Differential diagnosis of chronic cough in children

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ABSTRACT

A cough is considered chronic when it lasts >4 weeks. Chronic cough can be from a variety of causes. This article provides a structured approach to evaluating the child with chronic cough. Beginning with the disturbing cough that is absent once asleep, consistent with the habit cough syndrome, the diagnostic criteria for 10 causes of chronic cough are discussed. Using a structured approach to the differential diagnosis, common and uncommon causes can be identified. Well-established causes of chronic cough, such as asthma, are likely to be well known to the reader, whereas more recently identified etiologies, such as protracted bacterial bronchitis, are presented in more detail. The differential value of flexible and rigid bronchoscopy and bronchoalveolar lavage for aiding in the differential diagnosis is included for those entities where their use is essential.

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Cough is a common and troublesome symptom. Most common is acute cough, typically from viral respiratory infection and known colloquially as a chest cold. Some children have recurrent acute coughs from viral respiratory infections, a frequent manifestation of asthma in preschool age children. Particularly troublesome is chronic cough, defined as a cough lasting >4 weeks.

The extensive morbidity from chronic cough has been documented in a study of 190 children referred to a tertiary care center in Brisbane, Australia. More than 80% already had 5 unsuccessful physician visits for the cough, and 53% had >10 such visits. The median age of those children was 2.6 years. The symptoms substantially impacted sleep and school attendance.[1] The same group reported the identified etiology of chronic cough referred to major pediatric referral centers in Australia that used a standardized management pathway (Fig. 1).[2]

EVIDENCE-BASED EVALUATION OF CHRONIC COUGH IN CHILDREN

The purpose of this article is to provide a clinically relevant, data-driven approach to identify the cause of chronic cough in children, address management of cough syndromes, and discuss controversial causes of cough. Individual cases are presented to illustrate typical features that assist in recognizing the specific disorder discussed. Common etiologies of chronic cough are presented in the order identified by a diagnostic algorithm in use by the Allergy, Immunology, and Pulmonary Division at the University of Iowa Children's Hospital (Table 1).

Habit Cough Syndrome

Before subjecting the patient to diagnostic testing and medication, the possibility of habit cough should be considered. Habit cough, in its classic form, is characterized by a repetitive often loud, harsh, barking sound that has been described at times as sounding like a "barking dog" or "barking seal" (see a video of habit cough).[3] Unique to habit cough and the *sine qua non* is the complete absence of cough once asleep. Despite the absence of an organic basis for the cough, patients with habit cough can suffer considerable morbidity, including missed school, social isolation, and frequent unsuccessful pharmacotherapy for other presumed causes of cough. The following patient was the index case for our previous publication on the subject.[4]

Case Presentation. A 15-year-old girl was seen in our clinic with a history of coughing for 5 months. Her harsh barking cough multiple times per minute for much of the day was readily apparent during the clinic visit. This intractable coughing in a girl with an excellent school record, who liked school and who had many friends, had been kept out of school because the intrusive nature of the cough prevented being in a classroom. She had been subjected to extensive medical evaluation and treatment including two hospitalizations for i.v. antibiotics without benefit. The cough often interfered with falling asleep, but no cough was observed by her parents once she was asleep, and she was not awakened by cough. Her cough was stopped with 15 minutes of suggestion therapy; there was no subsequent recurrence.[4]

In the absence of specific behavioral treatment to stop the cough, the cough can persist for an extended period. A natural history report of habit cough syn-

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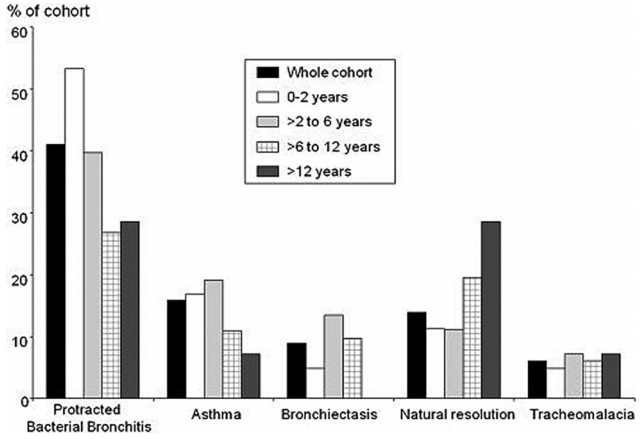

Figure 1. Distribution of the five most frequent diagnoses of children with chronic rough referred to several tertiary centers where a standardized management pathway was used. (Reproduced with permission Ref. 2.)

drome was described in 62 patients seen at the Mayo Clinic who continued to cough for a mean duration of >6 months with 16 of them still coughing >5 years after the diagnosis is made.[5]

A variation of habit cough syndrome, characterized by a softer sound, has the appearance in many cases of repetitive throat clearing. Although causing less actual disability, it is nonetheless annoying to those around the patient. As with the classic habit cough syndrome, it is absent once asleep. Not responsive to pharmacotherapy, cessation occurs within 15 minutes of suggestion therapy. Details of this method of suggestion therapy are described in the referenced publication which includes descriptions of and references for alternative behavioral methods including hypnosis.[6]

Because simple methods of suggestion therapy can stop the habit cough, generally within 15 minutes, prolongation of the habit cough should not be tolerated. Treatment is highly effective and reliable when confidently applied.

Because habit cough has been confused with Tourette syndrome, an understanding of each is important.[7] Tourette syndrome is characterized by multiple motor tics and at least one vocal (phonic) tic, not predominantly by actual repetitive cough or throat clearing. Referring to habit cough as psychogenic rather than habit cough can be counterproductive with regard to effective communication with the patient and parents. Other manifestations of somatization are generally not present.[4] However, there are occasional patients with more complicated psychopathology than just the habit cough syndrome.[8]

Pertussis Syndrome

Bordetella pertussis, the major organism causing classic whooping cough, is highly contagious and should always be considered for chronic cough <3-months duration because of its public health importance. The increase in immunization refusal and the apparent decreased duration of efficacy of the newer acellular vaccine have been associated with numerous local epidemics.[9] Also known as the 100-day cough, pertussis is characterized by a harsh nonproductive, spasmodic, cough that substantially interferes with sleep. It is often associated with posttussive nausea or emesis. Classic examples of whooping cough can be seen,[10,11] but whooping cough in previously immunized older children and adults is generally not associated with the classic whoop shown in the videos.[12] Transmission to infants results in a potentially life-threatening illness that often requires hospitalization. Macrolide antibiotics eliminate infectiousness but do not alter the clinical course of the very troublesome cough. *B. pertussis* is

Table 1 **Sequence of evaluation once a careful history is obtained including the age of onset, duration, other clinical problems, and response to medication**

A. Cough absent once asleep indicates likelihood of habit cough syndrome
B. Cough present <3 mo, especially if spasmodic, requires consideration of pertussis syndrome
C. Cough in infant with feeding warrants textured swallow study
D. Cough present since neonatal period, history of transient tachypnea of newborn, chronic otitis media, warrants consideration of PCD
E. Cessation of cough after a short course of an oral corticosteroid (see Table 2 for dosage) is consistent with asthma; further evaluation can determine an appropriate treatment plan
F. Failure to stop cough with the oral corticosteroid warrants further evaluation
   1. Chest x ray
      a. Lobar hyperinflation, suggests retained foreign body—consider rigid bronchoscopy
      b. Suggestion of airway inflammation or bronchiectasis warrants sweat chloride testing for CF
      c. Situs inversus totalis suggests a likelihood of PCD
      d. Normal chest x ray warrants further evaluation
   2. Flexible fiberoptic bronchoscopy with bronchoalveolar lavage can determine the following:
      a. Airway malacia, trachea, or bronchi
      b. Protracted bacterial bronchitis

CF = cystic fibrosis; PCD = primary ciliary dyskinesia.

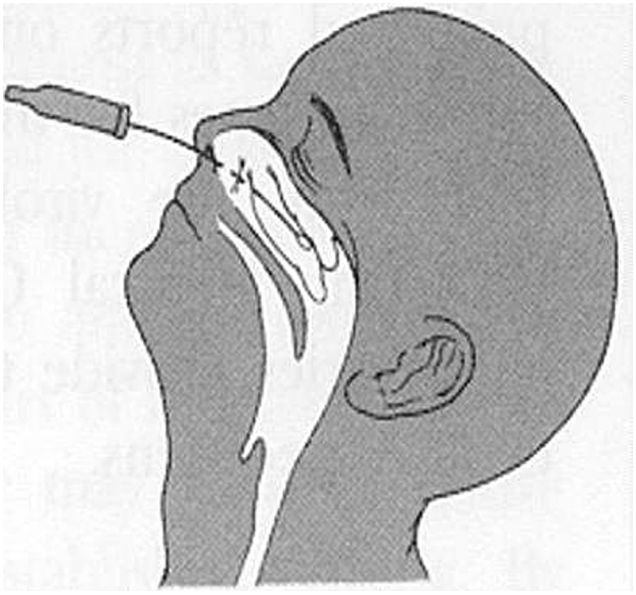

Figure 2. *Nasopharyngeal swab for obtaining sample to identify* Bordetella pertussis *antigen by polymerase chain reaction. The adsorbent material on the flexible wire probe should be of synthetic material such as polyester (not cotton). The swab should be inserted to the posterior nasopharynx and left there for 30 seconds before withdrawal.*

best identified by polymerase chain reaction obtained from a nasopharyngeal swab (Fig. 2).

Although *B. pertussis* is the most common and convincing etiology of this disorder, other organisms are sometimes also present.[13] However, the spasmodic nature of a nonproductive cough should always raise suspicion. Prolonged cough in 12–26% of college students and adults has been associated with documented *B. pertussis*.[14–16] In such cases, pertussis may not be obvious, and the longer the cough persists, the less likely a positive polymerase chain reaction will be found, especially if there has been previous treatment with a macrolide antibiotic.

Asthma

Although wheezing is traditionally the symptom most associated with asthma, a survey of school age children seen in the Allergy and Pulmonary Clinic at the University of Iowa Children's Hospital identified cough to be just as common as wheezing. Both were present in 85% of the children seen, and cough was the sole symptom present in 6% of these children with specialty assessment.[17] The most efficient and effective diagnostic test to identify chronic cough as a manifestation of asthma is a short course of an oral corticosteroid given in sufficient quantity to avoid a false negative response. Unfortunately, there are little data to support a specific dose recommendation or even to document a dose–response relationship for systemic corticosteroids in children. However, data in adults demonstrate a dose–response relationship over the range of 15–120 mg.[18] Based on the assumption that a dose–response relationship is also present in children, a diagnostic trial of corticosteroids for suspected asthma should use a sufficiently high dose to provide an outcome as definitive as possible (Table 2).

Table 2 **Empirical doses of oral corticosteroids for the purpose of identifying if chronic cough is from asthma**

	Dosage as Prednisone or Prednisolone*
<1 yr old	15 mg twice daily
1–3 yr old	20 mg twice daily
3–13 yr old	30 mg twice daily
>13 yr old	40 mg twice daily

Source: Ref. 19.
Based on the experience of the author, dosage is sufficiently high to provide a definitive assessment of a response consistent with a diagnosis of asthma.
**Some patients may have minor side effects including irritability or insomnia. Once this occurs, reducing the dose to once daily often decreases those adverse effects. Also, we have observed methylprednisolone to generally not cause those minor side effects (available in tablets only that may need to be crushed and added to soft sweet food for administration to young children).*

Alternatives, such as response to bronchodilator or even a trial of an inhaled corticosteroid is not sufficiently reliable. Although cessation of cough with an inhaled corticosteroid would support a diagnosis of asthma, the absence of response does not exclude asthma. Inhaled corticosteroids require proper delivery and patient cooperation. False negative results, *i.e.*, asthma is not identified when actually a cause of the cough, are more likely from a trial of inhaled corticosteroid because of variable technique of administration or inadequate effect of the inhaled corticosteroid on the extent of long-term airway inflammation in the child with chronic cough. A 7- to 10-day course of adequately dosed oral corticosteroid is a more reliable diagnostic trial that can provide the greatest and most rapid assurance for the presence or absence of asthma as the cause of the chronic cough.

Once asthma is confirmed by cessation of the chronic cough, subsequent evaluation and determination of treatment strategy can generally prevent return of the chronic cough.[19]

Persistent Bacterial Bronchitis

The awareness of persistent bacterial bronchitis (PBB) as an etiology of chronic cough has increased

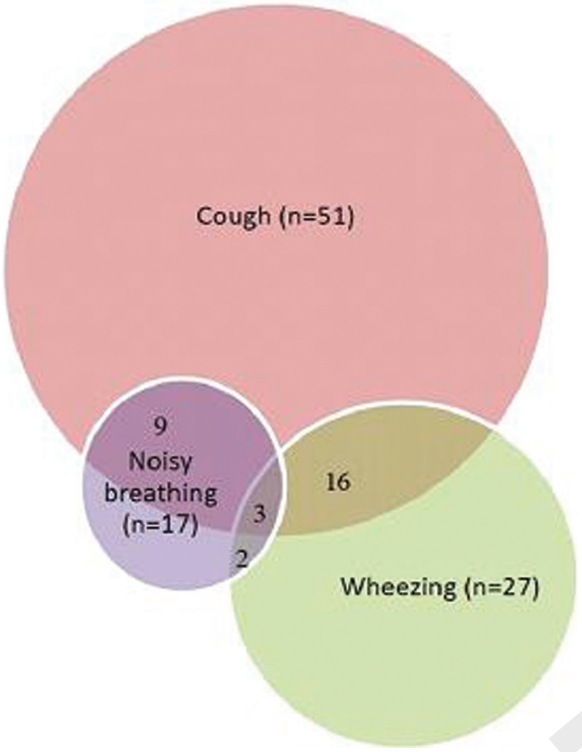

Figure 3. Symptoms at initial examination of 70 children found to have protracted bacterial bronchitis. The numbers in the overlapping portions of this Venn diagram illustrate the number of patients with two or three of the indicated symptoms. (Reproduced with permission from Ref. 20.)

with the publication of several recent reports.[2,20,21] PBB is often characterized by a chronic "wet" cough. We have also observed young children with wheezing and nonspecific noisy breathing (Fig. 3). The age of onset for this disorder is most commonly, but not exclusively, during the 1st year of life with 22% of the 70 in our study beginning during the 1st month of life.[20] Most referred to our tertiary care center had been symptomatic for many months (Fig. 4). The expectation of spontaneous cessation of symptoms, the absence of fever, and generally normal growth and development are the apparent reasons for the frequent delays in referral.

Confirmation of the diagnosis of PBB requires a bronchoscopy with a bronchoalveolar lavage. This procedure is best performed with a flexible pediatric bronchoscope with use of moderately light procedural sedation. That enables visualization of dynamic collapse of the trachea or bronchi (tracheomalacia or bronchomalacia), which was present in 74% of children with high colony counts of potentially pathogenic bacteria ($\geq 10^4$ colony-forming units [CFU]/mL). Airway malacia likely contributes to the retention of bacteria and associated inflammation by interfering with clearance of mucus from the airway distal to the dynamic collapse. The bacteria found in those elevated colony

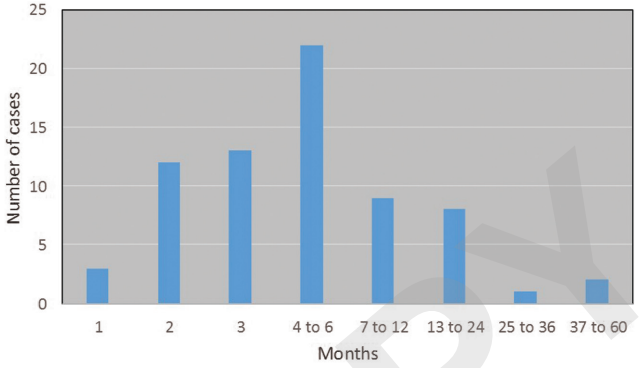

Figure 4. Duration of symptoms among 70 children referred to our tertiary care center subsequently found to have protracted bacterial bronchitis as a cause of their symptoms shown in Fig. 3. (Source: Ref 20.)

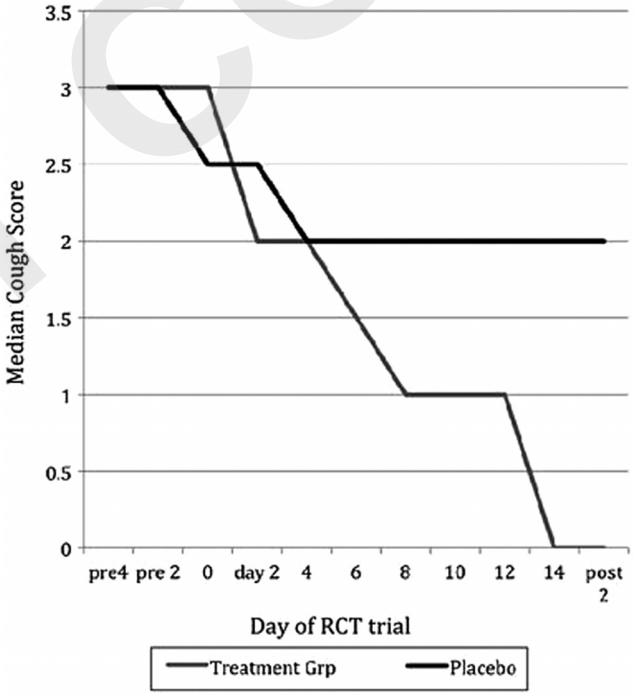

Figure 5. Randomized, double-blind, placebo-controlled clinical trial of 50 children with persistent bacterial bronchitis (PBB) who received amoxicillin/clavulanate (n = 25) or placebo (n = 25). (Reproduced with permission from Ref. 23.)

counts were the same as those found in otitis media, *Streptococcus pneumoniae*, *Haemophilus influenza*, and *Moraxella catarrhalis*.[20] These children have no other manifestations of bacterial infection to suggest a defect in adaptive immunity, and investigations have identified no defect in innate immunity.[22]

Successful treatment of PBB was established in a controlled clinical trial with oral amoxicillin-clavulanate. Treatment for at least 2 weeks was shown to gradually reduce and eliminate the cough (Fig. 5).[23] Our experience has been consistent with that report.

Relapse of PBB occurred in 43 of the 70 children with PBB in our study with successful retreatment in all.[20]

Case Presentation. A 21-month-old male infant had persistent cough since 3 months of age with occasional posttussive emesis and episodic dyspnea. There was a strong family history of asthma. He had been previously treated with albuterol, budesonide aerosol, and courses of prednisolone, all without clinical benefit. Flexible bronchoscopy showed segmental malacia of the right lower lobe and a cell count and differential of bronchoalveolar lavage fluid showed 25% of cells to be neutrophils (normal, <7%). Quantitative culture grew 500,000 CFU/mL of *S. pneumoniae*. Cessation of cough followed 2 weeks of amoxicillin-clavulanate (Augmentin ES600), 45 mg/kg per dose administered twice daily for 14 days. Subsequent recurrences after viral respiratory infections responded similarly. Some episodes were associated with dyspnea, retractions, and hypoxemia, suggesting that an asthmatic component also appeared to be present, but treatment with albuterol and oral corticosteroid was never effective without a 2-week course of Augmentin. This case illustrates the confusion that can occur when symptoms of asthma and PBB overlap requiring simultaneous treatment for both in some cases.

Although the long-term outcome of PBB has not been characterized, concern has been expressed that the chronic infections and peripheral airway inflammation could cause airway damage with consequent bronchiectasis.[24] Although we have not routinely performed chest computed tomography scans in these children, our general experience has been the frequent cessation of recurrent cough after about age 3 years, suggesting that airway damage has not occurred in those children who have been effectively treated.

Cystic Fibrosis

Cystic fibrosis (CF) is a heterogeneous recessive genetic disorder found in about one in 3000 live births among people of European descent that is now commonly diagnosed through newborn screening. However, false negative results, although uncommon, nonetheless, continue to occur. Most who are not identified through newborn screening are identified while young because of failure to thrive as a result of malabsorption from pancreatic dysfunction. However, ~15% have adequate pancreatic function, and some of those are not diagnosed until later in childhood or even as adults.[25]

Case Presentation. A 16-year-old well-developed athletic girl presented with chronic cough of 4 years duration. She had been diagnosed with asthma but had no response to any antiasthmatic treatment including inhaled corticosteroid. Pulmonary function was normal. When the cough did not respond to 40 mg of prednisone twice daily for a week, flexible bronchoscopy was performed. No anatomic airway abnormality was seen but 3115 neutrophils/mm^3 were present with <200 alveolar macrophages (normal is <7% neutrophils). A subsequent sputum culture grew >10,000,000 CFU of *Stomatococcus mucilaginosus* in addition to high colony counts of *Staphylococcus aureus* and *H. influenzae*. Because those were findings suggestive of CF, sweat chlorides were performed, which were within the normal range. However, when genetic analysis for CF was examined, deleterious mutations consistent with an atypical CF presentation was identified. Her subsequent clinical course over 10 years showed slowly decreasing pulmonary function despite continuing care although the chronic cough responded to treatment.

This case illustrates that CF can be present with normal sweat chlorides. This occurs in ~1% of patients with CF and is related to the specific mutations of the CF transmembrane regulator in the patient. Although sweat chlorides are the usual diagnostic test for CF, flexible bronchoscopy was able to identify cytology and bacteriology sufficiently consistent with CF to warrant genetic sequencing for the almost 2000 mutations of the CF transmembrane regulator, the defect of which causes the clinical manifestations of CF.[26]

Tracheomalacia

Dynamic collapse of the trachea can cause cough independent of the potential for tracheomalacia to be associated with PBB.[27] The coughing likely is stimulated by the anterior and posterior surfaces of a portion of the collapsing trachea making repeated contact and thereby causing a nidus of irritation. The cough often has a barking quality similar to the cough with croup (laryngotracheobronchitis).

Case Presentation. An 8-year-old girl had a 2-year history of harsh dry barking cough. The cough interfered with sleep nightly and was frequently associated with posttussive emesis. She had been treated with bronchodilators and sufficient systemic corticosteroids to make her cushingoid, hirsute, and growth suppressed. Flexible bronchoscopy with light procedural sedation showed severe tracheomalacia with kissing ulcerations where the anterior and posterior walls of the trachea made contact. The location of malacia was where the brachiocephalic (also called the innominate) artery crosses over the trachea.[3] Because of the severity, an aortopexy was performed. In this procedure, the aorta is tacked to the sternum with carefully placed sutures through the aortic intima.[28] Because the aorta and the brachiocephalic artery are attached to the an-

terior surface of the aorta by connective tissue, this effectively stents the anterior wall of the trachea by pulling it forward and thereby decreasing the localized tracheal collapse. This procedure was associated with cessation of the cough. Subsequent visualization of that area of the trachea with flexible bronchoscopy showed partial collapse of the trachea but, in contrast to previously, decrease in cross-sectional area never exceeded 50%, and contact of the anterior and posterior walls no longer occurred even with forced coughing.

Most cases of tracheomalacia in infants and toddlers are of lesser clinical consequence than the dramatic case report described. In some young children with tracheomalacia, a wet cough from PBB results as a consequence of interference with clearance of mucus requiring antibiotics as described previously. Growth and maturity appear to be associated with progressively decreased symptoms, either because of a larger airway or decreased compliance of the tracheal cartilage. Only rarely does the child with tracheomalacia have sufficient morbidity to warrant an aortopexy.

Dysphagia (Discoordinate Swallowing)

Some neurologically normal infants permit penetration of liquids into the upper trachea during swallowing. In the presence of a normal cough reflex, coughing results and may occur even from salivary penetration. The history indicates increased coughing with or after feeding. Because the airway penetrated substances are not retained in the respiratory tract because of the normal cough reflex, this transient aspiration is not harmful other than causing a chronic cough. Evaluation by a textured swallow study can identify the problem and adjustment of the consistency of the feeding may help alleviate the problem. Because these infants with an effective cough reflex are not at risk for chronic aspiration pneumonitis, alternatives to oral feeding are rarely indicated for this generally developmental disorder that improves with age.

Primary Ciliary Dyskinesia

This is a rare disorder estimated to occur ~1 per 15,000 births. It is a genetically heterogeneous recessive disorder that results in absence or uncoordinated ciliary movement.[29] More than 80% of infants with primary ciliary dyskinesia (PCD) have transient neonatal respiratory distress, suggesting a role for ciliary function in clearing fluid from the lungs after birth. Chronic coughing and recurrent ear infections begin in infancy and continue in an unrelenting manner throughout life as a result of the absence of normal mucous clearing from peripheral airways. The accumulation of airway mucous causes a chronic wet cough. One-half of those with this disorder have situs inversus totalis (complete reversal of the internal organs) as an apparent consequence of the need for embryonic or fetal ciliary movement to determine sidedness. The absence of ciliary movement results in random assignment of sidedness. Despite chronic cough, normal growth and development is common and progression of chronic lung disease is much slower than in CF. Pathogenic bacteria are not common in PCD. Although neutrophilia in sputum and bacteria are common, more benign organisms such as α-hemolytic streptococci are more common than pathogens common to CF and PBB. Other clinical manifestations of PCD are chronic otitis media from Eustachian tube dysfunction and male infertility due to immotile sperm.[30]

Treatment focuses on providing mechanical means of airway clearance. The chronic coughing can not be stopped, but effective mechanical airway clearance decreases mucus accumulation and helps maintain respiratory function. Judicious use of antibiotics is commonly added but data do not support their routine value. Other measures commonly used for the lung disease of CF are sometimes used but without supportive data of benefit.

Case Presentation. A 16-year-old boy was referred to us because of progressive severity of cough and decreased exercise tolerance. He had cough since infancy. Transient respiratory distress in the newborn period had been diagnosed as transient tachypnea of the newborn. He subsequently had frequent otitis media that had become chronic and associated with conductive hearing loss requiring hearing aids. Pulmonary function showed predominantly decreased vital capacity. With the history suggesting PCD, vigorous chest physical therapy and aerobic exercise were started to provide mechanical airway clearance. Pulmonary function gradually normalized and exertional intolerance improved to the extent that he was able to be normally active including athletic activities.

This case illustrates the typical delay in diagnosis for PCD, especially when situs inversus totalis is not present. The delay in diagnosing PCD probably occurs because of its relative rarity and lack of dramatic clinical effects beyond chronic cough and otitis media. Genetic testing can identify only some individuals with PCD.[31] Examination of ciliary movement under light microscopy can be performed from nasal scraping or tracheal biopsies. Normal ciliary movement and beat frequency can be examined through high-speed microscopic videography, but the technical ability to do that is limited to a few specialty centers. Electron microscopy of cilia was previously thought to be a gold standard for diagnosis, but normal ciliary ultrastructure has been reported in 30% of patients with PCD.[29]

Retained Foreign Body

Foreign body aspiration can result in retention for months to years in some cases, but chronic cough is only rarely a manifestation of a retained foreign body.[32] Recurrent bacterial pneumonia, lobar or lobular hyperinflation, and atelectasis are more common presentations. Development of bronchiectasis can occur from long-term retention of a foreign body. The most common foreign bodies are peanuts but almost any small object put in the mouth of a child can be aspirated. Vegetative materials such as peanut and plastics are not radiopaque. A foreign body may only be identified by bronchoscopy when other causes of chronic cough are not apparent.

Case Presentation. An 8-year-old boy presented with a chronic cough for many months. His parents thought it began when he developed a cold after a flu shot. However, his cough never improved and actually was worsening. His teachers complained that it is disruptive in class. Some days he will go without coughing, but then it recurs. Treatment with antibiotics, cough medicines, antihistamines, and an inhaled corticosteroid were all without benefit. On further review of his history, his mother remembered that the cough may have begun one evening after he returned from a night out at a movie theater where he had been eating popcorn. An inspiratory/expiratory chest film was performed that suggested hyperinflation on the right compared with the left. Rigid bronchoscopy found nondescript vegetative material and granulation tissue partially obscuring the right mainstem bronchus. Removal of the material was eventually associated with cessation of the cough.

This case shows the potential for a retained foreign body to cause chronic cough. It further illustrates that radiological findings can be subtle when the object is not radiopaque. When therapeutic trials of medication are not effective, bronchoscopy then becomes an important tool to identify the etiology of the chronic cough. In contrast to flexible bronchoscopy for examination of dynamic abnormalities, rigid bronchoscopy is appropriate when a foreign body is suspected because of its better ability to remove the object if found.

Unusual Causes of Chronic Cough

There are causes of chronic cough that have been described in individual cases. The following are a few seen at our own clinic.

Achalasia is a rare motility disorder of the esophagus that results from lack of enervation of the lower esophageal sphincter muscles and leads to dilatation of the proximal esophagus. We have seen two cases where chronic cough was the result of the dilated esophagus compressing the trachea (Fig. 6).[33]

Figure 6. *Dilated esophagus with an air–fluid level compressing the trachea. (Reproduced from Ref. 33.)*

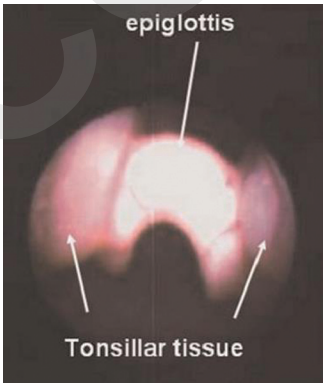

Figure 7. *Tonsils compressing the epiglottis in a 6-year-old girl with a history of cough for 3 months unresponsive to medication. Cough stopped after tonsillectomy. (Reproduced with permission from Ref. 34.)*

Another uncommon cause of cough seen jointly with our pediatric otolaryngologists occurred from large palatine tonsils making contact with and compressing the epiglottis (Fig. 7).[34] Another example of irritating the epiglottis as a cause of chronic cough was a 4-year-old boy who stated he coughed because he felt something in the back of his throat (Fig. 8).[35]

Controversial Causes of Cough

Chronic cough is ascribed to several causes based predominantly on anecdotal reports and popular belief. Despite claims to the contrary, they are not evidence based. Nonetheless, they are included in proposals for evaluating chronic cough in adults.[36] These include gastroesophageal reflux (GER), upper airway disease variably termed upper airway cough syndrome and postnasal drip, and sinusitis.

GER appears to be a particular favorite despite negative data.[37,38] Although there is certainly an association between GER and chronic cough from various causes including asthma and CF, there is no convincing

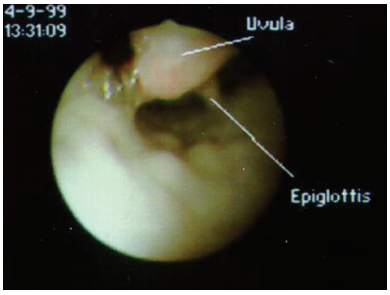

Figure 8. *Uvula resting on epiglottis in a 4-year-old boy with long-standing chronic cough. Uvulectomy eliminated the cough. (Reproduced with permission from Ref. 35.)*

evidence in the form of controlled clinical trials that treatment of GER decreases chronic cough. In fact, a physiological case can be made for chronic cough causing reflux. The strong impressions by some and the many uncontrolled anecdotal reports suggest that perhaps there is a small subpopulation for whom GER causes cough, but we currently do not know how to identify such individuals. The medical literature[38] and our experience provide little rationale for therapeutic trials of protein pump inhibitor medication for chronic cough.

The upper airway cough syndrome, postnasal drip, and sinusitis have been reviewed and we found no evidence to support those as a cause of chronic cough.[39–41] As with GER, there is an association of chronic cough with rhinitis and radiological opacification of the sinuses, but there is no evidence of one causing the other or that treating the upper airway symptoms or sinuses will effectively alter the cough. Certainly, postnasal drainage can cause a sensation that causes repeated throat clearing but that is different from a true cough.

A Rational Evidence-Based Guide to Diagnosing the Cause of Chronic Cough

Chronic cough can be a challenging and frustrating disorder for the patient, family, and physician. A diagnostic approach that combines a careful history and consideration of known evidence-based causes can rapidly provide an explanation for most children with chronic cough and thereby permit appropriate treatment decisions (Table 1). Flexible fiberoptic bronchoscopy has been an effective tool for expanding our knowledge of chronic cough. Although there continue to be occasional cases of chronic cough for which the etiology has eluded us, we are continuing to expand our knowledge and clinical experience in approaching this troublesome symptom.

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