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EVALUATION OF PERSISTENT COUGH IN CHILDREN

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CASE PRESENTATION

B.D. is a 3 year old who presents to the office for evaluation of a cough. It is difficult to believe that 3 years have gone by since B.D. was born to long-time patient L.D., a 33-year-old para 3003. B.D. was the full-term product of a low-risk pregnancy. Labor was uncomplicated except for a prolonged second stage. B.D. has had four ear infections to date and about six colds per year. L.D. is skilled at recognizing when B.D.'s colds can be cared for at home and when medical attention may be required. At this time, B.D. has been experiencing rhinorrhea, cough, and a temperature to 100°F. On evaluation in the office, B.D. appears active and well hydrated. No evidence of bacterial infection is present on physical examination and the diagnosis is made of viral upper respiratory tract infection. B.D. improves slightly during the following weeks, but then his older brother develops a cold. B.D. begins to cough more regularly at night and becomes somewhat more irritable. It is decided to reevaluate B.D. for his prolonged symptoms. At the time of reevaluation, B.D. still looks good. His nasal mucosa is mildly erythematous with bilateral clear discharge. He is active and playful. No evidence of inspiratory stridor, expiratory wheezing, or otitis media is found on physical examination. L.D. is upset. Her cousin's child has just been diagnosed with pneumonia, and L.D. is concerned that her son may develop this condition. She requests further diagnostic testing. Because the illness has lingered for 3 weeks, it is decided to perform a complete blood count, chest radiograph, and place a PPD. The hematocrit is 35%, and the white blood cell count is 7.8 mm^3 with a normal differential. The chest radiograph is clear. Two days later, B.D. returns to the office for an evaluation of his PPD. His skin test is negative. He is active, alert, and no longer coughing.

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Several questions come to mind in considering this case presentation. What is the natural history of the common cold? What types of signs and symptoms should we encourage parents to look for to distinguish complicated from uncomplicated colds? When and what types of tests are appropriate for evaluation of the persistent cough? Chronic cough can be defined as a persistent cough of more than 3-weeks duration. There are many causes, and most should be considered based on age of the child. Although the more common sources of chronic cough are to be stressed, the less common sources are not to be ignored. Infants are more likely to suffer with congenital malformations leading to chronic cough. Toddlers are prone to aspirate foreign bodies. School-aged children may present with signs and symptoms of allergic rhinitis or even cystic fibrosis. Adolescents may expose themselves to inhaled irritants such as tobacco or glue. The presence of psychogenic cough is also more prevalent in adolescents.

CLINICAL EVALUATION

The common cold is the most common reason that patients visit physicians. More lost school days occur because of the common cold than all other causes combined. The common cold is the most frequent upper respiratory tract infection (URI). Wald et al[20] studied the usual duration of community-acquired viral URI and the incidence of complications (otitis media/sinusitis) of these URI in infancy and early childhood. Children in daycare were found to be more likely to have protracted respiratory symptoms than children in home care. The mean duration for a single URI ranged from approximately 7 days (for 1–2 year olds in home care) to approximately 9 days (for children younger than 1 year old in daycare). The percentage of simple URIs lasting more than 15 days ranged from 6.5% (for 1-year-old to 3-year-old children in home care) to 13.1% (for 2-year-old to 3-year-old children in daycare). Symptoms of the common cold include sneezing, rhinorrhea, cough, mild sore throat, congestion, low-grade fever, and malaise. Acetaminophen, oral fluids, rest, and saline nose drops with gentle suction are the only treatments generally recognized as safe and partially effective. Symptoms usually abate in 5 to 7 days. When a child begins to recover and develops localized pain such as earache, chest, throat or facial pain, increased irritability or lethargy, decreased oral intake, high fever, a new purulent nasal discharge, difficulty breathing, or night and day cough, complications such as pharyngitis, sinusitis, otitis or lower respiratory tract infection should be suspected. The real challenge is to distinguish between recurrent or persistent colds that need more time and complications that require medical intervention.

Cough can persist after viral URI for several reasons. A patient occasionally may develop a dry, tic-like, irritative cough that may be present for days or weeks. Presumably the viral infection has irritated the airways and stimulates the cough receptors. Passive or active smoke inhalation may stimulate the cough receptors further. Removing environmental irritants and the passage of time may be the only modalities effective for this difficult cough.

After the URI, the next most common cause of chronic cough is caused by asthma. Cough variant asthma is an occult form of asthma in which the only sign or symptom is chronic cough.[8] It is a problem among all age groups that may go unrecognized. A trial of oral or inhaled bronchodilators with a spacer in young children and a metered-dose inhaler in older children is warranted in patients with or without wheezing and persistent cough after a laboratory evaluation excludes other, more complex, albeit less common, causes. Oral bronchodilators are considered for those children too young to use a spacer or for those for whom the cost of a home nebulizer would be prohibitive.

As many as 5% of acute URIs are complicated by an acute infection of the paranasal sinuses.[9] Persistent nasal discharge and chronic cough usually are caused by infections of the ethmoid or maxillary sinuses. These sinuses are present at birth, with frontal and sphenoid sinuses forming later. Inflammation from infectious and allergic processes may lead to obstruction of the sinus ostia and predispose to secondary bacterial infection. Drainage from the sinuses stimulates the cough receptors. The most common organisms for bacterial sinusitis are *Streptococcus pneumoniae, Moraxella catarrhalis,* and *Haemophillus influenzae.*

Bronchitis is a term used by parents and physicians. Unfortunately, this is a nebulous term without a clearly defined set of signs or symptoms. The term does not imply a specific cause, a treatment, or a prognosis. Because a significant degree of overlap exists between colds and asthma, the term *bronchitis* generally should be avoided and replaced with a more specific diagnosis. Because URIs and asthma have causes other than bacteria, antibiotics usually are not indicated.

Most chronic coughs fall into one of the three aforementioned categories: persistent or recurrent URI, reactive airway disease, or sinusitis. Despite the frequency of these diagnoses, other less common causes need to be remembered to avoid inappropriate reassurance or treatment. By considering the age of the child and the clinical circumstances, precise diagnosis can be achieved.[10]

In the infant younger than 3 months of age, the triad of staccato cough, tachypnea, and conjunctivitis should raise the question of chlamydia pneumonia. Tuberculosis or fungal infections may be seen in children and present as a chronic, hoarse cough thought to be caused by airway compression secondary to enlarged perihilar or paratrachial nodes. Pertussis starts with 2 weeks of mild rhinorrhea and cough before progressing to the characteristic paroxysms of cough or posttussive vomiting. Loud, brassy cough following a viral URI associated with attention seeking behavior and "la belle indifference" may indicate a psychogenic or habitual cough. Foreign body aspiration should be considered at every age, especially in the toddler. Even an esophageal foreign body can produce a chronic cough by pressing on the posterior pharynx. Overfeeding, a dysfunctional swallowing mechanism, gastroesophageal reflux and bottle propping can cause chronic aspiration, thereby producing chronic cough.[5] Other less common causes of chronic aspiration are congenital abnormalities such as tracheoesophageal fistula, laryngeal cleft, and adductor vocal cord paralysis.

Immune deficiency diseases can present with prolonged respiratory symptoms or multiple pneumonias.[4] HIV has become an important cause of immune deficiency in children. Unusual opportunistic infections such as *Pneumocystis carinii* pneumonia can be seen, but the most common manifestation of HIV disease in children is recurrent bacterial infection such as otitis media or pneumonia that usually responds temporarily to a standard antibiotic regimen. Lymphocytic interstitial pneumonia can complicate HIV infection and may persist with a nonproductive chronic cough, respiratory distress, failure to thrive, and pulmonary infiltrates.

Inability to mechanically clear mucus from the respiratory tract may cause trapping of foreign material and lead to chronic cough. Patients with cystic fibrosis present with cough, failure to thrive, and recurrent lower respiratory tract infections often secondary to *Pseudomonas.* These patients produce a thick, tenacious sputum that is difficult to clear from the airway. In the immotile cilia syndrome, an abnormality in the mucocilary apparatus results in frequent respiratory infections.

Other less common congenital problems causing chronic cough include any condition in which a large, aberrant, thoracic structure compresses the airway. Examples of this include anomalous great vessels, bronchogenic cysts, or pulmonary sequestration. A simple URI can produce respiratory compromise in these

conditions in addition to tracheobronchomalacia in which the central airways are soft and collapse more easily.

Few published reports detail the psychogenic cough. It generally is not thought of as rare, however. This cough is characterized as croupy and explosive. It never occurs during sleep and is not affected by antitussives. It usually is regarded as a respiratory tic and can be precipitated by various stimuli such as school phobia, attention seeking, or anxiety.

PATHOPHYSIOLOGY

Cough Stimuli

Cough is a reflex response of the respiratory tract to irritants in the form of mechanical, inflammatory, chemical, or thermal stimuli.[6] Dust, smoke, and foreign bodies are common types of mechanical stimuli, whereas extrinsic compression from tumor, lymph nodes, or enlarged anatomic structures is uncommon. Inflammation activates cough receptors because of hyperemia and edema of the mucous membranes. Organic compounds as well as acidic and basic vapors irritate receptors in the smaller airways. Inhalation of hot or cold air may stimulate cough where there is an underlying pathologic condition of the respiratory tract.

Cough Reflex

A reflex is a reproducible, neurally mediated response to a stimulus. In general, the components of a reflex arc include the peripheral sensory receptor, afferent pathway, cough center, and motor response unit. From the respiratory tract, the afferent pathway is mainly via the vagal and superior laryngeal nerves. The cough center is in the medulla. The afferent pathway is mainly via the phrenic and intercostal nerves. The motor unit is the diaphragm and intercostal musculature. The larynx, carina, and bifurcations of large bronchi are especially sensitive to mechanical stimuli, whereas the terminal bronchioles and alveoli are more sensitive to chemical stimuli. Interestingly, cough receptors also are found in the pharynx, external auditory canal, and stomach. If cerumen impinges on the eardrum, a chronic cough can be triggered and will persist until the canal is disimpacted of the cerumen.[3]

Anatomic Sequence

Air is inspired into the lungs. The air then is entrapped in the lungs by the closure of the epiglottis and the vocal cords. The abdominal muscles contract quickly and forcefully against the diaphragm in conjunction with contraction of the internal intercostal muscles. The pressure within the lungs rises sharply. An explosion of air occurs when the epiglottis and vocal cords open.

Pathophysiology of the Leading Causes of Persistent Cough

Viral URI

The common cold is a mild and self-limited syndrome caused by a viral infection of the mucosa of the upper respiratory tract. The symptoms are well known

and include sneezing, rhinorrhea, sore throat, and cough. The *rhinovirus* and the *coronavirus* cause up to 45% of all colds. Assorted other viruses such as *influenza, parainfluenza, respiratory synctial virus,* and *adenovirus* account for another 10% to 15%. Transmission appears to be via respiratory droplets and hand-to-hand contact. Self-inoculation then occurs on the conjunctival or nasal epithelium. The respiratory mucosa becomes hyperemic and edematous. With the onset of inflammation, the cough receptors are stimulated and the reflex is initiated.

Reactive Airway Disease

Asthma is characterized by airway obstruction that is reversible. Reduction in airway diameter is caused by smooth muscle contraction, epithelial inflammation, and mucous secretion into the lumen. Here too, the inflammation triggers cough receptors.[16]

Sinusitis

Production of cough in sinusitis is via two mechanisms. The postnasal drip into the pharynx associated with sinusitis serves as a mechanical stimulus, whereas the hyperemia of respiratory epithelium serves as an inflammatory stimulus.

HISTORY[2]

The history is of importance in determining the cause of persistent cough. Attention first should be directed at the symptom itself, eliciting duration and descriptive qualities of the cough as well as associated symptoms. Indicators of serious illness should be identified next. Identifying the age of the child will help to narrow the differential diagnosis. A more general history then may be obtained, including a prenatal and feeding history in the case of an infant. Growth and development, childhood illnesses, exposures, operations, injuries, hospitalizations, immunizations, medications, allergies, and psychosocial and family history also are necessary. Access to medical care for the child and the health belief system of the family, when evaluated, often will elicit enlightening and useful information.

Determining the duration of the cough is critical in sorting out persistent cough from recurrent cough. A frustrated parent may present with their child stating "Johnny has been coughing all winter!" On questioning, many of these chronic coughs will turn out to be a series of separate URIs not caused by a single pathophysiologic process.

Cough Characteristics

Once it has been established that the cough is indeed persistent for more than 3 weeks, characteristics of the cough may be noted. A cough productive of purulent sputum usually indicates an infectious cause from a bacterial or viral source. A productive cough usually occurs in children only after the age of 4 or 5 years old. A productive cough at a younger age should raise the examiner's index of suspicion for cystic fibrosis in the toddler age group of tracheoesophageal fistula or gastroesophageal reflux in infants. Viral infections tend to be recurrent. Bacteria that cause chronic cough include *Chlamydia, Mycoplasma, Bordatella pertussis,* and *Mycobacterium tuberculosis.* A cough producing thick, tenacious sputum may be

associated with cystic fibrosis. A dry, brassy, or stridorous cough may be associated with upper airway disease caused by foreign body aspiration, laryngitis, or laryngotracheobronchitis (croup). Paroxysms of cough are found in pertussis, cystic fibrosis, and foreign body aspiration. A paroxysm of cough followed by a whoop is the classic presentation of whooping cough caused by *B. pertussis.* The whoop rarely is seen in infants. A productive throat clearing indicates a postnasal drip associated with sinusitis. The staccato cough is associated with chlamydia pneumonia. A psychogenic cough that usually presents as dry and brassy may be bizarre, with a honking or barking quality. A cough associated with a wheeze is likely caused by asthma (Table 1).

Timing

Timing of the cough also carries certain implications. Cough that occurs with feeding implies aspiration and possibly a congenital abnormality. Reflux and overfeeding would be the more common cause in the infant, whereas tracheoesophageal fistula or laryngeal cleft are uncommon. A child who just enters daycare likely will experience an increased frequency of URIs, whereas seasonal variations may indicate an allergic cause. A temporal relationship to an irritant such as smoke or an allergen such as a pet may be established. Nighttime cough may signal reactive airway disease or sinusitis with recumbent postnasal drip. Cough that disappears with sleep should raise concern of a psychogenic cause. Cough that is worse on

Table 1. AGE-RELATED CAUSES OF PERSISTENT COUGH

Infant	
Viral URI	Common
Airway irritation (passive smoke)	
Chlamydia pneumonia	
Gastroesophageal reflux	
Tracheoesophageal fistula	
Laryngeal cleft	
Vocal cord paralysis	
Congenital heart disease	Uncommon
Toddler	
Viral URI	Common
Reactive airway disease	
Sinusitis	
Airway irritation (passive smoke)	
Foreign body aspiration	Uncommon
School-aged	
Viral URI	Common
Reactive airway disease	
Sinusitis	
Airway irritation (passive smoke and sniffing)	
Allergic rhinitis	
Cystic fibrosis	Uncommon
Adolescents	
Viral URI	Common
Reactive airway disease	
Sinusitis	
Inhaled irritants (smoking and sniffing)	
Psychogenic cough	
Immotile cilia syndrome	Uncommon

awakening may imply cystic fibrosis or bronchiectasis. Cough associated with exercise may be caused by exercise-induced asthma, cystic fibrosis, and bronchiectasis and rarely may suggest heart disease or extrinsic airway compression.

Associated Symptoms

An associated symptom such as hemoptysis raises the concern about such diseases as pulmonary tuberculosis, cystic fibrosis, bronchiectasis, or possibly foreign body aspiration. Headache, malodorous breath, and nasal discharge may signify a chronic sinusitis. Prolonged fever associated with weight loss indicates a more serious cause such as HIV infection.

PHYSICAL EXAMINATION[2]

The critical element of the physical examination is the general clinical impression. Does this child appear healthy, ill, or toxic? The signs and symptoms of serious disease should be considered early in the evaluation:

Persistent fever
Failure to grow or gain weight
Clubbing
Purulent sputum
Hypoxemia
Refractory chest radiographic infiltrates
Hemoptysis

With a URI, the child will appear mildly ill and have no significant fever. Rhinorrhea and pharyngeal erythema may be present, but the examination otherwise should be benign. In a child with reactive airway disease, URI symptoms may be present in addition to audibly harsh respirations, a prolonged expiratory phase, and wheeze. Musical rales may be present. A barrel chest suggests a chronic problem. The liver and spleen may be palpable because of hyperinflation of the lungs. Nasal polyps are suggestive of atopy.

Sinusitis in children is estimated to be a complicating factor in 5% to 10% of all URIs. Because children average six to eight colds per year, sinusitis is a common condition in primary care. Sinusitis typically presents with a nasal discharge of any quality (thin to thick and clear to purulent). The cough usually is present by day but is usually worse at night. Halitosis (bad breath) may be present. Facial pain and headache are useful indicators only after the age of about 10 to 12. Painless morning eye swelling may be noted by the parent in the school-aged population. Fever, if present, is usually low grade.[14]

The infant with tracheoesophageal fistula often will have early respiratory distress, cyanosis, excessive secretions in the oropharynx, and cough with feeding. Splinting may be seen as well. Tracheobronchial compression by anomalous or enlarged vessels causes an infant to have noisy breathing and a cough. The infant may attempt to optimize the airway by assuming an opisthotonos position.

Children between the ages of 6 months to 4 years are at particular risk of aspiration of foreign bodies. The initial response is usually gagging, coughing, and wheezing. If the foreign body has been allowed to remain, however, distal obstruction, mucous production, and inflammation may obstruct the airway, caus-

ing atelectasis or an infiltrate. Decreased breath sounds over the affected lung with inspiratory rhonchi and expiratory wheezing are found.

Inspection for stigmata of allergic disease will reveal a pale, boggy nasal mucosa, clear rhinorrhea, allergic shiners, and the nasal crease.

Chronic illness presents with generalized signs such as poor weight gain. Scattered diminished breath sounds, cyanosis, and digital clubbing are late signs of cystic fibrosis.

Tobacco abuse may be identified by the smell of tobacco or by nicotine stains, whereas sniffing glue and other substances may produce a clouded sensorium.

MANAGEMENT

The medical evaluation of chronic cough can present a significant challenge to the primary care provider. Despite the extensive differential, the three most common causes of chronic cough are viral URIs, reactive airway disease, and sinusitis. Looking carefully for signs and symptoms of serious disease (see list), recognizing that the age of the patient is associated with specific types of chronic cough (see Table 1), and understanding the character of the cough and its cause affect management decisions. By considering these three factors in addition to a thorough history and physical examination, many expensive, low-yield laboratory tests can be avoided. Although cost-effective, this approach must be combined with a skillful exploration of the parents' concerns and needs.

Failure to thrive, clubbing of the fingers, hypoxemia, persistent fever, purulent sputum, hemoptysis, and refractory chest findings point to a more complex diagnosis and should have an evaluation initiated with a chest radiograph, complete blood count, and PPD.

The younger the child is, the more likely a congenital cause for the cough will be found. Infants with congenital heart defects, laryngeal clefts, vocal cord paralysis, and tracheoesophageal fistula may present with chronic cough. Airway irritation secondary to passive smoke inhalation, chlamydia pneumonia, and gastroesophageal reflux also present in this age group.

Although toddlers may have reactive airway disease or sinusitis as a cause of their cough, one always must consider foreign body aspiration in this age group. If the chest radiograph is negative, inspiratory and expiratory films should be attempted. If the child is too young to cooperate, right and left lateral decubitus films can be substituted. These studies are designed to find air trapping, and if the history and physical examination are compatible, the patient should undergo bronchoscopy for evaluation and removal of the foreign body.

School-aged children are more likely to have reactive airway disease, allergic rhinitis, or sinusitis. If a thorough history, physical examination, and laboratory evaluation reveal nothing atypical of asthma, a trial of oral or inhaled β_2 agonists with or without a spacer can be tried. An older child may be able to perform a peak expiratory flow in the office to further assess bronchospasm in addition to pre– and post–bronchodilator therapy. It is important to counsel patients concerning the proper use of the inhalers and the correct dose before a decision is made to abandon this line of therapy. If the patient responds equivocally or partially to bronchodilator, a short course of high dose oral corticosteroid should be given. This is the patient who will benefit from chronic anti-inflammatory therapy. Sinus radiographs have significant false-positive and false-negative results in the presence of simple URIs and documented sinusitis. If sinusitis is expected clinically, a course of antibiotics should be administered.[14] Forty percent of sinusitis clears spontaneously, however. A frank discussion with the parents concerning

the value of antibiotics in this setting is generally prudent. MR imaging, rhinoscopy, ultrasound, and CT scans are not likely to be useful. A history of recurrent sinusitis and pneumonia should lead to a nasal biopsy to rule out immotile cilia syndrome.

Allergic rhinitis can be diagnosed by the general appearance of the child, nasal creases, allergic shiners, mucoid rhinorrhea, and mauve-colored nasal mucosa. A trial of antihistamines or topical steroid therapy is indicated, and consideration should be given to allergy evaluation if the pharmacotherapy is not effective.

Adolescents more frequently present with cough caused by inhaled irritants. If the cough is associated with unusual noises and absent at night, a psychogenic etiology should be considered.[15]

SUMMARY

Chronic coughing in children is a challenging problem for the busy clinician. A thoughtful and diligent approach that combines a working knowledge of the family, complete history, and physical examination with appropriate laboratory testing has the best chance of curing this difficult and often recalcitrant problem. As is usually the case in medicine, care of the patient and the family is often far more important than cure of a self-limited process.

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