Diagnosis and Treatment of Chronic Cough

March 3, 2017

Eric M. Davis, MD
Division of Pulmonary and Critical Care Medicine
University of Virginia Health System
Presenter disclosure:

- I have no relevant financial interests to disclose
Four learning objectives

• Review the morbidity of cough and underlying pathophysiology

• New guidelines and an algorithmic approach to chronic cough

• Understand the treatment options for cough associated with reflux disease

• Define unexplained chronic cough and review therapeutic strategies
Cough morbidity and impact:

- Why do we cough?
- How do we cough?
- Has anyone seen a patient with cough this week?
Coughing is good for the survival of the species

Clear the upper airway of secretions:
  - Mucus, noxious substances, foreign particles, and infectious organisms

It is a complicated process:
  - Inspiratory phase
  - Forced expiratory effort against closed glottis
  - Opening of the glottis with rapid expiration (sound)
The cough reflex:
- Transient receptor potential vanilloid-1 (TRPV-1) is a capsaicin receptor
Chronic Cough – Definitions:

- Chronic cough (> 8 weeks duration) impacts 8-10% of the adult population
- #1 medical reason for outpatient visit in 2001-2002 as per CDC records:

<table>
<thead>
<tr>
<th>Principal reason for visit and RVC code</th>
<th>Number of visits in thousands</th>
<th>Percent distribution</th>
<th>Total</th>
<th>Primary care offices</th>
<th>Surgical specialty offices</th>
<th>Medical specialty offices</th>
</tr>
</thead>
<tbody>
<tr>
<td>All visits</td>
<td>1,077,583</td>
<td>100.0</td>
<td></td>
<td>100.0</td>
<td>50.4</td>
<td>15.3</td>
</tr>
<tr>
<td>General medical examination</td>
<td>X100</td>
<td>71,939</td>
<td>6.7</td>
<td>100.0</td>
<td>81.8</td>
<td>3.0</td>
</tr>
<tr>
<td>Progress visit, not otherwise specified</td>
<td>T800</td>
<td>45,340</td>
<td>4.3</td>
<td>100.0</td>
<td>42.9</td>
<td>14.0</td>
</tr>
<tr>
<td>Cough</td>
<td>S440</td>
<td>33,119</td>
<td>3.1</td>
<td>100.0</td>
<td>73.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Postoperative visit</td>
<td>T205</td>
<td>24,629</td>
<td>2.3</td>
<td>100.0</td>
<td>17.1</td>
<td>69.4</td>
</tr>
<tr>
<td>Prenatal examination, routine</td>
<td>X205</td>
<td>22,279</td>
<td>2.1</td>
<td>100.0</td>
<td>88.4</td>
<td>–</td>
</tr>
<tr>
<td>Stomach pain, cramps, and spasms</td>
<td>S545</td>
<td>21,819</td>
<td>2.0</td>
<td>100.0</td>
<td>42.0</td>
<td>5.4</td>
</tr>
<tr>
<td>Symptoms referable to throat</td>
<td>S455</td>
<td>21,305</td>
<td>2.0</td>
<td>100.0</td>
<td>70.8</td>
<td>5.1</td>
</tr>
<tr>
<td>Fever</td>
<td>S010</td>
<td>17,437</td>
<td>1.6</td>
<td>100.0</td>
<td>65.3</td>
<td>*</td>
</tr>
<tr>
<td>Back symptoms</td>
<td>S905</td>
<td>17,019</td>
<td>1.6</td>
<td>100.0</td>
<td>49.6</td>
<td>14.5</td>
</tr>
<tr>
<td>Medication, other and unspecified kinds</td>
<td>T115</td>
<td>16,813</td>
<td>1.6</td>
<td>100.0</td>
<td>64.1</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Schappert SM and Burt CW Vital Health Stat 2006 from CDC
Chung KJ and Pavord ID Lancet 2008
Gibson PG and Vertigan AE. BMJ 2015;351:h5590
Chronic Cough – Age and sex are risk factors:

- A worldwide survey of 11 cough clinics (10,000 patients)
  - Female preponderance
  - Females may have heightened cough reflex sensitivity

**FIGURE 1** Age and sex distribution of all the patients presenting to the clinics.

Morice AH et al. ERJ 2014
Chronic Cough – Smoking and pollution are risk factors:

- Swiss smokers cough (SAPALDIA cross-sectional study):

<table>
<thead>
<tr>
<th>Table 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>REPORTED PREVALENCES OF RESPIRATORY SYMPTOMS</em> IN PERCENT (95% CONFIDENCE INTERVAL) BY SMOKING STATUS</em>*</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Chronic cough</td>
</tr>
<tr>
<td>Chronic phlegm</td>
</tr>
<tr>
<td>Chronic cough or phlegm</td>
</tr>
<tr>
<td>Wheezing without colds</td>
</tr>
<tr>
<td>Breathlessness during the day</td>
</tr>
<tr>
<td>Breathlessness at night</td>
</tr>
<tr>
<td>Breathlessness, day or night</td>
</tr>
<tr>
<td>Current asthma</td>
</tr>
<tr>
<td>Dyspnea on exertion</td>
</tr>
<tr>
<td>Chest tightness</td>
</tr>
</tbody>
</table>

* For exact definitions see Appendix.

- Never smokers were found to have greatest risk of chronic cough in response to environmental pollution

Zemp et al. Am J Respir Crit Care Med 1999
Chronic Cough – Why do we care?

- Chronic cough can last 6+ years on average
- It impacts quality of life:

<table>
<thead>
<tr>
<th>Table 3. Correlations Between Adverse Occurrences and Aggregate Sickness Impact Profile (SIP) Scores*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SIP Scores, Adverse Occurrence</strong></td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
<tr>
<td>Exhaustion</td>
</tr>
<tr>
<td>Lifestyle change</td>
</tr>
<tr>
<td>Cannot sing in church</td>
</tr>
<tr>
<td>Hoarseness</td>
</tr>
<tr>
<td>Aching all over</td>
</tr>
<tr>
<td><strong>Physical dimension</strong></td>
</tr>
<tr>
<td>Exhaustion</td>
</tr>
<tr>
<td>Others think something is wrong</td>
</tr>
<tr>
<td>Lifestyle change</td>
</tr>
<tr>
<td><strong>Psychosocial dimension</strong></td>
</tr>
<tr>
<td>Exhaustion</td>
</tr>
<tr>
<td>Inability to sleep</td>
</tr>
<tr>
<td>Lifestyle change</td>
</tr>
<tr>
<td>Aching all over</td>
</tr>
<tr>
<td>Hoarseness</td>
</tr>
<tr>
<td>Soiling of pants</td>
</tr>
<tr>
<td>Not going to movies</td>
</tr>
</tbody>
</table>

*N = 39.

Irwin RS et al. Chest 2014
Chronic Cough – Why do we care?

- Treatment can help with quality of life

Figure 3. Sickness Impact Profile (SIP) scores before and after successful treatment of chronic cough. Total SIP and psychosocial and physical dimension aggregate scores significantly decreased with elimination of chronic cough. Data for 28 patients are plotted as mean ± SE.

Chronic Cough – What are the most common causes:

- Cough hypersensitivity syndrome (coined by Alyn Morice)

**TABLE 1. Causes of Chronic Cough**

- Infectious: mycobacterial-, pertussis-, fungal-, and protozoal-related infections
- Airway disorders: asthma, NAEB, bronchiectasis, atopic cough, chronic bronchitis, sarcoidosis, aspiration, and airway foreign bodies
- Lung parenchymal diseases: interstitial lung diseases, pulmonary hypersensitivity syndrome, and sarcoidosis
- Tumors: benign and malignant tumors involving the airways and parenchyma
- Irritation of the external auditory meatus (the Arnold reflex)
- Upper airway cough syndrome: allergic and nonallergic rhinitis, chronic rhinosinusitis, and GERD
- Esophageal causes: GERD, laryngopharyngeal reflux, and tracheoesophageal fistula
- Drugs: ACE inhibitors and β-blockers
- Airway irritants: tobacco smoke, dust, fumes, and chemicals

ACE = angiotensin-converting enzyme; GERD = gastroesophageal reflux disease; NAEB = nonasthmatic eosinophilic bronchitis.
Chronic Cough – How to treat?

- We often treat the 3 most common causes:
  - Asthma
  - Upper airway cough syndrome (post nasal drip)
  - Reflux
- We often do not treat long enough.
- Patients don’t always get better!

Gibson P and Vertigan AE BMJ 2015
Chronic Cough – Are there guidelines?
### Chronic Cough - Guidelines:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC is defined as a cough persisting for longer than 8 weeks that remains unexplained after investigation and therapeutic trials conducted according to practice guidelines</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>CRC should only be diagnosed after thorough assessment at a cough clinic</td>
<td></td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Assessment should include the cough severity visual analog scale, cough quality of life questionnaires, and ambulatory cough monitoring</td>
<td></td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Objective testing of bronchial hyper-responsiveness and eosinophilic bronchitis or therapeutic corticosteroid trial</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>Speech pathology</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Inhaled corticosteroids are not recommended for patients with negative tests for bronchial hyper-responsiveness and eosinophilia</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Deal with patient stress and concern</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Treat exacerbating factors</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Minimize drugs</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Empiric trial of inhaled corticosteroids</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td></td>
<td>✔️</td>
</tr>
<tr>
<td>Empiric trial of proton pump inhibitors/consider reflux as a cause</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td></td>
</tr>
<tr>
<td>Antitussive therapy with narcotics</td>
<td>✔️</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td></td>
</tr>
</tbody>
</table>

Fig 5 | Comparison of cough guidelines in relation to chronic refractory cough (CRC). ACCP=American College of Chest Physicians; CICADA=Cough In Children and Adults: Diagnosis and Assessment; ERS=European Respiratory Society; BTS=British Thoracic Society; JRS=Japanese Respiratory Society

Gibson PG and Vertigan AE BMJ 2015
The ACCP (Chest) is in the process of updating the cough guidelines:

**TABLE 1: Spectrum of Topics for the Third Edition of the CHEST Cough Guidelines**

<table>
<thead>
<tr>
<th>Section</th>
<th>Topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introductory</td>
<td>Overview of the management of cough</td>
</tr>
<tr>
<td></td>
<td>Methodologies for the development of the management of cough: CHEST guideline and expert panel report</td>
</tr>
<tr>
<td></td>
<td>Anatomy and neurophysiology of cough</td>
</tr>
<tr>
<td></td>
<td>Global physiology and pathophysiology of cough</td>
</tr>
<tr>
<td></td>
<td>An assessment of intervention fidelity in studies on the diagnosis and treatment of chronic cough in the adult</td>
</tr>
<tr>
<td></td>
<td>Tools for assessing outcomes in studies of chronic cough: CHEST guideline and expert panel report</td>
</tr>
<tr>
<td></td>
<td>Classifying cough as an aid to suggesting differential diagnoses</td>
</tr>
<tr>
<td></td>
<td>Empirical management of cough</td>
</tr>
<tr>
<td>Acute cough</td>
<td>Common cold</td>
</tr>
<tr>
<td></td>
<td>Acute bronchitis</td>
</tr>
<tr>
<td></td>
<td>Allergic rhinitis</td>
</tr>
<tr>
<td></td>
<td>Community-acquired pneumonia</td>
</tr>
<tr>
<td>Subacute</td>
<td>Postinfectious</td>
</tr>
<tr>
<td></td>
<td>Pertussis</td>
</tr>
<tr>
<td>Chronic</td>
<td>Upper airway cough syndrome</td>
</tr>
<tr>
<td></td>
<td>Asthma</td>
</tr>
<tr>
<td></td>
<td>Nonasthmatic eosinophilic bronchitis</td>
</tr>
<tr>
<td></td>
<td>Gastroesophageal reflux disease</td>
</tr>
<tr>
<td></td>
<td>Chronic bronchitis/COPD</td>
</tr>
<tr>
<td></td>
<td>Bronchiectasis</td>
</tr>
<tr>
<td></td>
<td>Bronchitic and other nonbronchiectatic suppurative airway disease</td>
</tr>
<tr>
<td></td>
<td>Occupational and environmental factors</td>
</tr>
<tr>
<td></td>
<td>Drug-induced cough</td>
</tr>
<tr>
<td></td>
<td>TB</td>
</tr>
<tr>
<td></td>
<td>Intestinal lung disease</td>
</tr>
<tr>
<td></td>
<td>Lung cancer</td>
</tr>
<tr>
<td></td>
<td>Aspiration</td>
</tr>
<tr>
<td></td>
<td>Cardiac causes</td>
</tr>
<tr>
<td></td>
<td>Psychogenic, habit, and tic cough</td>
</tr>
<tr>
<td></td>
<td>Uncommon causes</td>
</tr>
<tr>
<td></td>
<td>Unexplained (refractory) chronic cough</td>
</tr>
<tr>
<td>Special groups</td>
<td>Pediatric age group</td>
</tr>
<tr>
<td></td>
<td>Immunocompromised host</td>
</tr>
<tr>
<td></td>
<td>Athletes</td>
</tr>
<tr>
<td></td>
<td>The elderly</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>Cough suppressant</td>
</tr>
<tr>
<td></td>
<td>Pharmacologic promotive therapy</td>
</tr>
</tbody>
</table>

*While cough due to many conditions such as asthma and aspiration will be discussed in the chronic category, these conditions can present acutely and subacutely. Nevertheless, the same principles of management apply once the diagnosis is made.*

**Cough Guideline and Expert Panel Report**

**Diagnosis and Management of Cough: CHEST Evidence-Based Clinical Practice Guidelines**

Individual topics are being updated to the Diagnosis and Management of Cough: ACCP Evidence-Based Clinical Practice Guidelines (January, 2006) as new evidence is evaluated. Currently updated articles include:

- Available Online First! Cough in the Athlete: CHEST Guideline and Expert Panel Report (Online First)
- Chronic Cough Due to Gastroesophageal Reflux in Adults: CHEST Guideline and Expert Panel Report (Chest 2016;150(6):1341-1360)
- Somatic Cough Syndrome (Previously Referred to as Psychogenic Cough) and Tic Cough (Previously Referred to as Habit Cough) in Adults and Children: CHEST Guideline and Expert Panel Report (Chest 2014;148(1):24-31)

Irwin RS et al Chest 2014
Approach cough with an algorithm:
Approach cough with an algorithm:

1. Careful review of management prior to referral.
2. Considering the following:
   - Any remaining investigations to be undertaken?
     - YES: Other investigation(s) review with results and treat as indicated.
     - NO: Were trials of therapy optimal?
       - NO: Optimize treatment.
       - YES: Patient adherent?
         - YES: Manage nonadherence.
         - NO: Make diagnosis of “difficult to treat” cough.
           - NO: Cough resolved.
           - YES: Consider the following:
             - Speech and language intervention.
             - Empiric trial of gabapentin.
             - Referral to specialist cough clinic.
             - Recruit to clinical trial.
   - NO: Cough resolved?
     - YES: Consider the following.
     - NO: Cough resolved.

Approach cough with an algorithm:

Evaluation of subacute or chronic cough in adults

- Cough 3-4 weeks
  - History, physical exam suggest post-nasal drip, asthma, or GERD
    - Treat accordingly
  - Cough resolved
    - Cough persists
    - Chest radiograph
      - Normal (or old unrelated abnormality)
      - Abnormal
        - Evaluate based on the nature of the radiographic abnormality
          - Treat accordingly
          - Cough persists
          - Cough resolved

- Cough 2-3 weeks
  - History, physical exam do not strongly suggest cause or do suggest pulmonary parenchymal disease
  - Pantelus sputum OR
    - Smoker OR
    - ACE inhibitor treatment OR
    - Immunocompromised host
    - Evaluate and treat accordingly (e.g., antibiotics; smoking cessation; stop ACE inhibitor)
    - Cough persists
    - Cough resolved

- Cough resolved?
  - YES
    - Other investigations to be undertaken?
      - YES
        - Careful review of test results
        - Any remaining investigations to be undertaken?
          - YES
            - Other investigations to be undertaken?
              - YES
                - Other investigations to be undertaken?
                  - YES
                    - Other investigations to be undertaken?
                      - YES
                        - Other investigations to be undertaken?
                          - YES
                            - Other investigations to be undertaken?
                              - YES
                                - Other investigations to be undertaken?
                                  - YES
                                    - Other investigations to be undertaken?
                                      - YES
                                        - Other investigations to be undertaken?
                                          - YES
                                            - Other investigations to be undertaken?
                                              - YES
                                                - Other investigations to be undertaken?
                                                  - YES
                                                    - Other investigations to be undertaken?
                                                      - YES
                                                        - Other investigations to be undertaken?
                                                          - YES
                                                            - Other investigations to be undertaken?
                                                              - YES
                                                                - Other investigations to be undertaken?
                                                                  - YES
                                                                    - Other investigations to be undertaken?
                                                                      - YES
                                                                        - Other investigations to be undertaken?
                                                                          - YES
                                                                            - Other investigations to be undertaken?
                                                                              - YES
                                                                                - Other investigations to be undertaken?
                                                                                  - YES
                                                                                    - Other investigations to be undertaken?
                                                                                      - YES
                                                                                        - Other investigations to be undertaken?
                                                                                                                  - YES
                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                 - YES
                                                                                                                                               - Other investigations to be undertaken?
                                                                                                                                                          - YES
                                                                                                                                                                - Other investigations to be undertaken?
                                                                                                                                                                    - YES
                                                                                                                                                                      - Other investigations to be undertaken?
                                                                                                                                                                           - YES
                                                                                                                                                                                   - Other investigations to be undertaken?
                                                                                                                                                                                     - YES
                                                                                                                                                                                                                     - Other investigations to be undertaken?
                                                                                                                                                                                                                           - YES
                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                               - YES
                                                                                                                                                                                                                                                                       - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                   - YES
                                                                                                                                                                                                                                                                             - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                           - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                                      - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                                               - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                           - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
                                                                                                                                                                                                                                                                                    - YES
                                                                                                                                                                                                                                                                                    - Other investigations to be undertaken?
Approach cough with an algorithm:

Evaluation of subacute or chronic cough:

1. History/physical exam
   - Cardiac, neurological cause likely?
     - Yes → Targeted diagnosis and treatment → Success?
       - Yes → No further action
       - No → No further action
     - No → Chest X-ray PA and lateral

2. Cough explained by result?
   - Yes → Further diagnosis and treatment
   - No → Chest X-ray PA and lateral

3. Lung function test
   - Normal lung function?
     - Yes → Is non-specific provocation pathological?
       - Yes → Cough due to IHHR
       - No → Further diagnosis and treatment
     - No → Smoking or exposure to hazardous material?
       - Yes → Absention?
         - Yes → Absention successful, cough subsided?
         - No → Further diagnosis and treatment
       - No → Normal ENT exam?
         - Yes → Reflux?
           - Yes → Treatment → Success?
             - Yes → Further treatment
             - No → Further diagnosis and treatment
           - No → Further diagnosis and treatment
         - No → Are HRCT scan and bronchoscopy normal?
           - Yes → Eosinophilia in sputum
             - Yes → Eosinophilic bronchitis
             - No → Further diagnosis and treatment
           - No → Are HRCT scan and bronchoscopy normal?
             - Yes → Eosinophilia in sputum
               - Yes → Eosinophilic bronchitis
               - No → Further diagnosis and treatment
             - No → Further diagnosis and treatment

Kardos P and the German Respiratory Society, Pneumologie 2010
Approach cough with an algorithm:

Iyer VN and Lim KG Mayo Clin Proc 2013


Kardos P and the German Respiratory Society, Pneumologie 2010
Approach cough with an algorithm:

**Evaluation of subacute or chronic cough in adults**

- **Cough ≥3 weeks**
  - History, physical exam suggest post-nasal drip, asthma or GERD
    - Treat accordingly
  - History, physical exam do not strongly suggest cause or do suggest pulmonary parenchymal disease
    - Purulent sputum OR Smoker OR ACE inhibitor treatment OR Immunocompromised host
      - Evaluate and treat accordingly (eg, antibiotics; smoking cessation; stop ACE inhibitor)
  - Chest radiograph
    - Normal (or old unrelated abnormality)
      - Evaluate based on the nature of the radiographic abnormality
        - Treat accordingly
        - Cough persists
        - Cough resolved
    - Abnormal
      - Sequentially treat (or evaluate) for the most common causes of cough*:
        - Upper airway cough syndrome (allergy skin testing, sinus CT)
        - Asthma (PFTs)
        - Non-asthmatic eosinophilic bronchitis (sputum eosinophilia)
        - GERD (esophageal pH monitoring)
      - Treat accordingly

- **Cough resolved**
  - Cough persists

- **Cough resolved**
  - Evaluate for less common conditions (eg, sputum tests, HRCT scan, esophageal pH probe monitoring, esophagoscopy, flexible bronchoscopy, cardiac studies)
  - Treat accordingly

- **Cough persists**
  - Cough resolved
  - Cough persists

**Unexplained chronic cough**
Approach cough with an algorithm:

**Evaluation of subacute or chronic cough in adults**

1. **Cough ≥3 weeks**
   - History, physical exam do not strongly suggest cause or do suggest pulmonary parenchymal disease
   - Purulent sputum OR Smoker OR ACE inhibitor treatment OR Immunocompromised host

2. Evaluate and treat accordingly (eg, antibiotics; smoking cessation; stop ACE inhibitor)

   - Cough persists
   - Cough resolved

**TABLE 1. Causes of Chronic Cough**

- **Infectious:** mycobacterial-, pertussis-, fungal-, and protozoal-related infections
- **Airway disorders:** asthma, NAEB, bronchiectasis, atopic cough, chronic bronchitis, sarcoidosis, aspiration, and airway foreign bodies
- **Lung parenchymal diseases:** interstitial lung diseases, pulmonary hypersensitivity syndrome, and sarcoidosis
- **Tumors:** benign and malignant tumors involving the airways and parenchyma
- **Irritation of the external auditory meatus:** (the Arnold reflex)
- **Upper airway cough syndrome:** allergic and nonallergic rhinitis, chronic rhinosinusitis, and GERD
- **Esophageal causes:** GERD, laryngopharyngeal reflux, and tracheoesophageal fistula
- **Drugs:** ACE inhibitors and β-blockers
- **Airway irritants:** tobacco smoke, dust, fumes, and chemicals

**Box 2 | Red flags: alarm symptoms and findings in chronic cough**

- Hemoptysis
- Smoker with >20 pack year smoking history
- Smoker over 45 years of age with a new cough, altered cough, or cough with voice disturbance
- Prominent dyspnea, especially at rest or at night
- Substantial sputum production: more than one tablespoon a day
- Hoarseness
- Systemic symptoms: fever, weight loss
- Complicated gastroesophageal reflux disease (GORD) symptoms associated with weight loss, anemia, overt gastrointestinal bleeding (hematemesis or melena), severe symptoms, dysphagia, odynophagia, or failure of empiric treatment for GORD
- Recurrent pneumonia
- Abnormal clinical respiratory examination
- Abnormal chest radiograph

Iyer VN and Lim KG Mayo Clin Proc 2013

Gibson PG and Vertigan AE BMJ 2015
Approach cough with an algorithm:

These three make up 70-90% of all chronic coughs
Treat sequentially based on clues from history and physical
Give yourself at least 3 months to see improvements

- **Asthma**
  - Corticosteroids, Bronchodilators, Anticholinergics, Avoiding triggers

- **Upper airway cough syndrome (post nasal drip)**
  - Decongestants, Antihistamines, Anticholinergics, Nasal steroids

- **Reflux**
  - Diet and exercise, Lifestyle modifications, Acid suppressing medication (?)
A 42 year old man presents with dry cough for 3 months duration. He denies any reflux symptoms or wheezing. He endorses a diet heavy with caffeine, chocolate, and alcohol.

On exam, he has a body mass index of 29 kg/m2, central adiposity, and clear lung fields.

We suspect he has reflux related cough.

He asks the following:
- How could this be reflux associated cough if I don’t have heartburn?
- Is my weight related?
- Can I just take a proton pump inhibitor?
Gastro-esophageal reflux triggers the cough pathway

- Reflux irritates cough receptors (even if no GI symptoms)
- Sensory receptors in the esophagus form part of the afferent limb of an esophageal tracheobronchial cough reflex
- Giving HCL in the esophagus leads to cough

[Graphs showing comparison between HCl and saline for number of coughs and cough latency with p < 0.001 for both]
Gastro-esophageal reflux triggers the cough pathway

- Reflux irritates cough receptors (even if no GI symptoms)
- Sensory receptors in the esophagus form part of the afferent limb of an esophageal tracheobronchial cough reflex
- Even saline (without acid) can cause cough in patients

*Figure 2. Results of distal esophageal acid perfusion testing, comparing the number of coughs precipitated by saline and acid in patients with that in control subjects.*

Ing et al. Am J Respir Crit Care Med 1994
Weight correlates with cough severity

- Being overweight is a risk factor for gastro-esophageal reflux and cough.

- High calorie and fat diets associated with worse baseline cough scores in a small weight loss clinical trial:

  Higher LCQ score = Less coughing

Smith et al. Cough 2013
Weight loss has been shown to improve cough severity scores

- Weight loss effectively treats cough symptoms in GERD even in absence of PPI

- Each arm had a significant change in a cough questionnaire score of 3.6 units or 2.5 units

Smith et al. Cough 2013
What about the role for acid suppressing medications?
Chronic Cough – PPI

Clinical Trial: High-Dose Acid Suppression for Chronic Cough: A Randomized, Double-Blind, Placebo-Controlled Trial

- Chronic cough > 8 weeks, non smokers and no asthma
- Baseline 24h pH study, methacholine challenge test, laryngoscopy
- Esomeprazole 40 mg bid or placebo 12 weeks
- Primary outcome cough-specific quality of life questionnaire (CQLQ)

Shaheen et al. Aliment Pharmacol Ther. 2011
39 to 45% of patients had a positive pH study

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>PPI (n=22)</th>
<th>Placebo (n=18)</th>
<th>p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>49.5 (12.0)</td>
<td>51.0 (11.6)</td>
<td>0.7</td>
</tr>
<tr>
<td>Sex (n, %)</td>
<td></td>
<td></td>
<td>0.4</td>
</tr>
<tr>
<td>Female</td>
<td>16 (73)</td>
<td>15 (83)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (27)</td>
<td>3 (17)</td>
<td></td>
</tr>
<tr>
<td>Race (n, %)</td>
<td></td>
<td></td>
<td>0.7</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>4 (18)</td>
<td>3 (17)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>17 (77)</td>
<td>15 (83)</td>
<td></td>
</tr>
<tr>
<td>Positive MCT (n, %)</td>
<td>8 (36)</td>
<td>5 (28)</td>
<td>0.6</td>
</tr>
<tr>
<td>Positive pH study (n, %)</td>
<td>10 (45)</td>
<td>7 (39)</td>
<td>0.7</td>
</tr>
<tr>
<td>GSAS frequency score (median, IQR)</td>
<td>16.2 (7.5, 30.4)</td>
<td>14.3 (6.7, 52.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>GSAS distress score (median, IQR)</td>
<td>1.3 (1.2, 2.0)</td>
<td>1.9 (1.4, 2.5)</td>
<td>0.07</td>
</tr>
<tr>
<td>CQLQ (mean, SD)</td>
<td>52.9 (12.0)</td>
<td>58.2 (11.8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Cough Severity Score (mean, SD)</td>
<td>2.9 (0.8)</td>
<td>2.8 (0.7)</td>
<td>0.8</td>
</tr>
<tr>
<td>Cough Frequency Score (mean, SD)</td>
<td>6.2 (1.8)</td>
<td>6.8 (2.0)</td>
<td>0.3</td>
</tr>
<tr>
<td>Reflux Finding Score (mean, SD)</td>
<td>7.6 (2.2)</td>
<td>8.3 (2.6)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

MCT: Methacholine challenge test; GSAS: Gastroesophageal reflux Severity Assessment Score; CQLQ: Cough Specific Quality of Life Questionnaire

* p values obtained via Student’s t-tests or rank sum tests for continuous variables, or chi-squared tests for categorical variables
No difference in cough questionnaire between the groups at 12 weeks

Shaheen et al. Aliment Pharmacol Ther. 2011
Chronic Cough – PPI

- No difference in outcomes even when isolating the “high acid” groups

---

**Table 4**

Comparison of primary and secondary outcomes between treatment groups stratified by pH study results.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline mean (SD)</th>
<th>End mean (SD)</th>
<th>Change mean (SD)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High acid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CQLQ</td>
<td>49.8 (12.7)</td>
<td>38.7 (13.6)</td>
<td>11.1 (9.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Cough Severity Score</td>
<td>2.9 (0.7)</td>
<td>1.8 (0.9)</td>
<td>1.1 (1.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Cough Frequency Score</td>
<td>5.6 (1.9)</td>
<td>2.2 (1.0)</td>
<td>3.4 (2.0)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Reflux Finding Score</td>
<td>7.3 (2.9)</td>
<td>7.3 (2.5)</td>
<td>0 (2.4)</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Low acid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CQLQ</td>
<td>55.4 (11.3)</td>
<td>46.7 (14.4)</td>
<td>8.8 (14.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>Cough Severity Score</td>
<td>2.9 (0.9)</td>
<td>2.0 (1.0)</td>
<td>0.9 (1.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Cough Frequency Score</td>
<td>6.7 (1.7)</td>
<td>3.7 (2.0)</td>
<td>3.0 (2.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Reflux Finding Score</td>
<td>7.8 (1.4)</td>
<td>6.6 (2.0)</td>
<td>1.1 (1.5)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline mean (SD)</th>
<th>End mean (SD)</th>
<th>Change mean (SD)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High acid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CQLQ</td>
<td>60.0 (12.3)</td>
<td>55.3 (10.7)</td>
<td>4.7 (9.4)</td>
<td>0.2</td>
</tr>
<tr>
<td>Cough Severity Score</td>
<td>2.9 (0.7)</td>
<td>2.3 (1.1)</td>
<td>0.6 (0.8)</td>
<td>0.1</td>
</tr>
<tr>
<td>Cough Frequency Score</td>
<td>8.0 (2.2)</td>
<td>4.3 (2.8)</td>
<td>3.7 (2.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Reflux Finding Score</td>
<td>9.7 (2.0)</td>
<td>9.3 (3.3)</td>
<td>0.4 (3.1)</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Low acid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CQLQ</td>
<td>57.1 (11.9)</td>
<td>50.5 (14.2)</td>
<td>6.6 (12.4)</td>
<td>0.1</td>
</tr>
<tr>
<td>Cough Severity Score</td>
<td>2.8 (0.8)</td>
<td>1.8 (1.0)</td>
<td>1.0 (1.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Cough Frequency Score</td>
<td>6.1 (1.5)</td>
<td>4.7 (2.5)</td>
<td>1.5 (2.8)</td>
<td>0.1</td>
</tr>
<tr>
<td>Reflux Finding Score</td>
<td>7.4 (2.6)</td>
<td>7.5 (3.7)</td>
<td>-0.1 (2.8)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Shaheen et al. Aliment Pharmacol Ther. 2011
Proton pump inhibitors have a strong placebo effect

- Mixed results in the randomized controlled trials with strong placebo effect of PPI therapy particularly in patients with normal esophageal pH.
Chronic cough and reflux:

- Any trial which included weight loss and/or lifestyle modifications had greatest impact.

- One such RCT showed that lifestyle modifications (elevate head of bed, no food for 2h before bed, avoidance of fatty meals/alcohol/caffeine/tobacco) and weight loss counseling worked in PPI and control group:

### Table 3. Treatment effects within each group

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control</th>
<th>PPI</th>
<th>PPI vs Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Change</td>
<td>CI 95%</td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Reflux Score</td>
<td>19</td>
<td>6.6 ± 12.5</td>
<td>0.6–12.7</td>
</tr>
<tr>
<td>Sig Global Improvement</td>
<td>18</td>
<td>50.0%</td>
<td>29%–71%</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reflux Severity</td>
<td>19</td>
<td>3.0 ± 6.1</td>
<td>0.1–6.0</td>
</tr>
<tr>
<td>Reflux Frequency</td>
<td>19</td>
<td>3.6 ± 7.1</td>
<td>0.2–7.0</td>
</tr>
</tbody>
</table>

Chronic cough and reflux:

- ACCP updated guidelines 2016:

Summary of Recommendations and Suggestions

2. In adult patients with chronic cough suspected to be due to reflux-cough syndrome, we recommend that treatment include (1) diet modification to promote weight loss in overweight or obese patients; (2) head of bed elevation and avoiding meals within 3 hours of bedtime; and (3) in patients who report heartburn and regurgitation, proton pump inhibitors (PPIs), H₂-receptor antagonists, alginate, or antacid therapy sufficient to control these symptoms (Grade 1C).

Summary of Recommendations and Suggestions

3. In adult patients with suspected chronic cough due to reflux-cough syndrome, but without heartburn or regurgitation, we recommend against using PPI therapy alone because it is unlikely to be effective in resolving the cough (Grade 1C).

Summary

- Healthy weight loss
- Lifestyle modifications and reflux precautions
- PPI if the patient has heartburn or regurgitation symptoms
- No PPI if no GI symptoms
Approach cough with an algorithm:

Evaluation of subacute or chronic cough in adults

- **Asthma**
  - Corticosteroids, Bronchodilators, Anticholinergics, Avoiding triggers
- **Upper airway cough syndrome (post nasal drip)**
  - Decongestants, Antihistamines, Anticholinergics, Nasal steroids
- **Reflux**
  - Diet and exercise, Lifestyle modifications, Acid suppressing medication (?)
Approach cough with an algorithm:

Evaluation of subacute or chronic cough in adults

- Cough ≥3 weeks
  - History, physical exam suggest post-nasal drip, asthma or GERD
    - Treat accordingly
  - History, physical exam do not strongly suggest cause or do suggest pulmonary parenchymal disease
    - Cough persists
    - Cough resolved
    - Chest radiograph
      - Normal (or old unrelated abnormality) or Abnormal
        - Evaluate based on the nature of the radiographic abnormality
          - Treat accordingly
          - Cough persists or Cough resolved
            - Sequentially treat (or evaluate) for the most common causes of cough*:
              - Upper airway cough syndrome (allergy skin testing, sinus CT)
              - Asthma (PFTs)
              - Non-asthmatic eosinophilic bronchitis (sputum eosinophilia)
              - GERD (esophageal pH monitoring)
            - Treat accordingly
Approach cough with an algorithm:

Evaluation of subacute or chronic cough in adults

- Cough ≥3 weeks
  - History, physical exam suggest post-nasal drip, asthma or GERD
    - Treat accordingly
    - Cough resolved
    - Cough persists
  - History, physical exam do not strongly suggest cause or do suggest pulmonary parenchymal disease
    - Evaluate and treat accordingly (eg, antibiotics; smoking cessation; stop ACE inhibitor)
    - Cough persists
    - Cough resolved
  - Purulent sputum OR Smoker OR ACE inhibitor treatment OR Immunocompromised host
    - Evaluate for less common conditions (eg, sputum tests, HRCT scan, esophageal pH probe monitoring, esophagoscopy, flexible bronchoscopy, cardiac studies)
    - Treat accordingly
    - Cough resolved
    - Cough persists

- Normal (or old unrelated abnormality)
  - Treat accordingly
  - Cough persists
  - Cough resolved

- Abnormal
  - Evaluate based on the nature of the radiographic abnormality
    - Treat accordingly
    - Cough persists
    - Cough resolved

- Sequentially treat (or evaluate) for the most common causes of cough*:
  - Upper airway cough syndrome (allergy skin testing, sinus CT)
  - Asthma (PFTs)
  - Non-asthmatic eosinophilic bronchitis (sputum eosinophilia)
  - GERD (esophageal pH monitoring)
  - Treat accordingly

Unexplained chronic cough
A 38 year old woman presents with chronic cough for almost 2 years. She has been treated sequentially for suspected asthma, gastro-esophageal reflux, and post-nasal drip.

Exam is notable for a normal BMI, normal HEENT and pulmonary examination. She is on no medications. Chest x-ray and PFTs have been normal.

She wants to know the following:
- What is my diagnosis?
- Do I need therapy?
- Is there a magic pill for this cough?
Systemic review of RCTs

- What is the efficacy of treatment compared with usual care for cough severity, cough frequency, and cough-related quality of life in patients with unexplained chronic cough

- 11 RCTs, 5 systematic reviews included
Chronic cough - definition:

- CHEST Expert Cough Panel:
  - Unexplained chronic cough:
  - Refractory chronic cough:

1. In adult patients with chronic cough, we suggest that unexplained chronic cough be defined as a cough that persists longer than 8 weeks, and remains unexplained after investigation, and supervised therapeutic trial(s) conducted according to published best-practice guidelines (Ungraded Consensus-Based Statement).

Chronic cough - guidelines:

Summary of Recommendations and Suggestions
2. In adult patients with chronic cough, we suggest that patients with chronic cough undergo a guideline/protocol based assessment process that includes objective testing for bronchial hyperresponsiveness and eosinophilic bronchitis, or a therapeutic corticosteroid trial (Ungraded Consensus-Based Statement).

• ACCP proposed algorithm:
Chronic cough - guidelines:

Summary of Recommendations and Suggestions

3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

5. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of gabapentin as long as the potential side effects and the risk-benefit profile are discussed with patients before use of the medication, and there is a reassessment of the risk-benefit profile at 6 months before continuing the drug (Grade 2C).

6. In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).
Chronic cough - guidelines:

• There is 1 good randomized controlled trial of 87 patients.

• 4 sessions of speech therapy vs healthy lifestyle education

Summary of Recommendations and Suggestions

3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

5. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of gabapentin as long as the potential side effects and the risk-benefit profile are discussed with patients before use of the medication, and there is a reassessment of the risk-benefit profile at 6 months before continuing the drug (Grade 2C).

6. In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).

Vertigan et al Thorax 2006
Chronic cough - guidelines:

Summary of Recommendations and Suggestions

3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

5. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of gabapentin as long as the potential side effects and the risk-benefit profile are discussed with patients before use of the medication, and there is a reassessment of the risk-benefit profile at 6 months before continuing the drug (Grade 2C).

6. In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).

- There is 1 good randomized controlled trial of 87 patients.
- 4 sessions of speech therapy vs healthy lifestyle education

Table 2  Examples of strategies in the treatment programme

<table>
<thead>
<tr>
<th>Component</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td>No physiological benefit from cough; capacity for voluntary cough control</td>
</tr>
<tr>
<td>Strategies to reduce cough</td>
<td>Identify warning signs for cough and replace with modified swallow technique, pursed lip breathing exercise, or relaxed throat breath</td>
</tr>
<tr>
<td>Reduce laryngeal irritation</td>
<td>Increase hydration, decrease exposure to irritating stimuli</td>
</tr>
<tr>
<td>Psycho-educational counselling</td>
<td>Internalising locus of control; acceptance that treatment is hard work; setting realistic goals</td>
</tr>
</tbody>
</table>
Chronic cough - guidelines:

There is 1 good randomized controlled trial of 87 patients.

4 sessions of speech therapy vs healthy lifestyle education

Summary of Recommendations and Suggestions

3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

5. In adult patients with unexplained chronic cough and negative tests, we suggest a therapeutic trial of gal as the potential side effects and the profile are discussed with patients b medication, and there is reassessm benefit profile at 6 months before co (Grade 2C).

6. In adult patients with unexplained chronic cough and a negative workup for acid gast reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).

Table 6 Comparison of clinical judgement of outcome of the intervention between treatment and placebo groups ($\chi^2$ test)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treatment (N = 43)</th>
<th>Placebo (N = 44)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful</td>
<td>38</td>
<td>6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unsuccessful</td>
<td>2</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Partially successful</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>
Summary of Recommendations and Suggestions

3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

5. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of gabapentin as long as the potential side effects and the risk-benefit profile are discussed with patients before use of the medication, and there is a reassessment of the risk-benefit profile at 6 months before continuing the drug (Grade 2C).

6. In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).
Chronic cough - guidelines:

Summary of Recommendations and Suggestions

3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

5. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of gabapentin as long as the potential side effects and the risk-benefit profile are discussed with patients before use of the medication, and there is a reassessment of the risk-benefit profile at 6 months before continuing the drug (Grade 2C).

6. In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).

Nonasthmatic chronic cough: No effect of treatment with an inhaled corticosteroid in patients without sputum eosinophilia

- 44 adults, age 45+
- 1 year of cough
- No asthma or otherwise known etiology
- Randomized and blinded to budesonide 400 mg bid x2 weeks or placebo
- Results: nonasthmatic chronic cough had no evidence of response to budesonide

Pizzichini et al. Can Respir J 1999
Chronic cough - guidelines:

Summary of Recommendations and Suggestions

3. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of multimodality speech pathology therapy (Grade 2C).

4. In adult patients with unexplained chronic cough and negative tests for bronchial hyperresponsiveness and eosinophilia (sputum eosinophils, exhaled nitric oxide), we suggest that inhaled corticosteroids not be prescribed (Grade 2B).

5. In adult patients with unexplained chronic cough, we suggest a therapeutic trial of gabapentin as long as the potential side effects and the risk-benefit profile are discussed with patients before use of the medication, and there is a reassessment of the risk-benefit profile at 6 months before continuing the drug (Grade 2C).

6. In adult patients with unexplained chronic cough and a negative workup for acid gastroesophageal reflux disease, we suggest that proton pump inhibitor therapy not be prescribed (Grade 2C).

- Cochrane review of 8 primary studies, 570 participants
- While ICS treatment resulted in a mean decrease in cough score of 0.34 standard deviations, the quality of evidence was low.
- International cough guidelines recommend that a trial of ICS should only be considered in patients with evidence of asthma or eosinophilic pulmonary disease

Johnstone KJ et al. Cochrane Airways Group 2013
Chronic cough - guidelines:

- Target neuronal pathways:
  - Gabapentin
  - Pregabalin

- Target microbiome and inflammatory pathways:
  - Azithromycin

- Target the cough reflex:
  - AF-219
Unexplained chronic cough – Gabapentin:

Gabapentin for refractory chronic cough: a randomised, double-blind, placebo-controlled trial

- 62 patients randomly assigned to gabapentin (up to 1800 mg daily dosage) or placebo

- Chronic cough > 8 weeks
  - All participants had previously been treated for asthma, reflux, and rhinosinusitis
  - Excluded smokers, chronic lung disease, ACE inhibitor usage, purulent sputum

- Treatment protocol:
  - 5 visits over 16 weeks
  - Start at 300 mg and titrate up until cough resolved or side effects intolerable

- Primary outcome was a change in cough score from baseline to 8 weeks

Ryan NM et al, Lancet 2012;380:1583-89
Unexplained chronic cough – Gabapentin:

- Cough scores were significantly improved in the gabapentin group.
Unexplained chronic cough – Gabapentin:

- Side effects were more common in the gabapentin group
- 31% adverse effect rate with gabapentin (vs 10% in placebo)
- 1 patient in each arm withdrew due to side effects

<table>
<thead>
<tr>
<th></th>
<th>Gabapentin (n=17)</th>
<th>Placebo (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blurred vision</td>
<td>1 (6%)</td>
<td>0</td>
</tr>
<tr>
<td>Depression</td>
<td>0</td>
<td>1* (17%)</td>
</tr>
<tr>
<td>Disorientation, confusion</td>
<td>2 (12%)</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3 (18%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Dry or very dry mouth</td>
<td>2 (12%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (18%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (6%)</td>
<td>0</td>
</tr>
<tr>
<td>Memory loss</td>
<td>1 (6%)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea, stomach pain</td>
<td>4 (24%)</td>
<td>2 (33%)</td>
</tr>
</tbody>
</table>

Data are number of events (%). n=total number of events associated with study drug. *Possible comorbidity (present before study).

Table 2: Adverse effects
Unexplained chronic cough – Pregabalin:

- Random allocation to speech therapy plus pregabalin (up to 300 mg daily) or speech therapy plus placebo for 14 weeks

- Enrolled 40 patients with chronic cough
Unexplained chronic cough – Pregabalin:

- Side effects were more common in the pregabalin group

**Table 5** Comparison of Side Effects Between Participants Taking SP + PREG and Participants Taking SP + PLAC

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>SP + PREG</th>
<th>SP + PLAC</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blurred vision</td>
<td>4 (20)</td>
<td>1 (5)</td>
<td>.003</td>
</tr>
<tr>
<td>Cognitive changes</td>
<td>6 (30)</td>
<td>1 (5)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9 (45)</td>
<td>1 (5)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>2 (10)</td>
<td>1 (5)</td>
<td>.197</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7 (35)</td>
<td>6 (30)</td>
<td>.535</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>2 (10)</td>
<td>.007</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>5 (25)</td>
<td>7 (35)</td>
<td>.197</td>
</tr>
<tr>
<td>Respiratory (eg, shortness of breath, increased cough)</td>
<td>3 (15)</td>
<td>3 (15)</td>
<td>NS</td>
</tr>
<tr>
<td>Weight gain</td>
<td>5 (25)</td>
<td>1 (5)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Dermatological</td>
<td>1 (5)</td>
<td>2 (10)</td>
<td>.197</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>0 (0)</td>
<td>2 (10)</td>
<td>.007</td>
</tr>
<tr>
<td>Fluid build-up</td>
<td>2 (10)</td>
<td>1 (5)</td>
<td>.197</td>
</tr>
<tr>
<td>Tight leg and feet muscles/cramps</td>
<td>2 (10)</td>
<td>1 (5)</td>
<td>.197</td>
</tr>
</tbody>
</table>

All data are No. (%) unless otherwise indicated. NS = not significant. See Table 1 and 2 legends for expansion of other abbreviations.

Vertigan AE et al. Chest 2016
Unexplained chronic cough – Azithromycin:

The Effects of Azithromycin in Treatment-Resistant Cough
A Randomized, Double-Blind, Placebo-Controlled Trial

- Randomized trial. 8 weeks of treatment

- Asthmatic patients included if had normal spirometry and no improvement with prednisone.

- Treatment with azithromycin 500 mg daily x3 days then 250 mg three times a week for 8 weeks

- Primary outcome was change in cough questionnaire at week 8

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Baseline Characteristics of Trial Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>Azithromycin (n = 22)</td>
</tr>
<tr>
<td>Age, a years</td>
<td>59.6 (11.0)</td>
</tr>
<tr>
<td>Female, %</td>
<td>73</td>
</tr>
<tr>
<td>BMI, b kg/m²</td>
<td>28.3 (4.0)</td>
</tr>
<tr>
<td>Smoking, b pack-years</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Asthma diagnosis</td>
<td>8/22 (36%)</td>
</tr>
<tr>
<td>Reflux symptoms</td>
<td>6/22 (27%)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>3/22 (14%)</td>
</tr>
<tr>
<td>PD_{20} methacholine, c μg</td>
<td>660.7 (0.6)</td>
</tr>
<tr>
<td>LCQ score a</td>
<td>10.2 (3.3)</td>
</tr>
<tr>
<td>Cough severity score a</td>
<td>6.4 (1.9)</td>
</tr>
<tr>
<td>FENO, c ppb</td>
<td>21.1 (0.6)</td>
</tr>
<tr>
<td>Blood neutrophils, x10^9/L</td>
<td>3.75 (3.25-4.6)</td>
</tr>
</tbody>
</table>

Unexplained chronic cough – Azithromycin:

![Graph showing changes in LCQ score over 12 weeks between Azithromycin and Placebo groups.]

**TABLE 2** Changes Within and Between Groups Between Baseline and Week 8

<table>
<thead>
<tr>
<th>Variable</th>
<th>Azithromycin (n = 21)</th>
<th>Placebo (n = 21)</th>
<th>Between Group P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomization</td>
<td>Week 8</td>
<td>P Value</td>
</tr>
<tr>
<td>LCQ score</td>
<td>10.2 (3.3)</td>
<td>12.6 (4.9)</td>
<td>.01</td>
</tr>
<tr>
<td>CSS</td>
<td>6.4 (1.9)</td>
<td>5.4 (2.9)</td>
<td>.07</td>
</tr>
<tr>
<td>FENO, a ppb</td>
<td>20.1 (0.06)</td>
<td>16.3 (0.06)</td>
<td>.01</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) unless indicated otherwise. CSS = cough severity score. See Table 1 legend for expansion of other abbreviations. a Geometric mean (log SD).

Hodgson et al, Chest 2016
Unexplained chronic cough – Azithromycin:

### Table 3: Characteristics of Clinical Responders vs Nonresponders in the Azithromycin Group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Responders (n = 11)</th>
<th>Nonresponders (n = 10)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>8 (73%)</td>
<td>8 (80%)</td>
<td>.7</td>
</tr>
<tr>
<td>Age, a years</td>
<td>59.1 (12.6)</td>
<td>60.5 (10.1)</td>
<td>.82</td>
</tr>
<tr>
<td>BMI, b kg/m²</td>
<td>30.9 (3.1)</td>
<td>26.3 (2.6)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Asthma</td>
<td>7 (64%)</td>
<td>0 (0%)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Reflux</td>
<td>3 (27%)</td>
<td>2 (20%)</td>
<td>.7</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>1 (9%)</td>
<td>1 (10%)</td>
<td>.94</td>
</tr>
<tr>
<td>Baseline LCQ a</td>
<td>10.0 (3.0)</td>
<td>10.0 (3.9)</td>
<td>.1</td>
</tr>
<tr>
<td>Baseline CSS a</td>
<td>6.4 (1.8)</td>
<td>6.7 (2.2)</td>
<td>.72</td>
</tr>
<tr>
<td>Baseline Fexa b</td>
<td>20.3 (0.58)</td>
<td>20.3 (0.54)</td>
<td>.1</td>
</tr>
<tr>
<td>Baseline sputum score a</td>
<td>3.7 (2.3)</td>
<td>3.6 (2.1)</td>
<td>.1</td>
</tr>
</tbody>
</table>

Data are presented as No. (%) unless indicated otherwise. See Table 1 and 2 legends for expansion of abbreviations.

*Mean (SD).

**Geometric mean (log SD).**

![Change in LCQ score](Hodgson et al, Chest 2016)
P2X3 receptors are expressed by airway vagal afferent nerves.

These receptors contribute to the hypersensitization of sensory neurons.

Activation could lead to chronic cough.

AF-219 is an oral P2X3 antagonist.
Unexplained chronic cough - guidelines:

Treatment of Unexplained Chronic Cough
CHEST Guideline and Expert Panel Report

Take home points:
- Inhaled corticosteroids were found to be ineffective for UCC
- Proton pump inhibitors are ineffective for UCC without GERD
- Multimodality speech pathology intervention improved cough severity
- Gabapentin is supported as a treatment recommendation
Unexplained chronic cough case:

- A 38 year old woman presents with chronic cough for almost 2 years. She has been treated sequentially for suspected asthma, gastro-esophageal reflux, and post-nasal drip.

- Exam is notable for a normal BMI, normal HEENT and pulmonary examination. She is on no medications. Chest x-ray and PFTs have been normal.

- She wants to know the following:
  - What is my diagnosis?
  - Do I need therapy?
  - Is there a magic pill for this cough?
Summary and Take Home Points:

1. Chronic cough carries significant morbidity and cost to our patients and healthcare community

2. Asthma, upper airway cough syndrome (post-nasal drip), and reflux are the most common causes of chronic cough

3. Trust your algorithm to guide your workup and treatment

4. The treatment of reflux cough syndrome involves diet, exercise, and lifestyle modifications. Use of an acid suppressing medication should be used only if dictated by GI symptoms

5. Unexplained chronic cough is difficult to treat. Longterm inhaled corticosteroids and acid suppressing medication are not recommended.

6. Consider speech therapy and gabapentin for unexplained chronic cough. Talk with patient about risks of gabapentin
Thank you!
Questions or comments:

Eric M. Davis, MD
emd9b@virginia.edu
434-982-0405