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Chest 2006;129;260-283
DOI 10.1378/chest.129.1_suppl.260S

Guidelines for Evaluating Chronic Cough in Pediatrics

ACCP Evidence-Based Clinical Practice Guidelines

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Objectives: **To review relevant literature and present evidence-based guidelines to assist general and specialist medical practitioners in the evaluation and management of children who present with chronic cough.**

Methodology: **The Cochrane, MEDLINE, and EMBASE databases, review articles, and reference lists of relevant articles were searched and reviewed by a single author. The date of the last comprehensive search was December 5, 2003, and that of the Cochrane database was November 7, 2004. The authors' own databases and expertise identified additional articles.**

Results/conclusions: **Pediatric chronic cough (*ie*, cough in children aged < 15 years) is defined as a daily cough lasting for > 4 weeks. This time frame was chosen based on the natural history of URTIs in children and differs from the definition of chronic cough in adults. In this guideline, only chronic cough will be discussed. Chronic cough is subdivided into specific cough (*ie*, cough associated with other symptoms and signs suggestive of an associated or underlying problem) and nonspecific cough (*ie*, dry cough in the absence of an identifiable respiratory disease of known etiology). The majority of this section focuses on nonspecific cough, as specific cough encompasses the entire spectrum of pediatric pulmonology. A review of the literature revealed few randomized controlled trials for treatment of nonspecific cough. Management guidelines are summarized in two pathways. Recommendations are derived from a systematic review of the literature and were integrated with expert opinion. They are a general guideline only, do not substitute for sound clinical judgment, and are not intended to be used as a protocol for the management of all children with a coughing illness. Children (aged < 15 years) with cough should be managed according to child-specific guidelines, which differ from those for adults as the etiologic factors and treatments for children are sometimes different from those for adults. Cough in children should be treated based on etiology, and there is no evidence for using medications for the symptomatic relief of cough. If medications are used, it is imperative that the children are followed up and therapy with the medications stopped if there is no effect on the cough within an expected time frame. An evaluation of the time to response is important. Irrespective of diagnosis, environmental influences and parental expectations should be discussed and managed accordingly. Cough often impacts the quality of life of both children and parents, and the exploration of parental expectations and fears is often valuable in the management of cough in children.** ***(CHEST 2006; 129:260S–283S)***

Key words: asthma; children; cough; evidence-based medicine; guideline; treatment

Abbreviations: ACE = angiotensin-converting enzyme; AHR = airway hyperresponsiveness; ARI = acute respiratory infection; ETS = exposure to tobacco smoke; GER = gastroesophageal reflux; GERD = gastroesophageal reflux disease; HRCT = high-resolution chest CT; ICS = inhaled corticosteroid; NO = nitric oxide; OTC = over the counter; RCT = randomized controlled trial; URTI = upper respiratory tract infection

Clinicians specializing in children's health are well aware of the limitations and possible adversity in the extrapolation of data from adults to children.[1,2] Child-specific guidelines are differentiated from those for adults in common respiratory diseases such as community-acquired pneumonia[3–5] and asthma.[6] However, rigidity in the adherence to child-specific data may also be disadvantageous to children, given

the relative paucity in pediatric research in comparison to research in adults.[1] In the area of cough, there are similarities but also clear clinical and physiologic differences between children and adults. Some adult definitions (*eg*, chronic bronchitis and COPD are not recognized diagnostic entities in the pediatric respiratory literature and main textbooks[7,8]) are inappropriate for children. Etiologic differences and frequency etiologies associated with cough are also evident from the literature.[9–11] Furthermore, adults and children also have different responses to some medications (*eg*, first-generation antihistamines that are efficacious for treating cough in adults are not only not beneficial in children when the evidence is critically evaluated,[12,13] but their use is also associated with more morbidity[14,15] in children when compared to adults). Personal and institutional practice may well differ from the evidence reviewed and presented in this article. This review is focused on chronic cough, and the data are limited to children unless specifically stated. Although the cutoff age for pediatric care in the United States is 18 years, we have chosen a lower cutoff age here (*ie*, 14 years of age) based on the limited evidence in the cough literature that adolescents are more like adults (*eg*, the response to over-the-counter (OTC) medications for cough as summarized in a Cochrane review[16]).

The Cochrane, MEDLINE, and EMBASE databases, review articles, and reference lists of relevant articles were searched and reviewed by a single author. All recommendations were based on the pediatric literature and current evidence, and were accepted by the panel on December 5, 2004.

Defining Cough in Children

Cough can be defined based on time frame (*ie*, duration of cough), quality (*eg*, dry or wet,[17] brassy, or staccato), or suggested etiology (*ie*, specific and nonspecific).[11] The majority of the terms defined below have been used in various publications.[11,18,19] The background for justification of the use of these terms has been reviewed elsewhere.[20] Chronic cough in children is defined as a cough of > 4 weeks duration based on the current data of cough related to acute upper respiratory infections in children.[21,22] This review and the evidence presented are also focused on nonspecific chronic cough (*ie*, cough in the absence of symptoms outlined in Table 1) as data on specific cough would encompass the entire spectrum of pediatric respiratory disease.

Clinical History, Examination, and Investigations

There is a general lack of data on the specificity and sensitivity of individual symptoms when evaluating cough in children. Furthermore, other than the validity of using dry/wet cough and brassy/nonbrassy in children,[17] there are few data on the validity of other cough characteristics and/or clinical examination. There are also only case series or cohort data relating to the value of available investigations for the evaluation of chronic cough in children. The data are summarized in Table 2.[66,73,74,79,80,88,89,94,103,105,106,117,252–261] As chronic cough can be associated with significant consequences (*eg*, a retained foreign body causing bronchiectasis), each child with chronic cough should be thoroughly reviewed and when appropriate relevant investigations should be performed. Clearly, the extent of investigations should be based on the clinical setting, population examined, and available expertise. Adverse events to investigations must be considered as, in children, some investigations such as CT scans have a higher risk from radiation and general anesthesia (if required) when compared with adults.

Etiologic Associations

Some of these aspects have been reviewed previously[9,23–25] and limited new data are presented (Table 3[9,89,94,103–105,175,177,262–264]) due to space limitations. Unlike adult data, the relationship between cough and upper airways disorders, asthma, gastroesophageal reflux disease (GERD) [as well as the frequency of these disorders] is less convincing in children. Other considerations for the etiology of nonspecific cough include the inhalation of a foreign body, airway lesions, environmental pulmonary toxicants, nonasthmatic eosinophilic bronchitis (poorly described in the pediatric literature), respiratory infections and postinfectious cough, the side effects of medications, and otogenic causes.

Evidence-Based Treatment

Based on the current knowledge of the large placebo effect seen in cough studies and shown in all randomized controlled trials (RCTs) in children,[12,13,26] data based on cohort studies must be interpreted with caution. Furthermore, the report-

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Table 1—*Pointers to the Presence of Specific Cough*

Abnormality	Examples of Etiology
Auscultatory findings	Wheeze-intrathoracic airway lesions (*eg*, tracheomalacia, asthma); crepitations, any airway lesions (from secretions), or parenchyma disease such as interstitial disease
Cardiac abnormalities	Associated airway abnormalities, cardiac failure
Chest pain	Arrhythmia, asthma
Dyspnea or tachypnea	Any pulmonary airway or parenchymal disease
Chest wall deformity	Any pulmonary airway or parenchymal disease
Digital clubbing	Suppurative lung disease
Daily moist or productive cough	Suppurative lung disease
Exertional dyspnea	Any airway or parenchymal disease
Failure to thrive	Any serious systemic including pulmonary illness such as cystic fibrosis
Feeding difficulties	Any serious systemic including pulmonary illness, aspiration
Hemoptysis	Suppurative lung disease, vascular abnormalities
Hypoxia/cyanosis	Any airway or parenchyma disease, cardiac disease
Immune deficiency	Suppurative lung disease or atypical infection
Neurodevelopmental abnormality	Aspiration lung disease
Recurrent pneumonia	Immunodeficiency, atypical infections, suppurative lung disease, congenital lung abnormalities, trachea-esophageal H fistulas

ing of cough is biased,[27] and Hutton et al[28] described the fact that "parents who wanted medicine at the initial visit reported more improvement at follow-up, regardless of whether the child received drug, placebo, or no treatment."

In general, the management of specific cough should be based on etiology. When the underlying condition or exacerbating factor is managed, cough subsequently resolves. For example, the severity and frequency of wet cough resolves following the management of an acute exacerbation of chronic suppurative lung disease. The management of specific cough encompasses the entire spectrum of pediatric pulmonology, which is well beyond the scope of this article. (A guideline for nonspecific cough, with its limited evidence, is presented in Figures 2 and 3, and the evidence is presented in the text and summarized in Table 4[12–16,74,75,79,90,91,122,207,208,211,215,225–227,231–233,237,265–271].) Irrespective of the cause of cough, particular attention to tobacco smoke exposure as well as parental expectations and concerns are advised, based on data on acute upper respiratory infections. When appropriate and when no pediatric data exist, readers are referred to the adult guideline, but this extrapolation should be cautiously accepted. If a trial of medications is warranted, "time response" (Table 4) should be considered, the child's case should be reviewed within the relevant time frame, and therapy with medications should be stopped when appropriate.

Introduction and Background

In the management of illnesses in children, the extrapolation of adult-based data to children can sometimes result in unfavorable consequences.[1,2,29] The pattern of respiratory illness in children is clearly different from that in adults; for example, viruses associated with the common cold in adults can cause serious respiratory illnesses such as bronchiolitis and croup in previously well young children.[30] Thus, it is not surprising that pediatric-specific guidelines exist for children in the management of common illnesses such as asthma,[6] GERD,[31] and community-acquired pneumonia.[3–5]

The physiology of the respiratory system in children is similar to that in adults in many ways. However, there are also distinct differences between young children and adults, including maturational differences in airway, respiratory muscle, and chest wall structure, sleep-related characteristics, respiratory reflexes, and respiratory control.[32–34] In the physiology of cough, gender differences in cough sensitivity that are well-recognized in adults[35] are absent in children.[36] In children, cough sensitivity is instead influenced by airway caliber (*ie*, FEV_1) and age.[36] the plasticity or adaptability of the cough reflex has been shown in animals,[37] and one can speculate that there are also maturational differences in the cough reflex.[38] In young children, the medical history is limited to parental perception and availability. The combination of these factors results in variations in differential diagnoses. As an example, the unknown inhalation of a foreign body (delayed diagnosis can result in permanent lung damage[39]) is not uncommon in children; the frequency of acute upper respiratory tract infections (URTIs) is age-related; studies from the 1940s to the 1960s have shown that children have 5 to 8 acute respiratory infection (ARI) episodes per year,[40] while in more recent studies[41] children aged < 5 years have 3.8 to

Table 2—*Summary of Studies That Described the Yield of Specific Investigations for Cough in Children

Study	Indication and Study Population	Key Findings and Authors' Conclusion	Additional Points or Limitations of Study/Test
Chest CT scans			
Coren et al[252]	Case series, chronic productive cough, tertiary hospital	Yield, 43%, where bronchiectasis was documented	Yield of CT scan in the evaluation of isolated cough without the presence of specific cough pointers (Table 1) is unknown
Sinus CT scans			
Tatli et al[253]	Case series, chronic cough, otolaryngology clinic	66% abnormal, but rhinorrhea, nasal congestion, sniffling, and postnasal drip had no significant relationship with paranasal sinus CT scan abnormality	50% asymptomatic children have incidental sinus abnormality[254]; poor concordance in diagnostic modalities[117]
Flexible bronchoscopy			
Callahan[88]	Case series, chronic cough, private clinic	Bronchoscopy assisted in the diagnosis in five (5.3%) children	
Thomson et al[89]	Case series, chronic cough, tertiary center	Airway abnormalities (mainly tracheobronchomalacia) present in 46%	Unknown cause and effect
Airway fluid/lavage and cellular assessment			
Fitch et al[105]	Case series, untreated persistent cough	3 of 23 children had asthma-type airway inflammation	
Zimmerman et al[94]	Case series, post infectious cough, treated and untreated asthmatic patients, tertiary hospital	6 of 11 children with post infectious cough had AHR, but airway eosinophils and eosinophil cationic protein were normal	
Gibson et al[103]	Cohort, community study; four groups (wheeze, cough, recurrent chest colds, control subjects)	"Persistent cough and recurrent chest colds without wheeze should not be considered a variant of asthma"	
Marguet et al[106]	5 groups: asthma, chronic cough, infantile wheeze, cystic fibrosis, and control	"Chronic cough is not associated with the cell profiles suggestive of asthma and in isolation should not be treated with prophylactic antiasthma drugs"	
Kim et al[255]	Cohort, "cough-variant asthma"	> 2.5% eosinophils in sputum were more likely to have classical asthma on follow-up	No control group
Colombo and Hallberg[256]	Evaluation of lipid-laden macrophage index as an indicator of aspiration as a cause of chronic cough		Increased lipid-laden macrophages index is found in other lung diseases in the absence of aspiration[257–259]; useful supportive but not diagnostic evidence
Airway hyperresponsiveness			
Chang et al[74]	RCT, chronic cough	AHR unpredictive of efficacy of inhaled salbutamol and corticosteroids (400 μg beclomethasone/d) for cough frequency or cough sensitivity in children with recurrent cough	Older studies on AHR mentioned in text
Strauch et al[260]	Cohort, community study	AHR associated with wheeze and dyspnea but not associated with dry cough or nocturnal cough once confounders were accounted for	
Galvez et al[73]	Case series, mixture of children and adults	Some had spirometric evidence of obstructive airways before AHR (FEV_1, 62%); 97% of AHR-positive subjects improved after asthma Rx; 87% of AHR-negative subjects also improved after asthma Rx	
Spirometry			
Hannaway and Hopper[80]	Chronic cough, hospital	12 of 20 children (60%) who performed spirometry had abnormalities	Spirometry is relatively insensitive[66,261]
	Chronic cough, hospital	6 of 8 children who had spirometry had $FEV_1 < 85\%$[79]	
Thomson et al[89]	Spirometry results were normal in all able to perform the test	Normal spirogram finding does not exclude underlying respiratory abnormalities	

*Rx = treatment.

Table 3—*Additional Studies Since Review[9] That Specifically Examined the Relationship Between Cough and Asthma, and Between Chronic Cough and Infections in Children*

Study	Indication and Study Population	Key Findings and Authors' Conclusion	Additional Points or Limitations of Study/Test
Asthma			
Thomson et al[89]	Case series, chronic cough, tertiary center (n = 49)	None had asthma as the sole final diagnosis; asthma was coexistent in 2 but cough was not related to asthma.	
Faniran et al[104]	Community-based study, chronic cough (n = 1,178)	"Cough variant asthma is probably a misnomer for most children in the community who have persistent cough"	See also studies[94,103,105,105] in Table 2
Infections			
Senzilet et al[262]	Adolescents and adults with cough of 7–56 days duration (n = 442)	20% had either laboratory confirmed or laboratory evidence of pertussis	
Hallander et al[177]	Prospective vaccine study—children (aged 3–34 mo) tested (*Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Bordetella parapertussis*, and *Bordetella pertussis*) if the child or household member coughed for > 7 d	115 etiologic agents were identified in 64% of episodes (99/155) with cough for < 100 d; most common single agent was *B pertussis* in 56% (64/115), with a median cough period of 51 d, followed by *M pneumoniae* in 26% (30/115), mean cough period of 23 days, *C pneumoniae* in 17% (19/115), 26 d, and *B parapertussis* in 2% (2/115)[177]	Other microbial studies were not done, and other possible etiologies of cough were not considered; a factor that needs to be considered when analyzing such results is determining whether the infectious agent isolated is the cause of the cough[263]
Tozzi et al[175]	Prospective study in children < 6 years of age	Median duration of cough in unvaccinated (for pertussis) children was 52–61 d, that for vaccinated children was 29–39 d; respective median duration of spasmodic cough was 20–45 d and 14–29 d[175]	In children who received the acellular pertussis vaccination, pertussis infection is clinically difficult to distinguish from diseases associated with coughing caused by *B parapertussis* and other viral or bacterial infections[264]

5 infections per person per year and adults have only 2. Respiratory tract carcinomas, which are not uncommon in adults, are very rare in children, and radiation from high-resolution CT (HRCT) scans of the chest in children carry higher risks.[42] While cough may be a manifestation of asthma in both adults and children, other common causes of cough and respiratory diseases in adults such as chronic bronchitis[43] and COPD are not recognized diagnostic entities in the pediatric respiratory literature and textbooks.[7,8] Thus, the management of childhood cough should be distinguished from that of adult cough, and it mandates a separate guideline that focuses on cough in children that is relevant to children < 15 years of age. This guideline, which is applicable in more affluent countries like the United States, the United Kingdom, and Australia, requires appropriate adaptations in other population settings[44] such as in Native American[45] and Australian[19] aboriginal communities in which bronchiectasis is relatively common (*ie*, 147 to 200 cases per 10,000 children).

Pediatric cough can be classified in several ways, including those based on etiology,[23] time frame,[11] characteristics (*eg*, moist vs dry),[17] and specific and nonspecific cough (Fig 1) with a degree of overlap. The definition of chronic cough in children, however, varies from 3 weeks[46,47] to 12 weeks in duration.[11,48] There are no studies that have clearly defined when cough should be defined as chronic or persistent. A systematic review[22] showed that cough related to an acute URTI resolves within 1 to 3 weeks in most children. A prospective cohort study[21] by the same group conducted in preschool children presenting to primary care showed that 10% of children were still coughing 25 days after a URTI. They did not describe whether those children with prolonged cough had complications of URTI such as pneumonia or bacterial bronchitis. Based on the natural history of URTIs and differences between adults and children, we define pediatric chronic cough as a daily cough lasting for > 4 weeks. In this guideline, only chronic cough will be discussed and its management summarized in two pathways (Fig 2, 3).

When considering cough in children, clinicians should be cognizant of some general issues, which

Table 4—*Summary of Therapies Used for Nonspecific Cough as Reported in Literature Based on Controlled Trials*

Therapy	Time to Response*	Level of Evidence	Data Limitation and Considerations
Antihistamines			
Chronic cough	1 wk	RCTs[265,266]	Adverse events,[13–15]; inconclusive data
Acute cough	Not relevant	Systematic review,[12] RCT[13]	Nonbeneficial
Antimicrobials	1–2 wk	Systematic reviews,[227] RCTs[225,226]	Some benefit, adverse events, cost/benefit ratio[267]
Asthma type therapy			
Cromones	2 wk	Systematic review[215]	Single open trial only[268]
Anticholinergics	No data	Systematic review[211]	No trials in children
Inhaled corticosteroids	2–4 wk	RCTs[74,90]	Small benefit if any, adverse event
Oral corticosteroids		No data	No RCTs, adverse events
β_2-agonist (oral or inhaled)	Not relevant	Systematic review,[210] RCT[74]	Non beneficial[74,91]; adverse events[91]
Theophylline	1–2 wk	Observational studies[75,79,80]	No RCTs, adverse events
Leukotriene receptor antagonist		No data	No trials in children
GERD therapy			
Motility agents	Not relevant	Single controlled trial[233]	No benefit, adverse events; systematic reviews on cisapride[269] and metoclopramide[237] showed no benefit for GER but cough was not an outcome measure
Acid suppression		No data	No RCT on proton pump inhibitors, adverse events
Food-thickening or antireflux formula	1 wk	Systematic review,[237] RCTs[231,232]	Inconclusive data; one reported increase in cough[231] and a second reduction[232]
Head positioning	Not relevant	Systematic review[237]	No benefit, systematic showed no benefit for GER, and cough was not an outcome measure[269]
Fundoplication		No data	No RCT, adverse events
Herbal antitussive therapy		No data	No RCTs
Nasal therapy			
Nasal steroids	1–2 wk	RCT[122]	Mainly adults and older children (> 12 yr of age) in RCT, beneficial when combined with antibiotics for sinusitis[270,271]
Other nasal sprays		No data	No RCT, adverse events
OTC cough medications	Not relevant	Systematic review,[12,16] RCT[13]	Non beneficial, adverse events[207,208]
Other therapies			
Steam, vapor, rubs		No data	No RCTs, adverse events (*eg*, burns)

*Time to response = expected reduction in cough severity if treatment is effective, as reported by trialists; No data = no pediatric data.

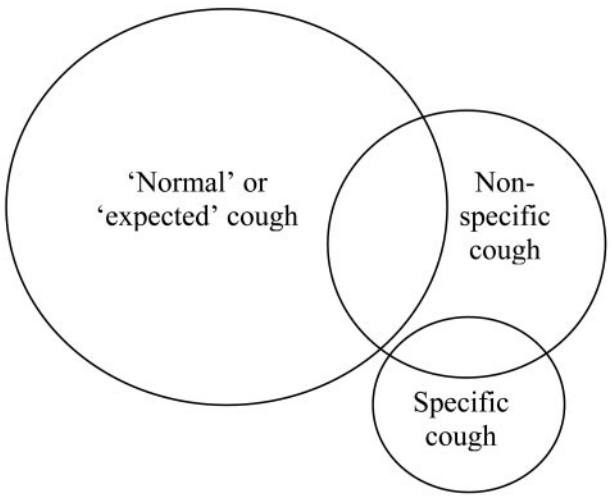

FIGURE 1. Classification of types of cough in children. The figure was reproduced from the article by Chang.[272]

are listed below. The limitations on subjective cough reporting have led to the advocacy for and development of objective measurements of cough in research circles.[27,49–51]

1. "Normal" children occasionally cough as has been described by two studies[52,53] that objectively measured cough frequency. The "medicalization" of an otherwise common symptom can foster exaggerated anxiety about perceived disease, and lead to unnecessary medical product delivery and services.[54] Cough in this situation is termed *expected cough*.
2. Questions about isolated cough are largely poorly reproducible,[55] and nocturnal cough in children is unreliably reported.[56,57] The κ value relating the chance-corrected agreement between answers to questions on cough ranges

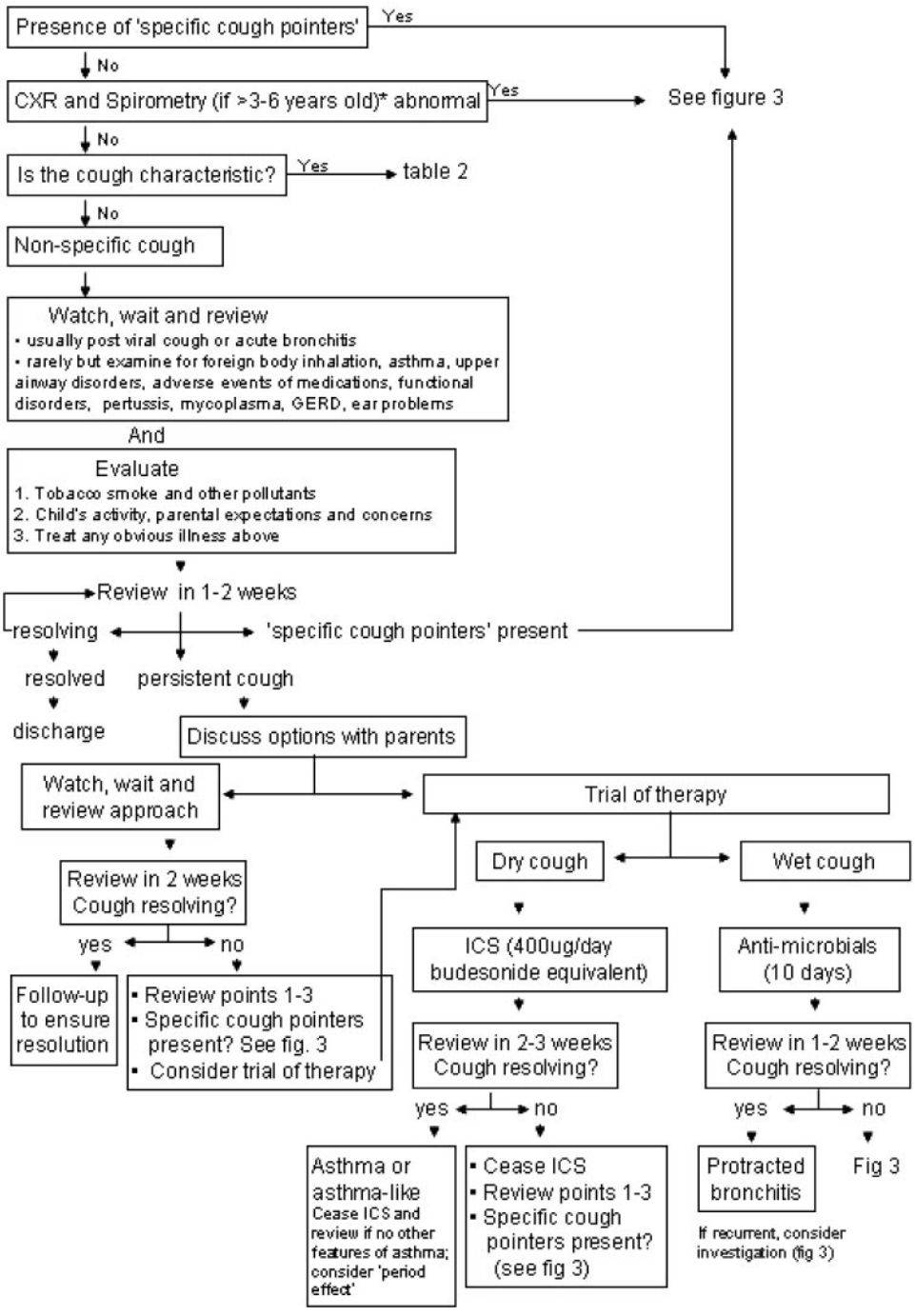

FIGURE 2. Approach to a child < 15 years of age with chronic cough. There are limitations to the algorithm, which should be read with the accompanying text. Spirometry can usually be reliably performed in children > 6 years of age and in some children > 3 years of age if trained pediatric personnel are present.[81] CXR = chest radiograph.

widely from 0.02 to 0.57.[27,55,58] In contrast, questions about isolated wheezing and asthma attacks are highly reproducible with κ values of 0.7 to 1.0.[55]

3. Cough is subjected to the period effect (*ie*, the spontaneous resolution of cough).[59] The therapeutic benefit of placebo treatment for cough has been reported to be as high as 85%.[60] The results of nonplacebo controlled intervention studies must be interpreted with caution.
4. In older children, cough is also subjected to psychological influences[61,62] because, as in

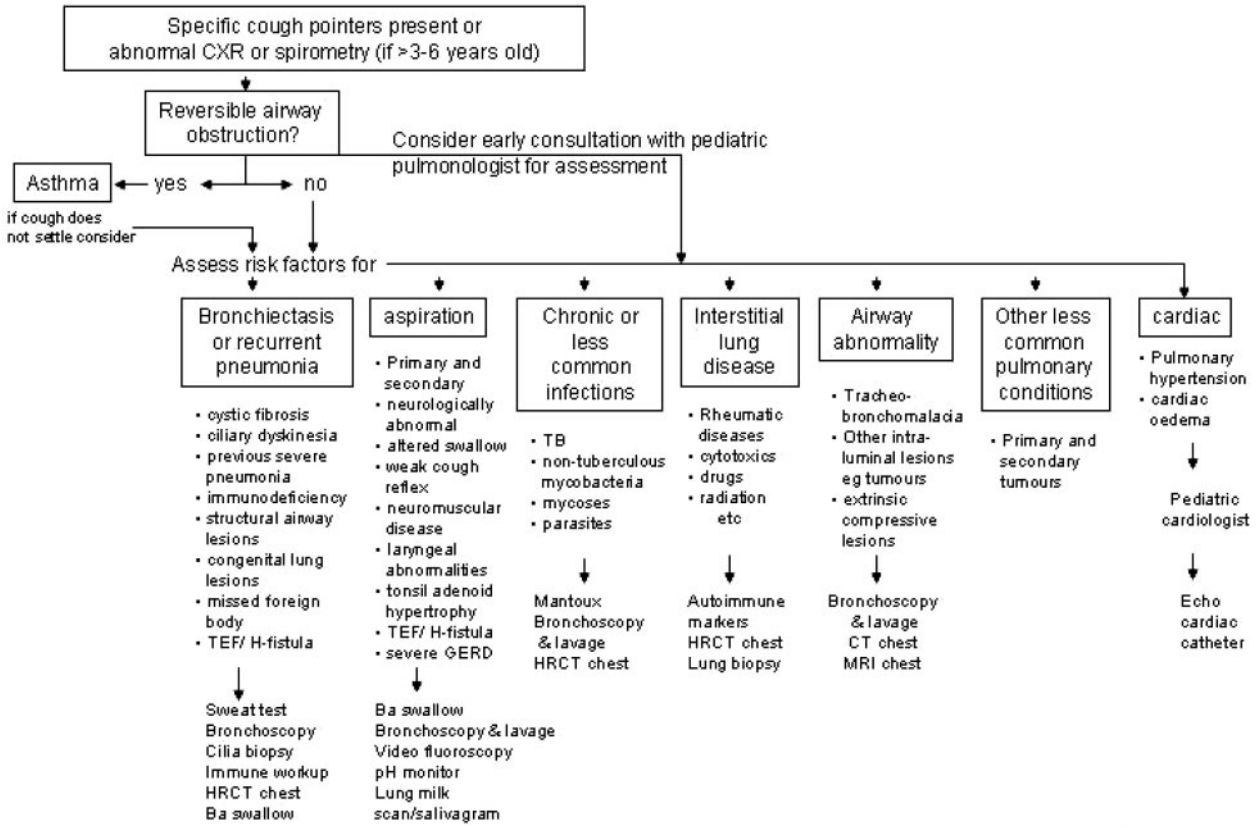

FIGURE 3. Approach to a child ≤ 14 years of age with chronic specific cough (*ie*, cough associated with other features suggestive of an underlying pulmonary and/or systemic abnormality). Children > 14 years of age should be managed as outlined in adult guidelines, but there is no good evidence concerning where the age cutoff for treatment should be. TB = tuberculosis; TEF = tracheoesophageal fistula.

adults, cough is cortically modulated.[9] Rietveld and colleagues[61,63] showed that children were more likely to cough under certain psychological settings.

5. The subjective perception of cough severity is dependent on the population that is being studied.[53] The reporting of childhood respiratory symptoms is biased, and parental perceptions of childhood cough play an important role.[27,28]

LITERATURE REVIEW OF RECOMMENDATIONS

To develop an evidence-based guideline, the following search strategy was utilized. Articles on diagnosis, etiology, treatment, and complications were searched separately. Articles published in the English language between January 1966 and December 2003 were identified from The Cochrane Register of Controlled Trials (CENTRAL), PubMed (1966 to December 2003), EMBASE (from 1997 to 2003), the list of references in relevant publications, and the authors' collection of references. The search strategy is presented in Table 5. A single author reviewed all abstracts identified from the search, and relevant articles were retrieved for full review. The searches were performed between September 1 and December 5, 2003. A final search of the Cochrane database only was conducted on November 7, 2004, using the search term "cough and children." All data presented are restricted to pediatric studies unless otherwise stated.

CHRONIC COUGH

The definition of chronic cough is a cough of > 4 weeks duration.

INVESTIGATING CHILDREN WITH CHRONIC COUGH: DIAGNOSTIC APPROACHES

Medical History and Physical Examination

Chronic cough in children secondary to respiratory diseases such as suppurative lung disease[19] and interstitial disease usually have a variety of other

Table 5—*Search strategy used*

ACE inhibitors and cough and children
Acute cough and children
Air pollution and trials and cough and children
Air pollution, randomized controlled study and children
Allergic cough and children
Allergy and chronic cough and children
Antihistamine and cough and children
Bronchoscopy and cough and children
Chronic cough and β-agonist and children
Chronic cough and children
Converting enzymes and cough and children
Cough and children
Cough guideline and children
CT scan and cough and children
Ear and cough
Education and cough and children
Eosinophilic bronchitis and children
GER and cough and children
Moist cough and children
Persistent cough and β-agonist and children
Pertussis and cough and children
Pertussis and cough and epidemiology
Pollution and cessation and cough
Pollution and cessation and cough and children
Postbronchiolitis and children
Postbronchiolitis cough and children
Postviral cough and children
Productive cough and children
Smoke and cessation and cough and children
Subacute cough and children
Treatment and cough and children
Vocal tics and children
Vocal tics and cough and children

Table 6—*Traditional Recognizable Cough in Children*

Cough Characteristic	Suggested Underlying Etiology or Contributing Factor
Barking or brassy cough	Croup,[247] tracheomalacia,[17,137,139] habit cough[62,184]
Cough productive of casts	Plastic bronchitis[248]
Honking	Psychogenic[249]
Paroxysmal (with/without whoop)	Pertussis and parapertussis[177,250]
Staccato	Chlamydia in infants[251]

specific clinical symptoms and signs.[64] However, a review of the medical literature found no reports on the specificity and sensitivity of these signs and symptoms. Based on expert opinion, children with chronic cough need to be carefully evaluated for the following:

- Symptoms and signs of an underlying respiratory or systemic disease (termed *specific pointers*) [Table 1]. When any of these symptoms and signs are present, the cough is referred to as *specific cough*.
- In some children, the quality of cough is recognizable and suggestive of a specific etiology (Table 6[17,62,137,139,177,184,247–251]). This significantly differs from the situation in adults in whom detailed questioning about the characteristics of cough was not diagnostically useful.[65] However, most of these cough characteristics recognized by pediatricians as "classical" or "traditional" have not been formally examined (*ie*, sensitivity and specificity are undefined). Of the cough characteristics presented in Table 6, only that of brassy cough has been formally evaluated.[17] The sensitivity and specificity for brassy cough (*ie*, for tracheomalacia) were 0.57 and 0.81, respectively.[17] The κ score for both intraobserver and interobserver clinician agreement for brassy cough was 0.79 (95% confidence interval, 0.73 to 0.86).[17]
- Possible exacerbating factors (see below) should also be evaluated, irrespective of the underlying etiology.

Investigations

Chronic productive purulent cough is always pathologic, and the workup usually involves detailed investigations that include the spectrum of available investigations (*eg*, chest HRCT scan), bronchoscopy, video fluoroscopic evaluation of swallowing, echocardiography, complex sleep polysomnography, and nuclear medicine scans. Determining the role of specific tests for the evaluation of lung disease is beyond the scope of this guideline because it would encompass the entire spectrum of pediatric respiratory illness. Table 2 outlines a summary of the available data when the yield (with significant abnormalities present) of tests used to investigate chronic cough were recorded.

Use of Chest and Sinus CT Scans

The chest HRCT scan is the current "gold standard" for evaluating small airway structural integrity and is more sensitive than spirometric indexes.[19,66,67] The utility of CT scans has to be balanced with the reported increased lifetime cancer mortality risk, which is age-dependent and dose-dependent. Although the risk is relatively negligible, children have 10 times the increased risk compared to middle-aged adults.[42] For a single CT scan examination of 200 mA, the lifetime attributable cancer mortality risk is 1 in 1,000 to 2,500 for a 2.5-year-old child.[42] Thus, while chest CT scans and, to a much lesser extent, sinus CT scans have definite roles in the evaluation of a child with cough, these should be uncommonly performed unless other symptoms are present. As radiation exposure and indications for conventional,

spiral, and HRCT chest scans are different and are dependent on the type of suspected lesion, prior consultation with a pediatric pulmonologist is recommended.

Flexible Bronchoscopy

Indications for flexible bronchoscopy in children with chronic cough include the following: (1) suspicion of airway abnormality, (2) localized radiology changes, (3) suspicion of an inhaled foreign body, (4) evaluation of aspiration lung disease and, (5) microbiological studies and lavage. In a European series,[68] chronic cough was the indication for 11.6% of the 1,233 pediatric bronchoscopies performed. Utility for flexible bronchoscopy is dependent on the child's medical history and the available expertise.

Airway Fluid/Lavage and Cellular Assessment

Currently, other than the assessment of airway specimens for microbiological purposes, the use of an airway cellular and inflammatory profile in children with chronic cough is currently limited to a supportive diagnosis and research rather than a definitive diagnosis. This is in contrast to that in adults with chronic cough in whom some have suggested the use of an airway inflammatory profile (*ie*, levels of primarily eosinophils) to direct therapy.[69,70]

Tests for Airway Hyperresponsiveness

Tests for airway hyperresponsiveness (AHR) are not used in routine practice in most pediatric pulmonary laboratories to diagnose asthma.[71] The presence of AHR does not mean that asthma is present in children,[72] and the demonstration of AHR in a child with isolated cough is unlikely to be helpful in predicting the later development of asthma[73] or the response to asthma medications.[74] Older studies[75–78] have stated that the presence of AHR in children with cough is said to be representative of asthma. However, these studies[75–78] were not placebo-controlled, and in them confounders were not adjusted for or unconventional definitions of AHR were used.

Spirometry

Spirometry is valuable in the diagnosis of reversible airway obstruction in children with chronic cough if an abnormality is present.[79,80] Spirometry can usually be reliably performed in children aged $>$ 6 years and in some children $>$ 3 years if trained pediatric personnel are present.[81]

Other Investigative Techniques

Airways resistance determined by the interrupter technique, which has not yet been established in clinical practice, may prove to be useful in detecting isolated cough associated with asthma.[82] Despite its application in research, there are still problems with intersubject variability and, hence, with the validity of its measurements when undertaken by different investigators.[83] To date, there have been no studies that have evaluated the role of nitric oxide (NO) or breath condensate in determining the etiology of chronic cough in children. There has been only one study[84] on bronchial biopsy in children with chronic cough. Heino and colleagues[84] described the association between ARI in children before the age of 1 year and epithelial inflammation in seven children with chronic cough ($>$ 3 months).[84]

Several studies[18,85,86] have described altered cough sensitivity (to capsaicin or acetic acid) in different disease processes. Increased cough sensitivity has been found in children with recurrent cough,[36] cough-dominant asthma,[86] and acute and postviral respiratory infections. However, tests for cough sensitivity are currently nondiagnostic, their sensitivity and specificity undefined, and their use still limited to research purposes.

Evaluation and Management of Children With Chronic Cough

For clinically practical reasons, we have divided cough into specific cough and nonspecific cough (Fig 1).[11] In specific cough, the etiology and necessity of further investigations is usually evident from the presence of coexisting symptoms and signs (Table 1). The presence of any of these symptoms suggests that the cough is likely indicative of an underlying disorder and that further complex investigations may be indicated. The type and depth of these investigations depend on clinical findings. Diagnoses that need to be considered include bronchiectasis, retained foreign body, aspiration lung disease, atypical respiratory infections, cardiac anomalies and interstitial lung disease, among others (see Fig 2, 3).

There are no published studies on the etiology of "dry cough" vs "moist/productive cough" in children. A moist cough putatively represents excess airway secretions.[17] Even in children with moist cough, though, a specific pediatric diagnostic category may not be found.[87] A chronic dry cough, on the other hand, may represent a dry phase of an otherwise usually moist cough.[17] Chronic cough in the absence of specific pointers (Table 1) in the medical history and physical examination is termed *nonspecific cough* (*ie*, cough is the only symptom). In nonspecific cough, the etiology is ill-defined; it has been speculated that the majority of cases are related to postviral cough and/or increased cough receptor sensitivity.[18,36] In the study by Callahan,[88] however, an

asthma-like condition was the most common diagnosis (the quality of cough was not specified in the study). After investigations are conducted (if necessary), some children may be found to have an underlying serious abnormality.[89] However, in the majority of children, nonspecific cough is most likely related to a nonserious etiology[23] or may spontaneously resolve, as evidenced in the placebo arms of RCTs[74,90,91] and cohort studies.[92–94] The remainder of this guideline discusses the available data on nonspecific cough. There is, though, an overlap among specific cough, nonspecific cough, and expected cough (Fig 1), and hence the need for a review of the case of any child with a chronic cough. Evidence-based management guidelines for cough associated with acute infections, as well as that associated with underlying respiratory and systemic disorders, are beyond the scope of this section, and disease-specific guidelines and/or evidence-based reviews for children are available for some diseases such as asthma,[6] community-acquired pneumonia,[3–5] bronchiolitis,[95] airway clearance methods,[96] and selective aspects of cystic fibrosis management,[97–99] in addition to that those provided by a United States-based resource (The National Guideline Clearinghouse [www.guideline.gov]). The list is far from exhaustive, and, although none of these guidelines are cough-specific, cough usually improves when the underlying disease is treated.

Recommendations

1. Children with chronic cough require careful and systematic evaluation for the presence of specific diagnostic indicators. Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A

2. Children with chronic cough should undergo, as a minimum, a chest radiograph and spirometry (if age appropriate). Level of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B

3. In children with specific cough, further investigations may be warranted, except when asthma is the etiologic factor. Level of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B

4. Children with chronic productive purulent cough should always be investigated to document the presence or absence of bronchiectasis and to identify underlying and treatable causes such as cystic fibrosis and immune deficiency. Level of evidence, low; benefit, substantial; grade of recommendation, B

Asthma, Asthma-Like Conditions, and Cough in Children

Children with asthma may present with cough. However, the majority of children with isolated cough do not have asthma.[9,10,100] The use of isolated cough as a marker of asthma is indeed controversial with more recent evidence[11,100] showing that in most children, isolated cough does not represent asthma. Some hospital-based clinical studies[101,102] of children presenting with chronic cough have found asthma to be the most common cause, but others have not.[87,89] There is little doubt that the etiology of cough would depend on the setting, selection criteria of the children studied,[89,103] follow-up rate,[104] and depth of the clinical history, physical examination, and investigations performed. When airway profiles have been examined in children with isolated chronic cough, the studies[103,105,106] have shown very few children with airway inflammation that is consistent with asthma. Cough associated with asthma without a coexistent respiratory infection is usually dry.[6] This topic has been previously reviewed.[9] With space limitations, only an update of further studies (in addition to the studies on airway fluid assessment outlined in Table 2) is summarized in Table 3. A review[107] relating measurements of cough severity to those of asthma severity is also available. A further difficulty relating cough and asthma is the fact that cough is the most common symptom in patients presenting to doctors in the United States and Australia,[108,109] and viral respiratory infections, which also cause cough, are said to account for 80% of childhood asthma exacerbations.[110] It would be difficult to ascertain whether cough is secondary to asthma or to the respiratory viral infection.

Upper Airways Disorders and Cough in Children

In adults, upper airway cough syndrome (previously referred to as *postnasal drip syndrome*) has been reported[111,112] as a common cause of chronic cough. In children, although nasal discharge and cough have been reported as the two most prominent symptoms in children with chronic sinusitis (for 30 to 120 days),[113] the supportive evidence of cause and effect in children is less convincing.[114] Although sinusitis is commonly diagnosed in childhood, it can be rarely proven, and it is not associated with cough once atopy and doctor-diagnosed allergic rhinitis are controlled for.[115] The relationship between nasal secretions and cough is more likely linked by common etiology (infection and/or inflammation causing both) or is due to the clearing of secretions reaching the larynx. Abnormal sinus radiographs may be found in 18 to 82% of asymptomatic children.[116] A systematic review of acute sinusitis in children con-

cluded that "diagnostic modalities showed poor concordance, and treatment options were based on inadequate data."[117]

Turktas and colleagues[118] described increased extrathoracic AHR without bronchial AHR to methacholine in a group of children presenting with chronic cough, and other studies[119,120] have linked extrathoracic AHR to sinusitis and rhinitis in adults. Whether the presence of upper airway abnormalities causes or is the consequence of extrathoracic AHR is unknown. The repeatability and validity of extrathoracic AHR in children is also ill-defined. Therapeutic approaches in managing children with allergic rhinitis have been well-summarized by Fireman.[121] A single RCT[122] on adolescents and adults (n = 245) with allergic rhinitis using cough as an outcome measure showed that daytime cough difference between the active treatment arm (with mometasone furoate) and placebo was significant (p = 0.049). In comparison, a larger difference between groups was found for nasal symptoms, and there was no difference in nighttime cough.[122] There have been no RCTs on therapies for upper airway disorders in younger children with nonspecific cough.

GERD and Cough in Children

Several studies[123,124] have reported that esophageal disorders can trigger cough in children, and this occurs by several mechanisms. Whether the sensory pathway stimulation described in animal studies[125] also occurs in children is unknown. However, while GERD can be the reason for persistent cough,[124,126] cough can also provoke gastroesophageal reflux (GER) episodes in adults.[127,128] Data on cough itself causing GER described in adults is unavailable in children.[128] Proof that GERD causes chronic cough in children is rare,[123] and the relationship between the two is most likely complex.[129] As cough is very common in children and respiratory symptoms may exacerbate GER, it is difficult to differentiate cause and effect.[130] Infants often regurgitate,[131] yet few well infants cough with these episodes. The effects of fundoplication on cough and other respiratory symptoms are inconsistent.[132,133] There are a limited number of studies that have looked at the causes of chronic cough in children prospectively, but those that are available suggest that GERD is infrequently the sole cause of isolated cough in children. One prospective study[101] of the causes of chronic cough in children found only one child with GERD out of a series of 38. A more recent retrospective study[89] found coexistent GERD in 4 of 49 children with chronic cough. In contrast to data in adults whereby GERD is a frequent cause of chronic cough,[134,135] there is indeed little current convincing evidence that GERD is a common cause of isolated chronic cough in children.

Airway Lesions and Cough

Chronic cough has also been well-described in children with airway lesions.[136–139] Gormley and colleagues[139] described that 75% of children with congenital tracheomalacia secondary to congenital vascular anomaly had persistent cough at presentation. How commonly airway lesions are found in asymptomatic children is unknown, and how the symptom of cough relates to airway lesions can only be postulated. Airway malacia impedes the clearance of secretions,[138] and it is plausible that the prolonged duration of cough in these children relates to a bronchitic process distal to the lesion. Stradling[140] has described bronchomalacia secondary to chronic bronchitis in adults. However, which is the cause and which is the effect are unknown. Nevertheless, recurrent infections and pneumonia on the side of the airway lesion have been well-described,[138] and so has the misdiagnosis of asthma in children with airway malacia disorders.[138,141] The relationship between airway lesions and cough is not straightforward. Although persistent cough is listed as an indication for flexible bronchoscopy,[68,142] its role in this context has yet to be defined prospectively.

Environmental Pulmonary Toxicants

Exposure to environmental smoke increases the susceptibility to respiratory infections,[143,144] causes adverse respiratory health outcomes,[145] and increases coughing illnesses.[146,147] Increased environmental tobacco smoke (ETS) exposure has also been described in cohorts of children with chronic cough compared to children without cough.[103,148] However, the Tucson study[149] concluded that, "cough was not associated with parental smoking during the first decade of life," which contrasts with other epidemiologic and clinical studies[103,145,146,150] showing a close link between childhood cough and ETS exposure.

Exposure to indoor biomass combustion increases coughing illness associated with respiratory infections with an exposure-response effect.[151] Exposure to other ambient pollutants (*eg*, particulate matter,[152,153] nitrogen dioxide, and gas cooking[154]) is also associated with increased cough in children in both cross-sectional studies[152,153] and longitudinal studies,[155] especially in the presence of other respiratory illness such as asthma.[152] Some studies,[156,157] however, have not shown this effect, and this may be

related partially to problems in questionnaire-based epidemiologic studies on isolated and nocturnal cough.[9,27]

Nonasthmatic Eosinophilic Bronchitis and Allergy

Nonasthmatic eosinophilic bronchitis, which is a well-described cause of chronic cough in adults,[158] has not been recognized in children. "Allergic cough" is a poorly defined condition even in adults, and its relationship to childhood cough probably represents an overlap with asthma, nonasthmatic eosinophilic bronchitis, allergic rhinitis, and adenoid tonsillar hypertrophy.[159] The association between atopy and respiratory symptoms has been the subject of many epidemiologic studies.[160,161] Some have described[160,161] greater respiratory symptom chronicity,[162] while others have not. Inconsistent findings regarding cough and atopy are also present in the literature; reports of increased atopy (or diseases associated with atopy) in children with cough have been found in cohort and cross-sectional studies[163,164] as has as the absence of influence of atopy.[74,90,165,166] Cough as a functional symptom can also be mistaken for an allergic disorder in children.[167]

Chronic Nocturnal Cough

The major problem in utilizing the symptom of nocturnal cough is the unreliability and inconsistency of its reporting when compared to objective measurements.[56,57,168] This has been reviewed,[107,169] and hence only salient points and recent articles will be mentioned. Nocturnal cough is often used as a direct indicator of asthma as children with asthma are often reported to have troublesome nocturnal cough.[170] However, in the community-based study by Ninan and colleagues,[165] only a third of children with isolated nocturnal cough (*ie*, the absence of wheezing, shortness of breath, or chest tightness) had an asthma-like illness. To date, there have been no studies that have objectively documented that nocturnal cough is worse than daytime cough in children with unstable asthma. One study[171] has shown that cough frequency was higher during the day than at night in a group of children with stable asthma who were receiving treatment with inhaled corticosteroids (ICSs) yet had elevated levels of NO but not sputum eosinophils, which is arguably the best marker for eosinophilic inflammation in adults with stable asthma.[172] Whether the increased NO is a marker of asthma instability or is related to other causes of elevated NO levels (such as environmental pollutants)[173,174] is unknown. It is possible that nocturnal cough is considered to be more troublesome than daytime cough.

Respiratory Infections and Postinfections Cough

Recurrent URTIs and infections such as pertussis can cause chronic cough (Table 3). The natural history of cough associated with URTIs in children 0 to 4 years of age in the community has been summarized.[22] *Postviral cough* is a term that refers to the presence of cough after an acute viral respiratory infection. However, this has not been well-studied, and little is known about its pathophysiology or natural history beyond 25 days.[21] When a child who has not fully recovered from a URTI-related cough acquires a subsequent URTI, the coughing illness may seem prolonged. In the review by Monto,[40] the mean annual incidence of total respiratory illness per person-year ranges from 5 to 8 in children < 4 years of age to 2.4 to 5.0 in children 10 to 14 years of age.[40]

Although pertussis, pertussis-like, and Mycoplasma infections classically cause cough that is associated with other symptoms, (*eg*, cough from pertussis infection is usually spasmodic,[175] and cough from Mycoplasma infection may be associated with other symptoms of a respiratory infection such as pharyngitis),[176] these infections can also cause persistent cough without other symptoms,[177] especially in the presence of process modifiers such as antibiotics and vaccination.[175] Pertussis should be suspected, especially if the child has had known contact with someone with a pertussis infection even if the child is fully immunized, as partial vaccine failure can occur.[178]

Medications and Treatment Side Effects

Chronic cough has been reported[179–181] as a side effect of the use of angiotensin-converting enzyme (ACE) inhibitors and of asthma medications immediately after inhalation,[182] and as a complication of chronic vagus nerve stimulation.[183] In one review,[181] chronic cough developed in only 1 of the 51 children (2%) who were treated with ACE inhibitors; yet, another study[180] reported cough in 7 of the 42 children (16.7%). In children, cough associated with ACE inhibitors resolves within days (*ie*, 3 to 7 days) after withdrawing the medication,[179,180] and may not recur when therapy with the medication is recommenced.[180]

Functional Respiratory Disorder (Psychogenic)

The many descriptions of cough with a functional or psychogenic overlay include the following: (1) habit cough, (2) tic cough, and (3) psychogenic cough. The distinctions between these categories may be unclear and possibly may reflect a spectrum of different severity.[62,184] This topic is covered in a

combined adult and pediatric section devoted to "habit cough and psychogenic cough."

Otogenic Causes: Arnold Ear-Cough Reflex

In approximately 2.3 to 4.2% of people, the auricular branch of the vagus nerve is present and the Arnold ear-cough reflex can be elicited (with bilateral occurrence in 0.3 to 2% of people).[185–187] The reflex can be elicited by palpation of the posteroinferior wall and rarely by palpation of the anteroinferior wall of the external acoustic meatus (ear canal).[185,187] Case reports[188–190] of chronic cough associated with ear canal stimulation from wax impaction, cholesteatoma, and acquired aberrant sensory referral post-cardiac transplant have been reported. In children, the significance of the ear reflex and cough was described as early as 1963,[191] although in 2002 it was reported again.[192] In our experience, this is a very rare cause of childhood chronic cough.

Inhalation of Foreign Body

Cough is the most common symptom in some series of foreign material inhalation but not in others.[193] In one series,[194] cough was present in 70% of patients, while other dominant symptoms included decreased breath sounds (53%) and wheezing (45%). A history of a choking episode was reported in 32% of patients, but when families were questioned in more detail the rate increased to 51%.[194] Presentations are usually acute,[195] but chronic cough can also be the presenting symptom in a previously missed foreign body inhalation.[196] A normal chest radiograph finding does not exclude foreign body inhalation, and a specific medical history should be sought because a missed foreign body can result in long-term pulmonary damage.[39]

Parental and Physician Expectations

Providing parents with information on the expected length of time until the resolution of ARIs may reduce their anxiety, and the need for medication use and additional consultation.[197] The appreciation of specific concerns and anxieties, and an understanding of why children present are thus important when caring for children with nonspecific cough. It has been argued[198] that quality of life is determined by expectations rather than by experience. Parental and professional expectations as well as the doctor's perceptions of patients' expectations influences consulting rates and the prescription of medications.[22,199,200] The use of cough medications and presentation to doctors were less likely in children with more highly educated mothers.[201] Mangione-Smith et al[202] described that "physicians' perceptions of parental expectations for antimicrobials was the only significant predictor of prescribing antimicrobials for conditions of presumed viral etiology and hellip." Earlier, Hutton et al[28] had showed that "parents who wanted medicine at the initial visit reported more improvement at follow-up, regardless of whether the child received drug, placebo, or no treatment." Physicians should be cognizant that "a parent navigating the Internet for information on the home management of cough in children will no doubt find incorrect advice among the search results."[203]

The concerns of parents presenting to general practitioners in the United States for their children's cough can be extreme and can include the following: fear of the child dying from choking; fear of asthma attack or cot death; and fear of permanent chest damage.[204] Other concerns that parents express are disturbed sleep and relief of discomfort.[204] Findings from a London specialist respiratory clinic were similar.[205] However, the burden of illness on children and their families has not been well-described.

Treatment of Nonspecific Cough

A summary of the treatment of nonspecific cough in children, the time to response, and the level of evidence is presented in Table 4. In the interest of space, only salient points will be discussed below, and readers are referred to the relevant studies for further information.

OTC Cough Medications

Systematic reviews have concluded that OTC cough medications have little, if any, benefit in the symptomatic control of acute cough in children,[12,16] and the American Academy of Pediatrics has advised[206] against the use of codeine and dextromethorphan for treating any type of cough. Moreover, the use of OTC cough remedies has been associated with significant morbidity and even with mortality.[207] OTC drugs are common unintentional ingestion medications in children < 5 years of age.[208] A Cochrane review[209] of symptomatic treatment of cough related to pertussis also found no significant benefit for therapy with diphenhydramine. A recent RCT[13] on two commonly used OTC cough medications and OTC medications containing antihistamine combinations are discussed below under the heading "Antihistamines." A review of these medications is available.[14]

Asthma Therapy

A systematic review[210] has shown that "there is no evidence to support using β_2-agonists in children

with acute cough and no evidence of airflow obstruction." There has been only one study[74] on the use of inhaled salbutamol in patients with chronic cough that also showed no benefit. There is also no evidence to support the use of anticholinergic agents[211] for the treatment of nonspecific cough in children. Nedocromil and cromoglycate reduce cough associated with asthma[212,213] and in children born prematurely.[214] A Cochrane review[215] has described an absence of data for its use. Old cohort studies have described the benefit of asthma therapy for that era (*ie*, oral orciprenaline, salbutamol syrup,[216,217] theophylline,[75,217] and metaproterenol with theophylline[79]) in abolishing cough.

Only two published RCTs[74,90] on ICSs for the treatment of chronic nonspecific cough in children exist, and both groups cautioned against the prolonged use of ICSs. There has been no RCT performed on the use of oral steroids for nonspecific cough in children. In cough associated with pertussis, dexamethasone provides no significant benefit for the symptomatic relief of cough.[209] Even in children with wheeze, an RCT[218] that was performed in 200 young children found that parent-initiated treatment with oral steroids conferred no benefit but was instead associated with a nonsignificant increase in hospitalizations ($p = 0.058$). Given that low-dose ICSs have been shown to be effective in the management of the majority of cases of childhood asthma,[219–221] and the reported significant adverse events occurring with high-dose ICSs,[222,223] we suggest the use of a 400 μg/d equivalent dose of budesonide (or beclomethasone) if a trial of asthma therapy is warranted. As the earlier studies[75,79,80,224] in adults and children that utilized medications for asthma for the era (*eg*, nonsteroidal agents such as theophylline[75] and major tranquilizers[224]) reported that cough related to asthma completely resolved after 2 to 7 days, we recommend reassessment after 2 to 3 weeks. Cough that is unresponsive to treatment with ICSs should not be treated with increased doses of ICSs. If the cough resolved with ICS use, clinicians should still be cognizant that the child does not necessarily have asthma, and the child should be reevaluated after asthma treatment has been stopped. The resolution of cough may occur with the period effect (*ie*, spontaneous resolution)[59] or a transient response.

Antimicrobials

There have been two randomized studies[225,226] that have examined the use of antimicrobial agents. Although the entry criterion was cough lasting for > 10 days, 23% of children had cough of > 30 days duration, and the mean duration of cough in the study by Gottfarb and Brauner[225] was 3 to 4 weeks. In both studies, nasopharyngeal colonization showed a predominance of *Moraxella catarrhalis*, and a significant improvement was seen in the antimicrobial treatment arm. In children with persistent nasal discharge or in older children with radiographically confirmed sinusitis, a Cochrane review[227] showed that a 10-day course of antimicrobial agents reduces the probability of the persistence of cough in the short to medium term. However, the "number needed to treat" was relatively high at eight patients.[227] In another systematic review[117] of uncomplicated sinusitis in children, the clinical improvement rate in RCTs was 88% with antimicrobial therapy and 60% with no antimicrobial therapy. The guidelines of the American Academy of Family Physicians[228] have suggested the restriction of antimicrobial use to those persons with acute sinusitis symptoms and cough that does not improve after 10 days. In a Cochrane review,[229] the use of antimicrobial agents confers no benefit in patients with acute cough associated with common colds.

Antihistamines

In contrast to the data in adults, the efficacy of antihistamine agents in relieving cough in children is minimal, if any. For acute cough, a systematic review[12] of antihistamine and nasal decongestion combinations and antihistamines in OTC medications has shown that these pharmaceuticals were no more likely than placebo to reduce acute cough in children. There have been, however, no studies on chronic cough. A recent RCT[13] also showed that diphenhydramine and dextromethorphan were no different than placebo in reducing nocturnal cough or sleep disturbance in both the children and parents. Like other RCTs, there was a significant improvement in both the placebo and active arms for the four cough-related outcomes measured.[13] In a metaanalysis[230] of antihistamine treatment for the common cold (in contrast to cough as an outcome measure), neither antihistamine monotherapy nor combinations of antihistamines with decongestants were effective in children (participants were ≤ 15 years of age) in reducing symptoms. However, in older children (one study included children > 12 years of age, but participants in the rest of studies were > 18 years of age) and in adults, "most trials show some beneficial effect on general recovery as well as on nasal symptoms."[230]

GERD Therapies

A clinical practice guideline[31] on the evaluation and management of children with GERD is available. There are no data on the time for resolution of

cough related to GERD in children, and no RCT has been conducted on the use of proton pump inhibitors for the treatment of cough in children. A Cochrane review[26] on GERD therapies (milk thickening[231,232] and cisapride or domperidone[233]) for cough has failed to find a beneficial effect. A therapeutic trial of high-dose proton pump inhibitors, arguably the best medication for acid-GERD associated cough in adults,[234–236] requires research in children. In a Cochrane review[237] on metoclopramide, thickened feedings, and positioning for GER in children < 2 years of age, the effect of metoclopramide on GER was not significant between treatment and placebo groups, and cough was not an outcome in these studies. Although case series have shown the link between supraesophageal symptoms and GER in children, there is a lack of convincing data, summarized as follows by Rudolph[238]: "No studies have definitively demonstrated symptom improvement with medical or surgical therapy for the latter symptom presentations." In the American guidelines for pediatric GER,[31] the section on upper airway symptoms included a discussion on cough and GER. It concluded that ". . . there is insufficient evidence and experience in children for a uniform approach to diagnosis and treatment."[31] While there has been a sporadic case report suggesting that cough can occur as an adverse event in reaction to therapy with omeprazole in adults,[239] there have been no pediatric reports.

Cessation of Exposure to ETS and Other Environmental Toxicants

In the management of cough in any child, irrespective of the etiology, attention to exacerbating factors is encouraged. The American Academy of Pediatrics has a policy statement on tobacco exposure in pediatrics.[240] There have been no RCTs that have examined the effect of the cessation of ETS or other toxic environmental exposure on cough in children. A single report[241] was found on the cessation of parental smoking as a successful form of therapy for cough in children. Behavioral counseling for mothers who smoke has been shown to reduce the ETS exposure of young children in both reported and objective measures of ETS.[242] However, the effect of ETS reduction on children's symptoms was not studied.[242] In one uncontrolled study,[243] house heating had the greatest impact on reducing nocturnal cough in children with asthma.

Physician and Parental Expectations

Educational input is most successful when it addresses the child's specific condition. Exploring and understanding the specific concerns of parents is initially required. Written information without discussion provides only modest benefit in changing perceptions and behavior.[244] In an RCT, Little et al[245] sent booklets and sheets that included information on minor respiratory tract infections and found that, while patients felt more confident managing their minor illness, the effect on subsequent attendance with a minor illness was only modest. Taylor et al[246] conducted an RCT examining the effect of a pamphlet and a videotape promoting the judicious use of antibiotics and found that their simple educational effort was successful in modifying parental attitudes about antibiotics and concluded "information about specific childhood conditions may be more effective in changing attitudes than more general information about antibiotic usage."[246]

Recommendations

5. In children with chronic cough, the etiology should be defined and treatment should be etiologically based. Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A

6. In children with nonspecific cough, cough may spontaneously resolve, but children should be reevaluated for the emergence of specific etiologic pointers (see Table 1). Level of evidence, low; benefit, substantial; grade of recommendation, B

7. In children with nonspecific cough and risk factors for asthma, a short trial (*ie*, 2 to 4 weeks) of beclomethasone, 400 μg/d, or the equivalent dosage with budesonide may be warranted. However, most children with nonspecific cough do not have asthma. In any case, these children should always be reevaluated in 2 to 4 weeks. Level of evidence, fair; benefit, intermediate; grade of recommendation, B

8. In children who have started therapy with a medication, if the cough does not resolve during the medication trial within the expected response time, the medication should be withdrawn and other diagnoses considered. Level of evidence, low; benefit, intermediate; grade of recommendation, C

9. In children with cough, cough suppressants and other OTC cough medicines should not be used as patients, especially young children, may experience significant morbidity and mortality. Level of evidence, good; benefit, none; grade of recommendation, D

10. In children with nonspecific cough, parental expectations should be determined, and the specific concerns of the parents should be

sought and addressed. Level of evidence, low; benefit, intermediate; grade of recommendation, E/B

11. In all children with cough, exacerbating factors such as ETS exposure should be determined and interventional options for the cessation of exposure advised or initiated. Level of evidence, low; benefit, substantial; grade of recommendation, B

12. Children should be managed according to the studies and guidelines for children (when available), because etiologic factors and treatments in children are sometimes different from those in adults. Level of evidence, low; benefit, substantial; grade of recommendation, B

13. In children ≤ 14 years of age with chronic cough, when pediatric-specific cough recommendations are unavailable, adult recommendations should be used with caution. Level of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B

Conclusion

Children with cough should be managed according to child-specific guidelines, which differ from those for adults as the etiologic factors and treatments in children are sometimes different from those in adults. In children, cough is very common and, in the majority of children, is reflective of expected childhood respiratory infections. However, cough may also be representative of a significant serious disorder, and all children with chronic cough should have a thorough clinical review to identify pointers that are suggestive of an underlying respiratory and/or systemic illness.

Cough in children should be treated based on etiology, and there is little evidence for using medications for the symptomatic relief of cough. If medications are used, it is imperative that the children are followed up and therapy with those medications stopped if there is no effect on the cough within an expected time frame. Evaluation of the time to response is important. Irrespective of diagnosis, environmental influences and parental expectations should be discussed and managed accordingly. Cough often impacts the quality of life of both children and parents, and the exploration of parental expectations and fears is often valuable in the management of cough in children.

Summary of Recommendations

1. Children with chronic cough require careful and systematic evaluation for the presence of specific diagnostic indicators. Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A

2. Children with chronic cough should undergo, as a minimum, a chest radiograph and spirometry (if age appropriate). Level of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B

3. In children with specific cough, further investigations may be warranted, except when asthma is the etiologic factor. Level of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B

4. Children with chronic productive purulent cough should always be investigated to document the presence or absence of bronchiectasis and to identify underlying and treatable causes such as cystic fibrosis and immune deficiency. Level of evidence, low; benefit, substantial; grade of recommendation, B

5. In children with chronic cough, the etiology should be defined and treatment should be etiologically based. Level of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A

6. In children with nonspecific cough, cough may spontaneously resolve, but children should be reevaluated for the emergence of specific etiologic pointers (see Table 1). Level of evidence, low; benefit, substantial; grade of recommendation, B

7. In children with nonspecific cough and risk factors for asthma, a short trial (*ie*, 2 to 4 weeks) of beclomethasone, 400 μg/d, or the equivalent dosage with budesonide may be warranted. However, most children with nonspecific cough do not have asthma. In any case, these children should always be reevaluated in 2 to 4 weeks. Level of evidence, fair; benefit, intermediate; grade of recommendation, B

8. In children who have started therapy with a medication, if the cough does not resolve during the medication trial within the expected response time, the medication should be withdrawn and other diagnoses considered. Level of evidence, low; benefit, intermediate; grade of recommendation, C

9. In children with cough, cough suppressants and other OTC cough medicines should not be used as patients, especially young children, may experience significant morbidity and mortality. Level of evidence, good; benefit, none;

grade of recommendation, D

10. In children with nonspecific cough, parental expectations should be determined, and the specific concerns of the parents should be sought and addressed. Level of evidence, low; benefit, intermediate; grade of recommendation, E/B

11. In all children with cough, exacerbating factors such as ETS exposure should be determined and interventional options for the cessation of exposure advised or initiated. Level of evidence, low; benefit, substantial; grade of recommendation, B

12. Children should be managed according to the studies and guidelines for children (when available), because etiologic factors and treatments in children are sometimes different from those in adults. Level of evidence, low; benefit, substantial; grade of recommendation, B

13. In children ≤ 14 years of age with chronic cough, when pediatric-specific cough recommendations are unavailable, adult recommendations should be used with caution. Level of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B

ACKNOWLEDGMENT: The authors thank Drs. Leroy Graham and Brent Masters for their evaluation of this manuscript.

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Chest 2006;129;260-283
DOI 10.1378/chest.129.1_suppl.260S