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# Developmental origins of asthma

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# Disclosures

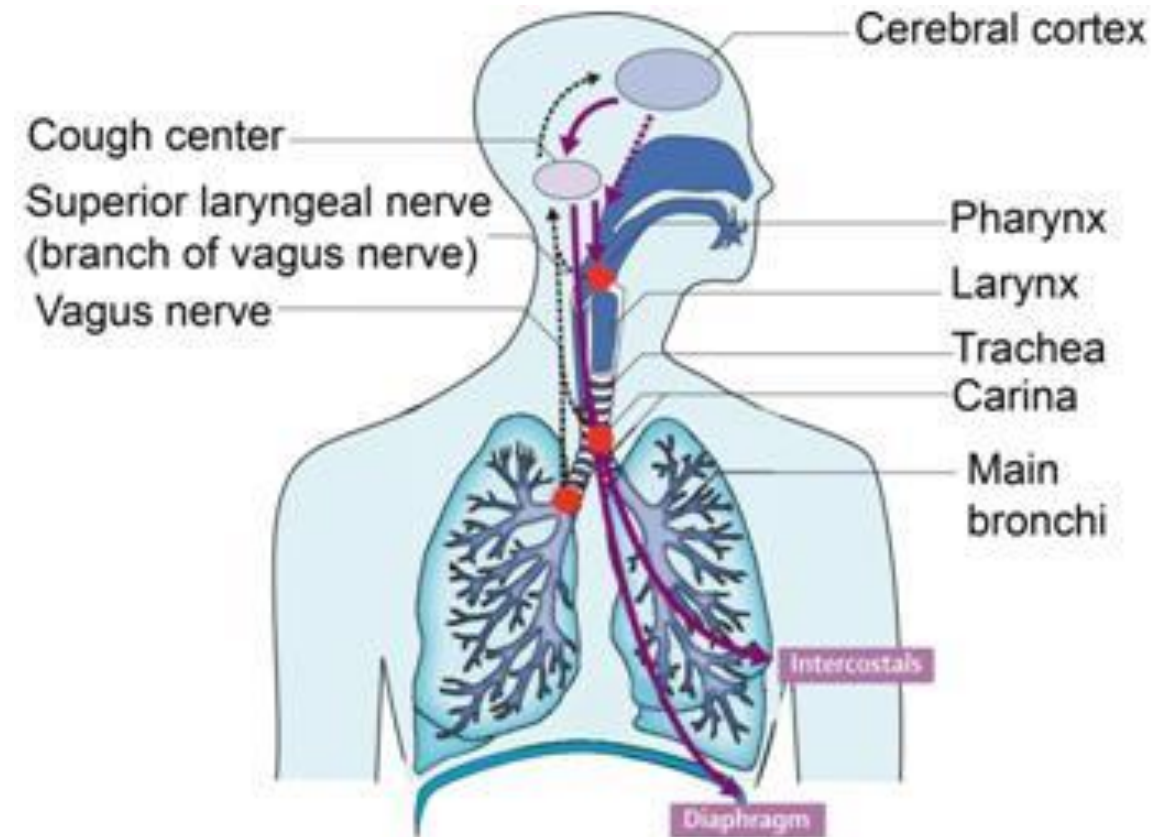
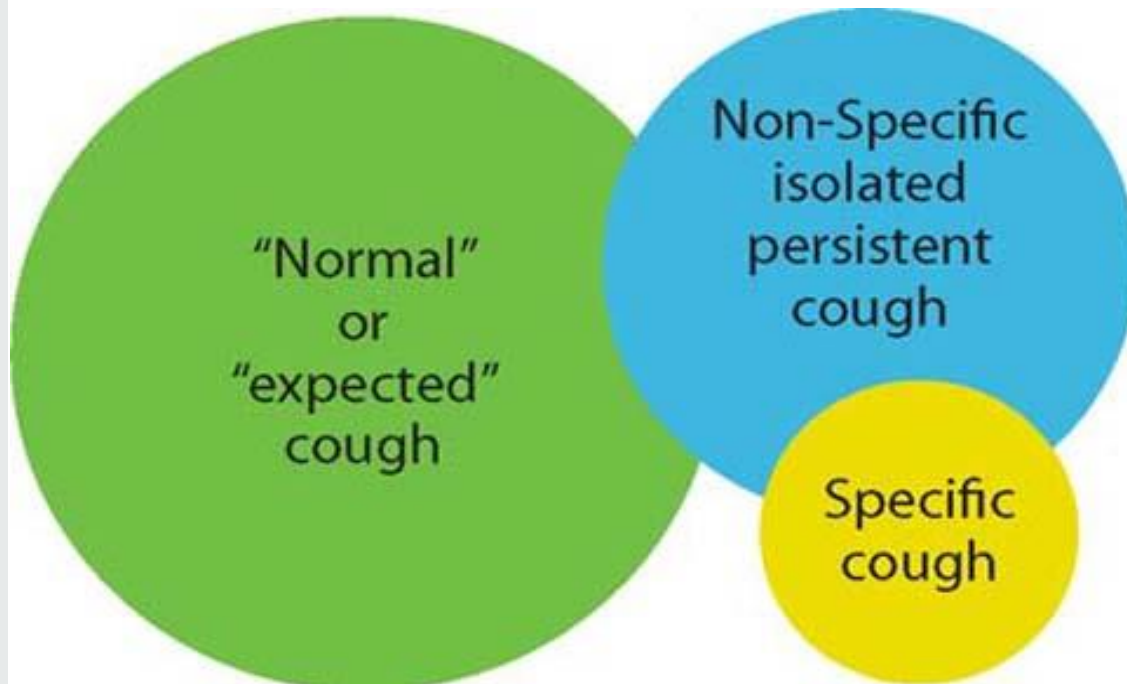
I have nothing to disclose

# Goals

1. Know what the clean hygiene hypothesis is and how microbes play a role in asthma development  
Understand the genetics of asthma development
2. Be familiar with what birth cohort studies have taught us about asthma's origins
3. Know what the asthma predictive index is and how to use it

# Definitions


- Chronic cough
  - CHEST: daily cough for more than 4 weeks in children  $\leq 14$  years of age
  - The British Thoracic Society: daily cough past 8 weeks (subacute is 4-8 weeks)
- Pediatrics are not small adults



<https://learn.pediatrics.ubc.ca/body-systems/respiratory-system/approach-to-a-child-with-a-cough/>

# Etiology

- Protracted bacterial bronchitis
- Asthma
- Post infectious cough
- Tracheobronchomalacia
- Bronchiectasis
- Habit cough
- Interstitial lung disease
- Pulmonary fibrosis
- Cystic fibrosis
- Aspiration
- GERD
- Primary Ciliary Dyskinesia
- Infectious: tuberculosis, mycoplasma, pertussis, Chlamydia, cocci, parasitic infections, etc.
- Congenital lung lesions
- Obstructive sleep apnea
- Compression from vasculature, tumor, lymphadenopathy
- Recurrent croup
- Bronchiolitis obliterans
- Allergic bronchopulmonary dysplasia
- Cardiac conditions
- Upper airway cough syndrome (postnasal drip cough)
- Immunodeficiency
- Surfactant deficiency
- Rheumatological causes
- Pulmonary hypertension
- Pulmonary edema
- Foreign body
- Tonsillar and adenoid hypertrophy

Type of cough	Diagnostic category
Dry	Post-infectious Airway inflammation Tic and somatic syndrome Extra-pulmonary Other specific diseases (e.g., tumors) Upper airway associations
Wet 	Airway infection Airway aspiration Airway anomaly Upper airway associations Other specific diseases

<https://doi.org/10.3389/fped.2022.850912>

# Recommended work up for all patients

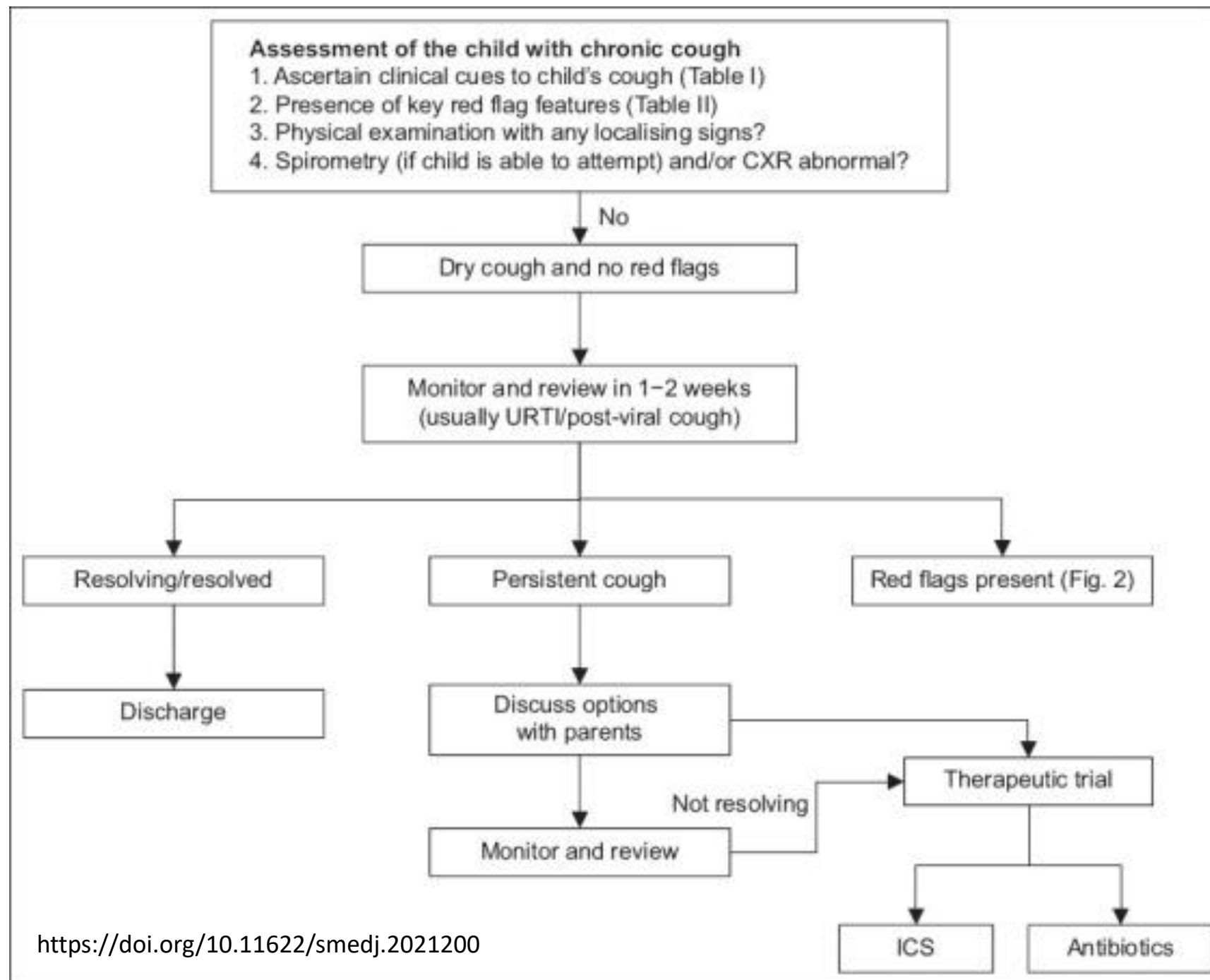
- Thorough history and exam
- Evaluate for airway pollutants such as tobacco smoke
- Chest Xray
- Spirometry with pre and post  $\beta$ 2 agonist

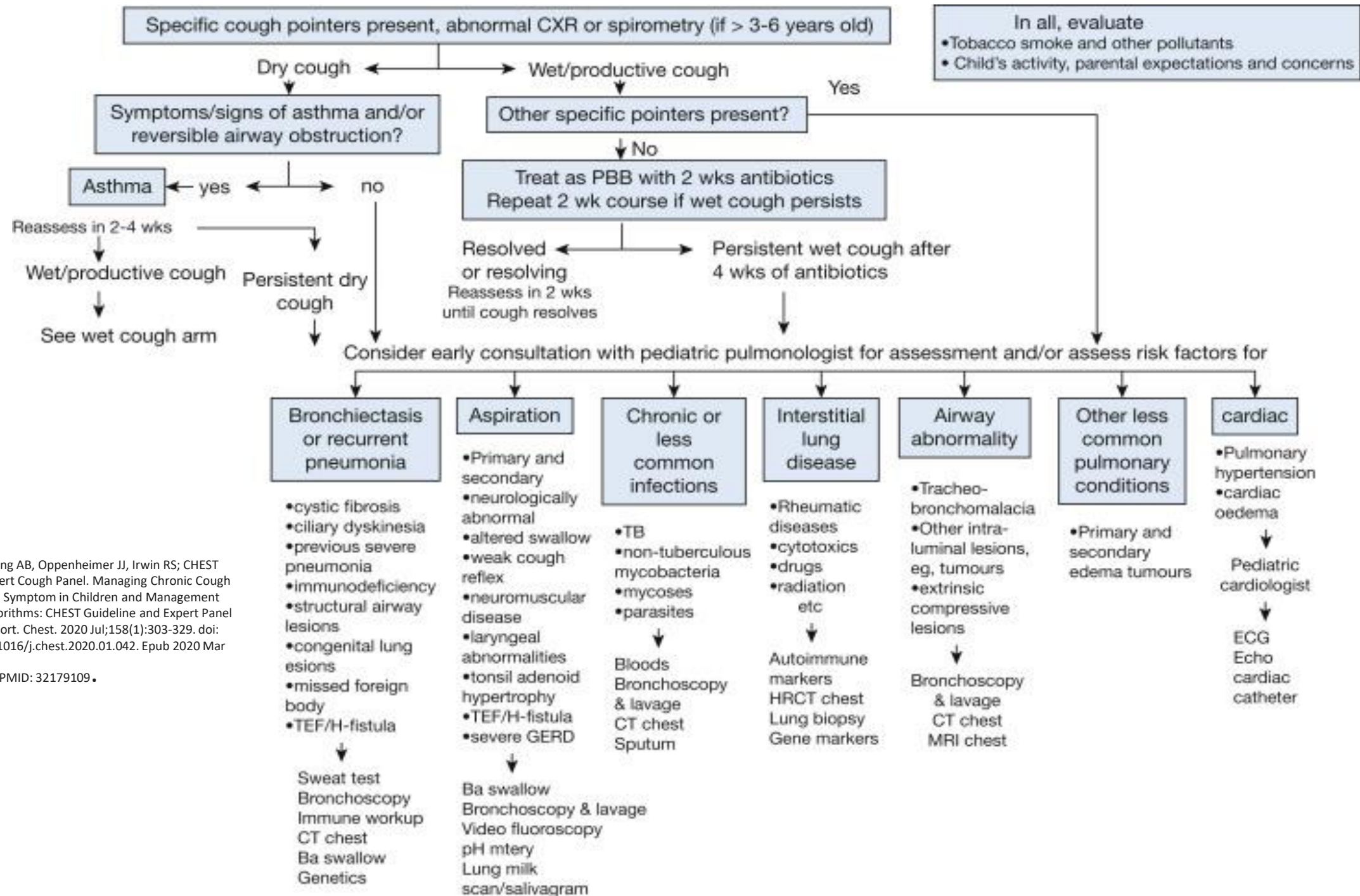
Key red flags	Possible aetiology
<b>History</b>	
Chest pain	Arrhythmia, asthma, pleuritic, functional
Choking	Foreign body inhalation
Dyspnoea or tachypnoea	Compromised lung function, or any chronic lung or cardiac disease
Daily wet or productive cough	Protracted bacterial bronchitis, suppurative lung disease, recurrent aspiration, atypical infections, TB
Exertional dyspnoea	Any airway or parenchymal disease
Facial pain/purulent nasal discharge	Chronic sinusitis, ciliary dyskinesia
Feeding difficulties/irritability and arching after feeds	Any serious systemic or pulmonary illness, aspiration lung disease
Hoarse voice/stridor	Laryngeal cleft/problems, airway abnormalities
Haemoptysis	Suppurative lung disease, vascular abnormalities
Recurrent infections	Immunodeficiency
Previous history of chronic lung or oesophageal disease (e.g. neonatal lung disease, oesophageal atresia)	Consider complications (e.g. H-type tracheoesophageal fistula, bronchiectasis, aspiration, asthma)
<b>Physical examination</b>	
Auscultatory findings	<ul style="list-style-type: none"> <li>• Wheeze: asthma, bronchitis, bronchiolitis obliterans, foreign body aspiration, airway malacia or stenosis, vascular rings, lymphadenopathy, mediastinal tumours; TB</li> <li>• Crepitations: any airway disease, parenchymal damage from interstitial lung disease</li> </ul>
Deformity of chest wall	Any chronic lung disease
Digital clubbing	Suppurative lung disease
Growth failure	Any serious systemic or pulmonary illness
Hypoxia or cyanosis	Any airway or parenchymal disease, cardiac disease
Neurodevelopmental abnormality	Aspiration lung disease

TB: tuberculosis

doi: 10.11622/smedj.2021200.







Chang AB, Oppenheimer JJ, Irwin RS; CHEST Expert Cough Panel. Managing Chronic Cough as a Symptom in Children and Management Algorithms: CHEST Guideline and Expert Panel Report. Chest. 2020 Jul;158(1):303-329. doi: 10.1016/j.chest.2020.01.042. Epub 2020 Mar

14. PMID: 32179109.

# Diagnostic work up to consider

- Sputum culture and/or cough swab
- Bronchoscopy
- CT scan
- FeNO or sputum eosinophils or eosinophilic blood count
- Sinus CT
- Echo
- Esophageal pH or multichannel intraluminal impedance monitoring
- Skin prick
- AFB testing
- Pertussis PCR and/or serologies

# Post Infectious Cough

- Post viral cough is the most common cause of chronic cough
  - Children <4 years have on average 5.0 to 7.95 respiratory illnesses per year
  - 10 % of children with respiratory illnesses have cough for >20 to 25 days
  - In one study 20% of children coughed > 28 days and a new or serious illness was found in 36 of the 117 children reviewed
- Pertussis
  - Paroxysmal cough
  - Median duration of cough in unvaccinated children <6 years 52 to 61 days
  - Median duration of cough in vaccinated children <6 years 29 to 39 days
- Mycoplasma
- Chlamydia

# Over the Counter

- Always ask families about herbs and supplements they using and/or have tried
- Honey may be useful in acute cough
- Antihistamines helpfulness is debatable with many studies showing no effect and some studies looking at allergic rhinitis showing usefulness
- OTC cough medicine had little to no effect on acute cough and are associated with adverse event



# CASES



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# Case

2-year-old present for chronic cough. The cough has been occurring for 3 months. He has been kicked out of multiple day cares due to the cough. The cough occurs day and night. There are no noticeable cough triggers. The cough keeps the whole family up many nights in a row. The child has no choking or trouble with feeds. No bottle in bed but mom does breast feed him overnight and co sleeps. The PCP has tried albuterol and Montelukast and Flovent 220 mcg 2 puffs BID. Mom does not think any of these things has helped.

PHx: born at term no complications, recently diagnosed with asthma

FHx: no family history of asthma but mom did have an inhaler as a small child

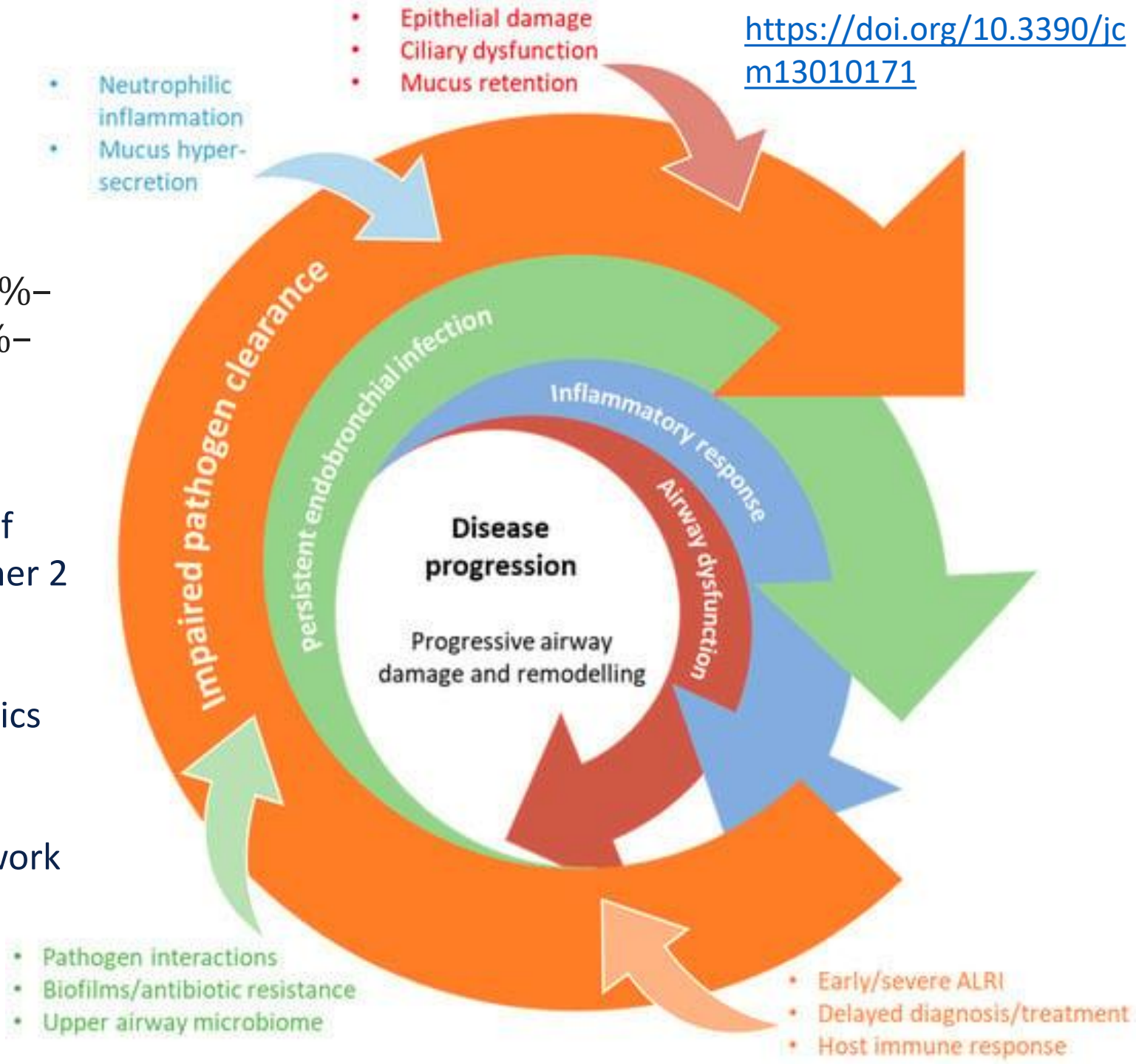
SHx: “in” daycare, no pets, lives with mom dad and siblings



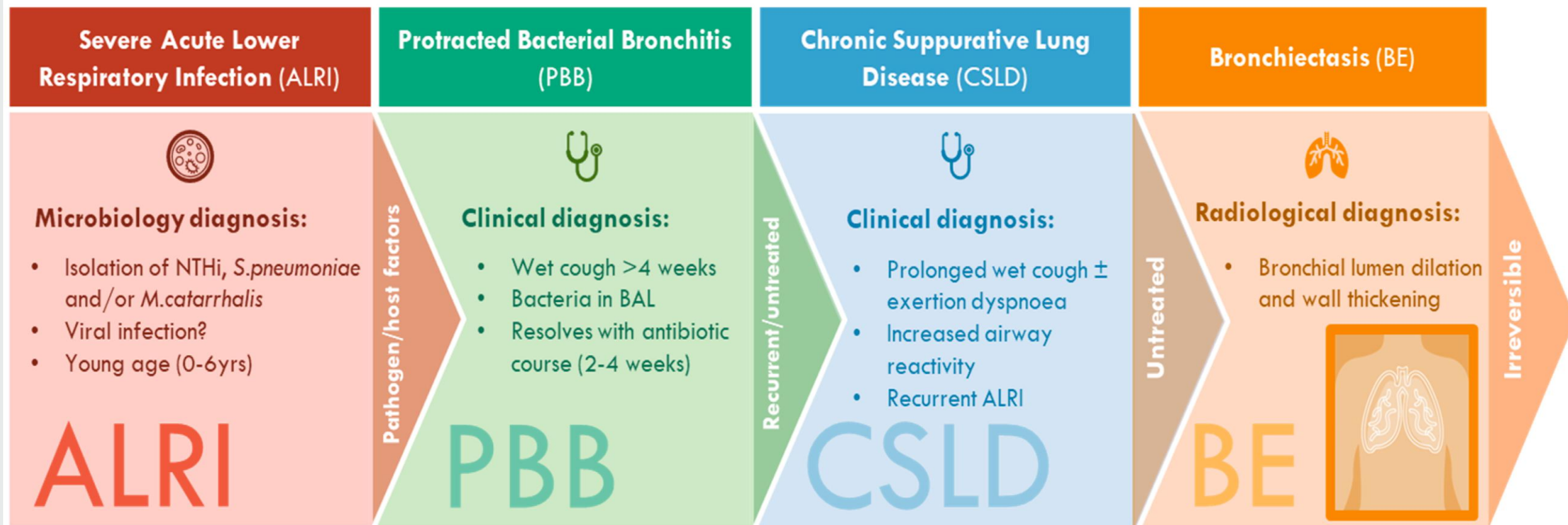
# Protracted Bacterial Bronchitis

- Wet/productive cough
- *Haemophilus influenzae* (28%–58%), *Streptococcus pneumoniae* (13%–58%) and *Moraxella catarrhalis* (17%–59%)
- BAL or sputum of  $>10^4$  cfu/ml is microbiologically PBB
- Treatment with 2 weeks of antibiotics if cough improves but persists give another 2 weeks
- If wet cough persists after 4 weeks of antibiotics further evaluation/diagnostics should be considered
- Can recur
- If having frequent recurrence further work up is indicating
- May need prophylactic antibiotics

<https://doi.org/10.3390/jcm13010171>







<https://doi.org/10.3390/jcm13010171>

# Case

5-year-old male with chronic cough. Cough has been going on forever per mom. The cough is wet sounding. There is no SOB with the cough. The PCP has tried albuterol and Flovent with no relief.

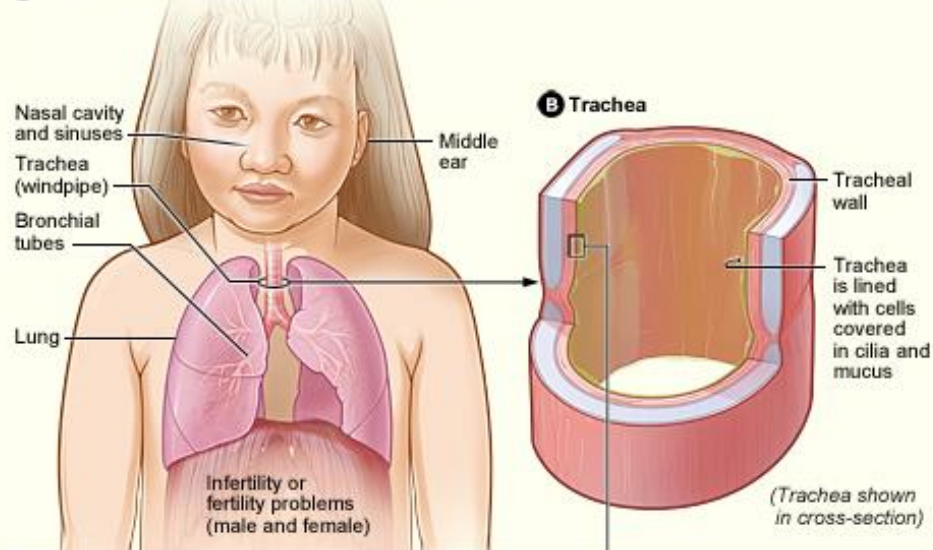
PMHx: no hospitalizations.

FHx: no history of asthma

SHx: lives with mom only dad is not in the picture, mom smokes outside and sometimes vapes inside, no pets, no siblings

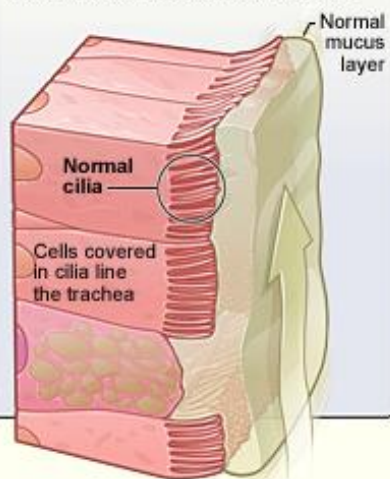
# Primary ciliary Dyskinesia

**A** Organs affected by primary ciliary dyskinesia



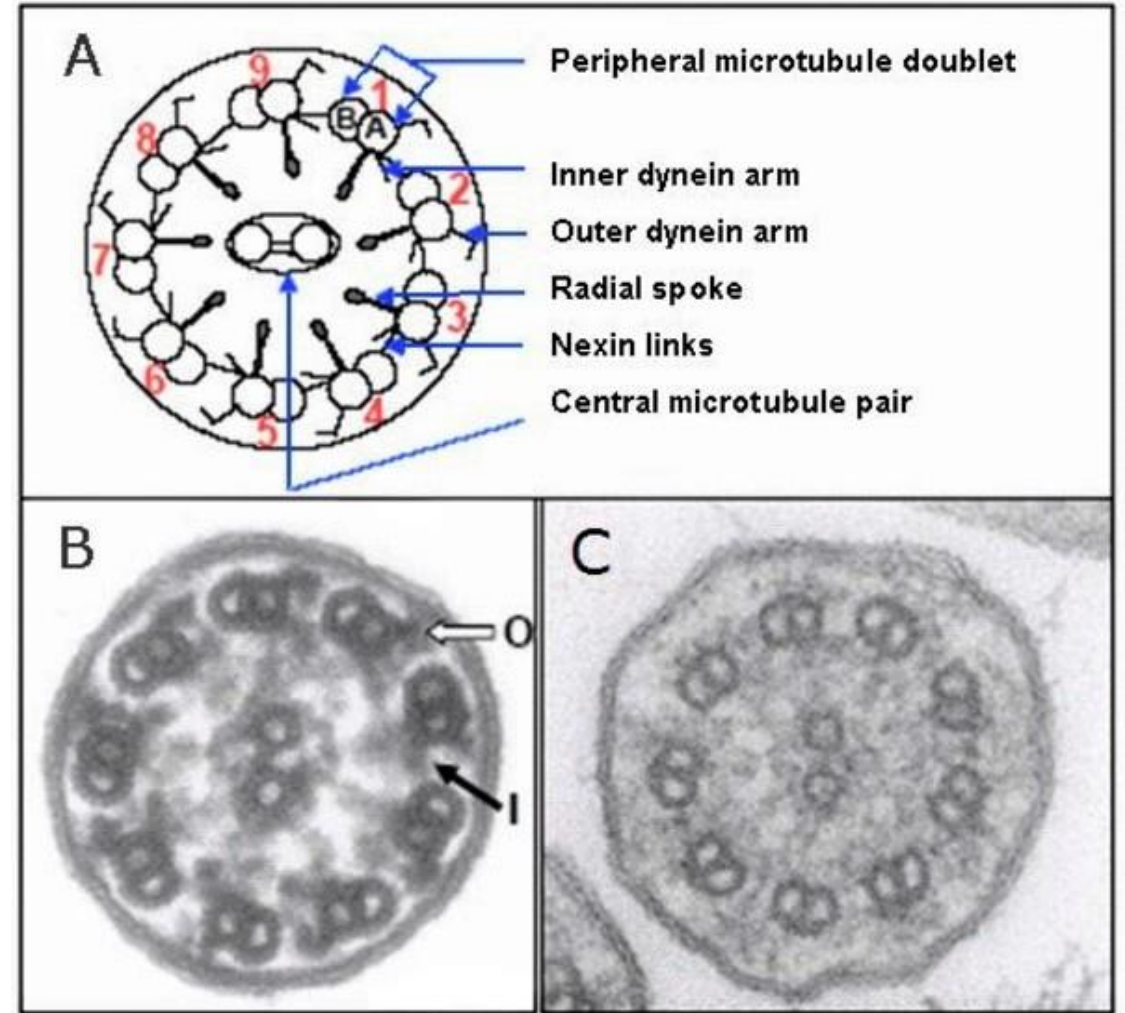
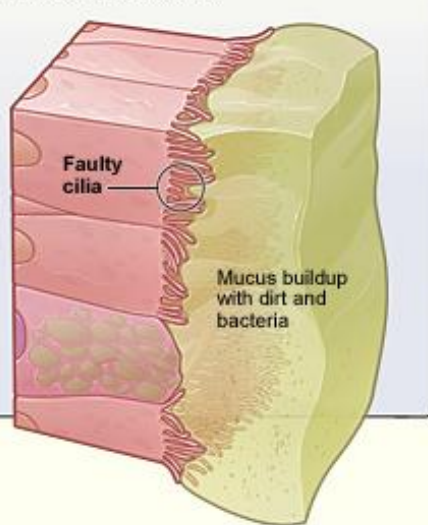
**C** Normal cilia lining trachea

Cilia move together in wave-like motions to transport mucus toward the mouth. The mucus contains dirt and bacteria.



**D** Faulty cilia lining trachea

Cilia are deformed and do not move together, causing a buildup of mucus. The mucus contains dirt and bacteria.



<https://www.ncbi.nlm.nih.gov/books/NBK1122/figure/pcd.F1/>

# Case

2-year-old male hospitalized for bronchiolitis history of 2 previous hospitalizations for bronchiolitis. This hospitalization has an albuterol response so was started on scheduled albuterol and prednisone.

PMHx: no eczema, no allergies, born a term no complications

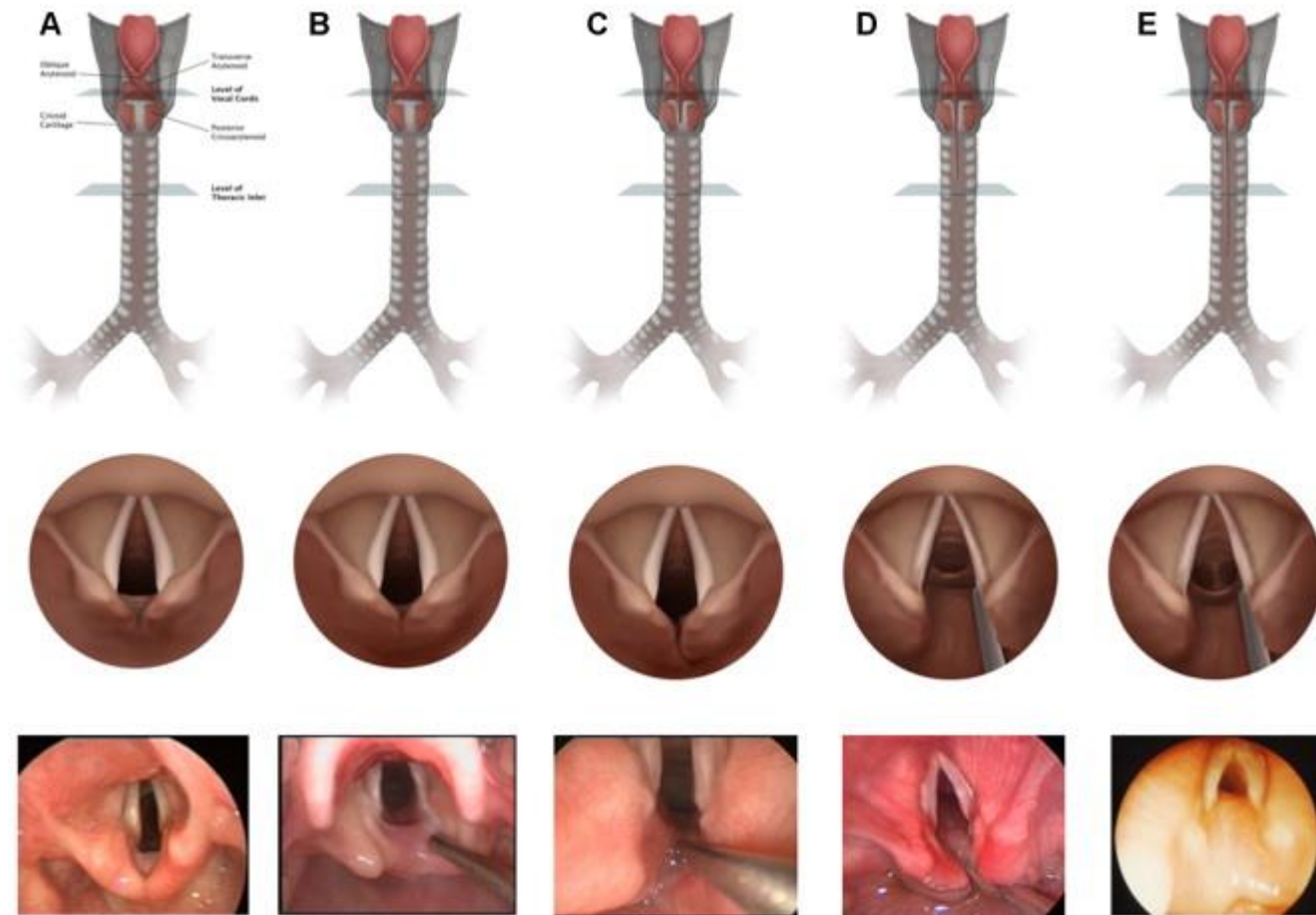
FHx: Dad had asthma as a child

SHx: lives with mom, dad, and siblings, 2 dogs at home, no smoke exposure



# Aspiration

- NO BOTTLES OR SIPPY CUPS IN BED OR JUST BEFORE BED
- Anatomical reasons can be present
- Multidisciplinary clinics are useful: GI, ENT, Pulmonary, Feeding specialist
- Work up: Swallow studies are sensitive but not specific, bronchoscopy for lipid index or lipid laden macrophages, chest imaging



[https://i0.wp.com/entokey.com/wp-content/uploads/2021/02/10-1055-b-006-163744\\_c052\\_f001.jpg?w=960](https://i0.wp.com/entokey.com/wp-content/uploads/2021/02/10-1055-b-006-163744_c052_f001.jpg?w=960)

# Case

3-year-old here with chronic cough. Per mom this cough all started 3-4 months ago and is intermittent. The PCP has prescribed albuterol and fluticasone which have not helped. He has had some antibiotics which did not help. He has had no troubles with coughs or colds prior to this starting 3-4 months ago.

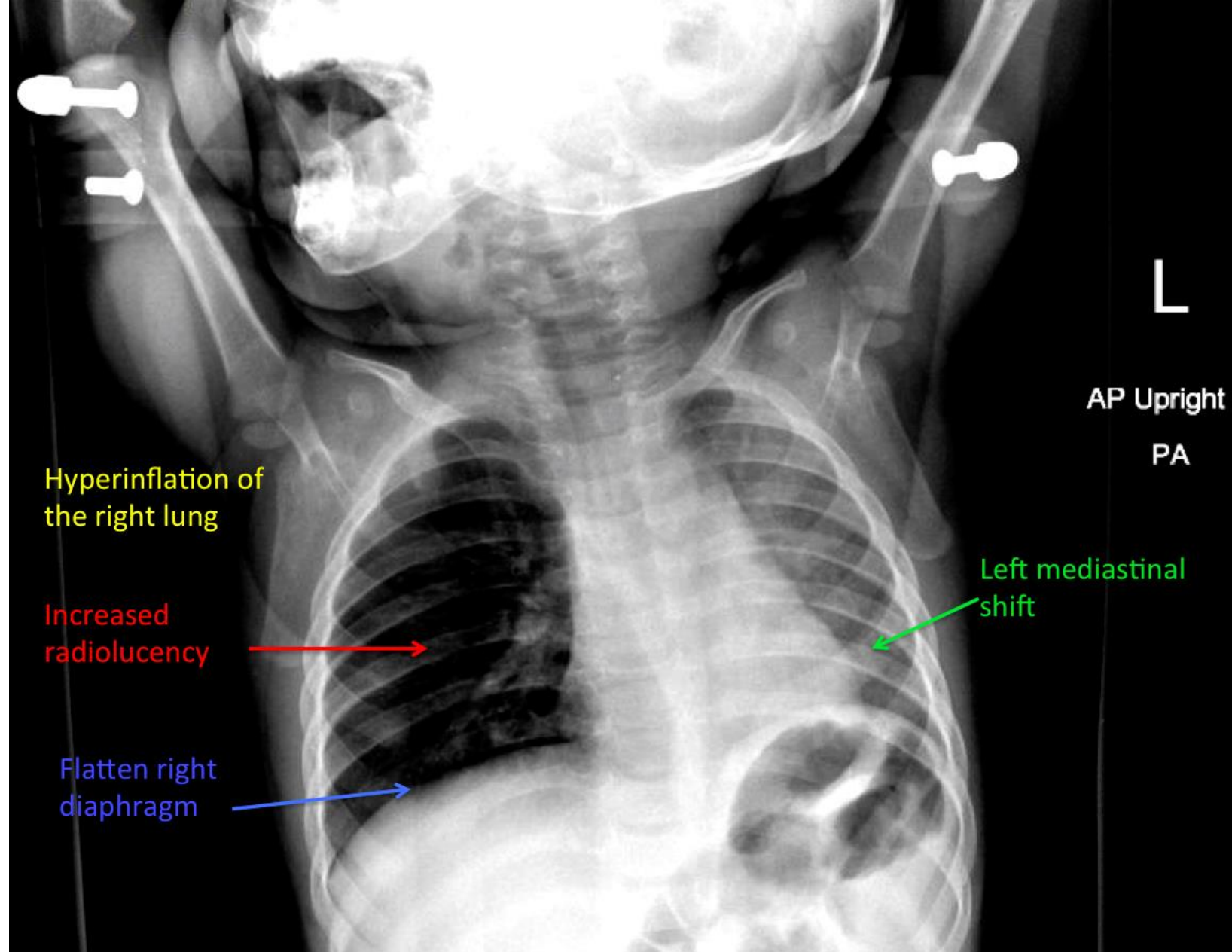
PMHx: born full term no complications, no previous hospitalizations

FHx: no asthma

SHx: has a turtle, no history of asthma

# Foreign Bodies

- Need a high index of suspicion
- Considered a medical emergency
- Symptoms can be variable based on location of foreign body
- Inspiratory and expiratory or right and left lateral decubitus chest xrays can be helpful if foreign body is causing ball valve effect
- Removal is with bronchoscopy



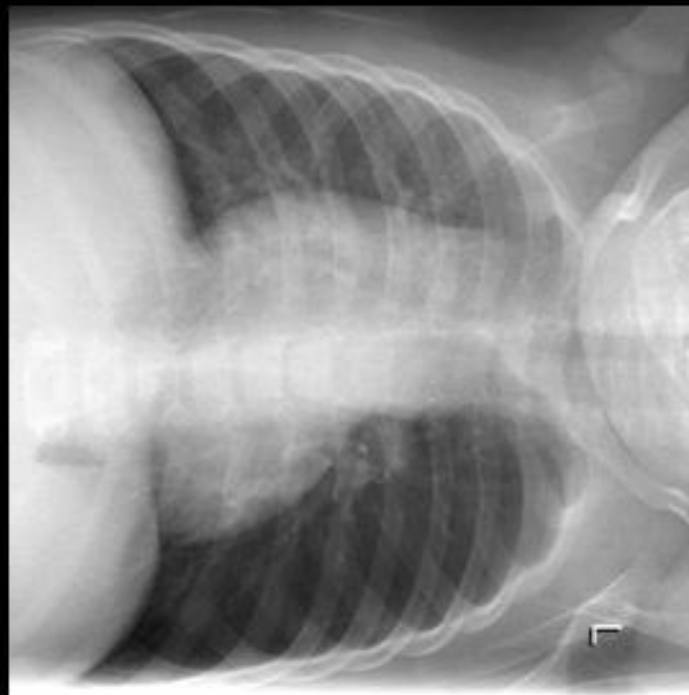
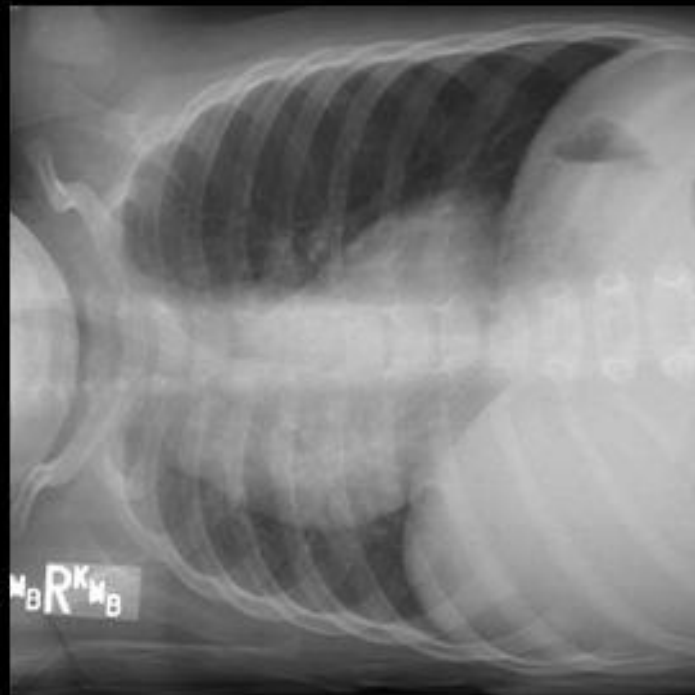
<https://jetem.org/wp-content/uploads/2018/07/Pediatric-Foreign-Body.-Chest-X-ray-Annotated.-JETem-2018.jpg>



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C.J.Lucaya





# Case

5-year-old with chronic cough. Has been treated with albuterol which may have helped per mom. Also given fluticasone HFA which did not help so mom stopped it.

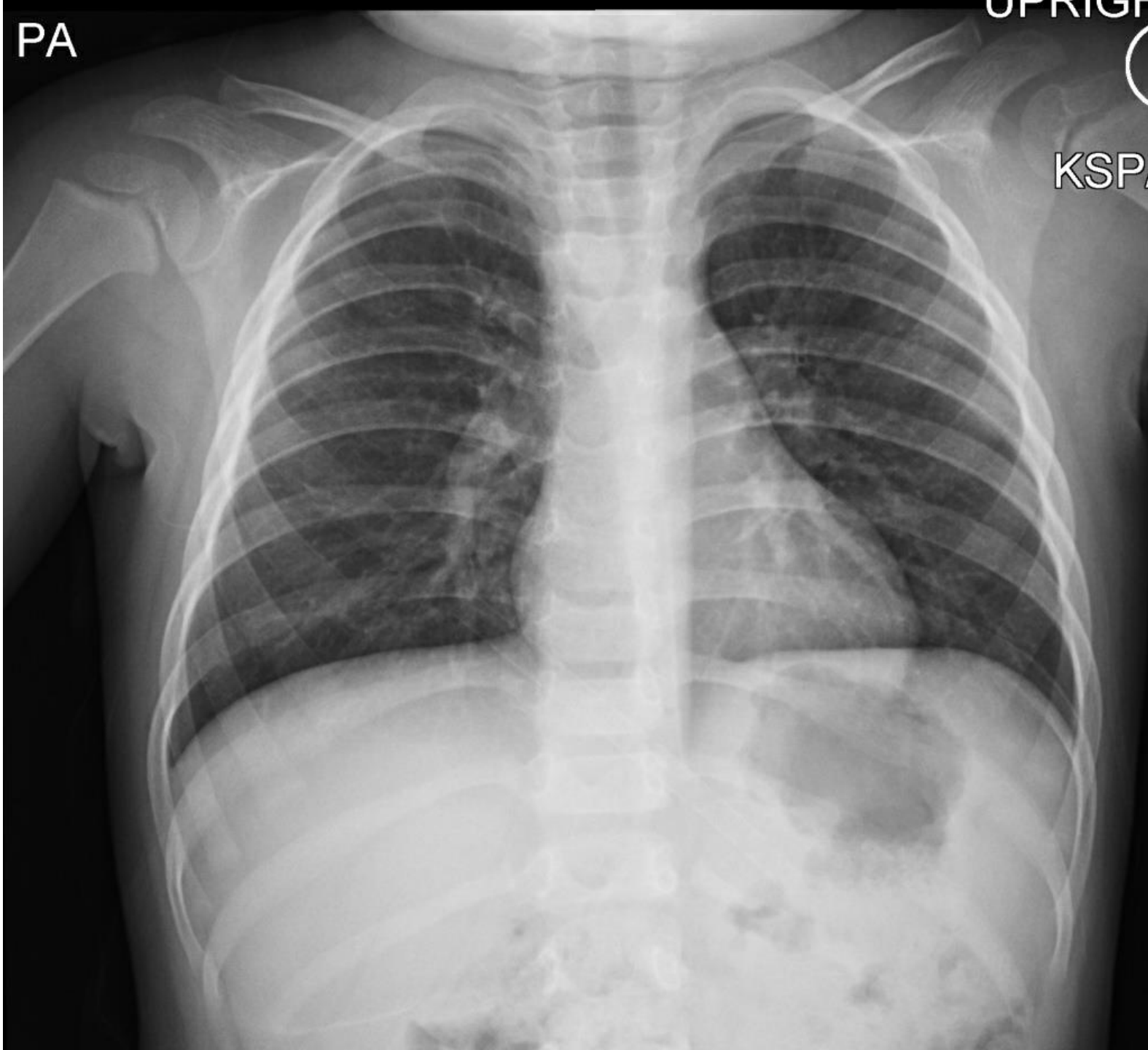
PMHx: history of right sided aortic arch reported on prenatal ultrasound, no hospitalization, born term, no NICU stay

FHx: none contributory

SHx: Lives with mom and dad, no pets, no tobacco exposure

PA

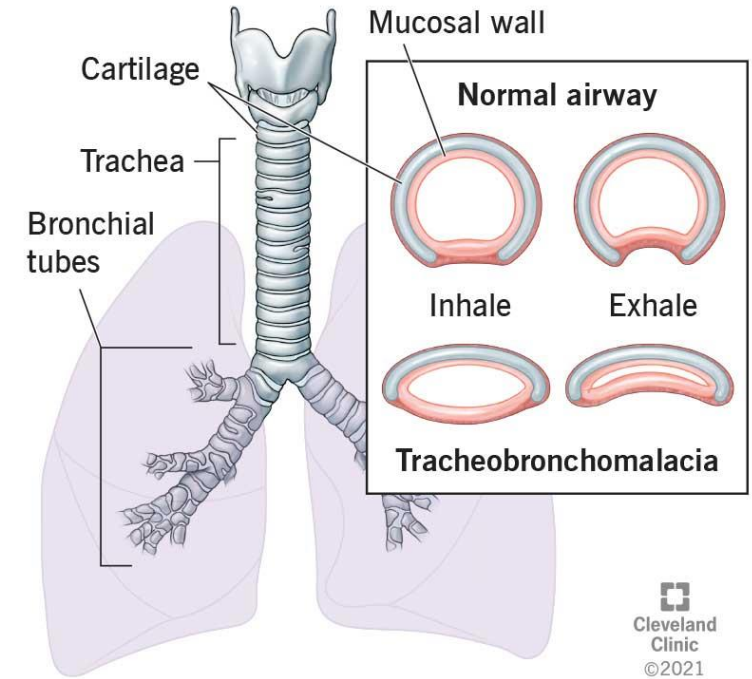
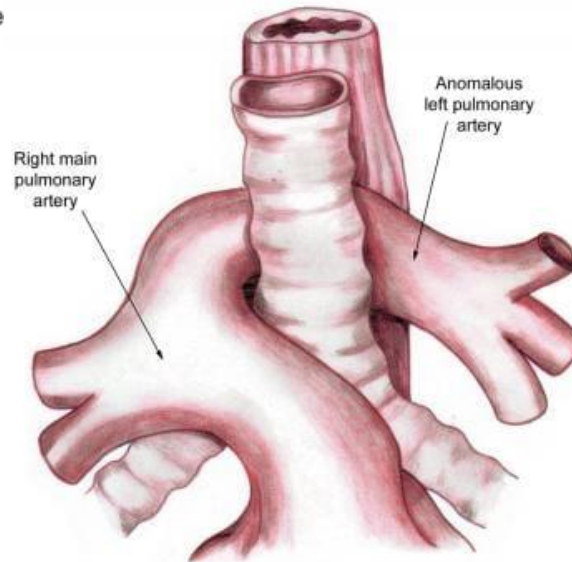
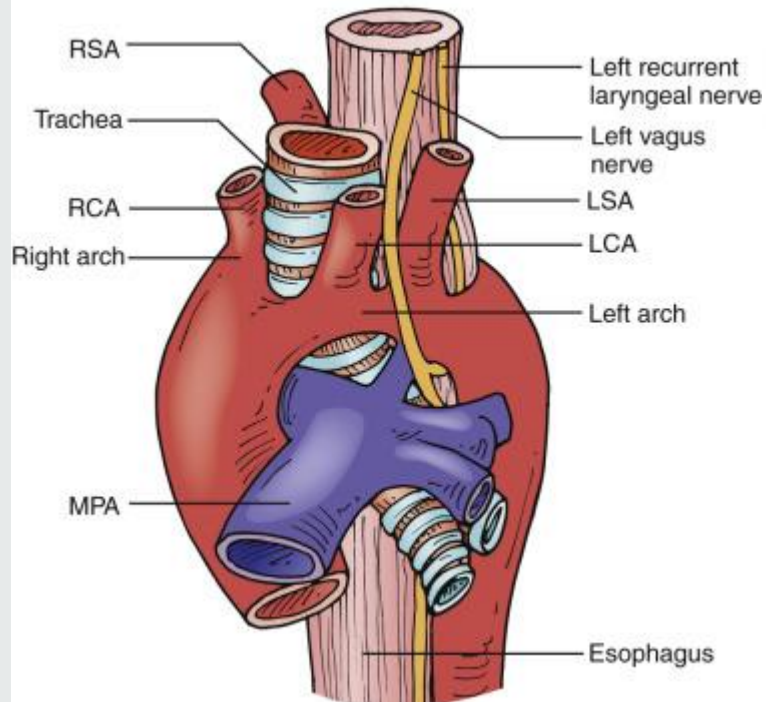
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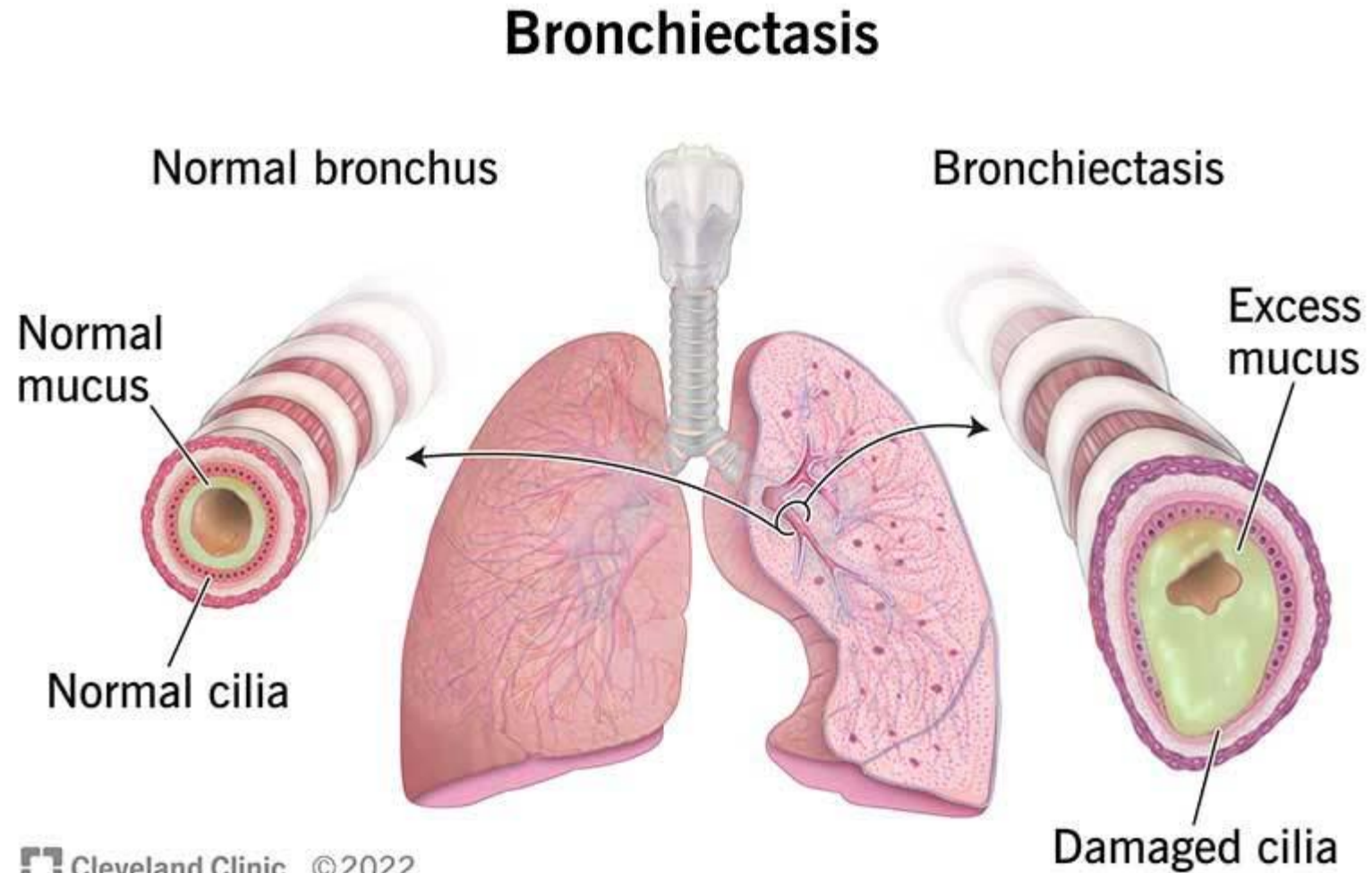
# Anatomical abnormalities

- Tracheobronchomalacia is often misdiagnosed
- Compression from vasculature, tumor, lymphadenopathy
- Bronchiectasis
- Impedes airway clearance

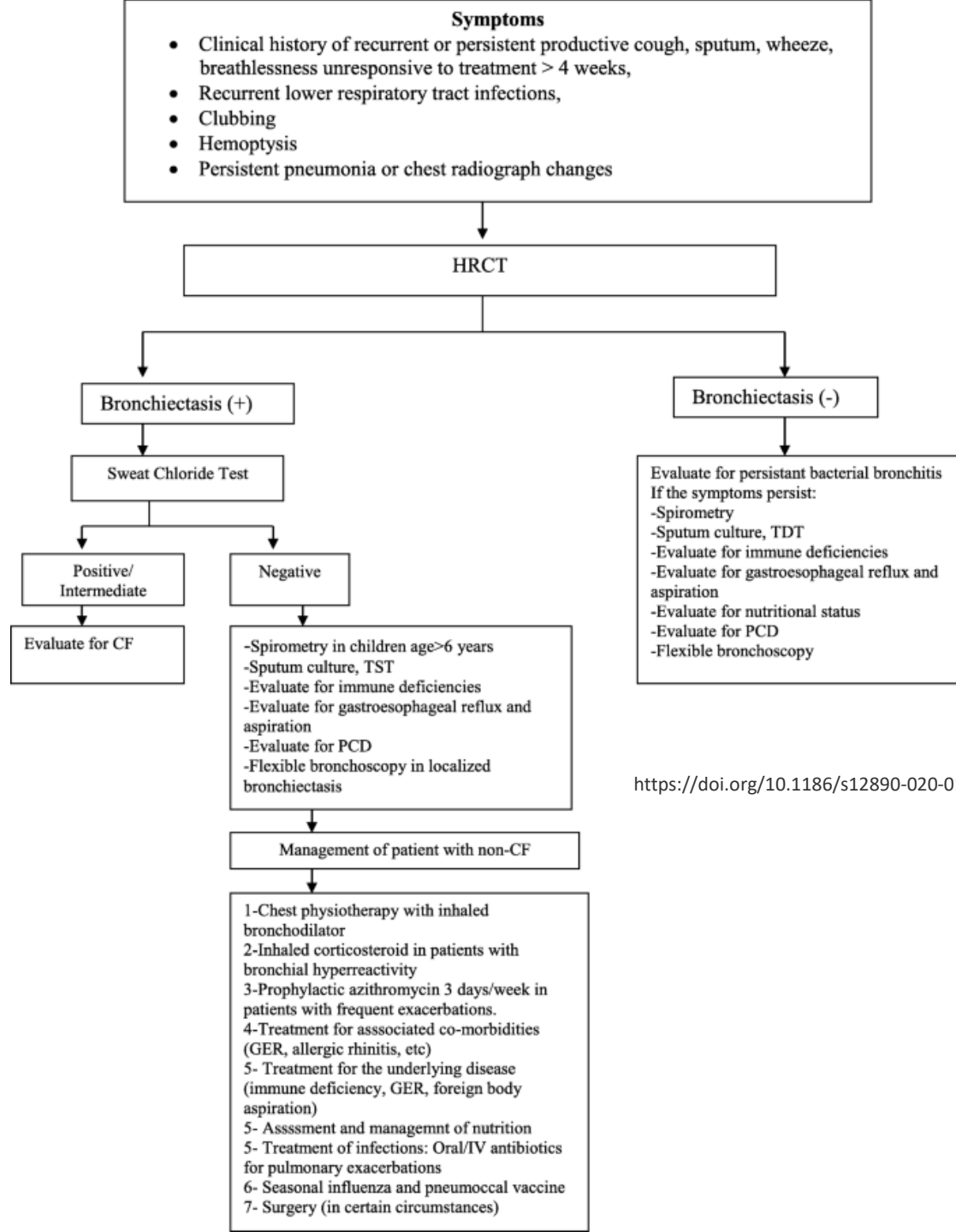


<https://my.clevelandclinic.org/-/scassets/images/org/health/articles/22061-tracheobronchomalacia-illustration>

# Bronchiectasis



# Bronchiectasis



<https://doi.org/10.1186/s12890-020-01214-7>

# Case

9-year-old female comes in for insistent cough for the past 1-2 months. She fell in the pool and had a “near” drowning event where she coughed out some pool water. Mom states that initially she had a wet cough for 1-2 days, but the cough changed in nature after that. Mom is very concerned that the Chlorine water damaged her lungs. The PCP has prescribed albuterol which did not help.

PMHx: healthy child, born full term no complications

FhX: no asthma

SHx: lives with mom dad and sibling, has no pets



# Habit/functional/psychogenic/somatic/tic cough

- Frequent nonproductive loud barking or honking cough
- Stops with sleep
- A respiratory illness or clinical reason for the cough is often an inciting factor
- Does not respond to medications such as albuterol or steroids
- Tic cough: core clinical features of tics that include suppressibility, distractibility, suggestibility, variability, and the presence of a premonitory sensation whether the cough is single or one of many tics
- Treatment: non-pharmacological trials of hypnosis or suggestion therapy or combinations of reassurance, counseling, or referral to a psychologist and/or psychiatrist

# Etiology

- Persistent bacterial bronchitis
- Asthma
- Post infectious cough
- Tracheobronchomalacia
- Bronchiectasis
- Foreign body
- Habit cough
- Interstitial lung disease
- Pulmonary fibrosis
- Cystic fibrosis
- Aspiration
- GERD
- Primary Ciliary Dyskinesia
- Infectious: tuberculosis, mycoplasma, pertussis, Chlamydia, cocci, parasitic infections, etc.
- Congenital lung lesions
- Obstructive sleep apnea
- Compression from vasculature, tumor, lymphadenopathy
- Recurrent croup
- Bronchiolitis obliterans
- Allergic bronchopulmonary dysplasia
- Cardiac conditions
- Upper airway cough syndrome (postnasal drip cough)
- Immunodeficiency
- Surfactant deficiency
- Rheumatological causes
- Pulmonary hypertension
- Pulmonary edema
- Tonsillar hypertrophy





# Thank you

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