ISSN: 2836-4961

Research article

General Surgery and Clinical Medicine

Cough and Protracted Bacterial Bronchitis (PBB) in Children Analytic View

Pablo Cortés-Borrego, MD

National Institute of Respiratory Diseases, Mexico Pediatric Pulmonary Service

***Corresponding Author**
Pablo Cortés-Borrego, MD, National Institute of Respiratory Diseases, Mexico Pediatric Pulmonary Service, pcortesborrego@gmail.com

Submitted: 25 Mar 2023; **Accepted**: 03 April 2023: **Published**: 17 April 2023

Citation: Cortes-Borrego P. (2023). Cough and Protracted Bacterial Bronchitis (PBB) in Children Analytic View. *Gen Surgery Clin Med, 1*(2), 72-81.

Abstract

The evolution of the concept of PBB is analyzed over time since it appeared as protracted Bronchitis, later protracted bacterial bronchitis (PBB), and finally its "clinical" version, which avoids the need to perform fiberoptic bronchoscopy in children [1-3]. However, this deviates in a significant manner from the principle on which the concept is based, giving rise to the idea of a disease that only affects children with the main characteristic of bacteriological isolation from lower airways.

On the other hand, the clinical diagnosis of PBB is made by excluding other diseases through so-called "pointers to specific cough, primarily for chronic cough1" with a posterior reference of signs and symptoms called specific cough pointers[2]. and Finally, in 2020, "Pointers to presence of specific cough" [4].

Comments are then made on how asthma (and early wheezing) and posterior nasal drip syndrome are ruled out as important causes of chronic and recurrent cough in children.

In conclusion, the causes of acute and chronic cough in children, with a few exceptions, are quite comparable to the causes of cough in adults. Therefore, an easy and more accurate way of diagnosing cough in children could be to reconsider our concepts of so-called cough pointers, upper airway cough syndrome, and asthma (and early wheezing) in children.

Background

The diagnostic entity of PBB has been described relatively recently (2006) as a clinical syndrome causing chronic cough in children and, since then, for rather practical reasons, it evolved and has increasingly departed from its original definition.

The original definition included
• History of chronic wet cough
• Positive bronchoalveolar lavage (BAL) culture (>105 colony-forming u/ml)
• Response to antimicrobial treatment with resolution of cough within two weeks [2].

Previously described as protracted bronchitis, the original definition of PBB subsequently evolved from a microbiological point of view, however isolating microorganisms from the tracheobronchial tree of children is not a risk-free task when sedation, fiberoptic bronchoscopy, and BAL are required, which leads one to consider the impossibility of doing this in most children with chronic cough. And with the introduction of new definitions of the syndrome, even if less firm, to help to make the diagnosis.

These new definitions are based on a later clinical version: Prolonged clinical bacterial bronchitis that eliminates the need for BAL, but openly recognizes that other causes of chronic wet cough need to be excluded [3, 4].

Other Proposed Definitions of Clinical PBB

• Chang et al define PBB as the presence of chronic wet cough (>4 weeks), resolution of the cough with antimicrobial treatment, and the absence of alternative etiologies.
• Bidiwala and collaborators recognize how unfeasible it is to make a microbiological diagnosis for PBB and maintain that clinical criteria should be used. However, it mentions that the proposed clinical definitions do not show the necessary specificity, nor do they distinguish it from other known causes of chronic cough [5].
• Asiloy et al defines prolonged bronchitis as the history of wet cough, response to antimicrobial therapy, and resolution of the cough within two to four weeks [6].
• Marchant et al define probable PBB as a history of wet cough and either a positive BAL culture or immediate response to antibiotic therapy, with resolution of cough within two weeks.

The four doctors have in common that they establish the diagnosis after the administration of antimicrobial therapy, so that PBB does not need bacterial isolation, and thus clinicians will have to rely only on the duration of the wet or productive cough to determine whether the antibiotic should be administered, and then observe its efficacy to confirm the diagnosis. It is a diagnosis based on the response to a certain therapy, such as applying low-dose inhaled steroids and short acting beta agonist for cough when asthma is suspected or a course of antihistamine for several weeks in the case of suspected "allergic cough" or with the treatment of cough-producing gastroesophageal reflux disease, without obtaining good results so far with this type of strategy [7, 8]. In general, the reviews evaluating certain treatments for cough have failed, and they only give a good response in a limited percentage of patients thus, no treatment has been effective enough to control cough [9].

What we are looking for in the clinical diagnostic process is to gather sufficient data through inquiry and observational study, with some paraclinical studies to support or rule out probable diagnoses to direct treatment. However, invasive studies should only be used if the benefit far outweighs the risk, which is not commonly associated with fiberoptic bronchoscopy [FBC] relation to cough, unless it is continuous cough for 8 weeks or longer and the diagnosis is not clear and FBC is expected to provide some help.

Pointers to Specific Cough (Mainly Chronic Cough)

By evaluating prior clinical data, the specific indicators of cough – primarily for chronic cough – are used to rule out other causes of cough, to make the diagnosis of PBB by exclusion. The danger is that these indicators are not very reliable in ruling out other alternatives in the diagnosis, leading to a biased diagnosis of PBB.

Initially, there were 16 cough indicators (Table 1)[2], some of which are not necessarily respiratory tract related and instead refer to syndromes that have little or nothing to do with cough; for example, immunodeficiency, heart disease or failure to thrive. This means that many chronic (or acute) coughs cannot be matched with the indicators on this list, consequently, the diagnosis of PBB is made erroneously by exclusion. Therefore, if we do not have reliable indicators, we will continue to make the diagnosis of PBB through a biased process.

Furthermore, referring to these cough indicators as being specific, may be related directly to the respiratory system of the children and ideally, as we will see later, with the characteristics, not only of the cough, but also with accompanying clinical data and signs that must be highly relevant to the distinction from other kinds of cough. All of these first identify the location in the airway where the cough stimulus occurs, in an attempt to explain the mechanism that suggests the possible direct cause or causes. It is true that this is not an exhaustive list, but it does not help the clinician in a clear way to distinguish the nature of the cough.

Table 1: Specific Indicators of Cough (Mainly, Chronic Cough)

Symptom/sign	Possible underlying aetiology*
Auscultatory findings (wheeze, crepitation, crackles, differential breath sounds)	Asthma, Bronchitis, congenital lung disease, foreign body aspiration, airway abnormality
Cough characteristics (e.g., cough with choking, cough quality, cough starting from birth)	Congenital lung abnormalities
Cardiac abnormalities (including murmurs)	Any cardiac illness
Chest pain	Asthma, functional, pleuritis
Chest wall deformity	Any chronic lung disease
Daily, moist or productive cough	Chronic bronchitis, suppurative lung disease
Digital clubbing	Suppurative lung disease
Dyspnea (exertional or at rest)	Compromised lung function of any chronic lung or cardiac disease
Failure to thrive	Compromised lung function, immunodeficiency, cystic fibrosis
Feeding difficulties (including choking/vomiting)	Compromised lung function, primary aspiration
Hemoptysis	Bronchitis
Immune deficiency	Atypical and typical respiratory infections
Medications or drugs	Angiotensin-converting enzyme (ACE) inhibitors, puffers, illicit drug use
Neurodevelopmental abnormality	Primary or secondary aspiration
Recurrent pneumonia	Immunodeficiency, congenital lung problem, airway abnormality
Symptom of upper respiratory tract infection	May coexist or be a trigger for an underlying problem
*This is a non-exhaustive list; only the more common respiratory diseases are mentioned	

Upper Airways Cough Syndrome

General indicators are not very specific. In addition, there is another bias by which the symptom of the upper respiratory tract infection is disqualified as a direct cause of cough, as in the column of "possible underlying etiology", which says: "May coexist or be a trigger for an underlying problem", which implies denying posterior drip syndrome as the sole cough mechanism in children [10, 11].

More recently, Chang et al (2020) reported on the possibility of upper airways disorders as a cough producer, considering sinusitis and putting it next to PPB [4].

As the causes of chronic cough encompass the entire spectrum of pediatric pulmonary and extrapulmonary diseases, the list that outlines the more common signs and symptoms is not exhaustive. Table 2 highlights (bold box) the new proposal for upper airway abnormalities and cough.

Table 2: Pointers to Presence of Specific Cough (2020)

Symptoms or signs	Examples of etiology
Auscultatory findings	**Wheeze (see below) Crepitations – any airway lesions from secretions) or parenchymal disease, such as interstitial disease**
Cardiac abnormalities	**Associated airway abnormalities,** cardiac failure, arrythmia
Chest pain	Arrhythmia asthma **(pleuritis excluded)**
Choked **(feeding difficulties separated in another cell)**	Foreign body inhalation
Dyspnea and tachypnea **(previously, dyspnea-exertional or at rest)**	Any pulmonary airway or parenchymal disease **(previously, "compromised lung function of any chronic lung or cardiac disease")**
Daily wet/productive cough (New symptom or sign)	Protracted bacterial bronchitis, suppurative lung disease, recurrent aspiration, atypical infections, TB. Diffuse "panbronchitis"
Facial pain/purulent nasal discharge (New symptom or sign instead of **"symptom of upper respiratory tract infection")**	**Chronic sinusitis** (protracted bacterial bronchitis), primary dyskinesia
Feeding difficulties	Any serious systemic including pulmonary illness such as cystic fibrosis
Growth failure **(previously, "failure to thrive")**	Any serious systemic illness including pulmonary illness
Hoarse voice/stridor (New symptom or sign)	Laryngeal cleft/problems, airway abnormalities
Hypoxia /cianosis	Any airway or parenchymal disease, cardiac disease.
Recurrent pneumonia	Immunodeficiency, **atypical infections, suppurative lung disease,** congenital lung abnormalities, **tracheoesophageal H-type fistulas.**
Recurrent infections	Immunodeficiency
Previous history of chronic lung or esophageal disease (e.g., neonatal lung disease, esophageal atresia)	Multiple causes (e.g., second H-type fistula, bronchiectasis, aspiration, asthma)
Wheeze monophonic	Large airway obstruction (e.g., foreign body aspiration, achalasia and/or stenosis, vascular rings, lymphadenopathy, and mediastinal tumors) TB should be considered in selected settings (e.g., high prevalence or HIV)
Whezze poliphonic	Asthma, bronchiolitis obliterants, bronchiolitis
TESTS	
Chest radiograph (other pan peribronchial changes) or spirometry abnormality	

In the highlighted cell, even though facial pain is an infrequent symptom in children with rhinosinusitis), in this new table, the infection of the upper airways is no longer considered as "can coexist" or "be a trigger" of an underlying problem, PBB or ciliary dyskinesia. Rhinosinusitis can be a cause of cough by spreading to a PBB in children, which in some of them can be facilitated by ciliary dyskinesia. This would also explain why a similar treatment (antimicrobial, 2-4 weeks) improves both conditions (rhinosinusitis and PBB), since both also share almost the same etiologic microorganisms and certain symptoms.

This leads to another reasoning in pediatric (and adult) respiratory health. If rhinosinusitis can carry pathogens to the bronchi, it can also carry them, perhaps less frequently, further down to the lung and be an important factor in causing not only PBB but also bacterial pneumonia.

If so, this would be a further step towards understanding one of the causes (possibly one of the most important) of chronic lung disease in children and/or recurrent pneumonia.

In fact, this has been considered by Benedictis and in a comparative chart of PBB and rhinosinusitis (Table 3), given the similarities between both entities, they are clearly related. I think there has been very little effort to rule out or confirm the diagnosis of rhinosinusitis even with simple studies.

In the same vein, the importance of rhinosinusitis is highlighted by speculation that rhinosinusitis may be the precursor to both PBB and in a lower level chronic suppurative lung disease, if left untreated.

Table 3: Main Clinical Characteristics of Protracted Bacterial Bronchitis and Upper Airway Cough Syndrome

	Protracted bacterial bronchitis	**Rhinosinusitis**
Cough	Chronic wet cough **No time predominance**	Recurrent wet/dry cough **(nocturnal* and early in the morning) Throat clearing**
Age	Preschool children	Toddlers, preschool children, school children
Personal history	Unremarkable	Daycare attendance Recurrent URI
Season	All	Cold season
General appearance	Coughing	Running nose, nasal crease, allergic shiners
Voice	Normal	Nasal
Respiratory sound	Rattle over the chest	Coarse sound from the upper airway
ENT evaluation	Normal	Post-nasal drip cobblestone pharyngeal mucosa View of secretions passing through the posterior pharyngeal wall
Allergy	Occasional	Frequent
Therapy	Respond to antibiotics	Response to nasal cleaning **Respond to antibiotics (if there is an infection)**

It should be noted that, for several authors, nocturnal and early-morning cough is more suggestive of postnasal drip (produced, for example, by common cold or rhinosinusitis), than other pathologies, when nocturnal cough is often used as a direct indicator of asthma in children. Thus, the existence of chronic, subacute, or recurrent rhinosinusitis may be a much more important factor than, for example, gastroesophageal reflux, in the case of pneumonia and, in particular, recurrent bacterial pneumonia [12-16].

Benedictis group reiterates, "There is a need for more studies of wet cough and not to assume that it is equivalent to lower airway infection in all children." Similarly, Toshiyuki (University of Kyoto) found that mechanical stimulation by postnasal drip evokes cough postnasal secretions in mice, and cough stops by closing the rhino-pharyngeal passage with cyanoacrylate (ensuring absence of inflammation in the lower airway). This allows us to understand the pathophysiological mechanism in patients, not only with rhinosinusitis, but also with the common cold (the most frequent cause of acute cough in humans). There should be no doubt that this mechanism produces cough in both children and adults, which gives the option of being able to do a pharmacological secretion blockage at this level and combat the cough, which in many individuals is likely to be excessive and intolerable [17].

Therefore, we might devise an algorithm (or several of them) to make a reasonably certain diagnosis of not only PBB, but also any kind of cough based on clinical symptoms, plus or minus routine laboratory tests, so physicians in the field can confidently make a diagnosis using cough as a key symptom – the goal of this paper – for which it is necessary to analyze some concepts in which there may be areas of confusion, such as asthma and cough due to upper respiratory tract disorders. Then, it is possible to propose algorithms for dealing with so-called nonspecific cough [18].

Asthma

In order to dismiss Irwin's method of diagnosing cough as useless in children, Chang's group refers to two papers: one of them, from Thompson with 49 children in which they found only two cases of asthma as a cause for cough of more than 4 weeks duration. The cohort of 49 children, were sent from several centers to a tertiary

care hospital with the diagnosis of chronic cough; however, they mention there was a probable patient referral bias. It also appears that asthmatic patients, who do not really represent a diagnostic problem, were treated at the primary care institution, and thus were not part of the sample studied [19, 20].

The other paper that also ruled out asthma as an important cause of chronic cough in children was written by Marchant, who is also from Chang's group in Australia. In 108 pediatric patients, 39.8% were diagnosed with PBB, and 22.2% had resolution without having made a diagnosis; asthma (or similar disease) was diagnosed in only 4.6%.

Table 4: Cases in Which Cough Was Not Diagnosed In Children (98 Patients)

Natural resolution	22.2%	Diagnosis was not made
Lost patients	4.6%	Diagnosis was not made
Uncertain diagnosis	6.1%	Diagnosis was not made
Total, patients without diagnosis	**42.3%**	**Total, percentage of cases in which diagnosis was not made**

These percentages can be explained by two reasons, the aforementioned bias, and the appearance of a new diagnosis at the time: PBB. Therefore, asthma should not cease to be an important diagnosis in terms of chronic cough in children, since several reviews, of chronic or subacute cough in children, asthma (or early wheezing) certainly plays an important role [21, 22]. On the other hand, the specific diagnosis of cough was not achieved in a large percentage of children sent with chronic cough.

If the diagnosis is only reached in 57.7% of the cases, we must rethink our approach, since this is much lower than 99% achieved by Irwin [23, 24]. We need to achieve the same effectiveness in children that he achieves in adults, in order to better guide pediatricians.

We know that, worldwide, pediatricians passionately advocate that childhood illnesses should be managed differently to adults, because extrapolation of adult data without adapting it to children can result in unfavorable consequences but discarding at all also can be detrimental [25].

Adults and the elderly, cough is often a result of physiologic decay and chronic abuse (e.g., chronic cough from smoking) [26, 27]. Children may present with multiple events of common cold (as many as 8-10 per year) so they tend to cough for more trivial and temporary causes (e.g., post-viral, common cold), and is often not given much attention, unless it is severe or long duration. In fact, one of the strategies for coughing in children is to do nothing when the so-called "expected cough" occurs, regarding therapy, there are also similarities. For example, all therapy for cough randomly tested against nonspecific cough is doomed to failure in both children and adults, even more, in adults, antihistamines and combinations of antihistamine/decongestant therapies have only modest if any, improvement, the same is true for children that show no improvement [28-30].

Non-specific cough and the difficulty, not only for its diagnosis (hence its name), but also for treatment make it necessary to further analyze what do we think it is, from another perspective.

"And thus, I was halfway between the apprehension of the concept of cough and the knowledge of an individual cough."

"I was caught between the singularity of his coughing, and my ignorance that it assumed the rather diaphanous form of a universal idea"

– Umberto Eco (paraphrased)

The Concept of Nonspecific Cough

Does nonspecific cough really exist? Or have we assumed that, in general, one cough is no different from another, and that the stimulus that produces it must necessarily originate from the same region of the tracheobronchial mucosa? Or is it from the pulmonary parenchyma? Or perhaps its origin is indirectly from the esophageal mucosa, as in the case of gastroesophageal reflux.

Traditionally, all coughs have been considered almost clinically the same and probably the prior differentiation has been made in reference to whether it is wet/productive or dry cough. Even subacute and chronic coughs have not been differentiated when making a diagnosis, which has led to confusion in differentiating them.

In the past, Dudgdale proposed devising an algorithm to make a reasonably certain diagnosis using cough as a primary key, so physicians working "in the field" can diagnose it with more certainty.

Therefore, it is proposed three algorithms, which include cough characteristics to make diagnosis easier. This means we must first accept upper airway cough syndrome (UACS) as one of the primary mechanisms of cough production in as many children as in adults. Second, we need to also accept that the bronchospastic phenomenon may explain subacute and chronic cough in many children, even in the cases absent of wheeze. In such cases, we must search for other indicators of the coughing mechanism, such as cough while running hard [31-35]. Once this is done, the following simple tables are proposed, in order to facilitate the diagnostic process in children with cough as a key symptom/sign:
Very specific indicators – accurate characteristics of certain types of coughs

Typical cough – cough that related to an illness
Cough according to age – different causes of cough at different ages

The following table shows the association between cough characteristics and its cause and indirectly, the anatomical region where the stimulus to produce the cough is located. For example, in children the possibility of observing them while running, since it is a common part of their active lives, and if they run a lot and this causes them to cough and sometimes even throw up, it makes one think of bronchial hyperresponsiveness (asthma not fully controlled or early wheezing), even if they do not have wheezing. These indicators are probably due to acute or subacute cough, though in some circumstances to chronic cough.

Table 1: Specific Indicators of Cough

Symptom or sign	Possible etiology
1. Cough when running, moderate to intense	Early wheezing/asthma
2. Night and/or morning cough	UACS (previously attributed to asthma)
3. Rhinorrhea (even if mild)	UACS
4. Clear throat (pharyngeal clearance)	UACS
5. Cough and wheezing	Asthma, early wheezing
6. Choking related to feeding	Foreign body aspiration Chronic aspiration
7. Tracheal (seal) cough	LTB
8. Dry or productive morning cough	UACS (If it is very productive: bronchiectasis)
9. Observation of discharge, any kind of secretion on the posterior pharyngeal wall (also by anterior nasal wall mucosa)	UACS

UACS: Upper airway cough syndrome. LTB: Laringotracheobronchitis. One cause does not rule out a concomitant cause. UACS as well as asthma, can be one of the main causes of acute, but also subacute and recurrent and chronic cough.

Cough due UACS should not be ruled out only by treating it with a systemic antihistamine-based treatment given its low efficiency [36].

On the other hand, there are very typical coughs such as the tracheal or "seal cough" that is strongly suggestive of laryngotracheitis (CROUP), or the cough accompanied by wheezing from asthma (or early wheezing).

Table 2: Typical Cough

COUGH QUALITY	PROBABLE DIAGNOSIS
1. **"Seal", "tracheal",** "metallic" or "dog" cough	**Laringotracheobrochitis (croup)** – Laringotraqueomalacia – Foreign body in airways – Psychogenic cough
2. **Cough with throat** clearing –Associated with throat clearing noise	**Upper Airway Cough Syndrome** – Rhinopharyngitis/common cold or rhinosinusitis if its lasts more than 10-12 days
3. Night cough – Mainly in the supine position – Improves slightly when sitting	**Upper Airway Cough Syndrome** – Asthma, early wheezing – Gastroesophageal reflux
4. Getting up in the morning	**Upper Airway Cough Syndrome** – Causes cough both, in the morning and at night – Bronquiectasis, more likely if accompanied by pulmonary suppuration
5. During or after exercise – Also, when laughing or when breath out forcefully	**Asthma** or early wheezing if less than 6 years old
6. Paradoxical – Long spells of incoercible and short coughs	**Whooping Cough** – Very typical with end stridor – Upper airway cough syndrome

7. Goose Squawk Cough like an old car horn	**Psycogenic cough**
8. Cough in Staccato From birth to 3-4 months old	**Chlamydia Trachomatis `**
9. Productive cough of bronchial mold casts	**Asthma** Plastic bronchitis (rare)

***Bold Letters** when diagnosis is feasible given the typical cough

Rhinosinusitis should be suspected in small children by the presence of mucopurulent rhinorrhea persisting beyond the usual 7-10 days for uncomplicated common cold [37].

Although severe throat clearing may also occur after events of upper gastroesophageal reflux which reach the upper airways. In children, gastroesophageal reflux has been associated in addition to nocturnal cough or recurrent croup.

Another way to evaluate cough in children is by grouping the most common causes of cough according to the different ages at which they usually occur. There can be many exceptions, but as a general guide it can be helpful.

The next table shows how age modifies not only the susceptibility but also causes of subacute or recurrent cough. At the beginning of life due to immaturity (or malformations), then its influence decreases while other factors become more important.

Like cough due to acute viral infections are more important in infants (as well as their persistence due to its sequelae) and in general bacterial causes are added later in life.

Table 3: Diagnosis of Cough According to Age

AGE GROUP	DIAGNOSIS
Infants – 1 to12 months	**1. Viral upper airways infections, can be recurrent (UACS)** 2. Asthma, early wheezing 3. Viral infections of lower airways (e.g., bronchiolitis) 4. Post-bronchiolitis sequalae 5. Gastroesophageal reflux disease 6. Bronchopulmonary dysplasia. Congenital malformations
Older infant and preschool children – 1 to 5 years old	**1. Rhinopharyngitis (viral) or bacterial rhinosinusitis +UACS** **2. Upper recurrent airways viral infections + UACS** 3. Early wheezing /asthma 4. Respiratory disease post-bronchiolitis 5. Pneumonia 6. Gastroesophageal reflux 7. Foreign body
School children – 6 to 16 years old	**1. Rhinopharyngitis (viral or bacterial) + UACS** 2. Asthma 3. Pneumonia 4. Gastroesophageal Reflux 5. Psychogenic Cough

A fourth table has been added considering that cough is particularly prone to being influenced by the placebo effect.

Table 4: Treatment for Secondary Cough

MEDICATION	CAUSE OF SECONDARY COUGH
1. Broncodilators	**Asthma, early wheezing**
2. Antibiotics	**Rhinosinusitis** – Protracted bacterial Bronchitis – Bacterial rhinopharyngitis – Other bacterial infections of the respiratory tract

One diagnosis that is easier to evaluate through direct treatment is asthma and cough variety asthma, manifested predominantly by cough, without wheezing and dyspnea. In fact, children under 5 years of age in whom spirometry cannot be performed or impulse oscillometry is not available, due to lack of cooperation and in whom symptoms that accompany cough could be doubtful, an inhaled bronchodilator treatment is a reliable way to make the diagnosis because the response is usually immediate and sometimes even spectacular therefore, there is less chance of confusion [38].

A good response to antimicrobial treatment for 2 to 4 weeks cannot differentiate between rhinosinusitis and a PBB.
Continuous cough (excluding recurrent cough) that lasts more than 8 weeks, requires a much more carefully study which may involve greater invasively and diagnostic acuity.

In relation to antihistamines and decongestants, it is worth mentioning that they are prohibited in children under 2 years of age. In UACS, cough due common cold/rhinosinusitis is not useful in children and doubtful useful in adults (3 weeks to respond) [39, 40].

Cough secondary to esophageal reflux. Gastro kinetics/proton pump inhibitors. Dr. Chang did not find any utility to treatment with gastro-kinetics and proton pump inhibitors in children with cough associated with gastroesophageal reflux.

Conclusion

The fact that common bacterial pathogens are extremely similar in rhinosinusitis and in PBB in children is significant. To date, no FBC studies have been conducted in children with acute and chronic rhinosinusitis to determine whether cough is related to upper airway infection that has spread to the lower airway causing PBB [41-46].

As a matter of fact, before this extension to the lower airways (and even during the same) the mechanism of cough is the posterior nasal discharge that later would be added to the other mechanism of cough, this is the bronchial stimuli, which is the cough triggered by the secretions at the tracheobronchial level [47, 48].

A cough mechanism does not necessarily rule out another mechanism existing at the same time in the same patient, so it is possible for the cough to be from stimuli of two (or more) different sites. It is also not uncommon for children to cough from rhinosinusitis – nocturnal or morning cough, and wet or dry cough – and that it exacerbates a pre-existing asthma. Thus, we would have two causes of cough in the same child, and not only has each one had its own characteristics, but also its own treatment.

Other Considerations

The agreement between clinicians and parents about the quality of cough (wet or dry) in children seems to be highly dependent on age, being better in children under two years of age [49]. In addition, different types of coughs can occur in the same patient, and probably in the same disease.

The modalities to exclude other causes of chronic cough in children with suspected PBB are not clearly defined.

A cough that seems to be mostly nonspecific may have associated signs (or symptoms) with which differentiation can be highly successful.

A cough whose stimulus comes from the lung parenchyma does not present in the same way as one that comes from the bronchi, and less so if the stimulus comes from larynx and hypopharynx. In that way, a cough due to bronchoconstriction cannot be the same as a cough whose stimulus is secretion in the upper airways. Cough is different according to some of these variables, but also according to age, previous health, different anatomies, and different laryngeal and bronchial spaces, or even from the lung parenchyma. And all of these influence the way a patient coughs.

Even so, many times one dry cough can be differentiated from another according to its cause if it is studied systematically.

Regarding cough in children, it is not desirable to discard all medical knowledge that has developed over time, especially in adults. It is necessary to establish explicit and specific differences in terms of etiologies, even though these differences may sometimes overlap in both groups. Since children are not young adults, this approach is not always justified and can occasionally be downright confusing.

It is very possible that by changing the indicators of cough and making them more specific, the possibility of carrying out studies focused on a more limited group of diagnoses, the percentage of effectiveness may increase. This would also necessarily require acceptance of posterior nasal discharge as an important cough mechanism in children, as well as the importance of asthma and early wheezing in a percentage of children with chronic or subacute cough as suggested by some authors.

Special thanks to priceless help in the preparation of this document: Dr. Carlos Borrego MD and Anaissa Galicia

References

1. Chang, A. B., Landau, L. I., Van Asperen, P. P., Glasgow, N. J., Robertson, C. F., Marchant, J. M., & Mellis, C. M. (2006). Cough in children: definitions and clinical evaluation. Medical Journal of Australia, 184(8), 398-403.
2. Marchant, J. M., Masters, I. B., Taylor, S. M., Cox, N. C., Seymour, G. J., & Chang, A. B. (2006). Evaluation and outcome of young children with chronic cough. Chest, 129(5), 1132-1141.
3. Chang, A. B., Upham, J. W., Masters, I. B., Redding, G. R., Gibson, P. G., Marchant, J. M., & Grimwood, K. (2016). Protracted bacterial bronchitis: the last decade and the road ahead. Pediatric Pulmonology, 51(3), 225-242.
4. Chang, A. B., Oppenheimer, J. J., Irwin, R. S., Adams, T. M., Altman, K. W., Azoulay, E., ... & Vertigan, A. E. (2020). Managing chronic cough as a symptom in children and management algorithms: CHEST guideline and expert panel report. Chest, 158(1), 303-329.
5. Bidiwala, A., Krilov, L. R., Pirzada, M., & Patel, S. J. (2015). Pro-con debate: Protracted bacterial bronchitis as a cause of chronic cough in children. Pediatric annals, 44(8), 329-336.
6. Asilsoy, S., Bayram, E., Agin, H., Apa, H., Can, D., Gulle, S., & Altinoz, S. (2008). Evaluation of chronic cough in children.

Chest, 134(6), 1122-1128.
7. Thomson, F., Masters, I. B., & Chang, A. B. (2002). Persistent cough in children and the overuse of medications. Journal of paediatrics and child health, 38(6), 578-581.
8. Chang, A. B., Lasserson, T. J., Kiljander, T. O., Connor, F. L., Gaffney, J. T., & Garske, L. A. (2006). Systematic review and meta-analysis of randomised controlled trials of gastro-oesophageal reflux interventions for chronic cough associated with gastro-oesophageal reflux. Bmj, 332(7532), 11-17.
9. Dicpinigaitis, P. V. (2011). Cough: an unmet clinical need. British journal of pharmacology, 163(1), 116-124.
10. Chang, A. B., & Glomb, W. B. (2006). Guidelines for evaluating chronic cough in pediatrics: ACCP evidence-based clinical practice guidelines. Chest, 129(1), 260S-283S.
11. Chung, K. F., Widdicombe, J. G., & Boushey, H. A. (2003). Cough: Causes, Mechanisms and Therapy.
12. De Benedictis, F. M., Carloni, I., Comberiati, P., Shields, M. D., Bush, A., & Chang, A. B. (2019). Wet cough and nasal symptoms in children: can we do better?. Frontiers in Pediatrics, 7, 459.
13. Brietzke, S. E., Shin, J. J., Choi, S., Lee, J. T., Parikh, S. R., Pena, M., ... & Rosenfeld, R. M. (2014). Clinical consensus statement: pediatric chronic rhinosinusitis. Otolaryngology–Head and Neck Surgery, 151(4), 542-553.
14. Yoder, K. E., Shaffer, M. L., La Tournous, S. J., & Paul, I. M. (2006). Child assessment of dextromethorphan, diphenhydramine, and placebo for nocturnal cough due to upper respiratory infection. Clinical pediatrics, 45(7), 633-640.
15. Chen, X., Peng, W. S., & Wang, L. (2019). Etiology analysis of nonspecific chronic cough in children of 5 years and younger. Medicine, 98(3).
16. Shields, M. D., Bush, A., Everard, M. L., McKenzie, S., & Primhak, R. (2008). Recommendations for the assessment and management of cough in children. Thorax, 63(Suppl 3), iii1-iii15.
17. Iwata, T., Ito, I., Niimi, A., Ikegami, K., Marumo, S., Tanabe, N., ... & Mishima, M. (2015). Mechanical stimulation by postnasal drip evokes cough. PloS one, 10(11), e0141823.
18. Dugdale, A. (2010). Protracted cough: problems and opportunities. Journal of paediatrics and child health, 46(1-2), 66-67.
19. Irwin, R. S., French, C. T., Lewis, S. Z., Diekemper, R. L., Gold, P. M., Adams, T. M., ... & Wiener, R. S. (2014). Overview of the management of cough: CHEST Guideline and Expert Panel Report. Chest, 146(4), 885-889.
20. Thomson, F., Masters, I. B., & Chang, A. B. (2002). Persistent cough in children and the overuse of medications. Journal of paediatrics and child health, 38(6), 578-581.
21. 21Holinger, L. D. (1986). Chronic cough in infants and children. The Laryngoscope, 96(3), 316-322.
22. Callahan, C. W. (1996). Etiology of chronic cough in a population of children referred to a pediatric pulmonologist. The Journal of the American Board of Family Practice, 9(5), 324-327.
23. Irwin, R. S., & Madison, J. M. (2000). The diagnosis and treatment of cough. New England Journal of Medicine, 343(23), 1715-1721.
24. Irwin, R. S., Corrao, W. M., & Pratter, M. R. (1981). Chronic persistent cough in the adult: the spectrum and frequency of causes and successful outcome of specific therapy. American Review of Respiratory Disease, 123(4), 413-417.
25. Chang, A. B. (2005). Cough: are children really different to adults?. Cough, 1, 1-15.
26. Simasek, M., & Blandino, D. (2007). Treatment of the common cold. American family physician, 75(4), 515-520.
27. Rubin, B. K. (2006). Pediatricians are not just small internists. Chest, 129(5), 1118-1121.
28. Chang, A. B., Van Asperen, P. P., Glasgow, N., Robertson, C. F., Mellis, C. M., Masters, I. B., ... & Morris, P. S. (2015). Children with chronic cough: when is watchful waiting appropriate? Development of likelihood ratios for assessing children with chronic cough. Chest, 147(3), 745-753.
29. Smith, S. M., Schroeder, K., & Fahey, T. (2008). Over-the-counter (OTC) medications for acute cough in children and adults in ambulatory settings. Cochrane database of systematic reviews, (1).
30. Simasek, M., & Blandino, D. (2007). Treatment of the common cold. American family physician, 75(4), 515-520.
31. Chang, A. B., Peake, J., & McElrea, M. S. (2006). Anti-histamines for prolonged non-specific cough in children. Cochrane Database of Systematic Reviews, (3).
32. Gao, F., Gu, Q. L., & Jiang, Z. D. (2019). Upper airway cough syndrome in 103 children. Chinese medical journal, 132(06), 653-658.
33. Michaudet, C., & Malaty, J. (2017). Chronic cough: evaluation and management. American family physician, 96(9), 575-580.
34. Benich III, J. J., & Carek, P. J. (2011). Evaluation of the patient with chronic cough. American family physician, 84(8), 887-892.
35. An, S. S., Fabry, B., & Mellema, M. (2005). Bibliography Current World Literature Vol 11 No. Current Opinion in Pulmonary Medicine, 11, 85-112.
36. De Sutter, A. I., Lemiengre, M., Campbell, H., & Cochrane Acute Respiratory Infections Group. (1996). Antihistamines for the common cold. Cochrane Database of Systematic Reviews, (3).
37. Schidlow, D. V., & Smith, D. S. (Eds.). (1994). A practical guide to pediatric respiratory diseases. Hanley & Belfus.
38. Reddel, H. K., Bacharier, L. B., Bateman, E. D., Brightling, C. E., Brusselle, G. G., Buhl, R., & Boulet, L. P. (2022). Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. American Journal of Respiratory and Critical Care Medicine, 205(1), 17-35.
39. Ostroff, C., Lee, C. E., & McMeekin, J. (2011). Unapproved prescription cough, cold, and allergy drug products: recent US Food and Drug Administration regulatory action on unapproved cough, cold, and allergy medications. Chest, 140(2), 295-300.
40. Pratter, M. R., Bartter, T., Akers, S., & Dubois, J. (1993). An

algorithmic approach to chronic cough. Annals of internal medicine, 119(10), 977-983.
41. Wald, E. R., Reilly, J. S., Casselbrant, M., Ledesma-Medina, J., Milmoe, G. J., Bluestone, C. D., & Chiponis, D. (1984). Treatment of acute maxillary sinusitis in childhood: a comparative study of amoxicillin and cefaclor. The Journal of pediatrics, 104(2), 297-302.
42. Gérvas, J., & Fernández, M. P. Curso a distancia sobre Uso Racional del Medicamento ARS XXI Madrid 2007.
43. Muntz, H. R., & Lusk, R. P. (1991). Bacteriology of the ethmoid bullae in children with chronic sinusitis. Archives of otolaryngology–head & neck surgery, 117(2), 179-181.
44. Bachert, C., Pawankar, R., Zhang, L., Bunnag, C., Fokkens, W. J., Hamilos, D. L., ... & Blaiss, M. (2014). ICON: chronic rhinosinusitis. World Allergy Organization Journal, 7, 1-28.
45. Isaacson, G. (1996). Sinusitis in childhood. Pediatric Clinics of North America, 43(6), 1297-1318.
46. Jiang, R. S., Hsu, C. Y., & Jinq-Wen, J. A. N. G. (1998). Bacteriology of the maxillary and ethmoid sinuses in chronic sinusitis. The Journal of Laryngology & Otology, 112(9), 845-848.
47. Kantar, A., Chang, A. B., Shields, M. D., Marchant, J. M., Grimwood, K., Grigg, J., ... & Everard, M. L. (2017). ERS statement on protracted bacterial bronchitis in children. European Respiratory Journal, 50(2).
48. Craven, V., & Everard, M. L. (2013). Protracted bacterial bronchitis: reinventing an old disease. Archives of disease in childhood, 98(1), 72-76.
49. Chang, B. A., Gaffney, J. T., Eastburn, M. M., Faoagali, J., Cox, N. C., & Masters, I. B. (2005). Cough quality in children: a comparison of subjective vs. bronchoscopic findings. Respiratory research, 6(1), 1-8.