

REVIEW

Chronic cough in childhood

Bruce K. Rubin

Correspondence to:

bruce.rubin@vcuhealth.org/ORCID: N/A

Doi

10.56164/PediatrRespirJ.2022.01

Department of Pediatrics, School of Medicine, Virginia Commonwealth University, Richmond, VA, USA

ABSTRACT

Chronic cough persisting for more than 4 weeks in children (8 weeks in adults), is one of the most common complaints leading to physician assessment. It is also a symptom responsible for the sale of billions of Euros each year, for mostly unnecessary over the counter medications.

While the cough reflex is similar in adults and children, the most common causes of chronic cough are currently thought to be different. This manuscript reviews these differences and how this, in turn, leads to different therapies for children with chronic cough.

IMPACT STATEMENT

Chronic cough in children has a different definition, different etiologies, and thus a very different diagnostic and therapeutic approach as compared with chronic cough in adults, as summarized in this review.

INTRODUCTION

Chronic cough is one of the most common reasons for adults and children to seek medical care. In adults, chronic cough is defined as a cough lasting more than 8 weeks in a nonsmoking, immunocompetent patient who has a normal chest radiograph, and has not been exposed to an environmental irritant (1) while in children, chronic cough is cough that lasts more than 4 weeks (2). This makes comparison of causes and therapy more challenging (3).

Physiologically, cough is an effective defense mechanism for airway clearance especially when there is an excess of thick but non-adhesive secretions in the airway (cough tenacity). This often arises when there is impaired mucociliary clearance (4). Secretions that are “thick” (viscous) are more effectively cleared by cough than secretions that are thin and watery which is one of the reasons that mucolytic agents are not effective in mobilizing sputum by coughing. As well, an effective cough requires sufficiently great expiratory airflow, referred to as cough peak flow, to detach and transport secretions (5). Children who are weak, with an ineffective cough may obtain benefit from using augmented cough ma-

KEY WORDS

Cough; asthma; protracted bacterial bronchitis; upper airway cough syndrome; gastroesophageal reflux disease; tobacco smoke.

neuviers or devices such as insufflators/exsufflators (e.g., CoughAssist, Philips Respironics). “Dry cough” will not respond to mucoactive medications.

Cough is also a very effective way of propagating infection. Aerosols containing bacteria or virions can travel a great distance depending on their size, measured as mass median aerodynamic diameter, and airflow velocity. As we have learned during the Covid-19 pandemic, correctly wearing a well-fitted mask is effective in protecting the wearer and more so, effective in protecting others.

COMMON CAUSES OF CHRONIC COUGH IN ADULTS – THE “BIG THREE”

Upper airway cough syndrome (UACS), formerly called post-nasal drip syndrome

UACS is reported to be the single most common cause of cough in adults with a prevalence up to 87% (6). The diagnosis of UACS is usually made by cough associated with nasal stuffiness after excluding recent upper respiratory tract infection (URTI), nasal drugs, and environmental exposure. There are no pathognomonic findings or objective test for UACS and no way to directly prove that the nasal symptoms caused the cough. Reported symptoms and signs are nonspecific and may include a dripping sensation and tickle in the throat, nasal congestion, mucus in the oropharynx, cobblestone appearance of oropharynx. The diagnosis is “confirmed” by response to specific therapy, and the absence of another cause of cough (6). Of note, sinus CT imaging is not helpful in making the diagnosis of UACS in children or adults (7). Therapy for rhinitis includes limiting environmental exposure and, in children, exposure to tobacco smoke is very important. Seasonal nasal allergy is usually treated with antihistamines and nasal corticosteroids. If a clinical effect is not seen in one week, the initial diagnosis should be reconsidered.

Gastroesophageal reflux disease (GERD)

GERD is very common occurring in about 40% of adults (8) with prevalence increasing with increasing body mass index. Chronic cough is present in 1/3 of adults with GERD symptoms and 44% of adults evaluated for chronic cough had abnormal acid reflux (9) but it is unclear if the

cough is due to reflux or caused by the reflux. In adults, the therapeutic response to antacid drugs is the most cost-effective tool for diagnosis and treatment of GERD.

Although 80% of asthmatic adults are reported to have a positive 24-hour esophageal pH monitoring suggesting GERD, antacid therapy does not improve asthma symptoms or pulmonary function in children with severe asthma and is associated with adverse side effects (10).

Cough dominant asthma (CDA) formerly called cough variant asthma

The change in terminology from cough variant asthma, suggesting that cough is the sole manifestation of asthma, to *Cough dominant asthma* was made because adults and children with CDA have clinical history and an objective examination consistent with asthma and allergies and have other manifestations of asthma, although cough may be most troublesome.

Although bronchoprovocation testing has been used to support the diagnosis of CDA, challenge testing is sensitive only when it produces the symptoms of cough, as well BHR is not diagnostic of asthma (11). Asthma consists of intermittent and reversible bronchospasm, airway inflammation (generally T2 in children) and mucus hypersecretion, CDA has been suggested to be a manifestation of secretory hyperresponsiveness, or a predominant mucus secretory response to challenge (12). Unlike smooth muscle contraction, which is rapidly reversible, mucus hypersecretion causes airflow limitation that reverses more slowly and depends upon secretion clearance from the airway. Secretory hyperresponsiveness involves activation of the extracellular regulated kinase, ERK 1/2, signaling which is steroid insensitive (13). CDA responds poorly to beta agonists or inhaled corticosteroids (ICS) but may respond to anticholinergic therapy. As noted in the next section, UACS, GERD, and CDA (the “big three” as designated by Richard Irwin), while common causes of chronic cough in adults, are rarely the cause of chronic cough in children.

PRIMARY DIAGNOSES IN CHILDREN WITH CHRONIC COUGH

The reason for the 8-week cut off for determining that a cough in adults is chronic, is that virus induced cough

after URTI is not uncommon and when studied at 3 to 4 weeks, many subjects will have post infectious cough and sensitive airways (14). This is likely to also be true in children. Airway inflammation associated with chronic cough may be due to the trauma of coughing and is similar to that of diseases thought to cause cough.

In 2006, Marchant and colleagues first reported that protracted bacterial bronchitis (PBB) is the most common cause of chronic cough persisting longer than 3 weeks in young children (15). In children, PBB is diagnosed by the presence of persistent “wet cough” and BAL neutrophils. Although it has been speculated that PBB can be “pre bronchiectasis”, the airways of children with PBB rarely contain purulent secretions. Cultures of bronchial lavage fluid in children with PBB often grow non-typable *Haemophilus influenzae* or *Moraxella catarrhalis* (16). Pediatric PBB can be effectively treated with a 2-week course of antibiotics, usually amoxicillin-clavulanic acid (17). In adults, PBB is a rare cause of chronic cough characterized by inflamed airways full of purulent material and often associated with established bronchiectasis or immunodeficiency. Recommended therapy is 3-6 weeks of intravenous antibiotics (18).

Do the “big three” often cause chronic cough in children? In the study by Marchant mentioned above, UACS, GER, and CDA combined were determined to be the cause of fewer than 12% of the patients studied. UACS probably does cause chronic cough in children although lack of clear diagnostic criteria makes this difficult to prove. However environmental tobacco smoke exposure is strongly associated with chronic cough in children and the mechanism for this association may be nasal inflammation and secretion (19).

On the other hand, GER probably does not cause chronic cough in children and therapy for GERD does not influence the course of chronic cough in children. Of note, GER is different from chronic aspiration, which can cause lung disease including bronchiectasis, and productive cough. Aspiration may or may not be associated with GER, but reflux alone does not appear to commonly cause chronic cough in children (20).

Does asthma produce chronic cough in children? Isolated cough dominant asthma is exceptionally uncommon in children. Earlier studies evaluating “cough variant asthma” in children were small and poorly controlled. A caveat here is that because there is a pervasive be-

lief among general pediatricians that asthma is one of the most common causes of chronic cough in children, many children who seek care from their paediatrician are prescribed beta agonists, steroids, and often antibiotics. If by chance, by time, or by intention these children stop coughing they are not referred to the specialists who conduct cough studies. On this basis, a group from Australia has published that is no value in using salbutamol or ICS for treating chronic cough in children (21). Chronic purulent cough is always pathologic and suggests the presence of bronchiectasis, which can be caused by immune deficiency aspiration, cystic fibrosis, primary ciliary dyskinesia, tuberculosis, etc. Unlike other causes of chronic cough, bronchiectasis is often seen in association with growth failure and the diagnosis is confirmed by CT scanning, less common causes of chronic cough in children include a retained airway foreign body, cardiac cough especially in association with pulmonary edema, and any chronic irritant exposure in the airway. Finally, there are the conditions known as psychogenic cough, habit or tic cough, cough due to secondary gain, and parental overconcern. These conditions are distinct and should not be confused although there can be some overlap (22). Psychogenic cough is thought to be a conversion response, generally to acute or chronic, physical, or emotional trauma or abuse. Secondary gain, as the term suggests, secondary gain implies that the coughing child is “using” the cough to get attention or to avoid doing something unpleasant such as attending school for the child who is repeatedly bullied. The child may be unaware of the connection between the coughing and the precipitating factor(s). I recall seeing a schoolboy in my cough clinic some years ago with a persistent cough that met the definition of habit cough as described below but responded poorly to suggestion therapy with cough recurrence. At follow up, the parents volunteered that his adult sister had progressively severe cystic fibrosis (not mentioned by them in the initial family history) and with each of her hospitalizations the brother’s cough became much worse. Family counseling by an outstanding psychologist finally brought this cough under control. Habit cough, sometimes referred to as tic cough, appears to be much more common in children than in adults (23). Habit cough is characterized by a prolonged, daytime cough that is sometimes preceded by an URTI. The underlying etiology is not known but is speculat-

ed to be associated with heightened cough sensitivity that is worsen by the cough itself. Unlike psychogenic cough, it is rarely associated with trauma. Although this is sometimes called “tic” cough, it is not associated with classic tic disorders such as Tourette syndrome.

A systematic review identified 18 uncontrolled studies, enrolling 223 patients of which 96% were children and adolescents (habit cough systematic review). Most of these patients (95%) had no cough during sleep and a barking or honking quality of cough was described in 8 studies. Hypnosis (3 studies), suggestion therapy (4), and counseling and reassurance (7) were the most commonly used interventions. Hypnosis was effective in resolving cough in 78% of the patients and improving it in 5%. Suggestion therapy resolved cough in 96% of patients (24). Dr. Miles Weinberger who is the acknowledged expert on habit cough, cured a girl of her cough remotely and her father recorded the session. This has now been posted on the internet (<https://youtu.be/jnQUvD8Qdj0>) and many patients from around the world have reported that watching this video recording and following the suggestion therapy along with Dr Weinberger has cured their cough.

Tracheal malacia may produce the brassy cough characteristic of habit cough. Acquired tracheomalacia is most commonly seen after prolonged intubation and mechanical ventilation and is fairly common in survivors of extreme prematurity. As well TE fistula and vascular ring can produce localized tracheomalacia with cough, especially with respiratory infection. Because bronchodilators relax airway smooth muscle, these drugs can worsen tracheal malacia and airway collapse (25). Children who have severe tracheal malacia probably should not receive beta agonist medications like salbutamol.

TREATMENT OF CHRONIC COUGH IN CHILDHOOD

Once the cause of the cough has been identified or assumed based on history examination, and testing when indicated, therapy should be directed toward treating the presumed cause. However, the therapeutic benefit of placebo treatment for cough is reported to be as high as 85% (26). In another study, parents who wanted cough medicine at the initial visit reported more improvement at follow up regardless of if the

child received antihistamines, cough suppressants or placebo (27). A beneficial response to therapy should be approached with cautious optimism.

There is no evidence for using airway clearance therapy for the treatment of cough that is not associated with chronic purulent expectoration (28). There is also no evidence for using over-the counter cough medications for the treatment of cough. This includes decongestants, antitussives, expectorants, hypertonic saline aerosol, or mucolytics. OTC cough medications have been associated with significant morbidity and even death (29).

CONCLUSIONS

Chronic cough in children is a very common and potentially vexing problem with diverse possible causes (30). Careful history, examination, and limited testing will usually identify the most likely cause. The use of specific management pathways has been shown to be useful in determining the most appropriate therapy for an individual patient (31).

COMPLIANCE WITH ETHICAL STANDARDS

Conflicts of interests

The Author has declared no conflict of interests.

Financial support

There were no institutional or private fundings for this article.

Authorship

Professor Bruce K. Rubin is the sole Author of this manuscript.

Author contributions

N/A.

Ethical approval

Human studies and subjects

N/A.

Data sharing and data accessibility

N/A.

Publication ethics

Plagiarism

N/A.

Data falsification and fabrication

N/A.

REFERENCES

1. Irwin RS, Baumann MH, Bolser DC, Boulet LP, Braman SS, Brightling CE, et al. Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(1 Suppl):1S-23S. doi: 10.1378/chest.129.1_suppl.1S.
2. Chang AB, Glomb WB. Guidelines for evaluating chronic cough in pediatrics: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(1 Suppl):260S-83S. doi: 10.1378/chest.129.1_suppl.260S.
3. Rubin BK. Pediatricians are not just small internists. *Chest*. 2006;129(5):1118-21. doi: 10.1378/chest.129.5.1118?
4. Rubin BK. Mucus, phlegm, and sputum in cystic fibrosis. *Respir Care*. 2009;54(6):726-32. doi: 10.4187/002013209790983269.
5. Brennan M, McDonnell MJ, Duignan N, Gargoum F, Rutherford RM. The use of cough peak flow in the assessment of respiratory function in clinical practice- A narrative literature review, *Respir Med*. 2022;193:106740. doi: 10.1016/j.rmed.2022.106740.
6. Irwin RS, Madison JM. The diagnosis and treatment of cough. *N Engl J Med*. 2000;7;343(23):1715-21. doi: 10.1056/NEJM200012073432308.
7. Diamant MJ, Senac Jr MO, Gilsanz V, Baker S, Larsson S. Prevalence of incidental paranasal sinuses opacification in pediatric patients: a CT study. *J Comput Assist Tomogr*. 1987;11(3):426-31. doi: 10.1097/00004728-198705000-00011.
8. Poe RH, Kallay MC. Chronic cough and gastroesophageal reflux disease: experience with specific therapy for diagnosis and treatment. *Chest*. 2003;123(3):679-84. doi: 10.1378/chest.123.3.679.
9. McGarvey LP, Heaney LG, Lawson JT, Johnston BT, Scally CM, Ennis M, et al. Evaluation and outcome of patients with chronic non-productive cough using a comprehensive diagnostic protocol. *Thorax*. 1998;53(9):738-43. doi: 10.1136/thx.53.9.738.
10. Writing Committee for the American Lung Association Asthma Clinical Research Centers; Lansoprazole for children with poorly controlled asthma: a randomized controlled trial. *JAMA*. 2012;307(4):373-81. doi: 10.1001/jama.2011.2035.
11. Pin I, Radford S, Kolendowicz R, Jennings B, Denberg JA, Hargreave FE, et al. Airway inflammation in symptomatic and asymptomatic children with methacholine hyperresponsiveness. *Eur Resp J*. 1993;6(9):1249-56. Available from: <https://erj.ersjournals.com/content/6/9/1249>. Accessed: Oct 6, 2022.
12. Rubin BK, Priftis KN, Schmidt HJ, Henke MO. Secretory hyperresponsiveness and pulmonary mucus hypersecretion. *Chest*. 2014;146(2):496-507. doi: 10.1378/chest.13-2609.
13. Kanoh S, Tanabe T, Rubin BK. IL-13-induced MU-C5AC production and goblet cell differentiation is steroid resistant in human airway cells. *Clin Exp Allergy*. 2011;41(12):1747-56. doi: 10.1111/j.1365-2222.2011.03852.x.
14. Irwin RS, Ownbey R, Cagle PT, Baker S, Fraire AE. Interpreting the histopathology of chronic cough: a prospective, controlled, comparative study. *Chest*. 2006;130(2):362-70. doi: 10.1378/chest.130.2.362.
15. Marchant JM, Masters B, Taylor SM, Cox NC, Seymour GJ, Chang AB. Evaluation and outcome of young children with chronic cough. *Chest* 2006;129(5):1132-41. doi: 10.1378/chest.129.5.1132.
16. Chang AB, Oppenheimer JJ, Weinberger MM, Rubin BK, Grant CC, Weir K, et al. Management of children with chronic wet cough and protracted bacterial bronchitis: CHEST Guideline and Expert Panel Report. *Chest*. 2017;151(4):884-90. doi: 10.1016/j.chest.2017.01.025.
17. Marchant JM, Masters IB, Champion A, Petsky H, Chang AB. Randomised controlled trial of amoxicillin clavulanate in children with chronic wet cough. *Thorax*. 2012;67(8):689-93. doi: 10.1136/thoraxjnl-2011-201506.
18. Schaefer OP, Irwin RS. Unsuspected bacterial suppurative disease of the airways presenting as chronic cough. *Am J Med*. 2003;114(7):602-6. doi: 10.1016/s0002-9343(03)00079-2.
19. Galway NC, Shields MD. The child with an incessant dry cough. *Paediatr. Respir Rev*. 2019;30:58-64. doi: 10.1016/j.prrv.2018.08.002.
20. Chang AB, Lasserson TJ, Gaffney J, Connor FL, Garske LA. Gastro-oesophageal reflux treatment for prolonged non-specific cough in children and adults. *Cochrane Database Syst Rev*. 2011;2011(1):CD004823. doi: 10.1002/14651858.CD004823.pub4.
21. Chang AB, Phelan PD, Carlin JB, Sawyer SM, Robertson CF. A randomised, placebo controlled trial of inhaled salbutamol and beclomethasone for recurrent cough. *Arch Dis Child*. 1998;79(1):6-11. doi: 10.1136/adc.79.1.6.
22. Vertigan AE, Murad MH, Pringsheim T, Feinstein A, Chang AB, Newcombe PA, et al. Somatic cough syndrome (previously referred to as psychogenic cough) and Tic cough (previously referred to as habit cough) in adults and children: CHEST Guideline and Expert Panel Report. *Chest*. 2015;148(1):24-31. doi: 10.1378/chest.15-0423.
23. MFA, Balfour-Lynn IM. Habit-tic cough: Presentation and outcome with simple reassurance. *Pediatr Pulmonol*. 2018;53(4):512-6. doi: 10.1002/ppul.23948.
24. Haydour Q, Alahdab F, Farah M, Barrionuevo P, Vertigan AE, Newcombe PA, et al. Management and diagnosis of psychogenic cough, habit cough, and tic cough: a systematic review. *Chest*. 2014;146(2):355-72. doi: 10.1378/chest.14-0795.
25. Hysinger EB, Panitch HB. Paediatric tracheomalacia. *Paediatr Respir Rev*. 2016;17:9-15. doi: 10.1016/j.prrv.2015.03.002.

26. Eccles R. The powerful placebo in cough studies? *Pulm Pharmacol Ther.* 2002;15:303-8. doi: 10.1006/pupt.2002.0364.
27. Hutton N, Wilson MH, Mellitis ED, Baumgardner R, Wissow LS, Bonuccelli C, et al. Effectiveness of an antihistamine-decongestant combination for young children with the common cold: a randomized, controlled clinical trial. *J Pediatr.* 1991;118(1):125. doi: 10.1016/s0022-3476(05)81865-7.
28. Hill AT, Barker AF, Bolser DC, Davenport P, Ireland B, Chang AB, et al. Treating cough due to non-CF and CF bronchiectasis with nonpharmacological airway clearance: CHEST Expert Panel Report. *Chest.* 2018;153(4):986-93. doi: 10.1016/j.chest.2018.01.014.
29. Gunn VL, Taha SH, Liebelt EL, Serwint JR. Toxicity of over-the-counter cough and cold medications. *Pediatrics.* 2001;108(3):E52. doi: 10.1542/peds.108.3.e52.
30. Chang AB, Oppenheimer JJ, Weinberger M, Grant CC, Rubin BK, Irwin RS. Etiologies of chronic cough in pediatric cohorts: CHEST Guideline and Expert Panel Report. *Chest.* 2017;152(3):607-17. doi: 10.1016/j.chest.2017.06.006.
31. Chang AB, Oppenheimer JJ, Weinberger MM, Rubin BK, Weir K, Grant CC, et al. Use of management pathways or algorithms in children with chronic cough: CHEST Guideline and Expert Panel Report. *Chest.* 2017;151(4):875-83. doi: 10.1016/j.chest.2016.12.025.