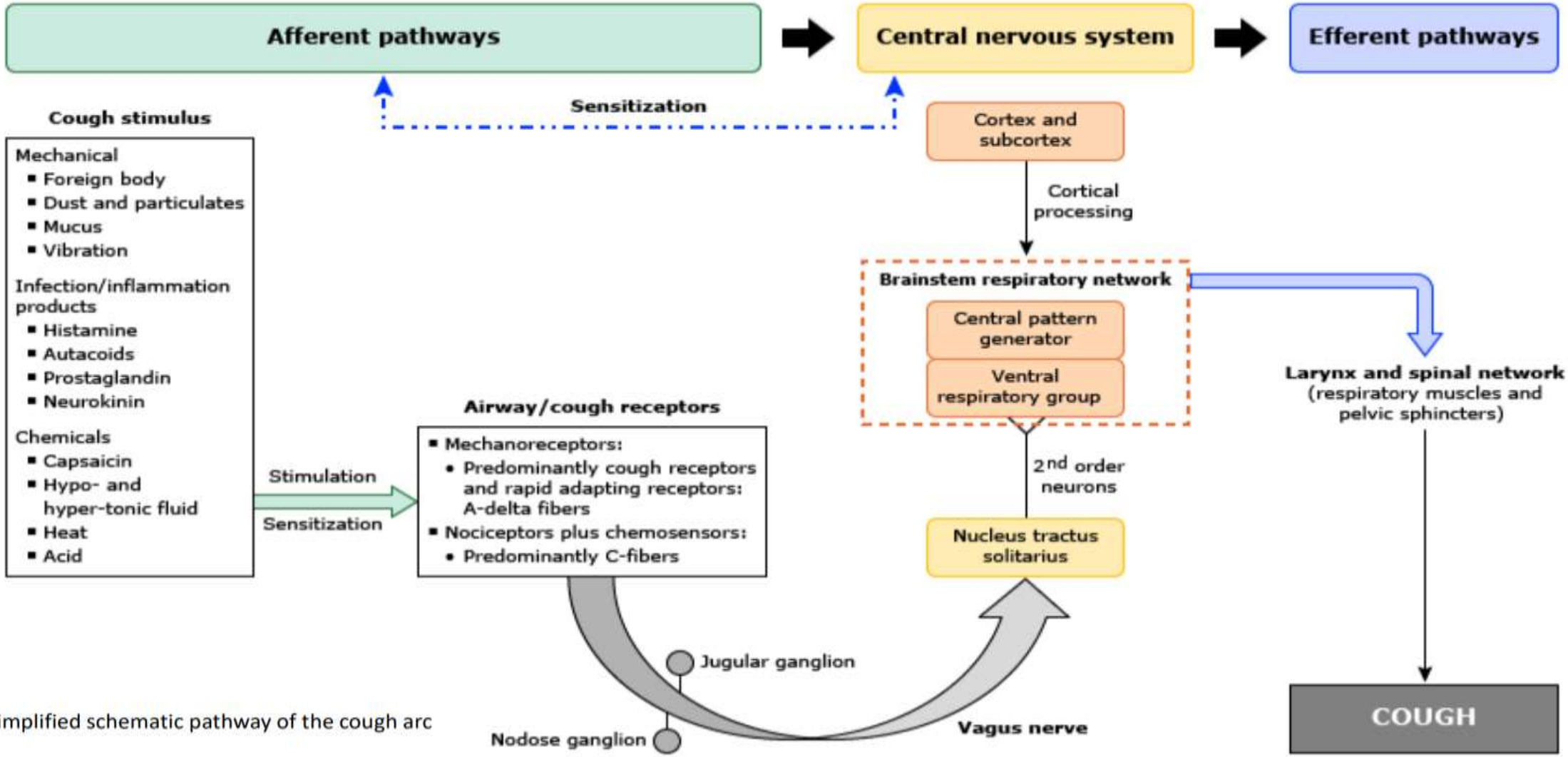
Approach to chronic cough

Dr. Samin Sharafian
Assistant professor of Allergy And Clinical Immunology
Shaheed Beheshti University Of Medical Sciences
Mofid Children's Hospital
Samin.sh2020@yahoo.com

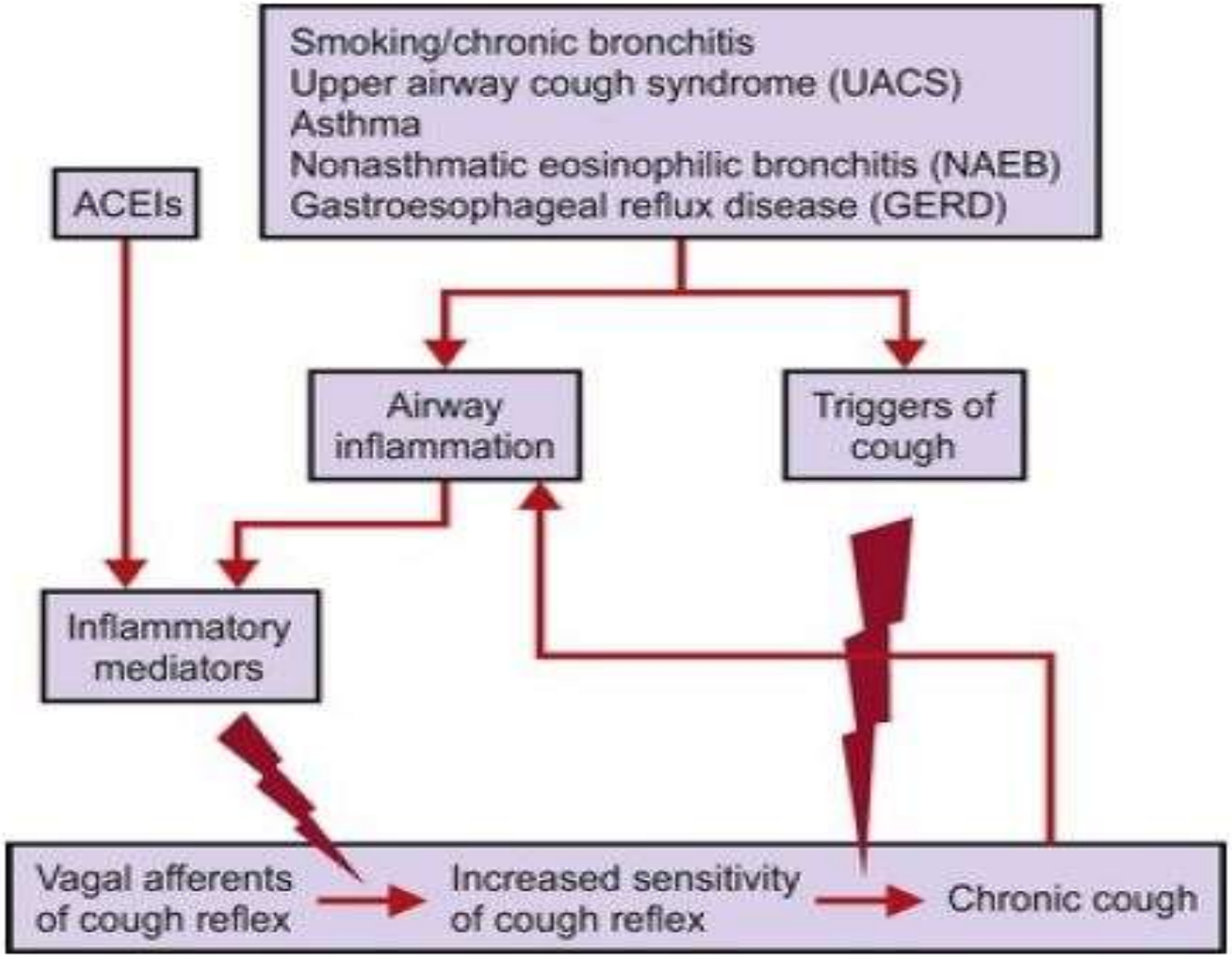
Introduction

- An effective cough is essential for maintaining respiratory health.
- Cough is the most common reason why patients acutely seek medica consult
- Cough as a symptom is sometimes trivialized by health professionals but is often distressing to parents irrespective of whether the cough is acute or chronic.
- In an outpatient pulmonary practice, evaluation and management of persistent cough can account for up to 40 percent of the practice volume

Normal cough mechanisms



Simplified schematic pathway of the cough arc



Definitions

- Acute cough :less than three weeks
- most commonly due to **an acute respiratory tract infection.**

- Other considerations include an acute exacerbation of underlying chronic pulmonary disease,
- pneumonia,
- pulmonary embolism.

- **subacute :** three to eight weeks
- **chronic more** than eight weeks
- "relentlessly progressive prolonged acute cough [>three weeks]…may warrant investigation before eight weeks“
- Patients who seek medical attention for chronic cough are more likely to be **female**.
- Women tend to cough more often and to have heightened cough reflex sensitivity compared to men

Case1

- A 14-month-old boy with cough since 3 months ago
- What do you ask his parents?

- Suddenly start
- Without URI symptoms
- Family history of asthma in his maternal aunt
- Salbutamol 2 puff q 6 hr for 3 months
- Unilateral Wheezing
- Decrease sound :unilateral
- CXR: NL

What is your diagnosis?

What do you do now?

Case 2

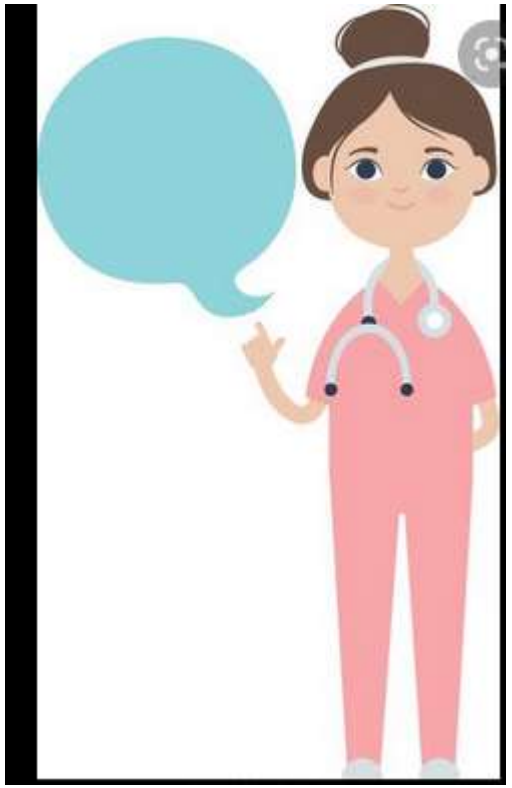
- A 2 –year-old girl with cough since early infancy
- Poor wait gain

  - What do you want to know?

- Diarrhea , 10 episodes a day
- Consanguine marriage
- 6 episodes of admission due to pneumonia
- Crackle
- clubbing

What do you do for patients ?

What is your diagnosis?



Case 3

- A 8-year-old boy with cough since 3 months ago
- Dry cough
- Nocturnal cough

What is important in history and physical exam?

- Family history : asthma in his uncle
- Dry skin
- Nasal stiffness and itching
- Exacerbate with exercise

What do you do for patients ?

What is your diagnosis?

Case 4

- A 13-year-old girl with cough since 2 years ago

- PMH:

✓Many admissions due to bacterial sinusitis and pneumonia since infancy

✓

History?

Physical exam?

- Consanguine parents
- Hypothyroidism
- Similar problem in her aunt
- Wt: Nl
- Clubbing
- No response to salbutamol

What do you do for patients ?

What is your diagnosis?

Epidemiology

persistent cough (>3 weeks duration), without colds

- children aged 5 to 11 and preschoolers 10 - 22 percent

Introduction

- Careful assessment of patients with chronic cough is important to identify any underlying disease
- **Etiologies** of chronic cough in children are **different** from those of adults and, thus, clinicians should use pediatric-specific cough guidelines.
- As an example, **gastroesophageal reflux** and **upper airway cough syndrome** (formerly known as postnasal drip syndrome) are thought to be common causes of chronic cough in **adults** but are controversial as common causes of chronic cough in children.

Etiologies of subacute and chronic cough in adults

✓The most common:

- **upper airway cough syndrome** (due to postnasal drip),
- asthma,
- gastroesophageal reflux post-infectious etiology angiotensin converting enzyme (ACE) inhibitors.

✓Other less common causes :

- non-asthmatic eosinophilic bronchitis,
- chronic bronchitis,
- bronchiectasis,
- neoplasm,
- foreign body or the pulmonary parenchyma (interstitial lung disease, lung abscess)

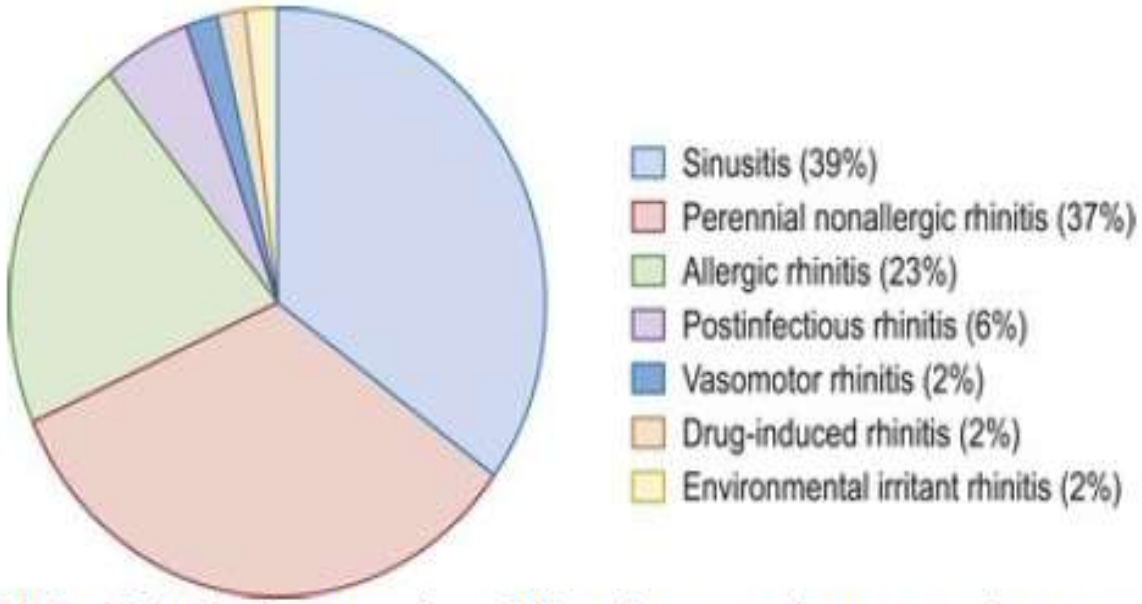


FIG. 60.3 Relative frequencies of disorders causing upper airway cough syndrome (UACS) in patients with chronic cough. Sinusitis, perennial nonallergic rhinitis, and allergic rhinitis account for a majority of the cases.[22] (Note that the percentages add up to more than 100% because in the data as reported,[22] some patients had multiple causes simultaneously contributing to UACS.)

Box 60.1

Causes of Chronic Cough in Adults

Intrathoracic Causes

Lungs and Airways

Asthma
Nonasthmatic eosinophilic bronchitis
Chronic bronchitis
Bronchiectasis
ACEIs
Sitagliptin
Inhaled medications
Chronic exposure to environmental and occupational irritants
Bronchogenic and metastatic carcinoma
Bronchial carcinoid
Foreign body or endobronchial suture
Broncholith
Infectious and noninfectious bronchiolitis
Chronic infectious pneumonias (e.g., bacterial, tuberculous, fungal,

parasitic)
Chronic infectious tracheobronchitis (as in tuberculosis or aspergillosis)
Chronic interstitial lung disease (e.g., sarcoidosis, HSP, IPF, asbestosis)
Pulmonary vasculitis (as in granulomatosis with polyangiitis)
Sjögren syndrome with xerotrachea
Relapsing polychondritis

Cardiovascular

Mitral stenosis
Left ventricular failure
Pulmonary thromboembolism
Enlarged left atrium
Vascular ring
Aberrant innominate artery
Aortic aneurysm
Pericardial stimulation by transvenous pacemaker

Pleura

Chronic effusion

Diaphragm

Transvenous pacemaker stimulation

Mediastinum

Neural tumors
Thymoma
Teratoma
Lymphoma
Metastatic lymphadenopathy
Intrathoracic goiter
Bronchogenic cyst

Head and Neck

Rhinitis and sinusitis
Nasal polyps
Rhinolith
Oropharyngeal dysphagia
Laryngeal disorders (e.g., vocal fold dysfunction, laryngomalacia)
Postviral vagal neuropathy
Recurrent aspiration
Elongated uvula
Chronically infected tonsils
Neurilemmoma of vagus nerve
Neuroma of internal laryngeal nerve
Ascending palatine artery aneurysm
Osteophytes of cervical spine
Mammomonogamus (*Syngamus*) *laryngeus* infection
Thyroiditis

Upper Gastrointestinal

Gastroesophageal reflux disease
Esophageal cyst or diverticulum
Tracheoesophageal fistula

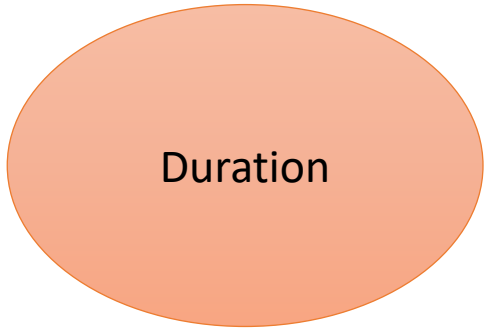
Central Nervous System

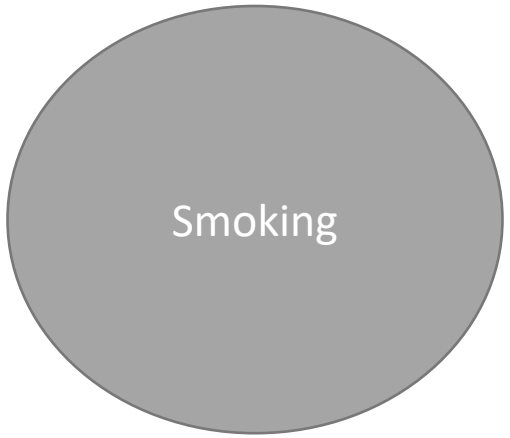
Somatic cough
Tic disorders
Gilles de la Tourette syndrome

Definitions and Common Causes of Cough in Adults and Children

Age Group	Type of Cough	Duration	Common Causes
Adults	Acute	<3 weeks	Common cold Exacerbation of lung disease (e.g., asthma) Acute environmental exposure Acute cardiopulmonary disease
	Subacute	3-8 weeks	Postinfectious cough Pertussis infection Exacerbation of underlying lung disease (e.g., asthma, COPD, bronchiectasis)
	Chronic	>8 weeks	Medications (ACEIs or sitagliptin) Smoking/chronic bronchitis Underlying lung disease UACS Asthma NAEB GERD
Children	Acute	≤4 weeks	Common cold Exacerbation of underlying lung disease Acute cardiopulmonary disease
	Chronic	>4 weeks	Asthma Protracted bacterial bronchitis Tracheobronchomalacia Chronic rhinosinusitis Recurrent aspiration GERD Underlying lung disease (e.g., bronchiectasis) Pulmonary infections (e.g., pertussis)

Diagnostic approach





key questions in evaluation and management of chronic cough

-Is there underlying chronic lung disease that requires further investigations and/or referral?

-Are therapies/medications indicated?

-Are there modifiable factors that exacerbate the cough, such as exposure to tobacco smoke?

-What is the psychosocial impact of the cough on the quality of life and function, and what are their expectations for treatment and outcomes?

Evaluation

- Targeted detailed history,
- Physical examination,
- Chest radiograph, and
- Spirometry (if the child is able) .

History

- Medications
- Social history and impact of cough
- Past medical history
- Neonatal history
- Previous hospitalizations and pulmonary disease
- Other medical problems
- Environmental exposures

Physical examination

General examination

Appearance	•**Poor growth** or thinness •**Dysmorphism, developmental delay**,
Skin	•**Eczema** – Suggests atopic disease. •**Other rashes** – Evidence of a recent rash raises the possibility of a triggering viral infection, or impetigo, more common in immune deficiency.
Head and neck	•Allergic "shiners," swollen nasal turbinates, nasal obstruction, nasal polyps, or allergic nasal crease – •Lymphadenopathy –immunodeficiency, malignancy, or chronic infection.
Ears	•Tympanic membrane scarring or otorrhea –primary ciliary dyskinesia. •Objects or disease in the ear canal –cough is triggered by the otogenic reflex
Mouth	•Hoarseness – Suggests aspiration or vocal cord dysfunction. •Tonsillar hypertrophy or pharyngeal cobblestoning –allergic disease. •High-arched or cleft palate –congenital anomalies. swallowing disorders or aspiration.

Heart	•Abnormal heart location – Dextrocardia in 50% of primary ciliary dyskinesia. •Abnormal heart sounds or pulses –congenital cardiovascular anomalies, pulmonary edema, or arrhythmia.
Abdomen	•Abnormal liver **size or texture** –chronic liver disease, due to cystic fibrosis. •Splenomegaly –portal hypertension, due to cystic, chronic infection, malignancy, storage diseases, or hemoglobinopathies. •Situs inversus in 50 percent of patients with primary ciliary dyskinesia •Rectal prolapse – Suggests cystic fibrosis.
Extremities	•Edema – Suggests cardiac disease. •Cyanosis or digital clubbing – Suggests bronchiectasis or interstitial lung disease.

Nonspecific cough

- Conversely, a "nonspecific" cough is defined as a chronic cough that does not have an identifiable cause after a reasonable evaluation.

- A chronic cough is more likely to be nonspecific if it is dry and there are no abnormalities identified on initial evaluation (ie, no "specific cough pointers"

Specific cough refers to a chronic cough that is ultimately attributable to an underlying physiologic cause (which is usually but not always of pulmonary origin).

Specific cough pointers

- Wet/productive chronic cough
- Wheezing or dyspnea
- Onset after an episode of choking (even if days or weeks prior)
- Neonatal onset of symptoms
- Any other associated medical conditions (cardiac, neurologic, autoimmune or immunodeficiency, or suspicion thereof)

Signs and symptoms suggesting a specific cause of cough in children (specific cough "pointers”

Specific chronic cough "pointer"	Possible major underlying etiology
History	
Pulmonary symptoms	
Chronic wet or productive cough*	Suppurative lung diseases (protracted bacterial bronchitis, chronic suppurative lung disease, bronchiectasis), aspiration, abscess, cavitations
Hemoptysis	Infection (eg, tuberculosis), interstitial lung disease, bronchiectasis, autoimmune lung disease
Wheeze (at rest or on exertion)	Asthma; bronchiectasis, eosinophilic disorders
Dyspnea (at rest or on exertion)	Asthma or any severe lung disease
Classically recognizable cough sounds¶	These cough characteristics (eg, barking, honking, whooping) often suggest a specific cause of cough¶
Recurrent pneumonia	Immunodeficiency, obstructed airways or any conditions causing bronchiectasis

Timing and triggers	
Symptoms from neonatal period	Congenital abnormality related to airways, immune function, or causes with predisposition to bronchiectasis (eg, primary ciliary dyskinesia)
Onset after an episode of choking	Inhaled retained foreign body
Cough worsens when child is anxious or attention is focused and is absent during sleep. Cough improves with distraction or suggestion and can be voluntarily suppressed	Habit cough (tic cough)
Child has disproportionate thoughts and anxiety about the seriousness of symptoms	Somatic cough disorder (psychogenic cough)

Associated symptoms or conditions	
Cardiac disease	Primary cardiac disease causing cough, tracheomalacia or primary ciliary dyskinesia
Neurologic and developmental abnormalities	Aspiration
Feeding difficulties	Laryngeal or trachea disorders, aspiration
Failure to thrive	Any severe lung disease, cystic fibrosis, immunodeficiency, indolent infections (eg, tuberculosis)
Exposure to tuberculosis, pertussis, and/or sick animals and travel history	Tuberculosis and other mycobacterium, pertussis, parasites (eg, Toxocara), and/or zoonoses (eg, trematodes, Strongyloides, Q fever)
History of deep infections ± immunodeficiency (primary or secondary to cancer treatment or medications)	Opportunistic infections (eg, fungal)
Autoimmune disease	Interstitial lung disease
Angiotensin-converting enzyme inhibitor use	Known adverse effect of angiotensin-converting enzyme inhibitor
Chronic fever	Indolent infection with or without immunodeficiency

Examination	
Digital clubbing	Bronchiectasis or interstitial lung disease
Chest wall abnormality	Any lung disease, neuromuscular disease
Wheezing or crepitations	Any lung disease; in particular, asthma, bronchiolitis obliterans, bronchiectasis (from any cause), bronchopulmonary dysplasia, heart failure, immunodeficiency and aspiration
Hypoxia	Any lung disease
Routine investigations/tests	
Abnormal chest radiography	Any lung disease
Abnormal spirometry	Obstructive or restrictive lung/chest wall diseases

Underlying causes of cough

Causes of chronic cough in children

Primary cause	Risk factors or mechanisms	Major evaluation method (in addition to clinical findings)
Pulmonary causes		
Aspiration* (recurrent small volume)	Primary **swallowing dysfunction or laryngeal disorders** (eg, laryngeal cleft, tracheoesophageal fistula), **gastroesophageal reflux, achalasia**	Swallowing assessment (eg, videofluoroscopic) and other evaluation as indicated¶
Asthma, cough-dominant asthma*	Genetics, environment, atopy, post acute respiratory infections	Lung function, airway hyperresponsiveness

Causes of chronic cough in children

Primary cause	Risk factors or mechanisms	Major evaluation method (in addition to clinical findings)
Pulmonary causes		
Chronic endobronchial suppurative disease* (protracted bacterial bronchitis, chronic suppurative lung disease, bronchiectasis)	**Cystic fibrosis** **Immunodeficiency** (primary or secondary) **Primary ciliary dyskinesia** **Aspiration** **Post-infections** (eg, tuberculosis, pneumonia, etc)	Sweat test, genetic screening Evaluation of immune function Cilia biopsy, genetic testing Chest CT, bronchoscopy Refer to "Aspiration" above
Chronic pneumonia*	Chronic **atelectasis, mucous plugging**, plastic bronchitis **Pathogens** include tuberculosis, nontuberculosis mycobacteria, mycoplasma, fungi, and chlamydia	Chest CT, bronchoscopy Relevant microbial assessment (eg, QuantiFERON gold and Gene Xpert for tuberculosis)

Causes of chronic cough in children

Primary cause	Risk factors or mechanisms	Major evaluation method (in addition to clinical findings)
Pulmonary causes		
Eosinophilic lung disease*	Primary or secondary (ie, related to parasitic disease)	Bloods and bronchoalveolar lavage
Inhaled retained foreign body*	Young child, history of choking (even if days or weeks before cough onset)	Bronchoscopy
Interstitial lung disease*	Primary genetic abnormality, post severe infection bronchiolitis obliterans, autoimmune disease, radiation, drugs	Relevant genetic or autoimmune test, with or without lung biopsy

Causes of chronic cough in children

Primary cause	Risk factors or mechanisms	Major evaluation method (in addition to clinical findings)
Pulmonary causes		
Mechanical inefficiency	**Tracheobronchomalacia** and other airway anomalies Vascular rings or other **anomalies** that cause tracheal narrowing	Dynamic bronchoscopy Chest CT with contrast Chest MRI (if vascular cause suspected)?
Noninfective bronchitis*	Exposure to **environmental pollutants** (eg, tobacco smoke, fungi, traffic)	History and removal of trigger
Postinfection (self-resolving)	Viral infections, pertussis, parapertussis	PCR and/or serology
Space-occupying lesions*	Cysts and tumors	Chest CT or MRI scan

ation
ry

Causes of chronic cough in children

Primary cause	Risk factors or mechanisms	Major evaluation method (in addition to clinical findings)
Extrapulmonary causes		
Causal role likely		
Cardiac*	May cause cough due to airway compression, pulmonary edema, or arrhythmia	ECG and other evaluation as indicated
Ear disease*	Oto-respiratory reflex (Arnold reflex), in which stimulation of the auricular branch of the vagus nerve triggers cough	Examination of the ear canal and removal of the object, or treatment of disease that is triggering the cough

Causes of chronic cough in children

Causal role likely		
Tic cough (habit cough) or somatic cough disorder (psychogenic cough)*	May be isolated, but more likely if other tics are present Some children have **generalized anxiety or disproportionate anxiety** about the seriousness of their symptoms	Suppressibility, distractibility, suggestibility, variability, and presence of a premonitory sensation; cough absent during sleep Response to behavioral therapy (eg, suggestion therapy)$^{\Delta}$ Children with somatic cough disorder may require referral to a psychologist and/or psychiatrist if unresponsive to suggestion therapy
Medications*	ACE inhibitors (common), any inhaled medication, proton pump inhibitors, other drugs (uncommon) Certain other medications (eg, cytotoxic drugs) may be associated with interstitial lung disease	Discontinuation of medication Evaluation for interstitial lung disease (eg, HRCT)

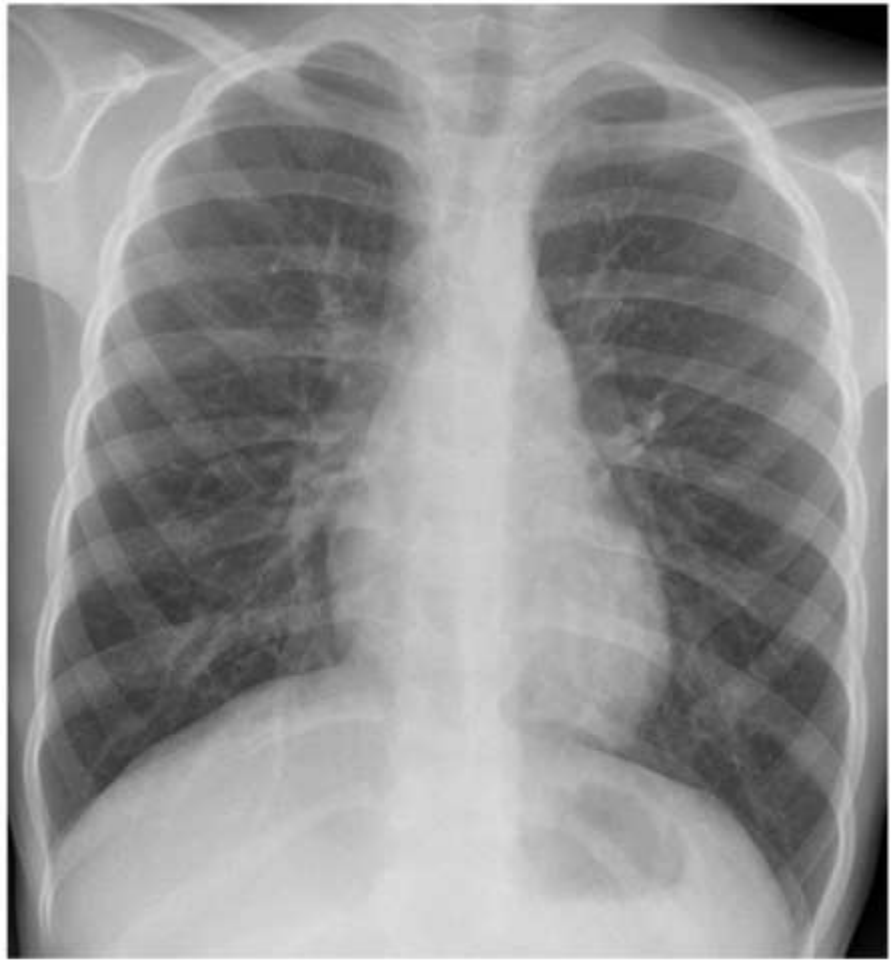
Causes of chronic cough in children

Primary cause	Risk factors or mechanisms	Major evaluation method (in addition to clinical findings)
Extrapulmonary causes		
Causal role unlikely		
Esophageal disorders	Gastroesophageal reflux (acid and nonacid)	Esophageal pH monitoring or impedance monitoring, with or without endoscopy
Upper airway pathology	Chronic sinusitis, obstructive sleep disorders◊	Evaluation guided by suspected disorder (CT, polysomnography)

Normal chest radiograph in a child with chronic cough

- Chest radiograph showing perihilar bronchial thickening only.

- This is a common finding in healthy children
- also in children with protracted bacterial bronchitis.



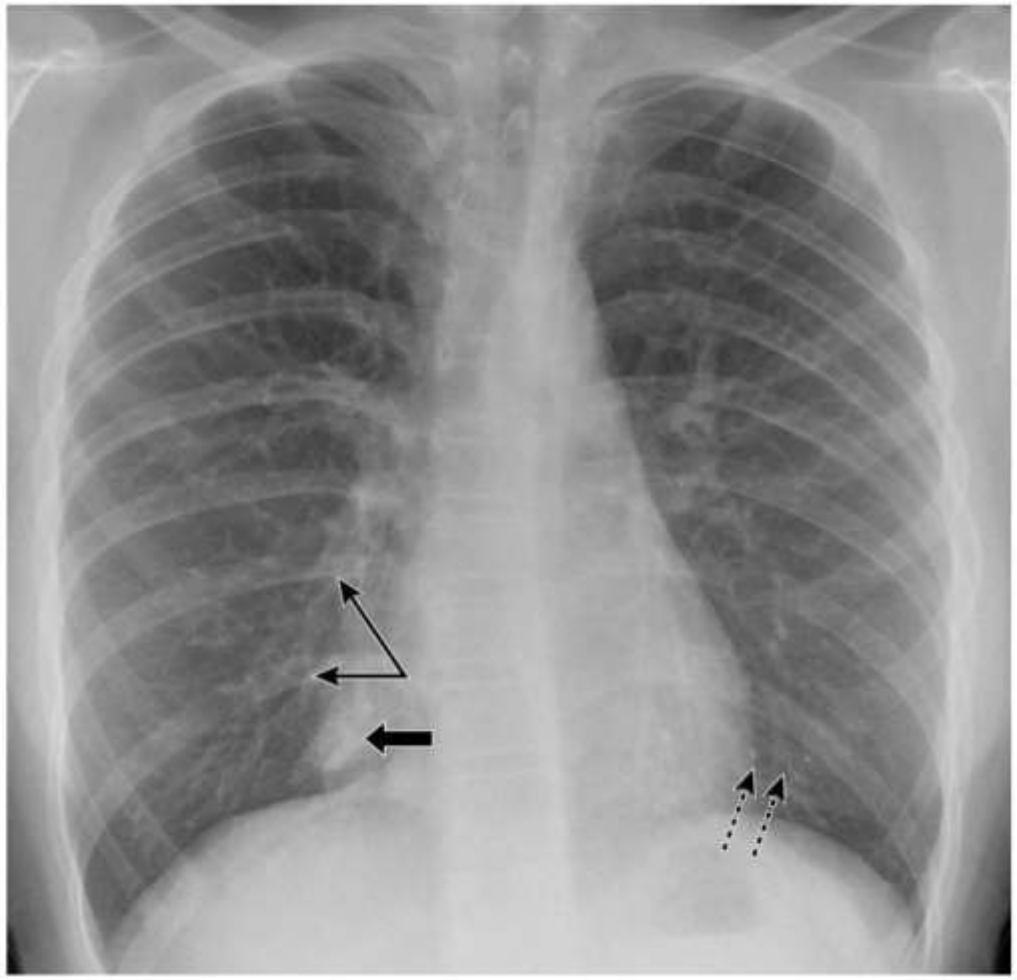
Airway foreign body

✓An expiratory chest radiograph

showing unilateral lung hyperinflation, suggestive of the presence of foreign body aspiration.

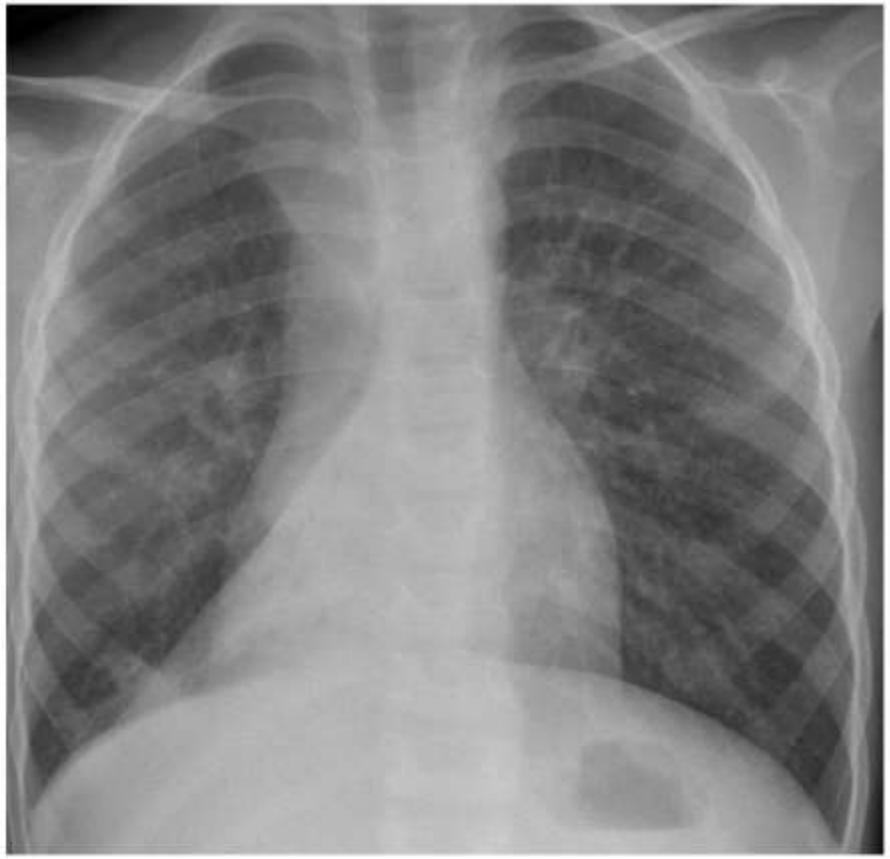
Radiographic features of bronchiectasis

Note that chest radiographs have very poor sensitivity for diagnosing bronchiectasis.



Primary ciliary dyskinesia

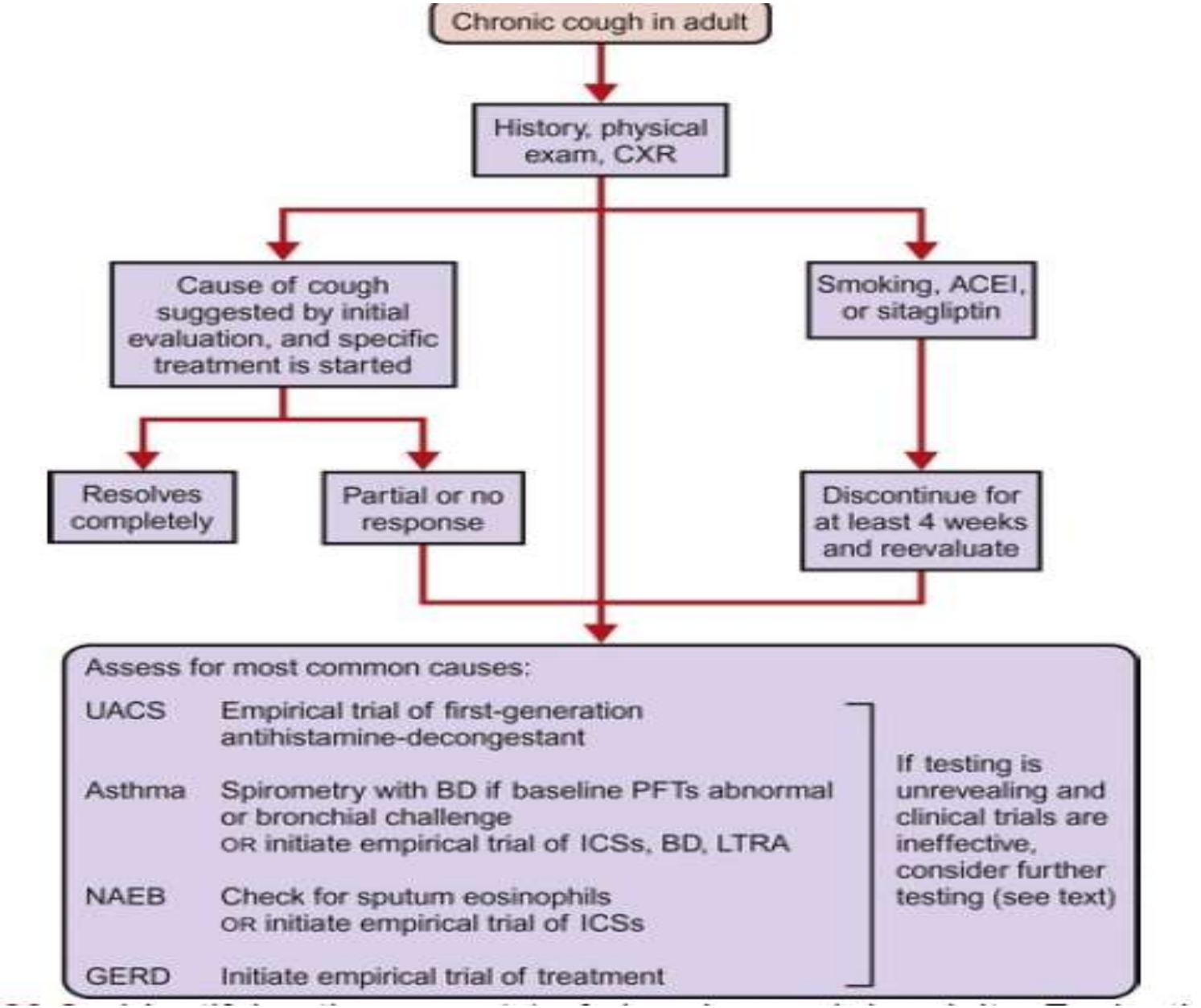
- Chest radiograph at the first presentation of a child.
- He was first referred at four years of age with a history of chronic wet cough for more than two years.
- He never had a prior chest radiograph.



- The chest radiograph shows **collapse of the right lower lobe,** which re-expanded after bronchoscopy and intravenous antibiotics.

- The ciliary biopsy showed immotile cilia, confirming the diagnosis of primary ciliary dyskinesia (PCD).
- The child also had heterotaxy syndrome, which is commonly associated with PCD.

Diagnostic and therapeutic approach


Chronic cough in adult
History, physical exam, CXR
Cause of cough suggested by initial evaluation, and specific treatment is started
Smoking, ACEI, or sitagliptin
Resolves completely
Partial or no response
Discontinue for at least 4 weeks and reevaluate
Assess for most common causes:
UACS
Empirical trial of first-generation antihistamine-decongestant
Asthma
Spirometry with BD if baseline PFTs abnormal or bronchial challenge
OR initiate empirical trial of ICSs, BD, LTRA
NAEB
Check for sputum eosinophils
OR initiate empirical trial of ICSs
GERD
Initiate empirical trial of treatment
If testing is unrevealing and clinical trials are ineffective, consider further testing (see text)

Additional investigations

- Flexible bronchoscopy: suspected foreign body aspiration. suspected airway malacia, tracheoesophageal fistula, or stenosis.

- perform bronchoalveolar lavage for bacterial, fungal, and mycobacterial cultures. Cilia brushings
- **Esophageal PH or multichannel intraluminal impedance (mii) monitoring**
- **Sinus imaging**: sinusitis is not a common cause of chronic cough in children
- Chest CT scans
- Tests for tuberculosis : in settings where tuberculosis is endemic or has a high prevalence at high risk for exposure,
- Allergy testing

All patients should be questioned about cigarette smoking, the use of ACE inhibitors, and about the presence of an upper respiratory tract infection at the onset of the cough.

Upper airway cough syndrome, asthma, and gastroesophageal reflux, alone or in combination, are responsible for approximately 90 percent of cases of chronic cough who had the following characteristics:

- Nonsmoker
- No use of an ACE inhibitor
- Normal or near normal and stable plain chest radiograph

ACE inhibitor induced cough features

- usually begins within one week of instituting therapy, but the onset can be delayed up to six months.
- often presents with a tickling, scratchy, or itchy sensation in the throat.
- typically resolves within one to four days of discontinuing therapy, but can take up to four weeks.
- generally recurs with rechallenge, either with the same or a different ACE inhibitor.
- is a more common complication in women than in men,
- does not occur more frequently in asthmatics than in non-asthmatics.
- is generally not accompanied by airflow obstruction

Non specific cough

- Watchful waiting –**waiting for two to four weeks**

- Medication trials –the cough is troublesome and if there is clinical evidence supporting asthma or if other specific causes have been excluded, empiric trial of bronchodilators (short-acting beta2 -agonists) or low-dose inhaled corticosteroids (<400 micrograms budesonide equivalent daily).
- Gastroesophageal reflux disease (GERD) is probably an unusual cause of chronic cough in otherwise healthy children. empiric trial of treatment for GERD for **four weeks**, using acid-suppressing medications such as a proton pump inhibitor (PPI)
- Assessing the response to therapy –two to four weeks, which is the "time to response" for most medications

Other management considerations

- Family expectations and counseling :

- parental worry can lead to the use of nonspecific medications, which may not be suitable due to lack of efficacy and safety concerns Cough suppressants –
- Over-the-counter cold and cough suppressants are not recommended for the treatment of chronic cough in children.
- we recommend against the use of opioid drugs such as codeine that may be effective in suppressing cough as evidence is limited, and these drugs are associated with serious side effects and the potential for abuse.
- Avoidance of tobacco smoke Alternative therapies –including honey and echinacea.

Thank you