Review Article

Pediatric cough as a symptom: Tips for management

Sandeep B Bavdekar¹, Agam Vora², Sonali Karekar³

From ¹Consultant Pediatrician and Chief Academics, Surya Hospitals, ²Medical Director, Vora Clinic, ³Medical Advisor, Medical Affairs, Pfizer Ltd., Mumbai, Maharashtra, India

ABSTRACT

Cough in children and adults is a commonly witnessed symptom that can be related to a serious underlying disease. It is a reflex phenomenon that protects the airways and lungs by eliminating mucus, inhaled irritants, pathogens, and particulates and further helps in clearing out the air spaces of accumulated secretions. However, cough in children and adults has some notable differences based on various parameters, including duration, symptoms witnessed, duration, and etiology. Therefore, the tools and processes commonly employed for evaluating cough in adults may not apply to pediatric patients. Furthermore, the management of cough, in general, should be based on the etiology instead of the underlying disease condition. There is a relative paucity of data related to pediatric cough in comparison to adult cough, making the management of cough challenging. This article provides a comprehensive review of cough management in children in Indian scenarios.

Key words: Anti-tussive agents, Children, Cough, Management

ough is a common symptom in children and adults. It is a defense mechanism that helps in the elimination of mucus, infectious particles, and other harmful matter including foreign bodies from various parts of the respiratory tract. At times, it can be related to an underlying serious disorder or may have grave repercussions such as hemorrhage or syncope. Based on the cough duration it is further classified as acute, subacute, or chronic cough. Even though the most of the cough is self-limiting and benign, lasting only for a short duration; it is a symptom that interferes with the children's daily activities and can cause anxiety to the parents [1,2].

Cough in children (pediatric age group) and adults differs based on the symptoms witnessed, duration, and etiology. Age influences cough-specific physiology, respiratory physiology, other physiological processes, and other systems (e.g., the immune system). Children (especially infants and young children) differ from adults in terms of maturational changes in the airway, respiratory muscle and chest wall structure, respiratory reflexes, respiratory control, and sleep-related characteristics. In adults, cough sensitivity is higher in women. In children, it is influenced by airway caliber and age [3]. The smaller airway caliber may affect the site of deposition of the inhaled particles [4]. Given these differences, the criteria used to assess cough in children differ from those used in adults and similarly, the tools and processes

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employed for evaluating adults may not apply to children [5,6]. Furthermore, the cough is indicative of an underlying disease, and treatment needs to be directed based on the underlying etiology. There is insufficient and scattered literature available on the management of pediatric cough as a symptom. Therefore, this article aims to provide a comprehensive review regarding the management of cough in children.

PATHOPHYSIOLOGY

Cough can be initiated voluntarily or it can occur spontaneously as a reflex event. Cough occurs as a result of a series of respiratory maneuvers involving a visceral sensation, a reflex motor reaction, and corresponding behavioral responses [7,8]. On stimulation by appropriate stimuli (such as excessive mucus or foreign substances, particulate/dust, chemical irritants), the mechanical and chemical receptors that are mainly present in the larynx, trachea, the carina, and the pharynx [7,9-11] initiate the cough reflex by sending afferent sensory inputs through the vagus nerve to the "cough center" in the medulla [9,10,12]. The putative cough center is distinct from the respiratory center and is under voluntary and involuntary control. After processing these inputs, the cough center initiates an efferent signal that travels through the vagus, phrenic, and spinal motor nerves to initiate a series of actions that produce cough [9,10]. There are three phases of cough which include, the inspiratory phase, the compressive phase, and the expiratory phase. During the inspiratory phase, the

Correspondence to: Dr. Agam Vora, Medical Director, Vora Clinic, Mumbai, India. E-mail: dragamvora@gmail.com

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air is inhaled in volumes that are nearer to the total lung capacity. With the closure of the glottis, this phase ends. In the compressive phase, the intercostal and abdominal muscles contract against a fixed diaphragm and a closed glottis to build up the pressure. This is followed by an expiratory phase in which there is the rapid and forceful expulsion of air due to the opening of the glottis.

In terms of respiratory physiology, children and adults differ considerably. The primary differences between children and adults in terms of general respiratory physiology factors influence cough frequency, collateral ventilation, the caliber of large and small airways, and the percentage of time spent in REM sleep [13,14]. In addition, in children, the paucity of collateral ventilation often results in a higher likelihood of developing atelectasis, which is considered to be the reason for children having right middle lobe syndrome which often manifests as chronic cough. Furthermore, in children, the effect of having small amounts of mucus in the small airways is likely to be different from that of adults having mucus in their large airways [13]. This explains the clinical usefulness of cough characteristics in children and not in adults in terms of explaining cough etiology [13,15]. In addition, during childhood, the brainstem reflex that controls cough undergoes a maturation process, which is primarily the reason for having different reference values for normal respiratory rate in children and adults. Furthermore, there are maturational differences in the airway, respiratory muscle and chest wall structure, sleep characteristics, respiratory reflexes, and respiratory control [2,3]. Furthermore, the predominant causes of cough would differ in children and adults [16]. Differences in immunological development also influence the degree and frequency of various respiratory infections including cough. Thereby, children younger than 3 years of age tend to have 4.3–5 episodes of acute respiratory infections per year in comparison to 1.9-2.2 episodes per year in adults [13,17]. Finally, the neurological system of children is more sensitive as compared to that of adults. The pathophysiology of cough, thus, differs for adult and pediatric patients [2].

CLASSIFICATION OF COUGH

Based on the duration, the cough has been variously classified as acute, sub-acute, and chronic cough (Table 1) [18]. Acute and sub-acute cough are common symptoms for which medical advice is sought from primary care clinicians. It is usually caused by viral upper respiratory tract infections (URTI). In most children, a cough due to URTI normally resolves spontaneously. The statistics show that there is an average of 8-10 episodes of URTI yearly in preschool children, in the cough may last for up to 2 weeks [19]. Children with chronic coughs, on the other hand, are often referred to specialists. In general, patients often visit general practitioners on multiple occasions before referral to specialists for further investigation and treatment is undertaken [18]. In children, recurrent cough is referred to as the cough that lasts for more than 10 days duration with a prevalence of four or more episodes in a year and is unlikely to occur in the absence of any given disease or abnormal physiological functioning [20].

Table 1: Definition of cough based as per various guidelines

Guidelines	Acute cough in children	Chronic cough in children
The CHEST guidelines [3]	-	In children <15 years old, the duration of cough lasting >4 weeks
The CICADA guidelines of Australia [8]	A protracted acute cough is a cough lasting between 2 and 4 weeks	In children <15 years old, the duration of cough lasting >4 weeks
The BTS guidelines [16]	Cough lasting <3 weeks	Cough lasting >8 weeks
The ERS guidelines [21]	-	Cough lasting >4 weeks

CHEST: The American College of Chest Physicians, CICADA: Cough in Children and Adults: Diagnosis and Assessment, BTS: The British Thoracic Society, ERS: The European Respiratory Society

Most guidelines define chronic cough as one lasting over 4 weeks, while acute cough is defined as one lasting for up to 2, 3, or 4 weeks [8,16,19,21,22].

Different guidelines provide different definitions for cough in children (Table 1) [8,16,19,21,22].

A cough can further be classified into a productive or nonproductive (or dry) cough. A productive cough is generally indicative of an increase in the amount of respiratory secretions and/or impaired clearance mechanisms. It is worth noting that such differentiation is difficult in younger children as those below the age of 5 years do not expectorate out the sputum and tend to swallow it. Such cough in children may lead to vomiting. The sputum color can also be observed in the vomitus. The presence of dry non-productive cough in children is usually indicative of viral infections, allergic disorders susceptible child, tuberculosis, or inhaled irritants. The appearance of isolated dry cough in children who otherwise appear healthy and have a normal chest radiograph could have one of the other conditions (including cough variant asthma, post-viral cough, frequently recurring viral bronchitis, allergic rhinitis, postnasal drip and sinusitis, and psychogenic cough). Persistent productive cough (moist or wet) may be noted in children with bronchiectasis or persistent pneumonia. Chest radiograph must be initiated in such patients to determine the presence of bronchiectasis or other specific suppurative lung conditions [16].

ETIOLOGY

In recent years, our knowledge of the neurophysiology of cough and clinical etiologies that are novel has been updated. The common causes of cough in various age groups are depicted in Table 2.

MANAGEMENT

In children, the management of cough should focus on identifying the etiology of the cough to arrive at an accurate diagnosis. The decisions regarding whether to investigate or not and the choice of investigating modalities are based on several factors including duration and severity of cough, accompanying complaints, history

Table 2: Salient causes of cough in children and adolescents [23-25]

Infants	Toddlers	Children	Adolescents
Acute	Infections Foreign matter Aspiration*	Infections Foreign matter	Infections
Recurrent	Asthma Gastroesophageal reflux Aspiration Secondhand smoke Cystic fibrosis* Congenital anatomical abnormalities*	Asthma Gastroesophageal reflux Secondhand smoking Cystic fibrosis*	Asthma Gastroesophageal reflux Aspiration Congenital anatomical abnormalities* Cystic fibrosis*
Chronic	Asthma Gastroesophageal reflux Aspiration Pertussis Passive smoke Congenital anatomical abnormalities* Cystic fibrosis*	Asthma Gastroesophageal reflux Pertussis Mycoplasma Passive smoke Congenital anatomical abnormalities* Cystic fibrosis* Psychogenic* Obstructive sleep apnea	Asthma Gastroesophageal reflux Smoking Congenital anatomical abnormalities* Pertussis Aspiration Tumour Cystic fibrosis* Tuberculosis* Psychogenic*
	Post-infection Immune deficiencies* Primary ciliary dyskinesia* Tourette syndrome*		

^{*}Rare causes

of allergies, family history, growth of the child, and abnormal findings on clinical examination, among others.

In addition, the importance of making a correct diagnosis cannot be overemphasized. A correct and carefully considered clinical diagnosis may suffice for an otherwise healthy child with acute cough (for example, a child with a short-duration cough with a cold). Children with chronic cough may need to undergo tests to confirm the diagnosis. Even children with short-duration cough may have to undergo appropriate diagnostic work-up if conditions such as gastroesophageal reflux or foreign body inhalation are suspected, or clinical features suggest the presence of a definitive disease [3,26]. Similarly, children with recurrent coughs require careful assessment. Strategies such as employing only symptomatic therapy and initiating empirical therapy without laboratory confirmation or proper evaluation are likely to fail, delay the institution of appropriate disease-directed therapy, and may, at times, be associated with serious consequences.

The treatment of cough in children should primarily be based on the underlying etiology instead of aiming to just suppress the cough. At the same time, symptomatic treatment does have a place in the management of cough.

Acute Cough in Children

Symptomatic treatment of acute cough requires antipyretics, good hydration, and aspiration of secretions. Honey has been recognized as a beneficial solution in improving cough and sleep difficulty in pediatric cough associated with URTI [5].

In a survey of 1998, children conducted across six cities in India from October to December 2017, it was found that 78% of children were prescribed first-generation antihistamines. The

second-generation antihistamines were prescribed to 76% of children and antibiotics were prescribed to 50% of the participating children. Mucolytics and expectorants were prescribed to 62% and 63% of children, respectively. Dextromethorphan was prescribed to 61% of children and codeine to 13% of children. Nutritional supplements were prescribed to only 12% of the population. Only 3% of children were prescribed corticosteroids in the form of nasal spray [27].

The drugs that are used in the symptomatic treatment of cough can be classified as demulcents, cough suppressants, and cough expectorants:

- a) Demulcents form a coating and soothe the inflamed pharyngeal mucosa, thereby reducing the frequency and strength of the afferent impulses transmitted to the cough center. Examples include honey and agents such as glycerin or liquorice available in the form of lozenges, oral drops, or oral liquids
- b) Cough suppressants as the name suggest repress the cough reflex and are also referred to as antitussive agents. They are classified based on their chemical structure and locus of action. The centrally acting cough suppressants include opioids (e.g., codeine, ethylmorphine, and pholcodeine) and non-opioid (e.g., noscapine and dextromethorphan) drugs. Peripherally acting drugs (e.g., prenoxiazine) are also available. Cough suppressants are indicated only for dry and irritating cough or when the cough is unduly tiring or disturbs sleep
- c) Cough expectorants (mucokinetic agents) either increase the bronchial secretions (e.g., sodium citrate, potassium citrate, guaiphenesin, and ammonium chloride) or decrease the viscosity of the secretions (e.g., bromhexine, ambroxol, acetylcysteine, and carbocysteine). Through these actions, these agents allow the patient to expectorate out the sputum more easily.

The American Academy of Family Physicians guidelines titled "Managing Chronic Cough as a Symptom in Children and Management Algorithms," published in 2020 have made some recommendations for managing non-specific cough [22]. The following table includes some of the recommended agents along with the commonly prescribed therapeutic agents for the symptomatic management of cough in children (Table 3).

Anti-histaminic agents do not have any cough suppressant or expectorant action. Those with anticholinergic actions may result in the drying of secretions. This may make the expulsion of sputum more difficult. They may have a role in the treatment of allergic cough [26,30].

Several fixed drug combinations (FDCs) marketed for the treatment of cough are available. Many of them are available as over-the-counter (OTC) or non-prescription drugs. Many times, these represent irrational combinations or may lead to unnecessary exposure to a non-indicated drug. For example, combining an antitussive agent with a cough expectorant is without any rationale. Prescribing a drug containing paracetamol, phenylephrine, cetirizine, and dextromethorphan to a child with just cough and fever would lead to unnecessary exposure to phenylephrine and cetirizine. More than 90% of the cough and cold preparations are FDCs with most of them containing at least 3–4 constituents. It has also been noted that most of these preparations contain more than one constituent of the same pharmacological group or with opposing action [34]. FDCs that contain ingredients with overlapping side effects (e.g., an anti-histaminic drug with an antitussive agent with sedation as a possible side effect) can potentiate harm. Many times, drugs in an FDC have a differing duration of action resulting in underdosing or overdosing of at least one of the constituents. Even a combination of drugs with similar actions (say, two cough expectorant agents) should be used only if there is definitive evidence of clinical benefit over (and safety) a single drug. Many times, parents initiate therapy with an OTC drug and then consult a physician. The physician should be careful in ensuring that there is no overlap of drugs used. A child whose cough does not show amelioration even after 2 weeks of treatment should be re-evaluated.

Chronic Cough in Children

The choice of treatment for chronic cough is dependent on the diagnosis. Chronic cough with no underlying cause is extremely rare in children. Based on the cause and severity of the cough, symptomatic treatment of the cough may or may not be required. For example, childhood asthma can be alleviated using inhaled corticosteroids and bronchodilators and no specific cough expectorants are required. Depending on the response and severity of manifestations, additional therapeutic measures [adjusting of doses, use of Leukotriene inhibitors, cromolyn, and long-acting beta-2 agonists] can be undertaken. Pertussis is treated with macrolide antibiotics. This may diminish the period of infectivity but the clinical course may not be significantly affected. Multiple systems are affected by cystic fibrosis and treatment with pancreatic

Table 3: Selected therapeutic agents used in the symptomatic management of cough in children

Demulcents

Honey [28-30]	Soothes the throat Has antioxidant properties		
	Uncertain clinical benefit but used for a dry		
	cough related to upper airway		
	Avoided in infants for the risk of botulism		
Cough-suppressive	e agents [26,31]		
Pholcodine [28]	Suppresses cough through its action on the		
	cough reflex Mild sedative effect. No analgesic action		
	In therapeutic doses does not cause depression of respiration, euphoria or CNS excitation. Psychological dependence unlikely Used in the treatment of dry (nonproductive) cough		
	Contra-indications: Known hypersensitivity to pholoodine, hepatic dysfunction, patients with risk of developing respiratory failure, age below 6 years, during an attack of asthma Adverse effects: Dizziness, nausea, and vomiting		
Dextromethorphan	Suppresses cough through its central action on		
[32,33]	the cough center in the medulla Structurally related to morphine. But does not have significant analgesic or sedative properties Used in the treatment of dry (non-productive) cough Avoid in children aged<12 years		
	Trigger's histamine release: Avoided in children with atopy or presence of severe allergic reaction Adverse effects: Nausea, vomiting, dizziness, restlessness, and lightheadedness		
Noscapine	Suppresses cough through its central action No sedative actions. No CNS or respiratory		
	depression. Addiction not reported Used in the treatment of dry (nonproductive) cough Adverse Effects: Nausea, vomiting, headache, dizziness, and tachycardia		
Cough-expectoran	ts [28,32]		
Guaiphenesin [33]	An expectorant that enhances the flow of respiratory tract secretions		
Bromhexine	Adverse effects: Headache, nausea, and vomiting Induces increased secretion of mucus and		
Biolinicanic	disturbs the chemical structure of the mucus resulting in the formation of less viscous mucus that is easier to cough out Used in the treatment of productive cough with viscid sputum		
	Adverse effects: Gastric irritation, headache, vomiting, dizziness, and sweating		
Ambroxol [29]	It probably induces increased secretion of mucus and also makes it less viscid Used in the treatment of productive cough in children over the age of 6 years. However, the beneficial effect on the frequency of exacerbations or lung functions has not been demonstrated consistently Adverse effects: Nausea, changed taste, years in a dry mouth, and distribute.		
vomiting, dry mouth, and diarrhea CNS: Central Nervous System			
CAS. Central Net vous System			

enzyme replacement therapy is the required management strategy. Some children will benefit from treatment with mucolytic agents and airway clearance therapy. Gastroesophageal reflux disease-induced cough should be managed using proton-pump inhibitors and/or surgery. Protracted bacterial bronchitis is usually treated with a 2-week regimen of amoxicillin-clavulanate. Identifying the causative infective agent determines the choice of antibiotic and treatment duration. Cough due to allergic rhinitis is treated with antihistamines and intranasal steroids. Sinusitis is managed using antibiotics, steam inhalation, and saline nasal drops [35,36].

TREATMENT OF COUGH BASED ON COMMON CLINICAL SCENARIOS

Cases of Isolated Chronic Dry Cough

For children with isolated chronic dry cough where the first line of investigation is inconclusive, a "watchful waiting" approach should be adopted. In the majority of the patients, within the next 3-4 weeks, they spontaneously become cough-free [26]. Such an approach is also applicable for cases of tic cough, a bizarre and honking cough that subsequently leads to an uneventful URTI. Such coughs disrupt daily life and further interfere with the activities of children, but they are notably absent when the child is asleep or distracted. In children with atopic cough, the "watchful waiting" approach may be bypassed when they have experienced persistent cough in the past [3,16,22,26]. In such cases, the recommended treatment involves a 4-8-week treatment with an adequate dose of inhaled corticosteroid (ICS) which should be followed by cessation and reassessment. The majority of patients would spontaneously get cough-free within the next weeks. The diagnosis of asthma should also be seriously considered. In cases, where isolated chronic dry cough does not get resolved even after watching waiting or ICS administration further specific investigations and management are recommended [3,16,22,26].

Cases of Isolated Chronic Wet Cough

In children, a wet cough usually indicates the presence of secretions within the airways. However, the etiology of isolated chronic cough is infectious. Globally, 40% of children in developing countries with chronic wet cough are diagnosed with protracted bacterial bronchitis (PBB) which covers three different endotypes: PBB clinical, PBB-extended, and PBBrecurrent Clinically, PBB is based on three diagnostic criteria which include (a) wet cough >4 weeks, (b) presence of no other signs and symptoms of other causes, and (c) resolution of cough symptom after 2 weeks of antibiotic treatment [26]. Even though there are different regimens proposed for isolated chronic wet cough, treatment with amoxicillin-clavulanate is the most recommended one. The duration of treatment often varies, the treatment may begin with a 2-week course; however, if the cough does not resolve, it may be extended to a period of 4 weeks. In cases, where 4 weeks of antibiotics are required to clear the wet cough, then a diagnosis of PBB-extended may be considered and in some cases, recurrent (>3 per year) episodes of PBB may be witnessed [3,16,22,26].

Cases of Chronic Cough with Additional Causes

In these cases, children usually present with chronic cough, suspicious medical history, abnormal clinical examination, abnormal Chest X-ray, and/or spirometry reports. Globally, primary care physicians are the ones who frequently encounter and evaluate children with chronic coughs. A persistent cough is troublesome and should always be carefully assessed [26].

Complications of Cough

In children, up to 12% of the cases experience some complications that are usually very mild and easily treatable. However, some children experience complications due to cough. The most common complication of cough witnessed in children includes otitis media, rash, diarrhea, and vomiting, and about 5% of pediatric cases progress to bronchitis or pneumonia [37].

CONCLUSION

The quality of life in both children and adults is often affected by cough. More commonly, the cough is short-lasting and is caused by self-limiting conditions such as viral infections. For most of these conditions that are easily diagnosed on clinical examination, providing symptomatic therapy may suffice. It is crucial to diagnose the underlying cause to prevent disease complications. Early diagnosis can be reached by monitoring of clinical course and undertaking appropriate diagnostic work-up expeditiously. Management of the underlying disorder using child-specific guidelines is of utmost importance.

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