. Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. Pediatrics 2007;120:855-64.
35. American Academy of Pediatrics Subcommittee on Management of Sinusitis and Committee on Quality Improvement. Clinical practice guideline: management of sinusitis. Pediatrics 2001;108:798-808.
36. Diament MJ, Senac MO, Gilsanz V, Baker S, Gillespie T, Larsson S. Prevalence of incidental paranasal sinus opacification in pediatric patients: a CT study. J Comput Assist Tomogr 1987;11:426-31.

Table II. Indicators (signs and symptoms) of specific cough in children based on history and physical examination

- Daily, wet, or productive cough
- Auscultatory findings (wheeze or crackles)
- Chronic dyspnea
- Exertional dyspnea
- Hemoptysis
- Duration >6 months
- Recurrent pneumonia
- Cardiac abnormalities (including murmurs)
- Immune deficiency
- Failure to thrive
- Digital clubbing
- Swallowing problems

Modified with permission.[13]

Table III. Prospective studies of etiology of cough in pediatric patients

	Marchant et al[21]	Khoshoo et al[22]	Asilsoy et al[23]
Patient population	108; prospective cohort referred to tertiary pediatric respiratory center	40; consecutive presentation to pediatric pulmonary clinic	108; consecutive presentation over 7 months
Setting	Royal Children's Hospital, Brisbane, Australia	West Jefferson Medical Center, New Orleans, LA	Children's Hospital and Research Center, Izmir, Turkey
Age	<18 years (median, 2.6 years)	9.3 years mean	6 to 14 years (mean, 8.4 years)
Definition of chronic cough	>3 weeks (median duration, 6 months)	>8 weeks	> 4 weeks (mean duration, 4 months)
Pertinent history	43% households cigarette smoke exposure; 62% onset cough at age <1 year; 89% wet cough	No cigarette smoke exposure	56% cigarette smoke exposure; 52% wet cough; 30% family history atopy
Evaluation	All: chest x-ray, spirometry in those age >6 years, bronchoscopy/BAL (n = 102) or induced sputum (n = 4), CF evaluation, quantitative IGs, IgE, mycoplasma, and pertussis antibodies Select: HRCT chest, pH probe	All: chest x-ray, PFT, bronchoscopy, methacholine challenge, sweat test, pH/impedance monitoring, allergy testing, quantitative IGs Select: EGD, barium swallow, sinus CT, chest CT, immune evaluation, A1AT testing	All: chest x-ray, PFT Select: Bronchodilator response, chest HRCT, bronchoscopy/BAL, GI scintigraphy, nasal mucosal transport time, sweat test, quantitative IGs, PPD, mycoplasma antibodies
Findings	PBB, 40%; natural resolution, 22%; bronchiectasis, 6%; asthma, 4%; UACS, 3%; GERD, 3%; habit, 1%; idiopathic, 5%; multiple causes, 55%	GERD, 28%; UACS, 23%; asthma, 13%; idiopathic, 10%; infection, 5%; aspiration, 3%; multiple causes, 20%	Asthma, 25%; PBB, 23%; UACS, 20%; GERD, 5%; bronchiectasis, 3%; natural resolution, 2%; TB/ mycoplasma, 2%; congenital malformation, 1%; multiple causes, 19%

PFT, indicates pulmonary function test; HRCT, high resolution chest CT; EGD, esophagogastroduodenoscopy; A1AT, alpha 1 antitrypsin.

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PULMONARY
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Review

Paediatric Problems of Cough

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SUMMARY: All children cough, but most children are normal. In a child with isolated cough, a detailed history and examination, followed in a small number of cases by targeted investigations, should allow the child to be placed in one of five diagnostic categories. These are normal child; the child with a serious illness such as cystic fibrosis, tuberculosis etc. the child with non-serious, but treatable causes of cough and wheeze, for example gastro-oesophageal reflux or postnasal drip; the child with an asthma syndrome and an overestimation of symptoms for psychological or other reasons by either or both of child or family. Treatment is of the underlying condition if appropriate. Non-specific treatment with cough syrups are not useful. Attention to environmental factors such as active and passive smoking, and exposure to dust and pets is important. The diagnosis of cough variant asthma should only be made in older children after variable airflow obstruction and response to bronchodilator has been demonstrated physiologically. In younger children, rational diagnostic criteria are an abnormally increased cough, with no evidence of any non-asthma diagnosis, a clear-cut response to a therapeutic trial of asthma medication, usually moderate dose inhaled corticosteroids, and relapse on stopping medications with second response to recommencing them. Some such children go on to develop more typical asthma, with wheeze and bronchial hyper-reactivity. It is important however, not to over-diagnose asthma in children who in fact have a chronic non-specific cough. Such children require no treatment, get better with time, and have normal long-term lung function.

KEY WORDS: Cough, Asthma, Bronchiolitis, Cystic fibrosis, Primary ciliary dyskinesia.

INTRODUCTION

The physician faced with a child with a chronic and relatively non-specific symptom such as cough first needs to decide into which of five categories to place the child:

1. Normal child (the diagnosis which requires the most skill and experience).
2. A child with a serious illness such as cystic fibrosis, tuberculosis etc. (rare, but essential to get right).
3. A child with non-serious, but treatable causes of cough and wheeze, for example gastro-oesophageal reflux or postnasal drip.
4. A child with an asthma syndrome.
5. Overestimation of symptoms for psychological or other reasons by either or both of child or family.

Initial assessment is with a careful history and physical examination. It should be noted that the likelihood of a child having a serious condition depends on the setting; in a community context, isolated cough rarely betokens anything serious, but in a tertiary level hospital, selection ensures that many more coughers have a serious underlying cause.

HISTORY TAKING

The evaluation of chronic cough is notoriously difficult. Coughing is universal in childhood at least at the time of viral upper respiratory infections. There is only poor correlation between objective measures of

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Table 1 Points to seek in the history suggesting alternative diagnoses.

- Is the child wheezing as well; if so, are the child/family really describing asthmatic wheeze, or a non-specific crackling noise?
- Upper airway symptoms – snoring, rhinitis, sinusitis
- Symptoms from the first day of life
- Very sudden onset of symptoms
- Chronic moist cough/sputum production
- Worse wheeze or irritable after feed, worse lying down, vomiting, choking on feeds
- Any feature of a systemic immunodeficiency
- Continuous, unremitting or worsening symptoms
- What happens when the child is asleep

cough such as diary cards or tape recorders and perception of severity by observers.[1,2] Ambulatory cough monitoring has been used predominantly in older children[3,4,5] to document how much coughing is normal, but is are not routinely available in clinical practice. The next step is to identify the pattern and severity of symptoms. The key distinction in the pattern of symptoms is to determine whether the child has symptoms solely at the time of a viral cold and is completely well in between colds, or whether there are additional symptoms in-between colds. If the latter, symptom frequency and triggers should be determined. Specific triggers may include exercise, excited emotional behaviour including laughing or crying, dust, exposure to furry pets (the English disease), weather or environmental temperature change, strong perfumes or aerosol sprays, and smoke from cigarettes or open fires.

The severity of symptoms should next be determined, both in terms of the disruption to the child and also to the family, in order to ensure that treatment is appropriately focussed. The family of a child who coughs intermittently but is not particularly breathless may merely be seeking reassurance that there is no serious underlying disease, rather than seeking a prescription for regular inhaled medication. Particularly in the child with symptoms between colds, specific questions which should be asked are summarized in Table 1. The upper airway can be the forgotten area of paediatric respirology.[6] Much the commonest cause of chronic cough is the catarrhal child with postnasal drip. Symptoms suggestive of obstructive sleep apnoea should be sought, including snoring, apnoeic pauses, restlessness, daytime somnolence and poor concentration. Adenotonsillectomy may be completely curative of the chronic cough, and prevent the (rare) dangers of failure to thrive, pulmonary hypertension and respiratory failure. In general, the earlier the onset of cough, the more likely that an important diagnosis will be found. Symptoms from the first day of life should always be investigated; they must be distinguished from symptoms starting at a few weeks of age, which may be due to an asthma syndrome. The mother should be asked whether the problem started literally from day one of life. If this is the case, structural abnormalities of the airway should be excluded. If there is prominent and persistent rhinitis from birth, then primary ciliary dyskinesia (PCD, Kartagener's syndrome) should be considered.[7] The very sudden onset of symptoms is strongly suggestive of endobronchial foreign body. Parents may not volunteer the history, and should be asked specifically whether choking on a foreign body is a possibility.[8] Note that even babies too young to bring their own hands to their mouth may have older siblings who may have pressed small objects onto their face. Possible endobronchial foreign body should be referred by telephone for immediate investigation.

Chronic sputum production or a moist cough when the child does not have a viral cold should always be a cause for concern. Although it may be due to postnasal drip or asthma, causes of chronic pulmonary sepsis (below) such as cystic fibrosis (CF), PCD and agammaglobulinaemia may need to be excluded.

Gastro-oesophageal reflux is suspected in an infant who is worse after feeds, is an irritable feeder and vomits or possets easily. A therapeutic trial of thickening of feeds, ranitidine or omeprazole, and domperidone is reasonable on clinical suspicion without further investigation. Choking on feeds, particularly in a child with known neurodevelopmental handicap or neuromuscular disease suggests that incoordinate swallowing due to bulbar or pseudo-bulbar palsy may be the cause of symptoms. Laryngeal cleft or H-type tracheo-oesophageal fistula may present with symptoms at the time of feeding.

Another pointer to the need to refer is whether there are any periods of remission. Although symptom-free periods do not exclude the possibility of a serious underlying disease, the child who has no days free of symptoms certainly merits critical consideration of alternative diagnoses. Finally, a history of systemic infections or poor weight gain in the context of chronic respiratory disease should never be dismissed lightly. Of particular importance is an overall assessment of the well-being of the child; on this above all hinges the decision on how far to pursue investigations.

PHYSICAL EXAMINATION

Most often there will be no physical signs. Digital clubbing is an obvious and important sign, but will not be found if not actively sought; children are not uncommonly referred with obvious chronic clubbing which has never been noticed. The upper airway should be inspected for rhinitis, and nasal polyps which are virtually pathognomonic of CF in this age

Table 2 Points to seek on examination suggesting alternative diagnoses.

- Digital clubbing, signs of weight loss, failure to thrive
- Upper airway disease – enlarged tonsils and adenoids, prominent rhinitis, nasal polyps
- Unusually severe chest deformity (Harrison's sulcus, barrel chest)
- Fixed monophonic wheeze
- Stridor (monophasic or biphasic)
- Asymmetric wheeze
- Signs of cardiac or systemic disease

Table 3 Differential diagnosis of cough.

- Upper airway disease – adenotonsillar hypertrophy, rhinosinusitis, postnasal drip
- Congenital structural bronchial disease – complete cartilage rings, cysts, webs
- Bronchial/tracheal compression – vascular rings and sling, enlarged cardiac chamber, lymph nodes enlarged by tuberculosis or lymphoma
- Endobronchial disease – foreign body, tumour
- Oesophageal/swallowing problems – reflux, incoordinate swallow, laryngeal cleft or tracheo-oesophageal fistula
- Causes of pulmonary suppuration – cystic fibrosis, primary ciliary dyskinesia, any systemic immunodeficiency including agammaglobulinaemia, severe combined immunodeficiency
- Misc. – bronchopulmonary dysplasia, congenital or acquired tracheomalacia, pulmonary oedema

group. The nature and severity of any chest deformity should be noted; although a severe Harrison's sulcus and pectus carinatum can be due to uncontrolled asthma, the more severe the deformity, the greater the likelihood of another diagnosis. Palpation of the chest with the palms of the hands during quiet breathing or, in an older child, during blowing or huffing may be a better way of detecting airway secretions than auscultation. Careful auscultation may, however, elicit unexpected findings such as crackles, fixed monophonic wheeze, asymmetric signs or stridor, all of which mandate a further diagnostic work up. Finally, signs of cardiac and systemic disease should be sought. Key features to be sought on physical examination are given in Table 2, and a summary guide to differential diagnosis in Table 3. Confirmatory diagnostic tests which may need consideration are listed in Table 4. It should be emphasized that the getting the decision whether to investigate right depends solely on an excellent clinical history and physical examination.

SPECIFIC CATEGORIES OF COUGH

This section covers a few common considerations in the assessment of the child with cough. Virtually any paediatric lung disease can cause cough; I here review topics of recurrent practical clinical importance. The reader is referred to standard monographs for descriptions of diseases such as cystic fibrosis which may present with cough.

Table 4 Investigations to be considered in the child with recurrent cough.

- Suspected oesophageal disease – pH probe, barium swallow, tube oesophagram, oesophagoscopy
- Suspected upper airway disease – polysomnography, RAST tests (radiograph of postnasal space is rarely useful)
- Suspected cystic fibrosis – sweat test, nasal potentials, genotype, stool elastase, faecal fat
- Suspected primary ciliary dyskinesia – saccharine test, nasal ciliary motility, electron microscopy including orientation studies, nasal and exhaled nitric oxide
- Suspected systemic immunodeficiency – immunoglobulins and subclasses; vaccine antibodies; lymphocyte subsets; lymphocyte and neutrophil function tests; HIV test
- Suspected structural airway disease – fibreoptic bronchoscopy
- Suspected tuberculosis – Heaf test, fibreoptic bronchoscopy and/or gastric lavage, combined with culture and PCR
- Suspected cardiovascular disease – echocardiogram, barium swallow to exclude a vascular ring or pulmonary artery sling, angiography
- Suspected bronchiectasis – high resolution CT scan, investigations for local or systemic immunodeficiency

A selective approach is necessary, depending on what clues have been elicited from history, examination and simple investigations. Abbreviations: CT = computed tomography; HIV = human immunodeficiency virus; PCR = polymerase chain reaction; RAST = radio allergy sorbent test.

'Nursery school syndrome'. Many in particular first time parents do not realize the frequency with which viral infections occur in toddlers when they first go to a child care facility (about every three weeks on average). These children have chronic infective rhinitis, cough vigorously and are well, although they may keep themselves and their families up at night. Reassurance should be given; cough linctuses are useless; and I suspect many seek the help of complementary therapists.

Post-bronchiolitic cough and other symptoms. Respiratory syncytial virus (RSV) bronchiolitis is a common scourge of infancy. Prolonged cough and wheeze are common after the acute illness. Inhaled steroids are valueless in these post bronchiolitic syndromes.[9,10,11] Although a therapeutic trial with bronchodilators or inhaled steroids is often attempted, especially in atopic children, it usually does not work. Parents should be reassured that long term the symptoms will improve[12,13] in the long term, and over-treatment should be avoided.

Coughing with viral colds. All children cough with colds. Excessive coughing even without wheeze may be a variant of asthma (below). Such symptoms solely at the time of viral colds under age one year are not miniature adult asthma. A number of physiological and prospective studies have shown that this phenomenon is not due to an inflammatory airway phenotype, but due to reduction in baseline airway calibre, almost certainly on a developmental basis. The first important principle is that lung function may

be influenced by the intra-uterine environment before birth. Two studies using tidal breathing indices of lung function,[14,15] and one using the squeeze technique to produce partial flow volume curves[16] have clearly demonstrated that infants have abnormal lung function very soon after birth; risk factors include a maternal history of atopy, maternal smoking and (interestingly and quite unexplained) maternal hypertension during the pregnancy. One group has suggested on the basis of complex physiological measurements that it may be abnormal airway wall compliance rather than calibre which is important in virus associated wheeze.[17] The second principle is that infants who cough and wheeze with colds have evidence of airway obstruction *before the first wheezing episode*. It has been confirmed by three large prospective studies[18,19,20] using different lung function measurements in different populations that infants who wheeze with viral colds have abnormal lung function *before their first wheezing episode*. Thus, current best evidence is that those who cough and/or wheeze with viral colds do so because of adverse effects on airway calibre prior to birth, probably in the second half of pregnancy. The third principle is that coughing and/or wheezing with viral colds may not be associated with either BHR or airway inflammation. Two studies showed no increase in BHR in children who wheezed with viral colds.[21,22] A study in which blind bronchoalveolar lavage was carried out in children at the time of elective surgery showed that children who wheeze with viral colds did not have inflamed airways, unlike the atopic asthmatics.[23] Long-term, children who wheeze with viral colds have normal lung function whether or not they are prescribed inhaled steroids.[24] Children who wheeze with viral colds in general respond poorly to inhaled steroids,[25] but a therapeutic trial may be justified (see above), but they should be discontinued if they do not work. There is no evidence that intermittent high dose inhaled steroids commenced at the onset of a viral cold are of any value. Most paediatricians (including myself) would be more inclined to use prophylactic inhaled steroids early in atopic children, even though many will outgrow their symptoms by the start of the school years.[26] There is clearly a huge need for a simple test to identify those infants with wheeze and cough who are at high risk for ongoing symptoms and long-term impairment of lung function. One study suggested that an elevation of ECP in non-atopic infants between acute episodes was predictive of ongoing symptoms, but there was considerable overlap between groups, making ECP useful only if it was very high.[27] A more promising study showed that a raised ECP at the time of the first episode was predictive of subsequent symptoms.[28] Neither study looked at whether outcome was affected by treatment. At the present time, a high serum ECP in a non-atopic infant with excessive viral induced cough might be considered an indirect marker for airway inflammation, and be a pointer towards early treatment with inhaled steroids. However, even this view is controversial, and, if a therapeutic trial showed no symptomatic benefit for inhaled steroids, then I would not persist with them, whatever the level of ECP. A more recent study[29] proposed a model based on atopic status and soluble IL-2 receptor, but this needs confirming in another prospective study.

Does true cough variant asthma exist? Cough is undoubtedly a common symptom of asthma; can it be the only symptom, and if so, how commonly? The answer will be different, depending on the setting in which the question is posed. There is no doubt that large epidemiological studies show that *in a community setting*, where by definition the vast majority of children are well, isolated cough is rarely due to asthma and rarely responds to asthma medications.[30,31] There is also no doubt that isolated cough may frequently be over-diagnosed as asthma.[32] Chronic non-specific cough frequently improves with time and without treatment.[33,34] However, in a specialist clinic, where a highly selected group of children are seen, children who cough in response to typical asthma triggers, and improve when treated with asthma medications are not uncommonly seen.[35] My diagnostic criteria are:

1. Abnormally increased cough, with no evidence of any non-asthma diagnosis.
2. Clear-cut response to a therapeutic trial of asthma medications (see below).
3. Relapse on stopping medications with second response to recommencing them.

Many children with chronic cough in fact have only a non-specific problem, and have been shown on bronchoscopic and blind lavage studies to have no evidence of eosinophilic airway inflammation.[36,37] Follow up studies show that most will get better over 1–2 years. Others, however, will show evidence of deterioration of BHR over time, wheeze, and develop the picture of classical asthma.[38] If coughing is troublesome and the precautions outlined above are followed, then there is little to be lost attempting a brief therapeutic trial. The only danger is that ineffectual and potentially harmful medication may be continued long term unless a trial off therapy is rigorous. In older children who can perform lung function, there is no justification for a therapeutic trial without making every attempt to document variable airflow obstruction.

Chronic paroxysmal cough. The importance of cough as a symptom of asthma has been so drummed into

us, that there is a real danger that every cough of any duration is treated as asthma. Fairly regularly I see children with paroxysmal cough, sometimes with vomiting or even whooping, of several weeks duration. Invariably they have had a failed trial of inhaled steroids. Some are undoubtedly due to pertussis, others probably a result of infection with mycoplasma or viruses. Typically, the child is well between paroxysms, but the paroxysms when they come are extremely distressing. The family should be reassured and commiserated with, and all treatment stopped. Some of these children may be left with a propensity to cough excessively with future viral colds. I have never seen a formal description of this syndrome, but it undoubtedly exists, and is not asthma.

'Honk' cough. This is absolutely characteristic – once heard, never forgotten. It is a loud, stereotyped, barking noise, quite unlike any organic cough. It is exceedingly irritating to all around, and continues unabated *until the child falls asleep*, quite unlike any cough signifying underlying disease. Unless the key question 'What happens when the child is fast asleep?' is asked, a series of negative investigations and escalating and useless therapeutic trials performed, with no benefit. Once the diagnosis is appreciated, symptoms may respond to relaxation and control of breathing exercises performed by a physiotherapist. If this approach fails, then psychological intervention is required. Not infrequently, quite profound disturbance is discovered. Although some believe that this is a variant of Tourette's syndrome, I have never yet encountered a child with isolated cough to whom I needed to give treatment with Haloperidol.

A few clinical catches. Cystic fibrosis characteristically causes failure to thrive as well as chronic cough. However, around 15% are pancreatic sufficient at diagnosis, and thus thrive – this frequently results in diagnostic delay. It should be noted that delayed diagnosis is not rare – 10–15% may not be diagnosed until adult life, usually presenting with respiratory rather than gastrointestinal symptoms.

Primary ciliary dyskinesia (PCD) is also frequently not considered, even in a child with dextrocardia and neonatal onset of symptoms, until bronchiectasis has developed. Typically, the child has rhinitis from birth (often fatuously diagnosed as being born with a cold!) which continues unabated. A chronic wet cough is common. This condition is not rare (estimated 1 in 15 000 live births), and failure of diagnosis can result in considerable iatrogenic upper airway morbidity, as well as progression to bronchiectasis.[7] Once the diagnosis has been made, however, the best evidence is that progression of respiratory disease can be halted, and upper airway morbidity avoided.[39,40]

THERAPEUTIC TRIALS OF ASTHMA MEDICATION IN CHRONIC CHILDHOOD COUGH

Ultimately, after a detailed evaluation, diagnostic doubt may remain and the question of a therapeutic trial is raised in particular for infants too young to perform lung function tests. If the main problem is cough and wheeze at the time of viral colds, and the physician is satisfied that the symptoms are sufficiently outside the normal range such that treatment is indicated, then intermittent bronchodilator therapy with either an anticholinergic or beta-2 agonist is suggested. Both medications may be tried; despite popular belief that there are no beta receptors in the airway under one year of age, there is definite physiological evidence that at least some children respond to inhaled beta agonists.[41] The drug delivery device should be a mask and spacer, with appropriate instruction in use. If intermittent therapy is unavailing, a trial with an anti-inflammatory medication should be considered. It may seem illogical to use an inhaled steroid in virus associated symptoms but occasionally a trial of inhaled steroids may be merited under carefully circumscribed conditions. Occasionally, there is a dramatically beneficial effect, and the family realize that in fact the child had interval symptoms that were not appreciated until they were treated.

The other circumstance under which I would consider a therapeutic trial is in the child with nonspecific chronic symptoms, especially if atopic. The choices would appear to be either inhaled bronchodilators, inhaled corticosteroids, or oral steroid. There are no evidence based data to guide the clinician in this dilemma; my own practice is to use moderately high dose inhaled steroids (for example, budesonide 800 mcg/day) via a spacer, with a mask if age-appropriate. If the child does not show any response, then asthma is a highly unlikely diagnosis. The alternative choices for a therapeutic trial would be high dose β-2 agonists, cromoglycate, or oral prednisolone. It is true that asthmatics should show some response to bronchodilators, but it is likely that if they fail, a trial of a more potent medication is likely to be performed to ensure that asthma can be ruled out, and the β-2 agonist trial only delays matters. Cromoglycate has been shown to be largely ineffective in children of this age.[42] Oral steroids are effective in asthmatics, but also treat allergic rhinitis and temporarily reduce the size of the adenoids, and so are not specific for lower airway inflammation, as well as having a greater potential for side-effects.

If the symptoms disappear after three months on inhaled steroids, the treatment must be stopped to ensure that the child has not improved coincidentally, after for example prolonged post mycoplasma or

post-viral cough. Only if symptoms recur on stopping inhaled steroids can the diagnosis of asthma be said to be established, and long term treatment instituted according to established guidelines. If there is no response to a therapeutic trial, then referral to a paediatrician with special expertise in respiratory medicine should be considered.

NON-PHARMACOLOGICAL MANAGEMENT OF COUGH

A detailed appraisal of environmental factors should be undertaken. Passive smoking is the most important adverse environmental factor impacting on respiratory health; the abject refusal of governments worldwide to tackle this is a scandal. Allergen avoidance is also important. The importance of different allergens varies between countries. In England, house dust mite and pet allergens (cats and dogs) are most important; each country will need to target their own important allergens. Recent evidence has underscored the importance of 'subclinical' allergen exposure. Allergen exposure in vitro may contribute to poor asthma control by reducing the binding affinity of glucocorticoid receptors.[43] In vivo, repeated allergen challenges in sensitized subjects with doses insufficient to cause acute changes in lung function resulted in increased bronchodilator use, worse bronchial hyper-reactivity and deterioration in airway inflammation.[44] Food allergy as a cause of symptoms is rare; in ethnic Asians, Coca-Cola, fried foods and very cold foods may provoke asthma.[45] In general, the search for an isolated food allergy which will cause cough to disappear is unrewarding. Environmental pollution may certainly worsen cough. The role of housing ('can I have a letter for the housing, doctor?') is controversial and has recently been debated.[46,47]

SUMMARY AND CONCLUSIONS

Cough is universal in childhood, but most children are normal. Clues that all is not well come from a well-taken clinical history and physical examination. If every child with cough is investigated, then all other work will cease. Careful clinical assessment should lead to targetted investigations in those children with suspicious or atypical features.

REFERENCES

1. Archer L N J, Simpson H. Night cough counts and diary card scores in asthma. Arch Dis Child 1985; 60: 473–474.
2. Falconer A, Oldman C, Helms P. Poor agreement between reported and recorded nocturnal cough in asthma. Pediatr Pulmonol 1993; 15: 209–211.
3. Munyard P, Busst C, Logan-Sinclair R, Bush A. A new device for ambulatory cough recording. Pediatr Pulmonol 1994; 18: 178–186.
4. Munyard P, Bush A. How much coughing is normal? Arch Dis Child 1996; 74: 531–534.
5. Chang A B, Newman R, Phelan P D, Robertson C F. 24-hour continuous ambulatory cough meter: a new use for an old Holter monitor. Am J Respir Crit Care Med 1996; 153: A501.
6. de Benedictis F M, Bush A. Hypothesis paper: Rhinosinusitis and asthma – epiphenomenon or causal association? Chest 1999; 115: 550–556.
7. Bush A, Cole P, Hariri M, et al. Primary ciliary dyskinesia: diagnosis and standards of care. Eur Respir J 1998; 12: 982–988.
8. Puterman M, Gorodischer R, Lieberman A. Tracheobronchial foreign bodies: the impact of a postgraduate educational program on diagnosis, morbidity and treatment. Pediatrics 1982; 70: 96–98.
9. Cade A, Brownlee K G, Conway S P, et al. Randomised placebo controlled trial of nebulised corticosteroids in acute respiratory syncytial viral bronchiolitis. Arch Dis Child 2000; 82: 126–130.
10. Richter H, Seddon P. Early nebulized budesonide in the treatment of bronchiolitis and the prevention of postbronchiolitic wheezing. J Pediatr 1998; 132: 849–853.
11. Everard M L. What link between early respiratory viral infections and atopic asthma? Lancet 1999; 354: 527–528.
12. Welliver R C. The role of RSV IgE in recurrent wheezing and asthma. In: Cloutier M M ed. RSV and asthma: is there a link? American Thoracic Society, USA 1998; 21–27.
13. Stein R T, Sherrill D, Morgan W J, et al. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. Lancet 1999; 354: 541–545.
14. Lodrup-Carlsen K C, Jaakkola J J, Nafstad P, Carlsen K H. In utero exposure to cigarette smoking influences lung function at birth. Eur Respir J 1997; 10: 1774–1779.
15. Stick S M, Burton P R, Gurrin L, Sly P D, LeSouef P N. Effects of maternal smoking during pregnancy and a family history of asthma on respiratory function in newborn infants. Lancet 1996; 348: 1060–1064.
16. Young S, LeSouef P N, Geelhoed G C, et al. The influence of a family history of asthma and parental smoking on airway responsiveness in early infancy. N Engl J Med 1991; 324: 1166–1173.
17. Frey U, Makkonen K, Wellman T, Beardsmore C, Silverman M. Alterations in airway wall properties in infants with a history of wheezing disorders. Am J Respir Crit Care Med 2000; 161: 1825–1829.
18. Martinez F D, Morgan W J, Wright A L, et al. Diminished lung function as a predisposing factor for wheezing respiratory illness in infants. N Engl J Med 1988; 319: 1112–1117.
19. Tager I B, Hanrahan J P, Tostesan T D, et al. Lung function, pre- and post-natal smoke exposure, and wheezing in the first year of life. Am Rev Respir Dis 1993; 147: 811–817.
20. Young S, O'Keeffe P T, Arnot J, Landau L. Lung function, airway responsiveness, and respiratory symptoms before and after bronchiolitis. Arch Dis Child 1995; 72: 16–24.
21. Clarke J R, Reese A, Silverman M. Bronchial responsiveness and lung function in infants with lower respiratory tract illness over the first six months of life. Arch Dis Child 1992; 67: 1454–1458.
22. Stick S, Arnot J, Landau L, Turner D, Sly S, LeSoeuf P. Bronchial responsiveness and lung function in recurrently wheezy infants. Am Rev Respir Dis 1991; 144: 1012–1015.
23. Stevenson E C, Turner G, Heaney L G, et al. Bronchoalveolar lavage findings suggest two different forms of childhood asthma. Clin Exp Allergy 1997; 27: 1027–1035.
24. Oswald H, Phelan P D, Lanigan A, et al. Childhood asthma and lung function in mid-adult life. Pediatr Pulmonol 1997; 23: 14–20.
25. Wilson N, Sloper K, Silverman M. Effects of continuous treatment with topical corticosteroids on episodic viral wheeze in preschool children. Arch Dis Child 1995; 72: 317–320.

Julia A. McMillan, MD

Investigating OTC cough and cold medications

Why did it take so long?

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On October 7, 2008, the president of the Consumer Health Care Products Association announced that makers of over-the-counter (OTC) cough and cold medications would voluntarily change the labeling on those products to indicate that they should not be used for children less than 4 years of age. This was the most recent victory, following filing of a petition to the Food and Drug Administration (FDA) in March 2007 by 14 Maryland pediatricians[1] calling for an end to the use of OTC cough and cold medications for children less than 6 years of age.

The petition highlighted both the risk of overdose and attendant adverse effects, as well as the lack of efficacy of these products in children. They cited, in particular, the deaths of four Maryland toddlers linked to cough and cold medications.

Just six months after that petition was filed, in October 2007—and days before an FDA advisory committee meeting on the subject—the makers of 14 OTC preparations intended for use in children less than 2 years voluntarily withdrew those products from the market.

In January 2008, the FDA issued a Public Health Advisory strongly recommending that "over the counter cough and cold products should not be used in infants and young children under the age of two because serious and potentially life-threatening side effects can occur from use of these products."[2]

The October 7 announcement by pharmaceutical companies that their labels will henceforth warn against OTC cough and cold medication use in children less than 4 years comes on the heels of the announcement of a year-long FDA review of these products, which began with public hearings just a week earlier. Previous published studies have found little to no benefit from use of antihistamines, decongestants, cough suppressants, expectorants, or from combinations of these agents in children.

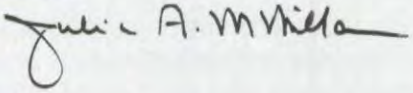
The reported adverse events have most often occurred because infants and children receive more than the "recommended" dose, because they receive more than one combination product containing the same ingredient, or because they receive a single product more often than recommended.

The imprecision with which many medications are dosed is highlighted in the clinical tip from Alvin Eden, MD, (p. 14 of this issue). Frequently these products are administered by parents without advice or recommendation from physicians, but, as Dr. Eden points out, pediatricians and pharmacists do not always provide precise instructions for parents even when they are consulted.

Pediatricians have known for decades that the estimated $286 million spent on OTC cough and cold medications for young children each year brings little to no relief, and potentially causes harm. The Centers for Disease Control and Prevention has reported that an estimated 7,000 children present to emergency departments annually because of ingestion of excessive cough and cold preparations.

Why has it taken so long for attention to be focused on ineffective, potentially risky products being used to treat self-limiting symptoms? Parents, understandably, have assumed that if pediatricians weren't objecting to the sale of these products, and if the FDA was allowing their sale with labeling explicitly suggesting an appropriate dose for infants and young children, they must be safe and they must work.

Congratulations to the Maryland pediatricians who filed the citizen's petition urging the FDA to investigate the safety and effectiveness of OTC cough and cold preparations. I'm just wondering where the rest of us have been all these decades. □



References

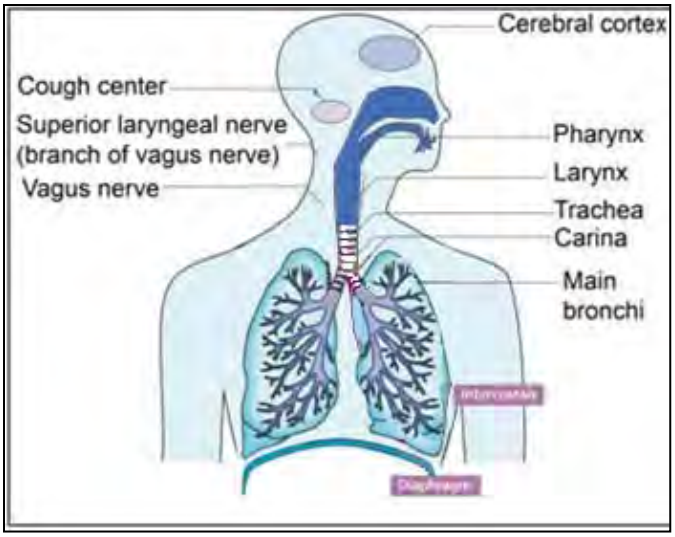
1. The Baltimore Statement on the Use of Over-the-Counter Cough and Cold Medications by Children Five and Under. Available at: www.baltimorehealth.org/press/OTC%20statement%20-%20final.pdf. Accessed Oct. 16, 2008
2. Transcript of FDA Press Conference on Cough and Cold Medicine. Available at: www.fda.gov/bbs/transcripts/2008/coughcold_transcript011708.pdf. Accessed Oct. 16, 2008

IMAGE: KATHRYN MILLER

Chronic Cough Quiz

1. **What is the role of cough?**

2. **Complete this diagram of the cough reflex. What conditions can cause ↑ or ↓CRS?**



(1) **Afferent pathway**:
Draw arrows and include cough receptors

(2) **Efferent pathway**:
Draw arrows

(3) **CNS cortical modulation:**
Draw arrows

- ↑CRS: _____
- ↓CRS: _____

3. **Fill in the following numbers related to chronic cough:**
   a) Percent of school-kids still coughing 10 days s/p common cold: _____
   b) Number of cough episodes per day in a "normal" child: _____
   c) Length of acute vs. subacute vs. chronic cough: _____
   d) 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, β2 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: A 5 year-old male 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?

Mom 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. Mom 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?

Mom 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? Which of Bush's 5 diagnostic categories (*from the PP&T article*) would you place him in?

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

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

Case 2: A 3 yo male presents with parental concern for prolonged cough x 2 weeks. Father describes the cough as "junky" or "wet-sounding". The cough occurs throughout the day ("at least 20 times") and also wakes him up at night ("at least 2 times"). Dad reports that his son is "wheezing" and he can feel his chest "rattling" when he hugs him. There is 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 he's *almost* 4"). He 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 J of Peds Algorithm, what will you recommend? Any other suggestions?

The patient returns 2 wks later, having followed your home-care advice, and dad reports that his son'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 their son hyper.

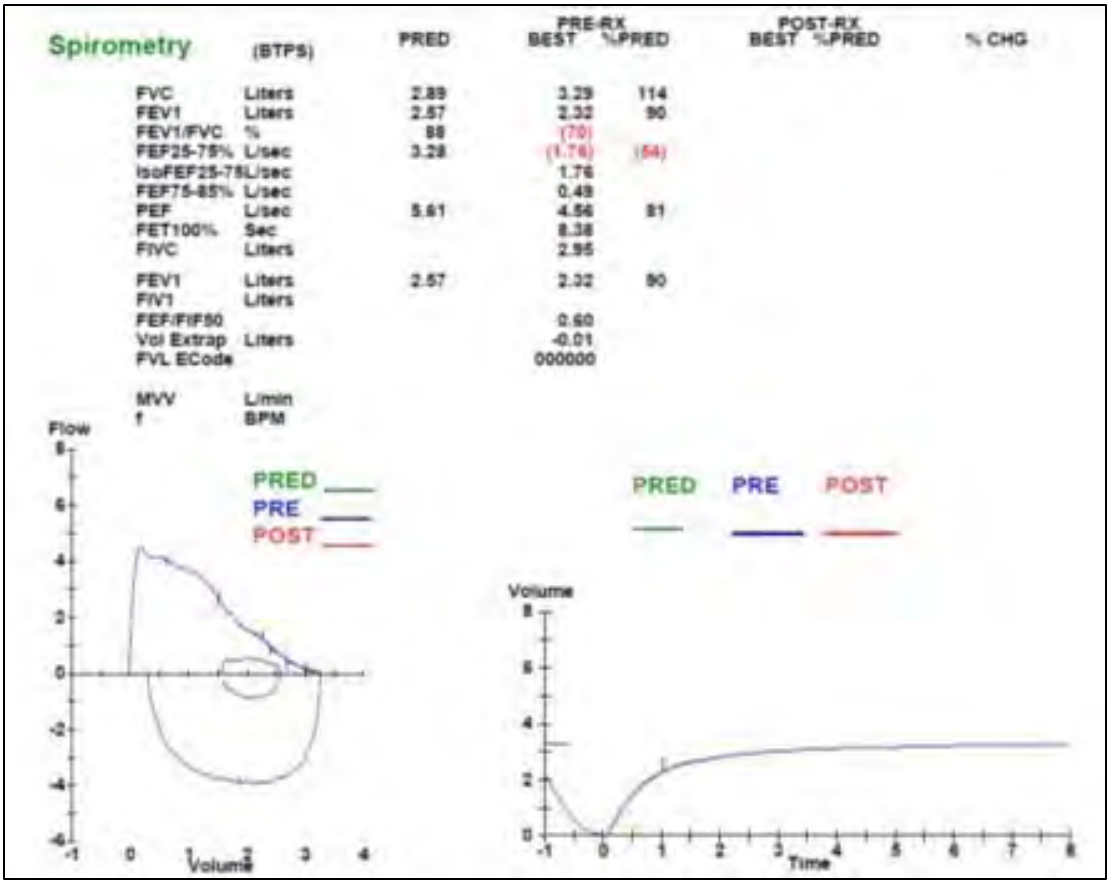
What is your working diagnosis? Which diagnostic category does this patient fit?

Using the J of Peds Algorithm, what will you recommend now? Any labs or other studies?

***Bonus Case 3*:** A 7 year old female 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.



Which of Bush's 5 diagnostic categories would you place this patient in? 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