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Pediatric Cough: Children Are Not Miniature Adults

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Abstract Pediatric cough-related issues, like most other conditions in particularly young children, share similarities but also have substantial important differences with adults. These can be understood from physiologically based domains simplified to (1) cough-specific, (2) general respiratory, (3) other direct systems such as the immune system, and (4) other general physiology. Among other reasons, these result in observed differences in etiology, management, and measurement of response between children and adults. For example, while empirical therapy for chronic cough is widely advocated for adults, it is not advocated for children. Indeed, there is some evidence that an empirical approach is potentially harmful; this is related to the use of medications and the delay in obtaining a correct diagnosis such as missed foreign body aspiration.

Keywords Cough · Children

Introduction

Pediatricians worldwide passionately advocate that childhood illnesses should be managed differently than adult illnesses. Extrapolation of adult-based data to children can result in unfavorable consequences [1, 2]. The pattern of respiratory illness in children is clearly different than that in adults; for example, viruses associated with the common cold in adults can cause serious respiratory illnesses such as bronchiolitis and croup in previously well young children [3]. The natural history of asthma in children is dominated by decreasing severity with age and in some, complete resolution [4], whereas asthma acquired in adulthood usually persists [5]. Thus, here we focus on childhood cough emphasizing the differences with that in adults. For a systematic evaluation of children with chronic cough, readers are referred to other publications [6–8] for a wider discussion.

Epidemiology: Prevalence and Burden of Illness

Cough is the most common reason for new medical consultations [9]. While there are no data on acute consultations specific for children, it is likely that the rate for children is higher than that for adults. The consumption of over-the-counter cough and cold medications is high worldwide; approximately one in ten children in the United States use a cough-and-cold medication in a given week [10]. Little accurate data on the prevalence of chronic cough in children are available as questionnaires for chronic cough assessment have limited validity [11]. Published data found that community prevalence of chronic cough in primary school-aged children (6–12 years) is 5–10% [12]. The prevalence is likely higher in preschool-aged children because retrospective [13] and prospective [14] studies have shown that the majority of children with chronic cough seen in clinics were young (median age = 2–3 years).

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Acute and chronic cough is associated with significant morbidity in both children and their parents [12, 15]. Parents report a high number of medical visits for cough before they visit a pulmonologist for their child's chronic cough. In one study, greater than 80% of children made 5 or more doctor visits and 53% made more than 10 visits before the child's first visit to a pediatric pulmonologist [15]. There are only three studies of children that have examined parental evaluations or concerns of their children's coughing illness. The Cornford et al. study [16] was in primary health, while the other two were hospital-based studies [15, 17]. In the two older studies [16, 17], the parents' main concerns were about disturbed sleep, discomfort, and that cough would cause permanent chest damage. A recent Australian study involving 190 families described that the most significant concerns and worries expressed by parents were feelings of frustration, being upset, sleepless nights, awakened at night, helplessness, stress, and sympathy for the child. Specific issues that bothered the parent(s) most were the cause of cough, cough related to a serious illness, their child not sleeping well, and cough causing damage [15]. Concerns and worries of parents outlined above were significantly reduced when the child's cough resolved [15].

Unlike adults with chronic cough, children with chronic cough do not have symptoms of anxiety [15]. Also, parents of children with chronic cough do not have symptoms of anxiety or depression but feel stress, which significantly subsides when the child becomes cough-free [15]. This contrasts with the data for adults with chronic cough who have associated anxiety and/or depression symptoms [18–21].

Why Children Are Different from Adults

Physiology-Based Reasons

Physiology drives the clinical manifestation of symptoms and signs on which clinical assessment is based. There is direct and indirect evidence that age has an impact on physiological domains that influence the clinical manifestation of conditions where cough is a dominant feature. These physiological domains relevant to cough can be simplified to (1) cough-specific physiology, (2) general respiratory physiology, (3) other direct systems such as the immune system that influence the respiratory system, and (4) other general physiology. These domains result in observed differences between children and adults in disease expression and hence common etiological factors, management, and measurement of response. Figure 1 provides a schematic framework outlining the concept using artificially divided physiology for simplification. It is beyond the scope of this article to provide a comprehensive review of all the factors mentioned above. Examples are highlighted below. For these reasons and others, common diagnostic categories that are present in children with cough differ from those of adults. For example, common acute illness with cough as the dominant feature, such as bronchiolitis and croup, does not occur in adults. Common causes of cough and respiratory diseases in adults, such as chronic bronchitis [22] and chronic obstructive pulmonary disease, are not recognized diagnostic entities in pediatric respiratory literature and the main textbooks [23]. Nonasthmatic eosinophilic bronchitis, which is relatively common in adult cohorts [24], is rare in pediatric studies that have examined airway cellularity [14, 25]. Protracted bacterial bronchitis, a recognized entity of chronic cough in children [7, 26, 27], is not described in adults.

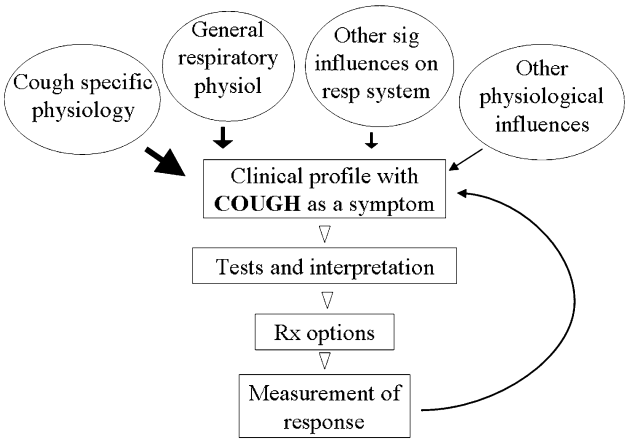

Fig. 1 Schematic framework of the influence of age on cough as a symptom in clinical medicine. The scheme outlines the artificially divided physiological (physiol) concepts for simplification, which translates to diagnostic categories, influences tests and their interpretation, treatment options, and measurement of responses that feeds back to the clinical profile and evaluation. Sig = significant

Cough-Specific Physiology Domain

Examples of cough-specific physiological differences include age- and gender-related variation in cough sensitivity. Gender does not influence cough sensitivity in young children [28], but in post-puberty children and adults, females have a higher cough sensitivity [29, 30]. In children, cough sensitivity is instead influenced by airway caliber (FEV_1) and age [28]. Also, the cough reflex is weak in premature infants and develops with maturity [31].

The laryngeal system is an integral component of the cough reflex [32]. A clear difference between children and adults (except the elderly) is reflected in the fact that young children, particularly those under 5 years of age, have an increased risk of inhaling foreign material, particularly

food like peanuts. This is (at least partially if not almost completely) related to immature laryngeal competency in protecting the airways against aspiration.

Plasticity of the central and peripheral components of the cough reflex has been shown [33]. While there is no direct evidence of greater plasticity in children's cough pathway compared with that of adults, one can speculate that the cough reflex has maturational differences also. Indirect evidence is that a child's neurological system has more plasticity than an adult's [34].

Respiratory Physiology-Specific Domain

General respiratory physiology factors of children and adults include differences in collateral ventilation, caliber of large and small airways, and percentage of time spent in REM sleep, all of which influence cough frequency [35]. The lack of collateral ventilation results in a higher likelihood of development of atelectasis. It is thought to be the reason why children may have right middle lobe syndrome that often manifests as chronic cough [36]. The effect of a small amount of mucus in the small airways of a child is likely to be different from that in the large airways of an adult. This likely explains why the characteristics of the cough have been shown to be useful in explaining its etiology in children [37] but are not clinically useful for adults [38]. Furthermore, distinct differences in respiratory physiology between young children and adults include maturational differences in airway, respiratory muscle, and chest wall structure, respiratory reflexes, and respiratory control, all of which impact on respiratory disease and hence the symptom of cough.

Other Systems that Directly Influence the Respiratory System

The immune system, which has its own developmental physiology [39], influences the degree and frequency of respiratory infections, and hence cough. Young children (younger than 3 years) have 4.3–5 episodes of acute respiratory infections (ARIs) per year, in contrast to the adult (aged >21 years) mean of 1.9–2.2 per year [40].

Other Physiology

Developmental cognitive aspects clearly differentiate children from adults. Also, children are more sensitive to the effects of toxicants and the environment compared with adults [41, 42]. For example the attributable cancer risk from radiation related to computed tomography is far higher in children than in adults [42].

Investigations and Assessing Response to Therapy

Several methods are available to objectively assess cough frequency, cough severity, and its response to therapy. Child-specific assessment tools are required for children because the adult assessment tools have limited applicability in children [43]. For example, in the assessment of cough sensitivity, inspiratory flow significantly influences results [44] and inclusion of questions about urinary incontinence and other adult-specific issues render adult cough-specific QOL questionnaires not applicable to children [45]. It can not be assumed that adult-based cough counters are reliable in children without validation studies because young children generate lower-amplitude EMGs and cough audio signals. The choice of the quantitative and objective cough indices performed is dependent on the setting and the reason for performing the measurement [46]. In clinical trials the response to therapy ideally includes objective measures (e.g., cough counters) in addition to patient-oriented outcomes (e.g., quality of life and subjective scores) [47]. Pediatric studies have documented that objectively measured cough frequency was related to both subjective cough scores and cough sensitivity and that the change in cough frequency also was related to the changes between cough scores and cough sensitivity [46, 48]. These data have recently been described in adults as well [49].

Evaluation of the Child with a Cough

The etiology and management of childhood cough should be clearly distinguished from those of adult cough [6, 7]. In contrast with adults, there is little role for empirical therapy, i.e., management of children with acute or chronic cough should be etiologically based [6, 7, 43]. Thus, defining the etiology of the cough is an important component of its evaluation.

Evaluation of a Child with an Acute Cough

Although viral ARIs are the most common cause of acute cough in children, all children need to be assessed adequately for other respiratory etiology such as inhalation of a foreign object, and for other infections such as pneumonia, bronchiolitis, and laryngotracheobronchitis. Acute cough may also be the presenting symptom of an underlying disorder; the presence of specific pointers (Table 1) should alert practitioners to the presence of an underlying problem.

Table 1 Pointers for the presence of specific cough

Auscultatory findings (wheeze, crepitations/crackles, differential breath sounds)
Cough characteristics (e.g., cough with choking, cough quality, cough starting from birth)
Cardiac abnormalities (including murmurs)
Chest pain
Chest wall deformity
Daily moist or productive cough
Digital clubbing
Dyspnea (exertional or at rest)
Exposure to pertussis, tuberculosis, etc.
Failure to thrive
Feeding difficulties and/or dysphagia (including choking/vomiting)
Hemoptysis
Immune deficiency
Medications or drugs (ACE inhibitor)
Neurodevelopmental abnormality
Recurrent pneumonia

Acute Respiratory Infections

Most coughs in early childhood are caused by viral ARIs [50, 51]. Fifty-six percent of the children with ARI were still ill 4 days after the initial consultation. The percentage fell to 26% on the 7th day and to 6% by the 14th day [52]. Cough, however, was not specifically reported in the study [52]. A systematic review of the natural history of acute cough in children aged 0–4 years and in primary care reported that the majority of children improve with time but that 5–10% develop bronchitis and/or pneumonia [50]. However, both studies were done a while ago (35–50 years ago) when the public health standards of sewerage, housing, etc. were very different than the current state in developed countries.

Children with acute ARIs can have pneumonia which can precipitate the first manifestation of an underlying congenital/developmental respiratory or immunological disorder [53]. The World Health Organization's (WHO) criteria for differentiating upper ARIs from pneumonia (and thus to use an antibiotic to prevent death) has been relatively widely studied [54, 55] in developing countries where the chest wall indrawing and respiratory rate are good predictors of the presence of pneumonia [55]. However, there is less information about its sensitivity and specificity in older children living in mainstream society in affluent countries where other risk factors [56] are absent and expectations for earlier treatment and accessibility to medications and medical service significantly differ. Pediatric-specific evidence-based guidelines for the management of community-acquired pneumonia have been published [57–59] to which readers are referred.

Inhalation of a Foreign Body

Cough is the most common symptom in some series of acute foreign material inhalation but not in others [60]. In one series, cough was present in 69.8% and other dominant symptoms were decreased breath sounds (52.8%) and wheezing (45.1%) [61]. Choking episode history was reported for 32% of patients, but when families were questioned about it further, the rate increased to 51%. Presentations are usually acute [62], but chronic cough can also be the presentation of previously missed foreign body inhalation [63].

Other Lung Pathology

Acute cough can be the presenting symptom of the entire spectrum of respiratory and nonrespiratory pathology, ranging from acute exposure to environmental pollutants [64] to acute lymphoblastic leukemia [65], which is beyond the scope of this article.

Treatment of Acute Cough

There are few efficacious options for the symptomatic treatment of acute cough. Honey has been shown to be beneficial in improving cough and sleep difficulty associated with childhood upper respiratory tract infection (RTI) [66]. Over-the-counter (OTCs) medications for cough confer no pharmacological benefit in the control of cough in children [67–69] but they have a placebo or nonpharmacological effect. Moreover, "OTC medications can be associated with significant morbidity and even mortality in both acute overdoses and when administered in correct

doses for chronic periods of time" [70]. The use of steam inhalation, vitamin C, zinc, and echinacea for upper RTI has been well summarized in the evidence-based medicine publication *Clinical Evidence* [71], where little benefit for symptomatic relief of cough for adults and children has been described. A single, small, randomized controlled trial (RCT) showed that treatment with nimesulide was associated with clinically significant improvement in cough and other signs and symptoms observed (rhinorrhea, nasal obstruction, pharyngeal redness, swelling of lymph nodes, and cough) [72]. In a RCT of children with acute cough but no history of asthma and with a normal chest examination, Bernard et al. [73] showed that oral albuterol was not effective in reducing cough frequency or duration. In a meta-analysis, Smucny et al. [74] likewise concluded that "there is no evidence to support using β_2 agonists in children with acute cough and no evidence of airflow obstruction." The American Academy of Family Physicians guidelines discourage use of antimicrobials except when rhinosinusitis and cough are present and not improving after 10 days [75]. Meta-analysis of antimicrobials for acute bronchitis (recent onset of productive cough without chronic obstructive pulmonary disease, sinusitis, or pneumonia) in children (older than 8 years) and adults showed a small benefit of 0.58 day but with significantly more adverse events [71].

Evaluation of a Child with Chronic Cough

The evaluation and management of a child with chronic cough have been published elsewhere [6, 8]; the topic is beyond the scope of this article. The key principles are as follows:

1. Defining cough types in accordance with different constructs is helpful. These constructs are not mutually exclusive and are based on (a) likelihood of an identifiable underlying primary etiology (specific and nonspecific cough) and (b) characteristics (moist versus dry, classical cough types such as brassy, staccato, etc.).
2. At a minimum all children with chronic cough should have spirometry (if age-appropriate) and a chest X-ray (CXR) [6]. The validity of this has been shown [37]. When a CXR taken for chronic cough is abnormal, the odds ratio of a specific etiology was 3.16 (95% CI = 1.32–7.62) [37].
3. Treatment for chronic cough should be etiologically based; that for specific cough (including almost all respiratory diseases) is beyond the scope of this article. Clinicians should be aware that cough is subjected to the period effect, i.e., spontaneous resolution. The benefit of placebo treatment for cough has been reported to be as high as 85% and therefore nonplacebo controlled intervention studies have to be interpreted with caution [11]. Evidence of lack of efficacy of treatment trials for nonspecific cough have been summarized [8].
4. If medications are tried for nonspecific cough, the child should be reviewed and "time to response" considered [6]. For example, for asthma-related cough, earlier non-RCT studies in adults and children that used medications for asthma for the time period (i.e., nonsteroids, theophylline, terbutaline, major tranquillizers) reported that cough completely resolved by 2-7 days [11]. Time to response is defined as the expected length of time for cough resolution in studies in which the cough treated was related to the etiology defined.
5. When reviewing any child with a cough irrespective of the etiology, exacerbating factors should be explored and addressed. There is little doubt that children with environmental tobacco smoke (ETS) exposure have an increased risk of having chronic [76, 77] and recurrent cough [78]. However, cough resolution was achieved in children exposed to ETS in several studies [14, 79], which suggests that ETS is not the sole etiology. The American Academy of Pediatrics policy on tobacco includes recommendations for tobacco cessation [80]. Other exacerbating factors include exposure to pollutants and secondary gains from having a cough.
6. Exploring and addressing parental expectations and fears is valuable when managing a child with a chronic cough. As discussed in the section Epidemiology: Prevalence and the Burden of Illness, parents presenting to doctors for their children's cough have significant concerns that cause parental stress [15]. Providing parents with information on the expected length of time for resolution of ARIs may reduce the anxiety and the need for medication for the child [52]. Parental and professional expectations as well as a doctor's perception of a patient's expectations influence consulting rates and the prescription of medications for ARIs [81, 82]. It is also known that information available from the internet provides incorrect advice on the home management of cough in children [83].

Summary

Like most other conditions in children, particularly young children, issues relating to pediatric cough have similarities but also have substantial important differences with adult cough. These can be understood from physiologically

based domains where direct and indirect evidence indicates that age influences physiological domains which influence the clinical manifestation of conditions where cough is a dominant feature.

The management of cough in children requires that all children with cough should be carefully evaluated and managed differently than adults because the etiological factors and treatment of children are significantly different than those of adults. While most children with acute cough (<2 weeks) have ARI, an assessment for inhalation of a foreign body, pneumonia, and other lower ARIs as well as other less common causes of cough is recommended. Children with chronic (>4 weeks) cough should be assessed for the presence of specific cough pointers and should at least have a chest radiograph and spirometry (if age-appropriate). In children with nonspecific cough (dry cough in the absence of cough pointers), cough usually spontaneously resolves but children should be reviewed for emergence of specific cough pointers. In all children with cough, exacerbating factors such as environmental tobacco smoke (ETS) exposure should be looked for and cessation by the smoker advised or initiated. Parental expectations and specific concerns of the parents should also be sought and addressed. The differences between adults and children are also exemplified in child-specific diagnosis such as protracted bacterial bronchitis and evidence-based cough guidelines.

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