Pediatric Cough

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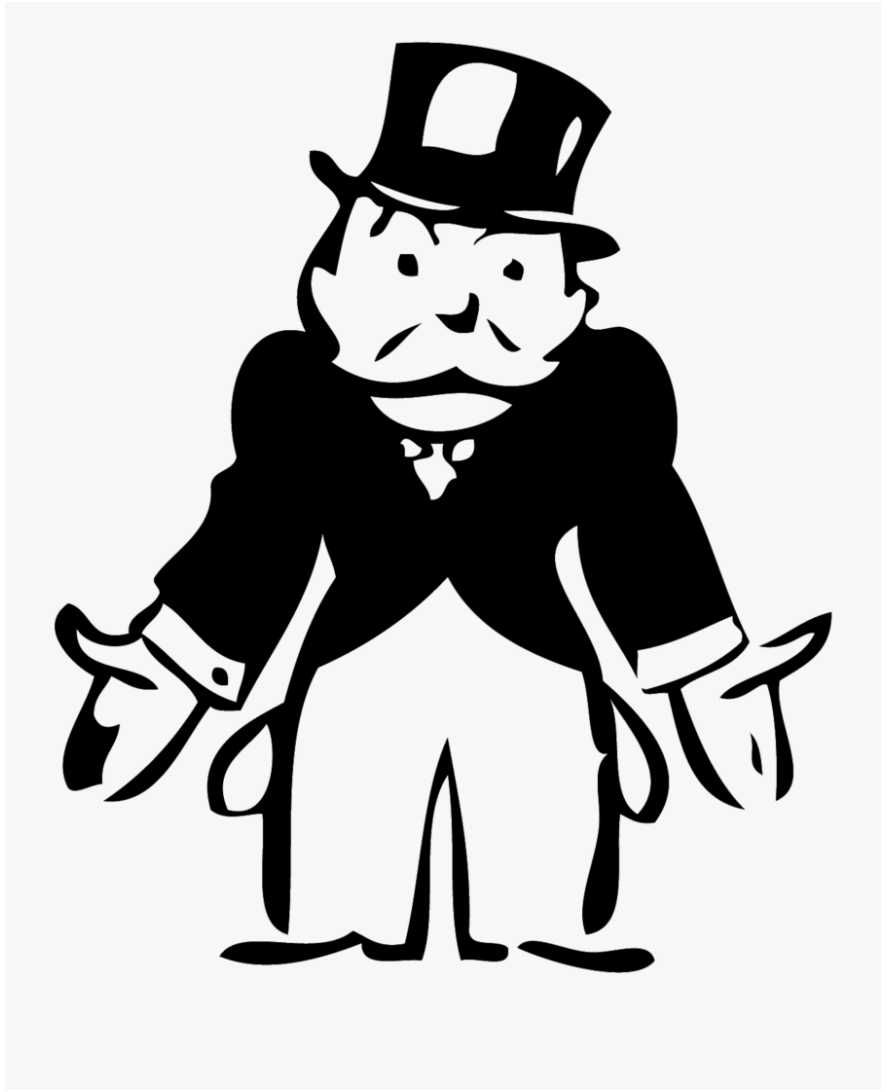
Objectives

- Understand cough pathogenesis, benefits, and harms
- Establish a framework for diagnosis
- Discuss value-based testing and treatment

Disclosures

- I have no relevant disclosures



What is “cough”?

- A physiologic and “normal” airway protective and clearance mechanism
  - Prevent aspiration
  - Clear excessive secretions or airway debris
- 3 Phases of cough
  - Inspiration
  - Glottic Closure (compression)
  - Expiration (explosive)
- Voluntary and/or involuntary depending on trigger and CNS development
- Among the most frequent reasons children will be brought to their doctor
  - Worrisome to parents
  - May disrupt sleep, work, school, and impair quality of life
  - Variably uncomfortable

Approach to cough in children

- Etiologies differ somewhat from adults (use appropriate algorithm)
- Emphasize stepwise diagnosis, treatment, and follow-up (avoiding low-value diagnostics and treatments)
- Age and situational context helpful
- Characteristics and duration are key factors (especially important with chronic cough)

- Definition of Pediatric Chronic Cough is > 4 weeks (until age 15)

Refractory Chronic Cough & Cough Hypersensitivity Syndrome

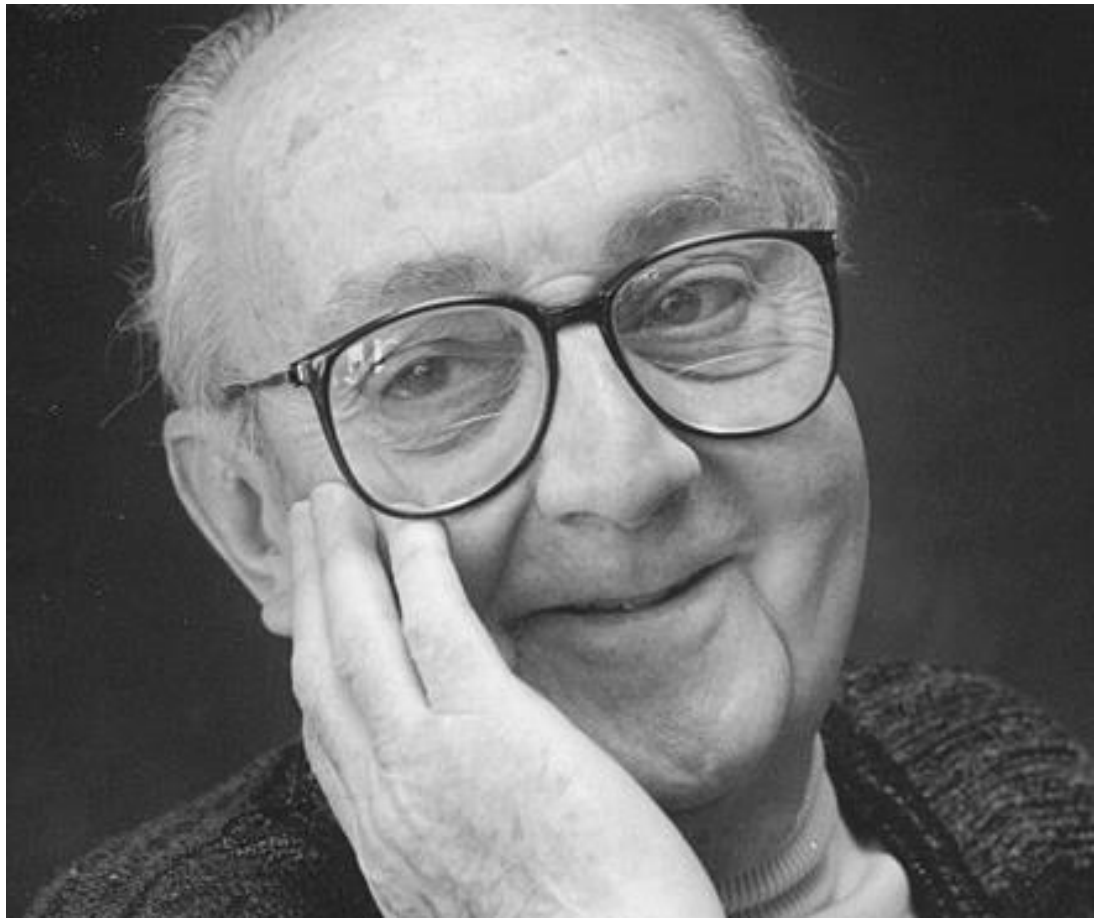
- NOT CONSIDERED APPROPRIATE DIAGNOSES IN CHILDREN

- So, for the purposes of our talk, consider:
  - Etiologies among children with chronic cough are well defined
  - Underlying diagnosis of cough is commonly found through stepwise assessment (or cough resolves along the way)
  - Directed treatment has very high success rate in pediatric chronic cough

Chang et al. J Clin Med. 2023 Aug; 12(15): 4879. doi: 10.3390/jcm12154879

“All models are wrong, some are useful”

-George Box
(1976)



In other words:

The utility of the guideline(s) is that it generally steers us, and the families we care for, in a direction that avoids unnecessary worry, testing, and treatment, while ultimately resulting in the desired outcome.

Cough is often normal in all ages (but especially in kids)

- Normal or ”expected” cough is the mainstay of acute cough
- Children <10y cough 11-34 times per day without illness
- Parental reports of cough severity/frequency is *unreliable*
  - Child report of severity is better
- The pediatric (<15 yo) definition of *chronic cough* is >4wks (adult >8wks)

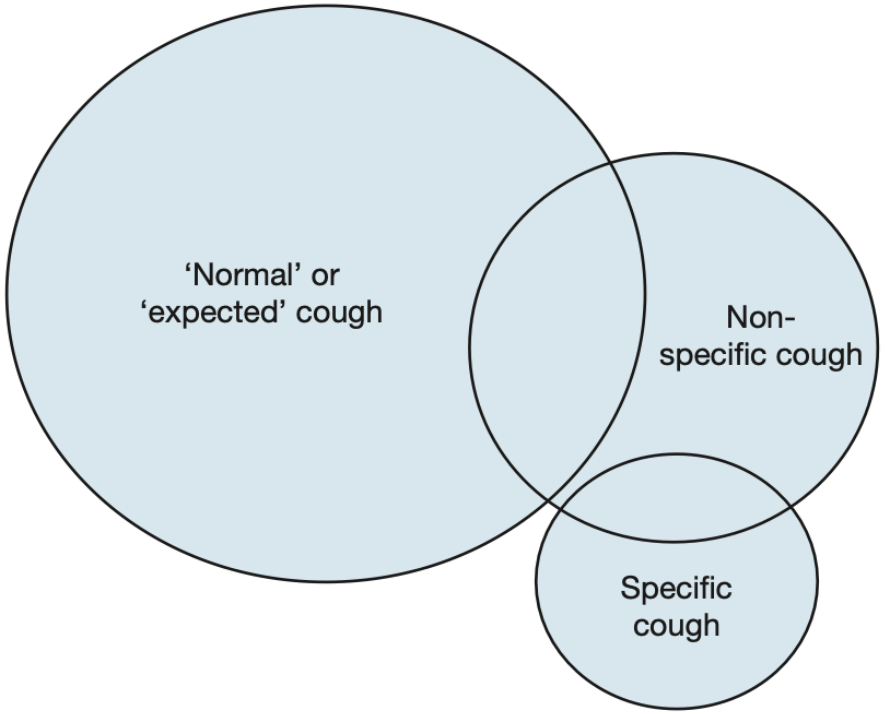


Figure 1 – *Classification of types of cough in children. ‘Expected cough’ refers to coughing illness reflective of common upper respiratory viral infections in an otherwise child where the cough duration is usually < 2 weeks but may be longer in a small minority.*

CHEST 2020; 158(1):303-329

Development of Cough Reflex

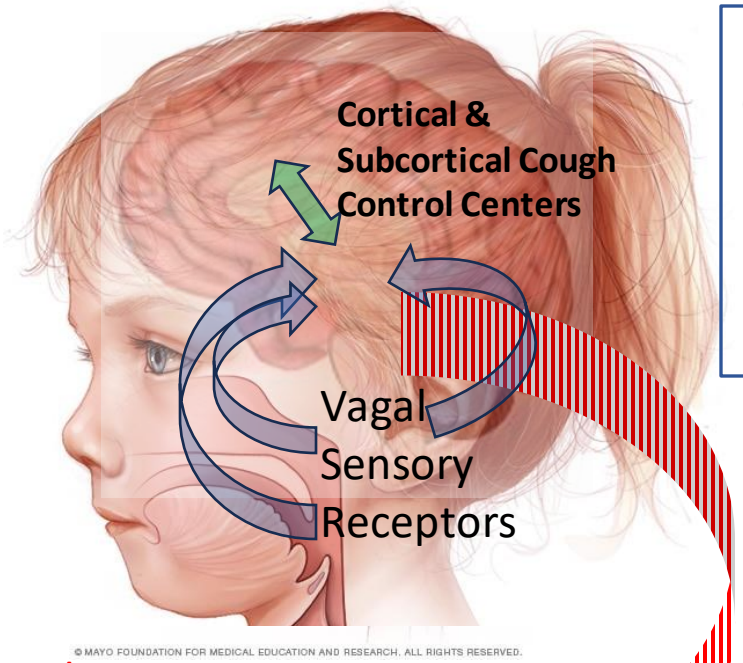
- Can trigger cough with pharyngeal stimulus in
  - 10% of 27wk premies
  - 90% of term infants
- Infants up to 2 months corrected age may be triggered to swallow, default to “Dive Reflex”, or go apneic (fun times)
  - Apnea/breath holding
  - Glottic Closure (reflexive)
  - Startled appearance (eyes wide open)
  - Varying color change (red/purple to pale)
  - Resolves with in-breath, often with crying

Sensory Pathways in upper respiratory tract key to ”urge to cough” (UTC)

- Arnold’s Nerve Ear-Cough Reflex – stimulation of the auricular branch of the vagal nerve elicits cough
  - Children with or without chronic cough have similar rates of this
  - Adults with CC have 11-fold higher rates than healthy adults
- Sensory nerves in the pharynx may be triggered by numerous stimuli
  - Cranial nerves X (Vagus) and IX (Glossopharyngeal) share distribution
  - Mechanical (e.g., mucous, post-nasal drip, unexpected bolus/ misswallow)
  - Chemical/irritation (e.g., capsaicin, cigarette smoke, dry throat)
  - Inflammation (e.g., viral infection)

Murgia et al. Pediatr All Immunol Pulm 2020 (33); DOI 10.1089/ped.2019.1135

”Voluntary” Cough Pathway



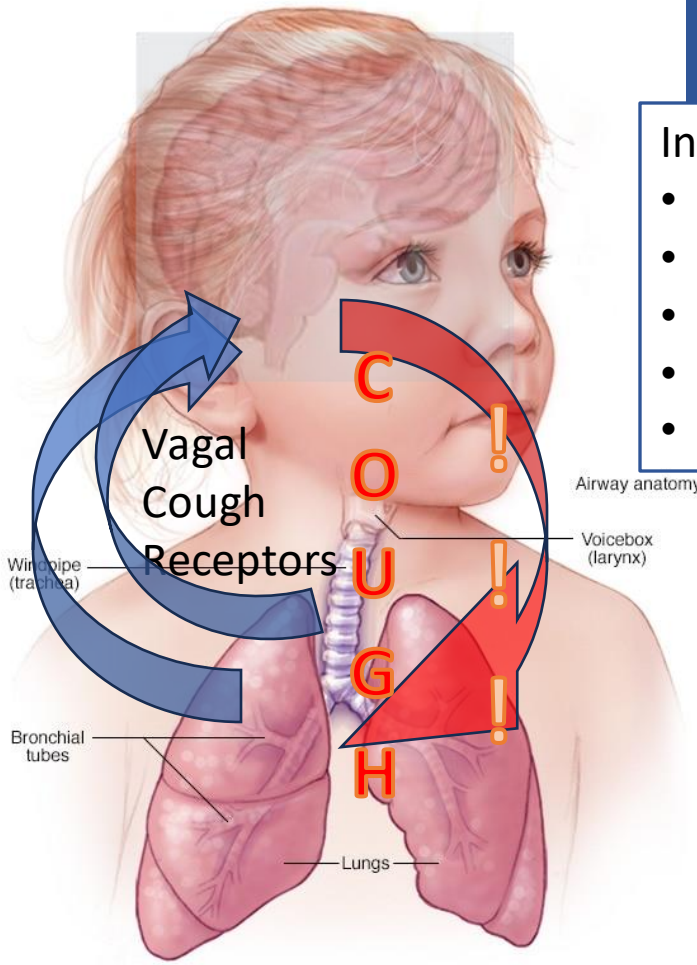
Cortico-medullary Response

Urge to Cough/Swallow

- URTI/Inflammation
- Post-nasal drip
- Gag reflex
- Irritant/dryness

- Cough
- Clear Throat
- Try to Ignore (which is learned/developed) or do something about it (which is taught, bought, or *prescribed*)

Reflexive Cough Pathway



Brainstem Neural Network

Involuntary cough

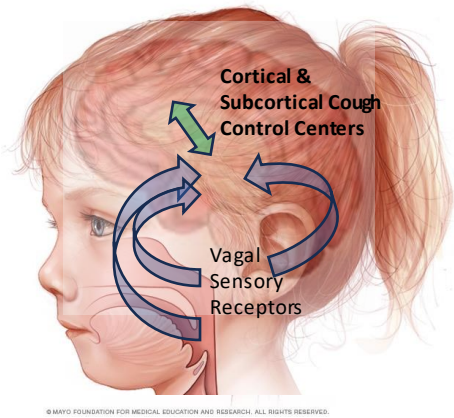
- Pneumonia
- Asthma
- Bronchitis
- Pertussis
- FB in LRT

URTI, cough, and… concern

- With URTI, cough may last for some time
  - Resolves in 10 days in half of cases
  - Resolves in 25 days in 90%
- Frequent of URTIs in young children may give the appearance of prolonged/chronic cough
  - 7-13 febrile illnesses/year, many of which are respiratory
  - Concentration of URTIs in winter
- Cough most noticed at night (keeping child and parent awake)

URTI cough is multifactorial

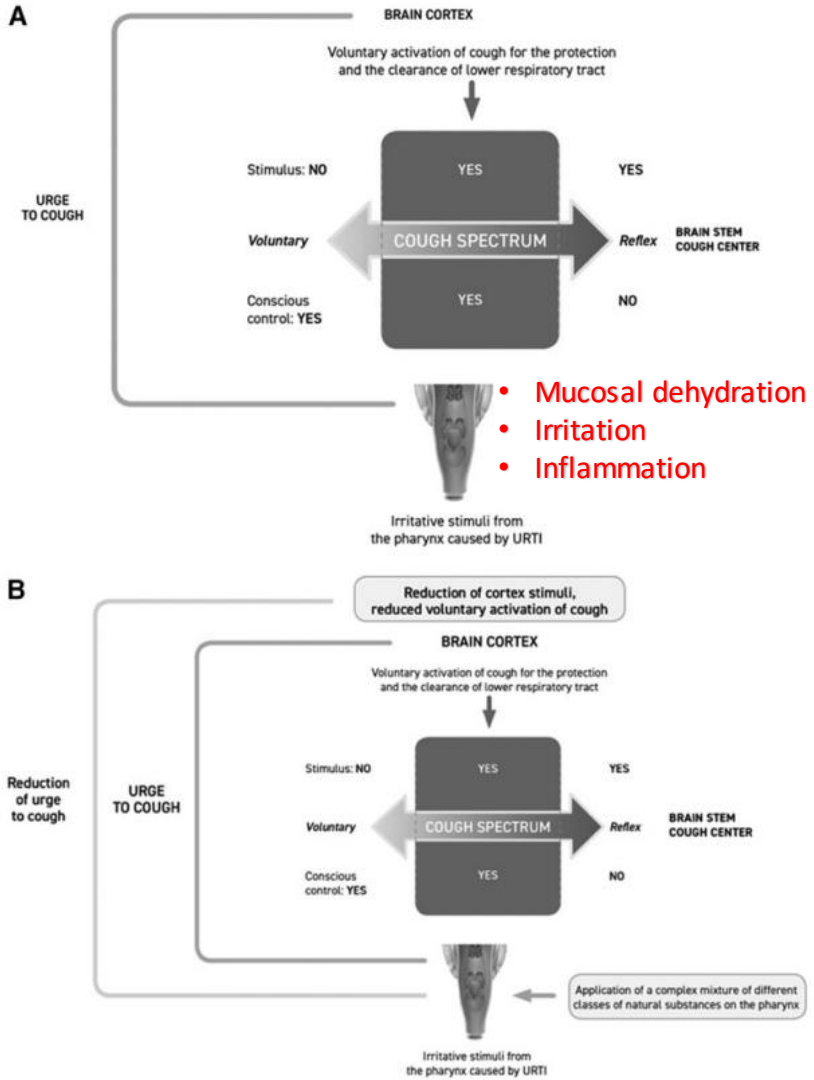
- Direct inflammation in nose, nasopharynx, oropharynx, and other airways
  - Mix of cough types depends on focus of inflammation and developmental age
  - Inflammation may enhance sensory receptor sensitivity
- Irritation (airway dryness due to mouth breathing)
- Mechanical (post-nasal drip sensation)



- Sensory ”Voluntary” pathway by age
  - Ability to override UTC is learned in later childhood
  - Young children may simply keep coughing

Murgia et al. Pediatr All Immunol Pulm 2020 (33); DOI 10.1089/ped.2019.1135

Antitussives: Low effect in URTI



- Medications with "antitussive" properties (cough suppressants) are largely ineffective
- FDA and AAP: do not give to any child <2y, and avoid children <6.
- Natural polysaccharides and honey seem better than meds

Murgia et al. Pediatr All Immunol Pulm 2020 (33); DOI 10.1089/ped.2019.1135

Cohen et al. Pediatr 2012;130:465-71

HONEY vs Medication: Moving away from "Cough Reflex" inhibitors for acute and non-specific cough

- Acts locally (pharynx)
  - Produces lubricant, demulcent, and protective barrier effect
  - Sweet!
  - Mucoadhesive, anti-inflammatory, anti-microbial, antioxidant
  - Not for < 1 y.o. (botulism)
- Natural plant-derived polysaccharides may have similar properties

  - *Plantago lanceolata*, marshmallow root, mallow flower
- Nasal Saline, Humidifier

- Codeine, dextromethorphan: Centrally-acting antitussives
  - No better than placebo
  - Risk of side-effects significant
  - Yuck!
- Antihistamines: Not effective for non-allergic cough; side effects
- Gabapentin is right out

Murgia et al. Pediatr All Immunol Pulm 2020 (33); DOI 10.1089/ped.2019.1135

Cohen et al. Pediatr 2012;130:465-71
Morice et al. Eur Respir J 2020;55(1)

Chronic Cough

Managing Chronic Cough as a Symptom in Children and Management Algorithms: CHEST Guideline and Expert Panel Report

*Anne B. Chang, PhD; John J. Oppenheimer, MD; and Richard S. Irwin, MD, Master FCCP; on behalf of the CHEST Expert Cough Panel**

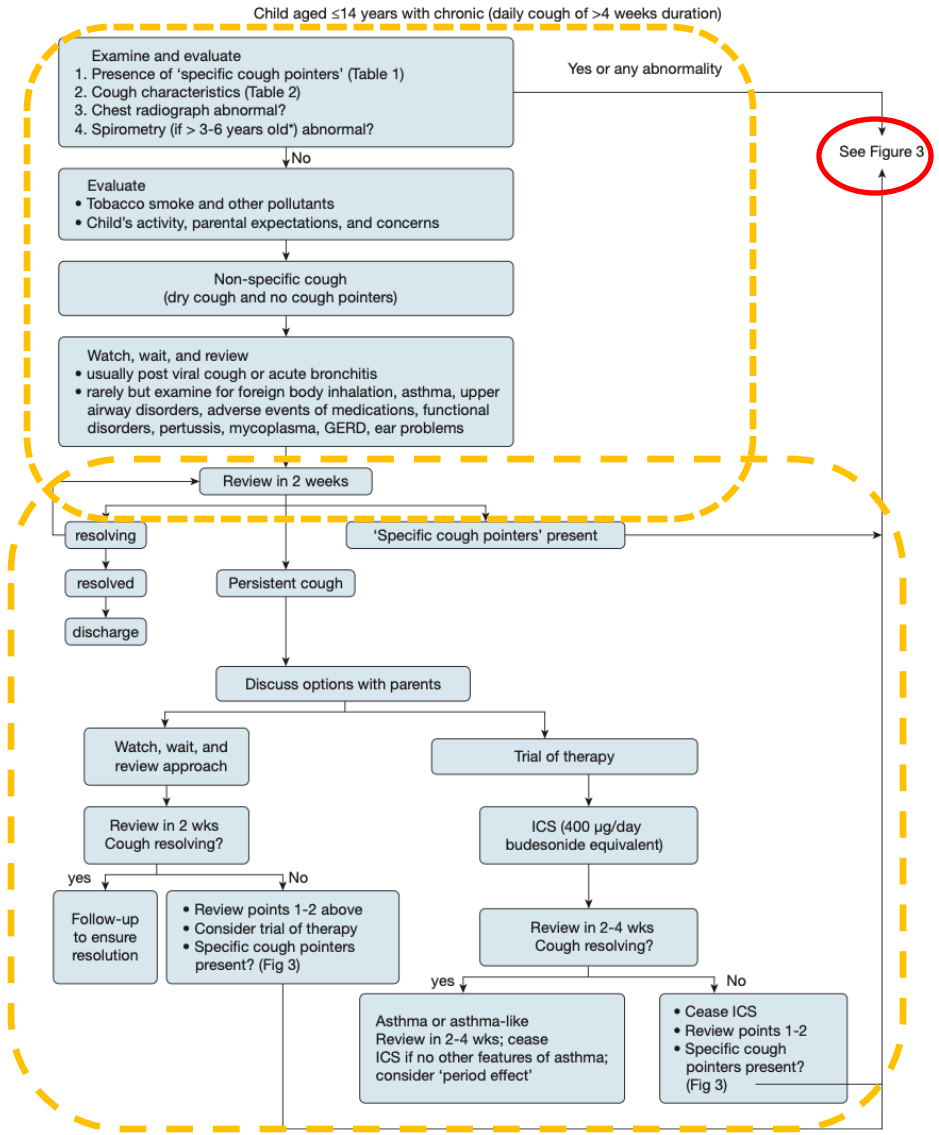


Figure 2 – *Approach to a child aged ≤ 14 years with chronic cough. Children aged > 14 years should be managed as outlined in adult guidelines but there is no good evidence when the age cutoff should be. The algorithm should be read with the accompanying text. *Spirometry can usually be reliably performed in children aged > 6 years and in some children > 3 years if trained pediatric personnel are present.[33] GERD = gastroesophageal reflux disease; ICS = inhaled corticosteroids.*

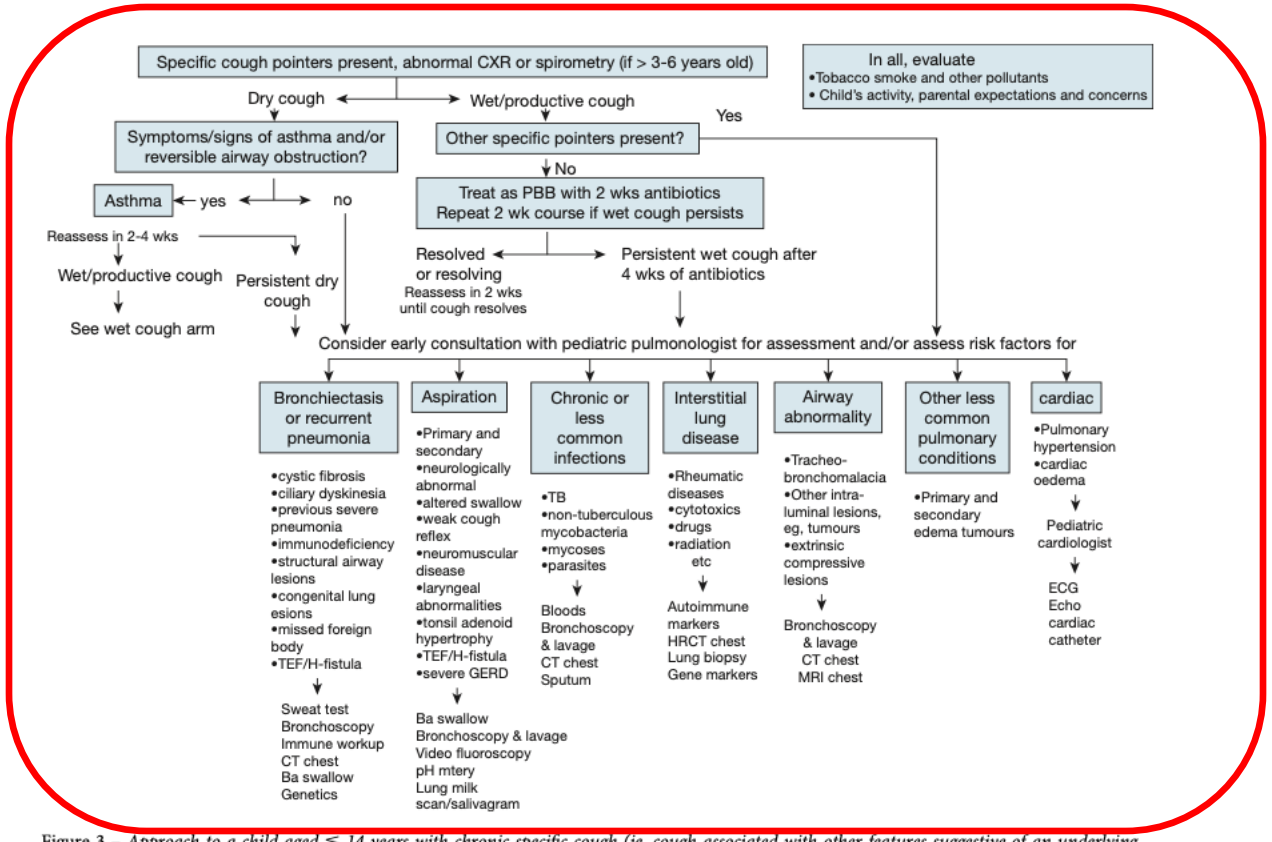


Figure 3 – *Approach to a child aged ≤ 14 years with chronic specific cough (ie, cough associated with other features suggestive of an underlying pulmonary and/or systemic abnormality). CXR = chest radiograph; HRCT = high-resolution CT; PBB = protracted bacterial bronchitis; TEF = tracheal-esophageal firstula. See Figure 2 legend for expansion of other abbreviation.*

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Child with Chronic Cough (daily cough > 4wks)

Examine and evaluate
1. Presence of specific cough pointers (Table 1)
2. Cough characteristics (Table 2)
3. Chest radiograph abnormal?
4. Spirometry (if > 3-6 years old*) abnormal?

Yes → Specific Cough

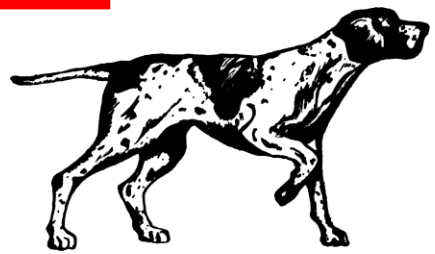
No

Evaluate
- Tobacco smoke and other pollutants
- Child's activity, parental expectations, and concerns

Non-specific cough
(dry cough and no cough pointers)

Watch, wait, and review
- usually post viral cough or acute bronchitis
- rarely but examine for foreign body inhalation, asthma, upper airway disorders, adverse events of medications, functional disorders, pertussis, mycoplasma, GERD, ear problems

Review in 2 weeks



Point 1

TABLE 1 Pointers to Presence of Specific Cough[a]

Abnormality	Examples of etiology
Symptoms or signs	
* Auscultatory findings	Wheeze–see below Crepitations–any airway lesions (from secretions) or parenchyma disease such as interstitial disease
Cardiac abnormalities	Associated airway abnormalities, cardiac failure, arrhythmia
Chest pain	Arrhythmia, asthma
Choked	Foreign body inhalation
* Dyspnea or tachypnea	Any pulmonary airway or parenchyma disease
Chest wall deformity	Any pulmonary airway or parenchyma disease
Digital clubbing	Suppurative lung disease
* Daily wet/productive cough	Protracted bacterial bronchitis, suppurative lung disease, recurrent aspiration, atypical infections, TB, diffuse panbronchiolitis
* Exertional dyspnea	Any airway or parenchymal disease
Facial pain/purulent nasal discharge	Chronic sinusitis (protracted bacterial bronchitis), primary ciliary dyskinesia
* Feeding difficulties	Any serious systemic including pulmonary illness, aspiration
Growth failure	Any serious systemic including pulmonary illness such as cystic fibrosis
* Hoarse voice/stridor	Laryngeal cleft/problems, airway abnormalities
Hemoptysis	Suppurative lung disease, vascular abnormalities
* Hypoxia/cyanosis	Any airway or parenchyma disease, cardiac disease
Neurodevelopmental abnormality	Aspiration lung disease
Recurrent pneumonia	Immunodeficiency, atypical infections, suppurative lung disease, congenital lung abnormalities, trachea-esophageal H-type fistulas
Recurrent infections	Immunodeficiency
Previous history of chronic lung or esophageal disease (eg, neonatal lung disease, esophageal atresia)	Multiple causes (eg, second H-type fistula, bronchiectasis, aspiration, asthma)
* Wheeze–monophonic	Large airway obstruction (eg, from foreign body aspiration, malacia and/or stenosis, vascular rings, lymphadenopathy, and mediastinal tumors) TB should be considered in selected settings (eg, high prevalence or HIV)
* Wheeze–polyphonic	Asthma, bronchiolitis obliterans, bronchiolitis
Tests	
Chest radiograph (other than peribronchial changes) or spirometry abnormality	Any cardiopulmonary disease

[a]As the causes of chronic cough encompasses the entire spectrum of pediatric pulmonology and extrapulmonary diseases, this list outlines the more common symptoms and signs and is not exhaustive.

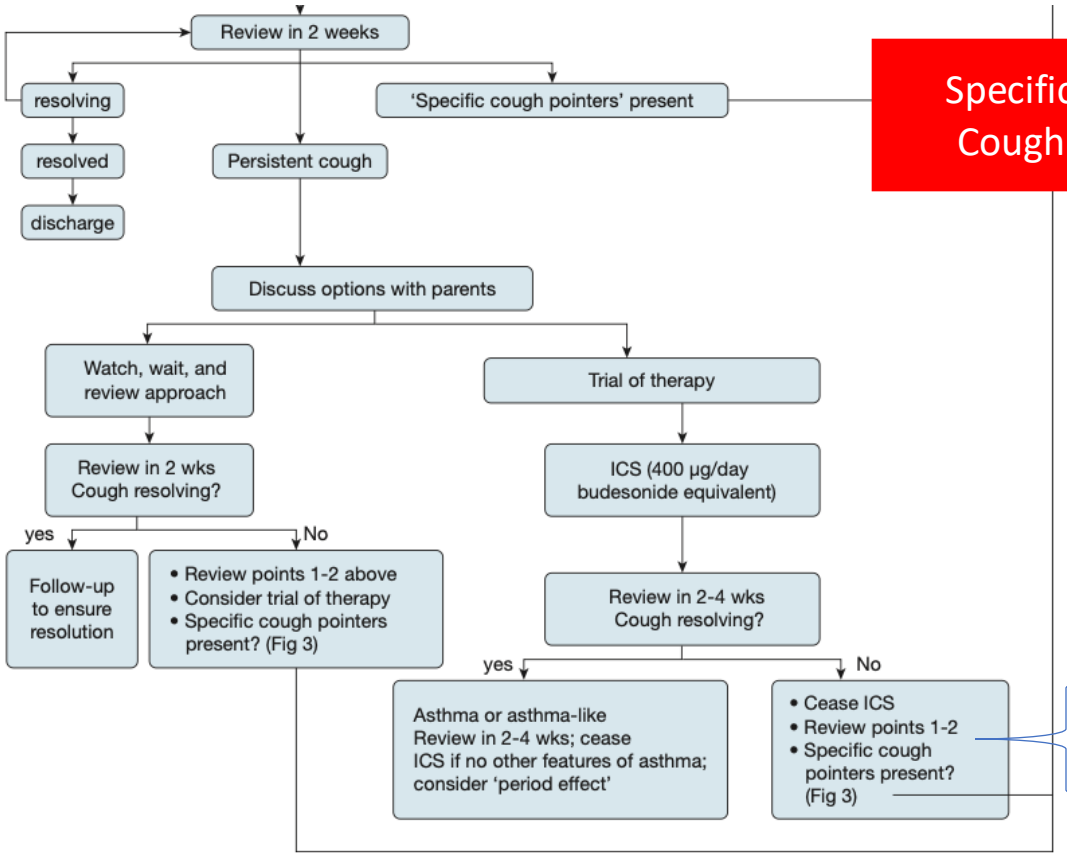
Point 2

TABLE 2 Classical Recognizable Cough in Children

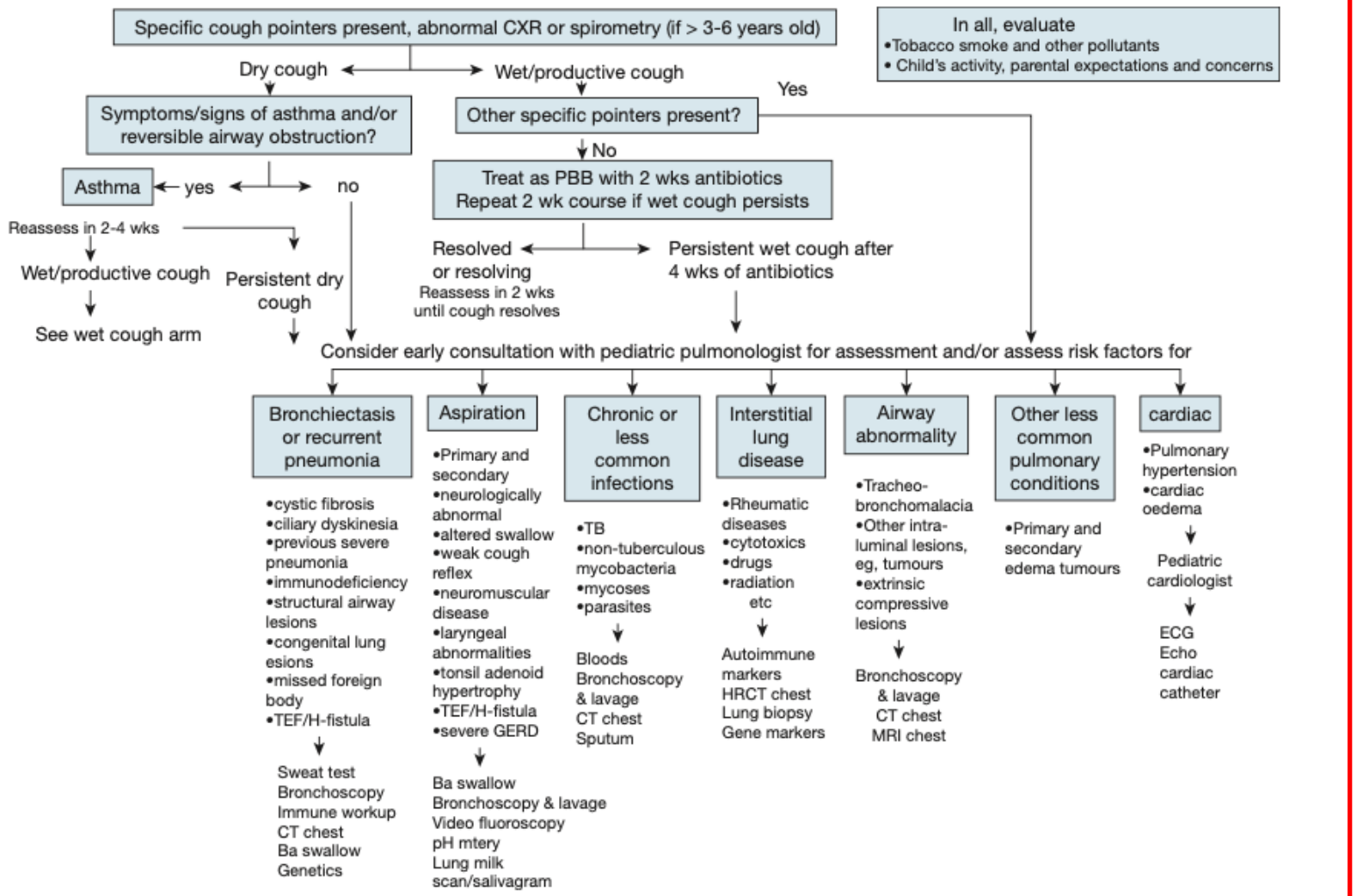
Cough Characteristic	Suggested Underlying Etiology or Contributing Factor
* Barking or brassy cough	Croup,[34] tracheomalacia,[35] habit cough[36]
Cough productive of casts	Plastic bronchitis[37]
Honking	Psychogenic[38]
* Paroxysmal (with/without whoop)	Pertussis and parapertussis[39,40]
Staccato	Chlamydia in infants[41]

https://www.youtube.com/watch?v=FXnWgwGMcJk

Sometimes, the saga continues…



1. Cough Pointers?
2. Cough Characteristic?



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Persisting cough (>4wks) with signs suggesting a given cause:

- Possible Asthma (+wheeze/low FEV1/reversible)
- Possible PBB (Wet/productive cough, normal CXR, no other pointers)
- Pointers indicative of an etiology

Key point: <u>Interventions linked to known or suspected cause</u>

Lack of response: consider extending for another course or alternative diagnosis

Follow-up or consultation should link to expected outcome/timeframe and/or need for invasive testing

Physician and Parental Expectations

- Recognize burdens of chronic cough: Concern, medical care, and impaired quality of life
- Establish reasonable expectations around expected time to resolution and treatment options
  - Use condition-specific teaching resources (non-specific resources are ignored)
  - Pay attention to parent concerns
  - In non-specific cough, recognize and share low value of many common treatments; avoid this trap

TABLE 3] Summary of Therapies Used for Non-specific Cough as Reported in Literature Based on Controlled Trials

Therapy	Time to Response[a]	Level of Evidence	Data Limitation and Considerations
Anti-histamines			Adverse events (especially with H1 antagonist)
Acute cough	1 wk	Systematic review (with OTC medications[193])	Non-beneficial from 3 RCTs in children
Chronic cough	2 wk	Systematic review[194]	Non-beneficial in systematic review.[194] Single small study showed benefit by 2 wk of treating allergic cough in children with pollen allergy with cetirizine[195]
Anti-microbials (for chronic wet/productive cough)	2 wk	Systematic reviews and meta-analysis[73]	Some may require 4 wks[73]
Asthma type therapy			
Cromones	2 wk	Systematic review[196]	Single open trial only[197]
Anti-cholinergics	4 wk	Systematic review,[198] single case series[199]	No trials in children. Case series unclear
Inhaled corticosteroids	2-4 wks	RCTs,[45,46] systematic review[141]	Small benefit if any, adverse event
Oral corticosteroids	Not relevant	No RCTs	No RCTs, adverse events[200]
Beta-2-agonist			Adverse events[47]
Acute cough	Not relevant	Systematic review[201]	Non-beneficial
Chronic cough		Systematic review,[140] RCT[46]	Non-beneficial
Theophylline	1-2 wk	Observational studies[202-204] Systematic review[205]	No RCTs, adverse events
Leukotriene receptor antagonist		Systematic review[142]	No trials in children
GERD therapy			
Motility agents	Not relevant	Single controlled trial[206]	No benefit, adverse events, systematic review on metoclopramide[207] showed no benefit for GER but cough was not an outcome measure
Acid suppression	Not relevant	Systematic reviews[5-7]	Adverse events
Food thickening or anti-reflux formula	1 wk	Systematic review,[5] RCTs[208,209]	Inconclusive data; one reported increase in cough[208] and a second reduction[209]
Head positioning	Not relevant	Systematic review[207]	No benefit, systematic showed no benefit for GER and cough was not an outcome measure[210]
Fundoplication		No data	No RCT, adverse events
Herbal anti-tussive therapy		No data	No RCTs
Nasal therapy			
Nasal steroids	1-2 wk	RCT[156]	Mainly adults and older children (> 12 y) in RCT, beneficial when combined with antibiotics for sinusitis[211,212]
Other nasal sprays		No data	No RCT, adverse events
Over the counter			Adverse events[214,215]
Acute cough	Not relevant	Systematic review[11,193]	Honey maybe beneficial, other OTC medications were non-beneficial
Chronic cough		Systematic review for codeine[213]	No studies
Physical therapies steam, vapor, rubs		No data	No RCTs, adverse events eg, burns

No data = no pediatric data.
GER = GI gastroesophageal reflux; OTC = over-the-counter; RCT = randomized controlled trial.
[a]Time to response = expected reduction in cough severity if treatment is effective, as reported by trialists.


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