

الله أكبر  
الحمد لله



# Approach to chronic cough

**Dr Effat Rafiee Pulmonologist**  
**Zanjan university of medical science**

# Review

- Epidemiology and ethiology
- Most frequent
  - Asthma
  - GERD
  - NAEB
  - UACS
- Approach&Management
- Refractory cough
- pitfall



# Epidemiology and etiology

# Epidemiology

- Cough prevalence varies by age
- Asthma and UACS are more common in young
- COPD and GERD are more common in older
- It is unclear why chronic cough is more prevalent in women
- Age-related hormonal changes may contribute

# Etiology

- Intrathoracic
- Extrathoracic



# Etiologies: intrathoracic

## Lungs and Airways

1

- Asthma
- Nonasthmatic eosinophilic bronchitis
- Chronic bronchitis
- Bronchiectasis
- ACEIs
- 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

## Pleura

2

- Chronic effusion

## Diaphragm

3

- Transvenous pacemaker stimulation

## Mediastinum

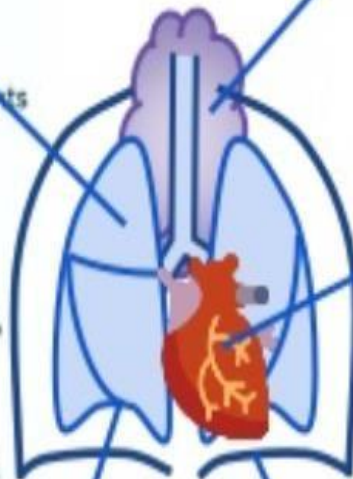
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- Neural tumors
- Thymoma
- Teratoma
- Lymphoma
- Metastatic lymphadenopathy
- Intrathoracic goiter
- Bronchogenic cyst

## Cardiovascular

4

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



# Etiologies: extrathoracic

## 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



## Central Nervous System



- Psychogenic or habit cough
- Tic disorders
- Gilles de la Tourette syndrome

## Upper Gastrointestinal



- Gastroesophageal reflux disease
- Esophageal cyst or diverticulum
- Tracheoesophageal fistula





Approach & Management

History	Reasons
Onset	To determine acute/subacute or chronic causes of cough
Aggravating factor, relieving factor	<ul style="list-style-type: none"> <li>• Cough due to GERD affected by postural changes, post meal</li> <li>• Cold induced or MDI relieved cough in asthma or COPD</li> </ul>
Sputum colour	Normal sputum: clear to white colour, thin, odourless tasteless Yellow-green: bacterial infection Rust-colored: pneumonia
Sputum character	Mucoid or mucopurulent: cigarette smokers as a result of chronic bronchitis Commonly purulent in bronchiectasis
Sputum amount	Significant volumes: more than 1 cup per day

<b>History</b>	<b>Reasons</b>
<b>Fever</b>	<b>Ongoing infection</b>
<b>Noisy breathing</b>	<b>Wheezing suggest asthma/COPD</b>
<b>Loss of appetite, loss of weight, hemoptysis</b>	<b>Suggesting Tuberculosis, malignancy</b>
<b>Allergy, nasal obstruction or congestion, rhinorrhoea, sneezing, facial pain, post-nasal drip or repetitive throat clearance</b>	<b>Suggesting Rhinosinusitis</b>
<b>Dyspepsia, heartburn, waterbrash</b>	<b>GERD</b>
<b>Medication used</b>	<b>ACE-inhibitor</b>
<b>Occupation</b>	<b>Exposure to asbestos, chemical or cigarette smoke</b>
<b>Family history</b>	<b>Asthma, tuberculosis, lung cancer, cystic fibrosis</b>
<b>Social history</b>	<b>Contact with PTB suggesting PTB</b>

# Physical Examination

Physical examination	Reasons
General condition such as altered conscious level, accessory muscles usage, cyanosis, grunting, nasal flaring, clubbing, nicotine stain	To assess severity and to look for respiratory distress
Vital signs	Fever – infection Tachycardia, tachypnea – respiratory distress Pulsus paradoxus – asthma
Nasal polyps	Allergy rhinitis
Pharynx: erythema, a cobblestone appearance of posterior pharyngeal mucosa or mucoid secretions dripping from the nasopharynx	Post nasal drip
Chest: Hyperinflated  Silent chest Crepitations, wheezing	Suggest air trapping due to chronic disease Severe asthma Pneumonia, asthma, heart failure

Physical examination	Reasons
CVS: Displaced apex beat, raised JVP, loud P2, RV heave	Cor pulmonale
Eczema, transverse nasal crease, injected conjunctiva	Signs of atopic disease
Lymphadenopathy	To suggest infection

- Abnormal physical signs are rare in a chronic dry cough
- Wheeze may be audible on examination but is usually absent in cough variant asthma (CVA)
- ✓ Evaluation of chronic cough merits a **chest Radiography**
- ✓ Examination of **expectorated Sputum**

# Most common causes

- Asthma
- GERD
- UACS
- Non Asthmatic eosinophilic bronchitis





Most common  
causes



Asthma

- Prevalence 28%
- mechanism
  - Inflammatory mediators directly induce cough
  - sensitize vagal afferent
- Diagnosis
  - Symptom
  - PFT



Most common  
causes

GERD

- **Prevalence** :10% of chronic cough
- **Silent GERD:** 43% - 75% of GERD patients present with cough only
  - Aspiration
  - Irritating hypopharynx and supraglottic larynx
  - Distal esophageal-bronchial reflex



Most common  
causes

GERD

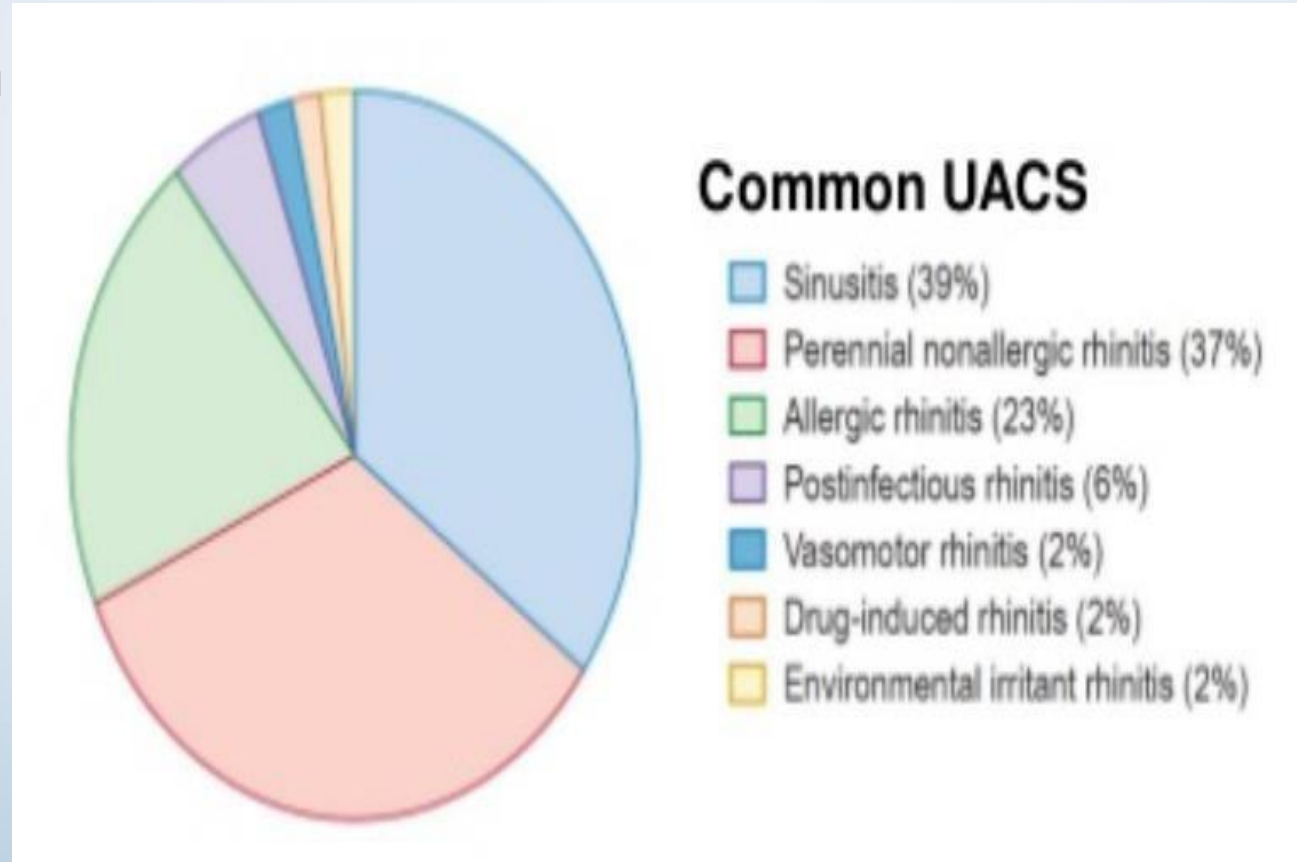
## ➤ Diagnosis

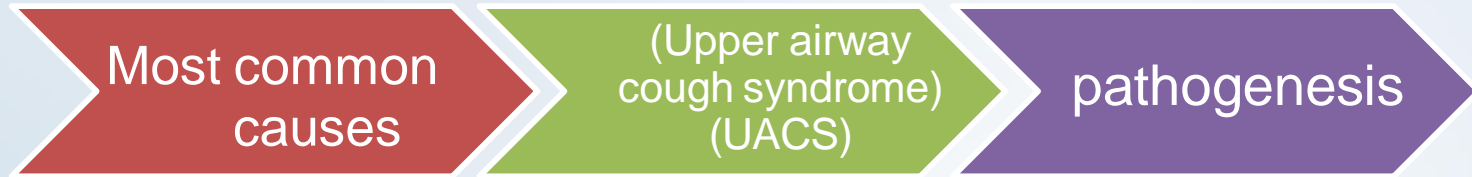
- ✓ **Symptom of GERD:** heartburn, sour taste, Retrosternal burning after meals or on recumbency , and throat pain, dysphonia, hoarseness, frequent throat clearing, a globus sensation, and sore throat; often, posterior vocal cord laryngeal inflammation with edema, erythema, contact ulceration, pachydermia, and/or granuloma is visible
- ✓ **Barium swallow:** reflux to the level of the mid-esophagus or higher
- ✓ **24-hr pH and impedance monitoring:** gold standard (usually performed after treatment failure)

Most common  
causes

(Upper airway cough syndrome)  
(UACS)

- Definition





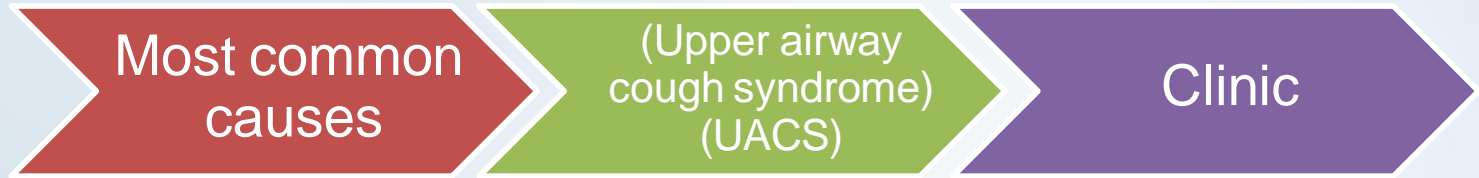
1. Postnasal drip

stimulation of cough receptors located in the hypopharynx or larynx

2. Direct irritation of nasal mucosa (gate keeper)

cough reflex is up-regulated during stimulation of nasal afferents in order to minimize the spreading of the pathological process from the nasal cavity to other parts of the respiratory tract

3. Airway inflammation



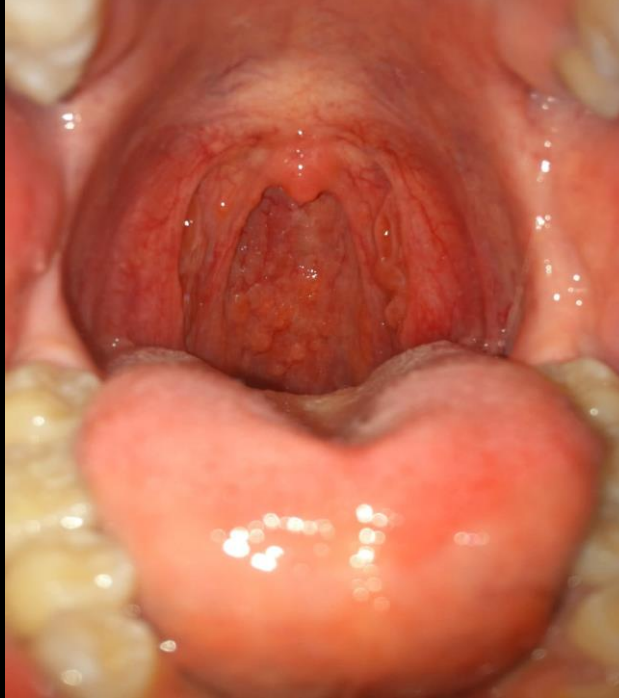
- ✓ Self reporting PND 80%
- ✓ Self reporting PND without cough(Silent PND)
- ✓ Comorbidity with Asthma
- ✓ Comorbidity with GERD



Most common  
causes

(Upper airway  
cough syndrome)  
(UACS)

Diagnosis



Most common  
causes

(Upper airway  
cough syndrome)  
(UACS)

Diagnosis



## Most common causes

## Non asthmatic eosinophilic bronchitis

- Eosinophilic airway inflammation without variable airflow obstruction or airway hyperresponsiveness
- Diagnostic tests:
  - Spirometry: normal
  - Methacholine challenge: normal
  - Sputum or BAL eosinophilia: >3% eosinophils
- Diagnostic/Therapeutic trial:
- inhaled corticosteroid for  $\geq 4$  weeks
- Characteristically resistant to bronchodilator but responds ICS
- Confirmed diagnosis if responded to ICS

## Most common causes

## Non asthmatic eosinophilic bronchitis

**TABLE 3. Differentiating NAEB, Asthma, and Cough Variant Asthma**

Feature	NAEB	Classic asthma	Cough variant asthma
Symptoms	Cough	Dyspnea, chest tightness, cough, wheeze	Cough
Atopy	Same as the general population	Increased	Increased
Airway hyperresponsiveness	Absent	Present	Present
Bronchodilator responsiveness	Absent	Present	Present
Corticosteroid responsiveness	Yes	Yes	Yes
Sputum eosinophilia	Always present	Usually present	Usually present
Mast cells in airway smooth muscle bundles	Absent	Present	Present

# ACEI Induced cough

- ✓ Incidence: 5% - 35% of patient taking ACEI
- ✓ Onset: hours - months after initiation
- ✓ Management : Switching to Angiotensin II receptor antagonist
- ✓ Cough usually resolves within 4 weeks, may up to 3 months

# Postinfectious Cough

- Prevalence 11% to 25%
- 25% to 50% following Mycoplasma or Bordetella pertussis infection
- In children, chronic cough include viruses (respiratory
  - syncytial virus and parainfluenzae), Mycoplasma, and Chlamydiae
- cough of B. pertussis usually lasts for only 4 to 6 weeks (but can last longer) and is spasmodic with a typical whoop
- TX
  - Inhaled corticosteroids
  - Oral steroids
  - Inhaled Ipratropium bromide

Macrolide antibiotics or trimethoprin/Sulfamethoxazole are effective in eliminating B. pertussis but do not alter the subsequent clinical course



# • Psychogenic or habit cough

- children
- diagnosis after exclusion of other causes
- **throat-clearing noise** nervous and self-conscious person
- **“honking” or “barking”** quality
- associated with a **depressive illness**, and long-standing cough may in turn cause depression
- cough **etiologies specific for this age** group need to be considered: congenital abnormalities, vascular rings and tracheobronchomalacia, pulmonary sequestration or mediastinal tumors; foreign bodies; aspiration; and heart disease

# Approach in Adults

## 1 Identify obvious causes

- Diagnosis based on Hx, PE, CXR → **specific treatment**
- Often multiple etiologies
- Consider exacerbation of chronic diseases

### Red Flags

- Hemoptysis
- Voice disturbance
- Dysphagia
- Vomiting
- Dyspnea
- Systemic symptoms
  - Fever
  - Weight loss
  - Edema
- Recurrent pneumonia
- Abnormal PE / CXR
- Smoker
  - Age > 45 + new symptom
  - Age > 55 + smoke > 30PY

### Smoking

### ACEI

### 4 Most common

Upper airway cough syndrome

Asthma

NonAsthmatic eosinophilic bronchitis

Gastroesophageal reflux disease

- Allergy Asthma Immunol Res. 2018 Nov;10(5):591-613.  
 - CHEST Guideline and Expert Panel Report. Chest 2018;153:196-209.  
 - J Allergy Clin Immunol 2019;143:100-110

### May not helpful in diagnosis

- character: paroxysmal, loose, productive, dry
- sound quality: barking, honking
- timing: nocturnal

- no obvious cause found
- not fully response after optimal & adequate treatment

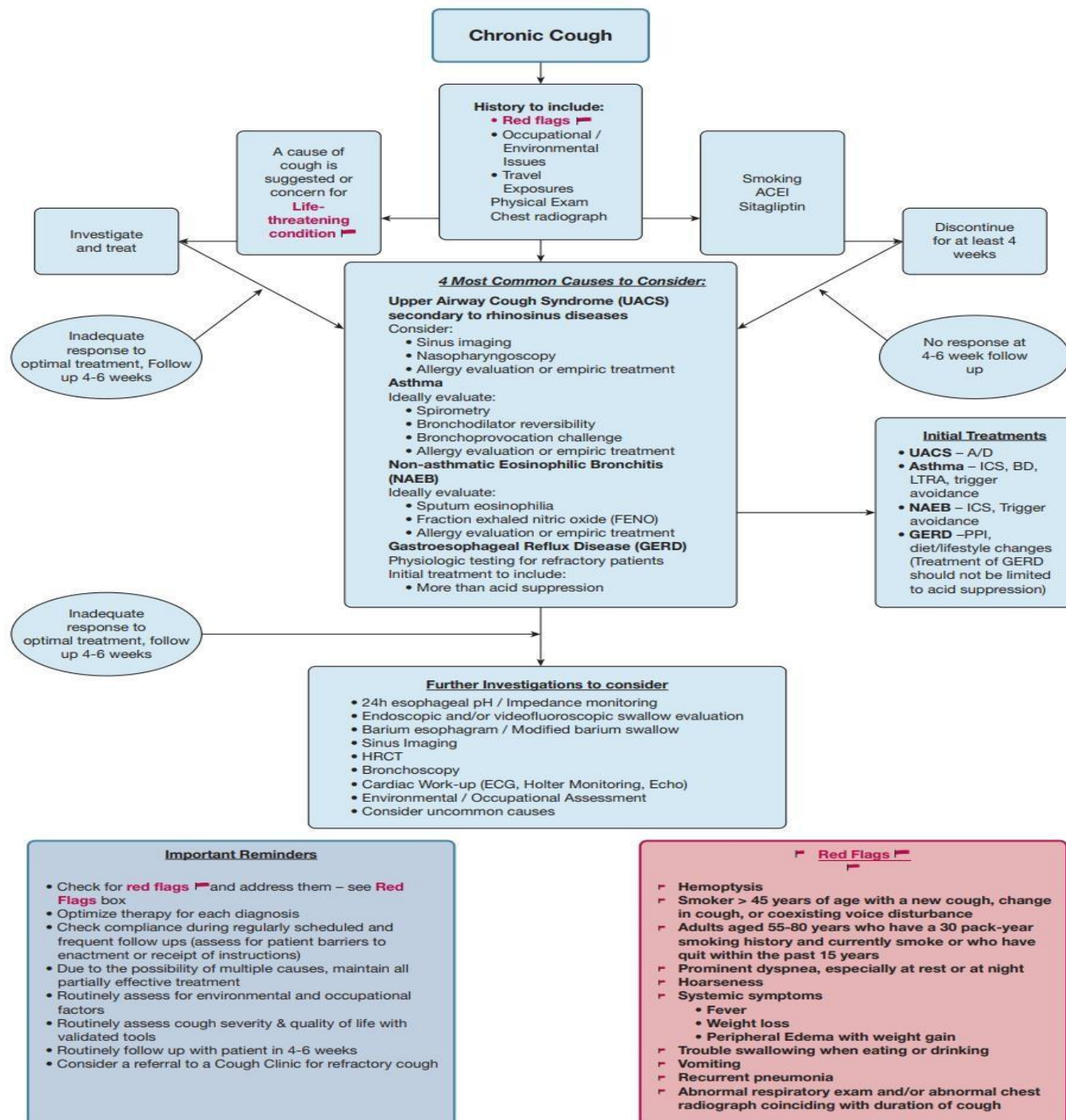
## 2 Investigation +/- empirical treatment for common causes

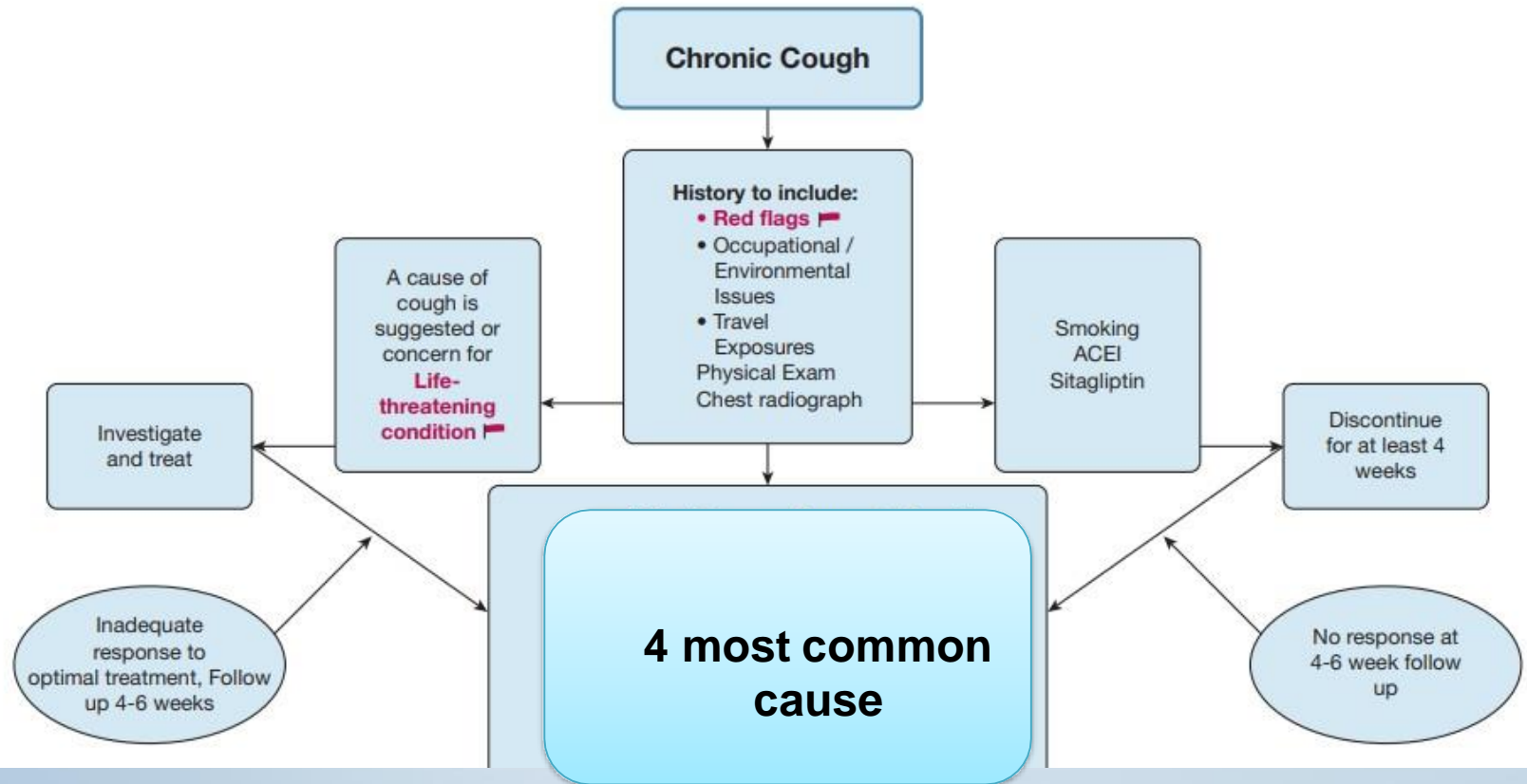
- negative study
- not fully response after treatment

## 3 Further investigation

- negative study

## 4 "Unexplained chronic cough"





**4 Most Common Causes to Consider:**

**Upper Airway Cough Syndrome (UACS)  
secondary to rhinosinus diseases**

Consider:

- Sinus imaging
- Nasopharyngoscopy
- Allergy evaluation or empiric treatment

**Asthma**

Ideally evaluate:

- Spirometry
- Bronchodilator reversibility
- Bronchoprovocation challenge
- Allergy evaluation or empiric treatment

**Non-asthmatic Eosinophilic Bronchitis (NAEB)**

Ideally evaluate:

- Sputum eosinophilia
- Fraction exhaled nitric oxide (FENO)
- Allergy evaluation or empiric treatment

**Gastroesophageal Reflux Disease (GERD)**

Physiologic testing for refractory patients

Initial treatment to include:

- More than acid suppression

**Initial Treatments**

- **UACS** – A/D
- **Asthma** – ICS, BD, LTRA, trigger avoidance
- **NAEB** – ICS, Trigger avoidance
- **GERD** –PPI, diet/lifestyle changes (Treatment of GERD should not be limited to acid suppression)

Inadequate response to optimal treatment, follow up 4-6 weeks

**Further investigation**





### **Further Investigations to consider**


- 24h esophageal pH / Impedance monitoring
- Endoscopic and/or videofluoroscopic swallow evaluation
- Barium esophagram / Modified barium swallow
- Sinus Imaging
- HRCT
- Bronchoscopy
- Cardiac Work-up (ECG, Holter Monitoring, Echo)
- Environmental / Occupational Assessment
- Consider uncommon causes



### Red Flags

- ┆ Hemoptysis
- ┆ Smoker > 45 years of age with a new cough, change in cough, or coexisting voice disturbance
- ┆ Adults aged 55-80 years who have a 30 pack-year smoking history and currently smoke or who have quit within the past 15 years
- ┆ Prominent dyspnea, especially at rest or at night
- ┆ Hoarseness
- ┆ Systemic symptoms
  - Fever
  - Weight loss
  - Peripheral Edema with weight gain
- ┆ Trouble swallowing when eating or drinking
- ┆ Vomiting
- ┆ Recurrent pneumonia
- ┆ Abnormal respiratory exam and/or abnormal chest radiograph coinciding with duration of cough

## Important Reminders

- Check for **red flags**  and address them – see **Red Flags** box
- Optimize therapy for each diagnosis
- Check compliance during regularly scheduled and frequent follow ups (assess for patient barriers to enactment or receipt of instructions)
- Due to the possibility of multiple causes, maintain all partially effective treatment
- Routinely assess for environmental and occupational factors
- Routinely assess cough severity & quality of life with validated tools
- Routinely follow up with patient in 4-6 weeks
- Consider a referral to a Cough Clinic for refractory cough

# Unexplained chronic cough

- ✓ cough that **persists longer than 8 weeks**, and remains unexplained **after investigation**, and supervised **therapeutic trial(s)** conducted according to published best-practice guidelines
- ✓ *Idiopathic or refractory or unexplained* cough
- ✓ **12-42 %** of patients did not fit into any categories despite vigorous diagnostic and therapeutic efforts.

- middle-aged **women**, onset at **menopause**
- associated **autoimmune disorders** such as autoimmune hypothyroidism
- **enhanced cough reflex**
- complain of a persistent **tickling** sensation in the throat leads to **paroxysms** of coughing
- **trigger factors** : changes in ambient temperature, taking a deep breath, laughing, talking over the phone for a few minutes, and exposure to cigarette smoke or other irritants such as aerosol sprays or perfumes or to certain odors
- **increase neural profiles** that express the neuropeptide, calcitonin gene-related peptide (**CGRP**), and the calcium channel, **TRPV<sub>1</sub>**, in the airway epithelium of chronic coughers that could contribute to the increased cough reflex

# cough hypersensitive syndrome(CHS)

- an **idiopathic** cough
- **neuropathic** syndrome
- chronic persistent cough that has **lasted for more than 8 weeks**
- trigger symptoms and sensations indicating the presence of an enhanced cough reflex
- **persistent tickling or irritating sensation in the throat** (feeling of an itch) or a choking sensation, and it may sometimes be felt in the chest, which often leads to **paroxysms of uncontrollable coughing**
- **Triggers** ; lying down, eating, singing, talking, laughing, and taking a deep breath (through mechanoreceptors); changes in ambient temperature (through thermoactivation); aerosols, scents, odors, and cigarette smoke
- **Vagal nerve neuropathy ,sensory laryngeal neuropathy** laryngospasm, or paradoxical vocal cord dysfunction
- **neuromodulatory therapies** directed at controlling hypersensitive cough, should be tried



**pitfalls**

# Common pitfall in management

## Failure to recognize that

- Etiologies of chronic cough may be **multifactorial**
- GERD and UACS can also **produce phlegm**
- **Cough can be the only manifestation** of:
  - Cough variant asthma
  - Silent UACS
  - Silent GERD



# Common pitfall in management

## **Premature abortion** of treatment

- Asthma, UACS: up to 4 weeks
- GERD: up to 6 months

## Fail to recognize **environmental exposure & co-morbid**s

- Asthma, UACS, NAEB: Allergen avoidance
- GERD: OSA, CCB treatment, foods, lifestyle

## **Premature labelling** of

- Psychogenic cough
- Idiopathic cough
- Unexplained cough



A woman with curly hair, wearing a white t-shirt, is shown from the chest up. She has her eyes closed and a joyful expression, with her arms raised high in the air. In her right hand, she holds a light blue surgical mask by its ear loops. The background is a bright blue sky with scattered white clouds. The overall mood is one of triumph and relief. The image is framed by a light blue border with diagonal grey and orange stripes in the top-left and bottom-left corners.

**THANK YOU**