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REVIEW

Evaluation of chronic cough in children: a practical approach

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ABSTRACT

Cough is one of the main causes of seeking medical care worldwide. Cough that persists for more than a few weeks is very tasking to the patient and family, both financially and psychosocially. The latter is particularly notable when cough is chronic (> 8 weeks) and the patient is a child.

Whereas acute cough in children is mostly caused by an infection, chronic cough can have numerous respiratory tract and extra-respiratory causes and mechanisms. An early recognition of the underlying cause would lead to early and precise treatment that, in some cases, may require multiple medical consults. Towards such an objective, this article is designed to provide a practical, easy-to-follow guideline for evaluating chronic cough in children.

A skillful medical history-taking of the present illness, past history, family history, and environmental history, followed with a comprehensive physical examination can provide very valuable clues for selecting supportive, cost-effective investigative tests. In addition to the currently available standard evaluation tests, technological advances are leading to the recent development of practical devices for objective assessment of cough characteristics which in turn enhance precise evaluation.

IMPACT STATEMENT

This article provides an easy-to-follow practical approach for evaluation of chronic cough in children. It should facilitate early identification of the underlying cause, prescribing the appropriate management, and limiting the illness' negative impact.

KEY WORDS

Childhood chronic cough; chronic cough causes; cough characteristics; radiologic findings in cough; cough assessment devices.

Introduction

Cough is basically an innate reflex that acts as a defense mechanism – primarily to clear the respiratory tract of excessive mucus or to expel a foreign body. Healthy children normally cough several times a day with an average of 11 times a day; more in cold weather than on warm days (1). However, cough can be a symptom of illness and a potent method of spreading respiratory infections. It is one of the most common reasons for seeking medical care worldwide and contributes substantially to the healthcare costs. It accounts for 4.7% to 23.3% of all reasons for pediatric primary care visits (2). Apart from the financial burden, the psychosocial effects of chronic cough in children, compared to adult patients, impact family dynamics and peer relationships differently.

Definition and Classification

Cough from acute respiratory infection usually resolves within a few weeks. Chronic cough in children is generally defined as a cough persisting for more than 4 weeks (3, 4). According to these guidelines, the pediatric population is generally defined as pre-pubertal children younger than 14 years. In contrast, the British Thoracic Society defines chronic cough in children as a cough lasting for more than 8 weeks (5), which is similar to adults, but this cut-off is considered too long in children (6, 7). Children are not small adults, their cough can have different causes (4, 8, 9). The differential diagnosis of cough in young children is distinct from older children and adults.

Cough may be classified in different ways, *i.e.*, according to its mechanisms, characteristics, causes, or as non-specific *vs* specific. Non-specific cough is typically dry with a normal chest X-ray (CXR) and spirometry; it mostly follows a respiratory viral infection and resolves spontaneously without serious sequelae. Specific cough may be wet or dry and is associted with abnormal findings by lung auscultation and/or CXR, along with other symptoms such as dyspnea, hemoptysis, recurrent pneumonia, swallowing problems, or failure to thrive.

The objective of this review is to provide a practical approach for evaluating chronic cough in children. Awareness of the various causes is crucial for conducting an appropriate evaluation, including medical history-taking, physical examination, and selection of diagnostic procedures and laboratory tests. To enhance the usefulness of this article in clinical practice, more information is presented in simplified tables in lieu of long texts.

Causes of Chronic Cough

The underlying causes of chronic cough can be simply divided into respiratory and extra-respiratory (**Table 1**) – a broad spectrum reflecting the marked heterogeneity of cough phenotypes. Furthermore, cough can be stimulated or provoked by a large number of mechanical, thermal, chemical, and inflammatory mediators (**Table 2**). Such agents act through different complex pathophysiological mechanisms and pathways (10, 11).

According to a review by Rubin (12), chronic cough in children is often preceded by viral respiratory infection. Protracted bacterial bronchitis is one of the most common causes of persistent wet cough in young children. Gastroesophageal reflux rarely causes chronic cough in children. Also, isolated-cough-variant asthma without objective airway findings appears to be rare in children. Chronic purulent cough should prompt evaluation for bronchiectasis, immune deficiency, aspiration, cystic fibrosis, or ciliary dyskinesia. Functional cough disorders include psychogenic cough, habit cough, and cough associated with secondary gain – which can be hard to differentiate from each other; psychologic consult would help in diagnosis and management.

Evaluation of Chronic cough IN CHILDREN

Multiple guidelines and diagnostic algorithms for the evaluation of chronic cough have been published (1, 3, 9, 13-18). We present a simplified yet comprehensive guideline that is easy to follow and applicable in clinical practice.

Appropriate evaluation starts with a thorough skillful medical history-taking followed by a comprehensive physical examination with emphasis on, but not limited to, the respiratory tract. According to the information gathered from these two procedures, a differential diagnosis that guides the selection of appropriate diagnostic procedures and laboratory tests can be formulated.

Medical history

It cannot be overemphasized that a skillful history-taking plays a pivotal role in the assessment of chronic cough in children (9, 19, 20). Medical history should include the present illness history, past history, family history, and environmental history. Since in most cases the information is obtained through the parents, a special skill is required on the part of the health provider, parents may not volunteer important information unless specifically prompted.

Present illness history

Information-gathering should begin with the cough's onset and its circumstances. Onset during early infancy may be related to prematurity, congenital malformations, neonatal illness, interventions, conditions predisposing to aspiration, or chronic pulmonary disease such as bronchopulmonary dysplasia (BPD) or cystic fibrosis. A sudden onset of cough while playing with small toys or eating should raise suspicion of foreign body aspiration or a tracheoesophageal fistula. The cough should be assessed in terms of its initial characteristics, course over time, triggers, exacerbating factors, and associated symptoms such as fever, night sweats, dysphagia, and weight loss. Hemoptysis may suggest foreign body aspiration, bronchiectasis, tuberculosis, lung abscess, hemosiderosis, heart failure, neoplasm, vascular lesions, endobronchial lesions, and clotting disorders. Obtaining information on current or past medication can be valuable in knowing the response to past therapies or as potential cause – a dry cough may develop after prolonged asymptomatic use of angiotensin-converting enzyme (ACE) inhibitors. Information on the characteristics of cough can provide valuable clues to the underlying etiology (21) (**Table 3**).

Past medical history and comorbidities

Past medical history should be evaluated for perinatal history, including prematurity, neonatal illnesses, interventions, and BPD. In addition, a history of severe respiratory infections like pertussis and adenoviral bronchiolitis should be taken into consideration. A recent case-control study (22) revealed that children with chronic cough exhibited higher rates of allergic diseases compared to controls: allergic rhinitis was present in about 75% *vs* 24%, food allergy in 60% *vs* 28%, and eczema in 55% *vs* 31%.

Family history

Information should be obtained regarding a family history of illness, particularly chronic cough and atopy, especially asthma. A family history of allergy was noted in 72% of children with chronic cough *vs* 28% in children without cough (22). Chronic cough in a family member may lead to the development of habit cough in a child. Tobacco smoking by household members can be a primary or a major contributory factor. The family dynamics may not only contribute to exacerbation of the child's cough but can also be the cause of psychogenic cough.

Environmental history

Environmental exposures should be explored, including indoor, outdoor, and geographic factors (23-26). Indoor exposures include allergens such as pets, mold, and dust mites, as well as irritants such as tobacco smoke, wood burning stoves, fumes, and cleaning chemicals. Outdoor exposures may include pollens, mold, and nearby industrial pollution. Geographical and endemic factors should also be considered, particularly exposure to

parasitic and fungal infections. Compared with children without cough, children with chronic cough had higher exposure to household smoking (55% *vs* 21%) and mold (29% *vs* 7%) (22).

Physical Examination

Children with chronic cough should undergo a comprehensive physical examination, starting with the general appearance, vital signs, and main body systems, particularly the respiratory and the cardiovascular systems (**Table 4**). Physical findings can point to possible underlying causes of cough (**Table 5**). External ear examination may reveal a foreign body which may be as small as a tiny piece of paper or a hair lodged against the tympanic membrane, inducing reflex cough through stimulation of the auricular branch of the vagus nerve (27). Failure to thrive may point to cystic fibrosis or other chronic pulmonary diseases. Dyspnea, tachypnea, cyanosis, or finger clubbing typically indicate chronic airway obstruction, substantial pulmonary parenchymal disease, or cardiac disease. On lung auscultation, crepitations suggest alveolar secretion whereas localized decreased breath sounds indicate consolidation or atelectasis. Skillful chest percussion may reveal areas of lung consolidation, cavitation, or pleural effusion.

LABORATORY INVESTIGATIONS

A vast array of laboratory tests is available for a comprehensive evaluation of chronic cough. Multiple factors should be taken into consideration including availability, the child's age, and cost. They can be broadly classified into two main groups: initial basic tests and additional selected tests (**Table 6**).

Initial basic tests

A routine complete blood count (CBC) may suggest infection or reveal anemia, eosinophilia or cytopenia that warrant further investigation. Radiologic imaging of lungs and paranasal sinuses can reveal important findings. Common chest radiograph (CXR) abnormal findings and their potential clinical significance are presented in **Table 7**.

Spirometry (with flow-volume loop), including pre- and post-bronchodilator or exercise testing can help assess airway obstruction and reversibility. A concave expiratory flow-volume curve is suggestive of asthma, whereas a flat inspiratory loop would indicate an extra-thoracic airway obstruction such as inducible laryngeal obstruction (vocal cord dysfunction). It is important to note that normal CXR and/or spirometry findings do not exclude the need for further pulmonary investigation. A study showed that the use of CXR and spirometry in initial evaluation of children with chronic cough showed specificities of 93% and 94% respectively, but their sensitivities were only 19% and 17% (28).

Radiologic imaging of the paranasal sinuses may include a Waters' view X-ray, but CT scan, if feasible, has better sensitivity and specificity for revealing abnormalities. Expertise is needed in interpreting sinus imaging because some findings may be transient or not clinically relevant

(3). Initial signs of sinus pneumatization are noted at birth for the maxillary and ethmoid, at 9 months for the sphenoid, and after the age of 5 years for the frontal (29). For practical purposes, the maxillary and ethmoid sinuses can be radiologically visualized in young infants, the sphenoids become apparent at 3-5 years, and the frontals at 7-12 years (30-32).

Additional selected tests

Additional diagnostic tests should be individualized and judiciously selected (**Table 6**). In some cases, certain CXR views may be needed such as decubitus for pleural effusion or films during inspiration versus expiration for localized airway obstruction. In screening for tuberculosis, to differentiate between infection and immunity, interferon-gamma release assays, such as QuantiFERON-TB or T-SPOT.TB, are preferred over the tuberculin Mantoux skin test (33).

Suspicion of pertussis requires confirmation with PCR testing. In screening for cystic fibrosis, genetic testing for CFTR gene mutations is superior to sweat chloride testing (34). Screening for primary ciliary dyskinesia can be by electron microscopy examination of respiratory tract brush biopsy or by genotyping for mutations in the PCD gene, but normal finding does not exclude the disease (35). For bronchial hyperresponsiveness, mannitol challenge is preferred over methacholine (36). A suspicion of Heiner syndrome (**Table 8**) would be supported by a high serum titer of IgG antibodies to cow milk proteins (37, 38); the presence of iron-laden macrophages in bronchoalveolar lavage or lung biopsy would indicate pulmonary hemosiderosis (**Figure 1**).

Advanced tools for assessing cough characteristics

Recent years have witnessed the development of many new methods and devices for objective assessment of cough frequency, intensity, and reflex sensitivity (**Table 9**). They were initially developed primarily for research studies. Most of these tools are expensive and require specific expertise for administration and interpretation, and so far, have shown varying degrees of correlation with subjective assessment. Several devices have been adapted for easy clinical use. Selected devices will be briefly mentioned here; details are available in other publications (39-43).

Several ambulatory cough frequency monitors are available; the most commonly used are VitaloJAK and Leicester Cough Monitor. Others are Hull Automatic Cough Counter, LifeShirt, Cayetano Cough Monitor, LR102, and PulmoTrack-CC. Cough intensity can be assessed with measuring the expiratory flow rate, electromyogram activity of respiratory muscles, and cough sound amplitudes. For assessing the cough reflex sensitivity, capsaicin and citric acid have been used for controlled inhalation challenge tests. More recently, there has been an increased focus on advanced technology to develop wearable, low-cost, real-time, and patient-friendly devices for the acquisition and automatic assessment of cough sounds.

The Hyfe Cough Monitor is a smartwatch-based system, which is connected to its software application. It is an artificial intelligence-powered cough detection system designed to passively and continuously monitor cough in real-world conditions. In a multicenter observational study, the results of the Hyfe Cough Monitor wrist-worn device were compared with manually counted coughs; it demonstrated high sensitivity (90.4%), a low false positive rate (~1.03/hour), and a very strong correlation (r = 0.99) between its automated counts and manual count (44).

Hoyos-Barcelo *et al*. (45) proposed a smartphone-based cough detection system which can classify cough in a noisy environment with 88.94% sensitivity and 98.64% specificity. Similarly, Kvapilova *et al*. (46) used continuous smartphone sound recordings combined with machine learning algorithms to measure cough frequency and distinguish between dry and wet cough, with reported sensitivity and specificity of 88% and 86% respectively.

The LEOSound-system is an automated lung sound monitor, functioning as a "long-term stethoscope". It can continuously record lung sounds using an ambient microphone and three small bio-acoustical sensors. One of the sensors is attached to the patient's trachea and the other two to the back (47). In children, the sensitivity of cough detection was 89% and its specificity was 99%, with a strong correlation (r = 0.85) with subjective measures (48).

Another wearable portable automatic cough counting device containing acquisition and reception software has been recently developed (43). It includes a small microphone connected to a controller, Bluetooth module, and software that enables real-time cough counting. The cough sensor is designed to be worn on the body (*e.g*. on the collar near the mouth) and paired with a host tablet app for long-term monitoring. It has the advantages of denoising and high degrees of accuracy, with sensitivity, and specificity at 93.24%, 97.58%, 86.97%, respectively. In comparison to other devices which are often larger, stationary and require offline processing, this system is compact, wearable, and suitable for daily long-term use. With the continued advances in technology, more advanced devices for objective cough monitoring are expected in the coming years.

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Table 1. *Causes of chronic cough*.

Respiratory tract		Extra-respiratory	
Mechanical	**Thermal**	**Chemical**	**Mediators**
Upper: disorders of nose, sinuses, pharynx, larynx, ear canal	Cold air	Capsaicin	Histamine
Mucus	Hot air	Citric acid	Bradykinin
Foreign body	Cold water ingestion	Osmotic agents	Prostglandin-F2α
Lower: trachea, bronchi, lungs, pleura		Tobacco smoke	
Instrumentation			
Inflation/deflation			

Cardiovascular: heart failure, vascular rings, anomalies of large blood vessels

Neuromuscular: swallowing disorders

Gastroesophageal: gastroesophageal reflux, diaphragmatic hernia

Medications: angiotensin-converting enzyme inhibitors; cytotoxic drugs

Functional: Psychogenic, habitual, secondary gain

Table 2. *Cough stimuli.*

Table 3. *Cough characteristics may point to the underlying cause.*

Modified from (21).

Cough Characteristic	Possible Underlying Condition
Honking, not during sleep, stops upon request	Psychogenic, habit, secondary gain
Nocturnal	Postnasal drip (Upper airway cough syndrome), asthma, allergens in bed
Post-exercise	Asthma, cough-dominant asthma
Environmental exposure	Respiratory allergy
Associated with stridor	Laryngeal obstruction, foreign body, pertussis
Spasmodic, inspiratory whoop	Pertussis
Staccato	Chlamydia pneumonia
Brassy, barking	Croup, laryngitis, tracheitis, tracheomalacia
Productive, purulent sputum, worse in morning	Immunodeficiency, foreign body, cystic fibrosis, bronchiectasis, ciliary dyskinesia

Table 5. *Significance of physical findings in subjects with chronic cough.*

Physical finding	**Possible underlying condition**
Failure to thrive	Cystic fibrosis, other chronic pulmonary disease
Tachypnea or dyspnea	Substantial airway or pulmonary parenchymal disease
Cyanosis	Chronic airway or parenchyma disease, cardiac disease
Digital clubbing	Suppurative lung disease, cyanotic heart disease
Lymphadenopathy	Neoplastic disease, tuberculosis
Chest wall deformity	Any chronic airway or parenchymal disease
Lung auscultation	Wheeze, rhonchi, crepitations, decreased breath sounds
Chest percussion	Consolidation, cavitation, pleural effusion
Cardiac abnormalities	Associated airway abnormalities, cardiac failure
Neuromuscular disease	Aspiration lung disease

T*able 4.* *Physical examination in chronic cough.*

Adapted from (1); (9); (13); (21).

Table 6. *Tests for evaluation of chronic cough*.

Initial basic tests	**Additional selected tests**	
Complete blood count with differential	Chest radiograph (CXR) specific views	Nasal brush biopsy
Chest radiograph (CXR)	Chest high resolution computed tomography (HRCT)	Bronchial challenge
Sinus X-ray or computed tomography (CT)	PPD or QuantiFERON	Rhinolaryngoscopy
Spirometry:	Cystic fibrosis (sweat/genetic)	Bronchoscopy
Flow-volume loop	Allergy evaluation	Bronchial or lung biopsy
Pre- / post-bronchodilator	Immunodeficiency evaluation	Esophageal pH monitoring
Pre- / post-exercise		

Table 7. *Clinical significance of chest X-ray abnormal findings.*

Abnormal finding	**Possible clinical significance**
Peribronchial accentuation	Chronic asthma, cystic fibrosis, chronic bronchitis
Peribronchial accentuation with macro-nodularity or railroad sign	Bronchiectasis
Asymmetry in aeration or vascular markings	Partial airway obstruction
Right middle lobe infiltrate	Atelectasis from mucus plugging or foreign body
Pleural effusion or pneumothorax	Parenchymal lung disease
Hilar lymphadenopathy	Tuberculosis, fungal infection, sarcoidosis, neoplasm
Large heart or pulmonary artery	Heart failure, pulmonary hypertension
Shifted cardiac shadow	Substantial atelectasis
Right-sided heart	*Situs inversus*, ciliary dyskinesia
Multiple lung infiltrates	Milk-induced pulmonary disease (Heiner syndrome) (Table 8)

Modified from (21).

Table 8. *Milk-induced chronic pulmonary disease (Heiner syndrome).*

Chronic or recurrent lower respiratory symptoms, often associated with upper respiratory and GI symptoms and failure to thrive. Cow's milk is the most common, but not the only, causative food.
CXR may show patchy infiltrates, localized atelectasis, consolidation, peribronchial infiltrate, hilar lymphadenopathy, pleural thickening, or reticular density.
CBC may show eosinophilia and/or iron deficiency anemia.
High titers of serum IgG antibodies (precipitins) to multiple cow's milk protein fractions.
Pulmonary hemosiderosis in severe cases.
Symptoms begin to improve within several days after dietary elimination, but radiologic improvement may take several weeks.

Table 9. *Advanced tools for assessing cough characteristics (40-48).*

Device	**Use**
VitaloJAK and Leicester Cough Monitor; Hull Automatic Cough Counter; LifeShirt; Caytano Cough Monitor; Pulmo Track-CC.	Ambulatory monitors for objective cough frequency assessment.
Expiratory flow rate, electromyogram activity of respiratory muscles, and cough sound amplitude	Objective assessment of cough intensity.
Capsaicin and citric acid inhalation challenge	Controlled inhalation challenge tests for assessing cough reflex sensitivity.
Hyfe Cough Monitor	AI-powered smartwatch device for passive, continuous, real-world cough monitoring.
Smartphone-based cough detection systems	Smartphone sound recording, detect and classify cough in noisy environments, can distinguish dry from wet cough
LEOSound system	Automated lung sound monitor using ambient microphone and bio-acoustic sensors attached to the trachea and back.
Wearable collar cough counter	Compact wearable microphone paired with a Bluetooth-enabled tablet app for real-time, long-term cough counting

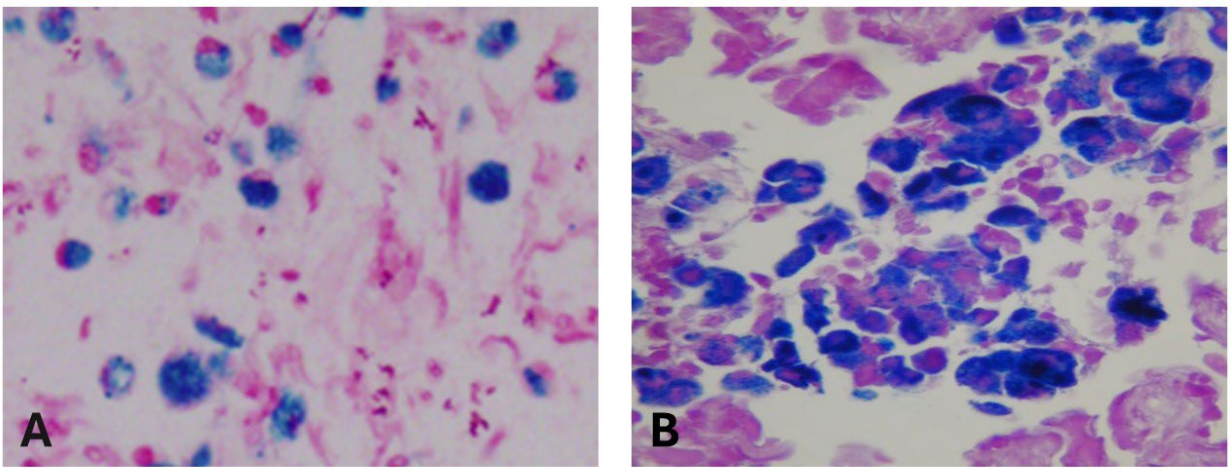

Figure 1. *Iron-laden macrophages (Prussian blue stain) in bronchoalveolar lavage (A) and in lung biopsy (B) from 2 children with Heiner syndrome with pulmonary hemosiderosis*