Cough

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M III Medicine Clerkship

Question:

- The 2006 American College of Chest Physicians Consensus Evidence-Based Guidelines statement on the management and diagnosis of cough is:
  - A. 10 pages
  - B. 20 pages
  - C. 100 pages
  - D. 300 pages

Cough:

- 30 million outpatient physician visits per year
  (many for cough associated with common cold)
- Up to 40% of outpatient pulmonary practice can consist of evaluation/treatment of chronic cough
- Billions of dollars spent on treatments for cough (most of which are partially or minimally effective)

Physiology:

- A vigorous cough can generate expiratory air velocities up to:
  - A. 5 L/sec
  - B. 10 L/sec
  - C. 100 miles per hour
  - D. 500 miles per hour

Physiology:

- Very important protective role
- Impaired cough: elderly, newborn, lung transplant, neuromuscular disease
- Animal studies show vagal afferent nerves initiate cough reflex (terminate in airway mucosa/airway wall down to terminal bronchioles/parenchyma)

Physiology:

- Rapidly adapting receptors (RARs)
  - Respond to changes in mechanical properties
  - Airway diameter, length, pressures
- Slowly adapting stretch receptors (SARs)
  - Role less defined
- C-fibers
  - Majority of airway afferent nerves
  - Respond to noxious mechanical or chemical stimuli
- Nerves also from chest wall, diaphragm, esophagus, stomach, pericardium, pharynx, larynx
**Physiology:**

- **Higher cortical control of the reflex as well**
  - Cough suppression
  - Voluntary cough
- **Gender differences**
  - Women may have higher cough reflex sensitivity

**Table 1—Properties of Nerve Fibres Nerve Fibres Innervating the Airways**

<table>
<thead>
<tr>
<th>Property</th>
<th>Thick</th>
<th>Thin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (µm)</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Conduction speed</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>Threshold (mV)</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>Frequency (Hz)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**Inspiratory phase**

- Inhale some amount of air
- Higher lung volumes will allow more positive intrathoracic pressure and thus higher flow and dynamic airway compression (further enhancing velocity)
- Effective cough can be generated at pressures (inhaled volume) much lower than maximum, ie effective cough can occur with small inhalational volume

**Compressive phase**

- Glottis closure (about 0.2 sec)
- Followed by expiratory effort (thoracic and abdominal muscles)
- Maintained lung volumes but intrathoracic (and intraabdominal) pressure rises – up to 300 mm Hg
- Transmission of this pressure explains some of the GU, GI, CNS, and musculoskeletal complications of cough

**Expiratory phase:**

- Glottis opens and high pressures promote high flow rates
- Initial burst up to 12 L/sec
- Dynamic compression of central airways (further enhances air flow velocity)
- Can occur without glottic closure
  - “Huff” cough (open glottis)
  - Endotracheal tube or tracheostomy
Classification:

- Acute: < 3 weeks
- Subacute: 3 to 8 weeks
- Chronic: > 8 weeks

Acute Cough

Acute cough:
- Most common: upper respiratory tract infection
- Rule out life-threatening conditions:
  - pneumonia, severe asthma, PE, heart failure, etc
- Exacerbation of pre-existing condition:
  - asthma, bronchiectasis, UACS (upper airway cough syndrome), COPD
- Environmental/occupational
  - Toxins, smoke, dust, animals, etc

Acute cough is often caused by an upper respiratory tract infection. It is important to rule out life-threatening conditions and consider exacerbation of pre-existing conditions. Environmental factors can also contribute to acute cough.

Cough in the common cold:
- Most common cause of acute cough
- U.S. adults 2 - 4 colds/year
- 200 viruses capable of common cold
- Key points:
  - First generation antihistamine (brompheniramine) and decongestant (pseudoephedrine – sustained release)
  - Naproxen may decrease cough
  - Newer non-sedating antihistamines ineffective
  - Maxillary sinus CT abnormal in 87% - do not diagnose bacterial sinusitis in first week
  - Cough may be sustained for 2-3 weeks

Subacute Cough

Subacute cough is post-infectious, occurring at least 3 weeks after an acute respiratory infection. It is often characterized by airway inflammation, bronchial hyperresponsiveness, and impaired mucociliary clearance. Management may involve trials of inhaled ipatropium or inhaled steroids, with severe cases potentially requiring prednisone 40 mg daily short course and central acting antitussive (codeine).
Post-infectious:
- If severe paroxysms, posttussive vomiting, inspiratory whooping sound consider B. pertussis
- Nasopharyngeal aspirate or polymer swab for culture (PCR not recommended)
- Presumptive diagnosis: acute and convalescent sera antibodies
  - Fourfold increase in IgG or IgA to PT consistent with recent infection
- Macrolide antibiotic and isolate first 5 days treatment
  - Reduces coughing and spread of disease

Chronic cough:
- Which of the following commonly leads to a diagnosis in the etiology of chronic cough?
  - A. Chest CT scan
  - B. 24 hour esophageal pH monitoring
  - C. Bronchoscopy
  - D. Sinus x-rays

Chronic cough:
- Recommendation:
  - Patients with chronic cough with normal CXR, nonsmokers, not on an ACE inhibitor should be investigated for one or more of the following:
    - UACS (formerly post-nasal drip)
    - GERD
    - Asthma
    - NAEB (nonasthmatic eosinophilic bronchitis)
- Any of these can present with cough alone
- Description or character of cough not predictive

Chronic cough:
- Western hemisphere – non-smoker and non-ACE inhibitor cough 92-100% cases explained by one or more of the triad:
  - UACS
  - GERD
  - Asthma

UACS:
- Most common cause of chronic cough
  - And acute cough as well (common cold)
- Formerly known as postnasal drip syndrome
- Throat clearing, hoarseness, nasal congestion, cobblestoning of oropharyngeal mucosa
- No pathognomonic findings
  - Some have cough as only symptom
- Best test is response to treatment

Table 1—Summary of Most Common Causes of Cough Reported in the Literature

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>31</td>
<td>15</td>
<td>20</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>31</td>
<td>15</td>
<td>20</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>31</td>
<td>15</td>
<td>20</td>
<td>15</td>
<td>20</td>
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<tr>
<td>GERD</td>
<td>31</td>
<td>15</td>
<td>20</td>
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<tr>
<td>Asthma</td>
<td>31</td>
<td>15</td>
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</tr>
<tr>
<td>UACS</td>
<td>31</td>
<td>15</td>
<td>20</td>
<td>15</td>
<td>20</td>
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</tbody>
</table>

PA = Pseudomonas; CB = chest x-ray; CB = chest x-ray; FB = frontal sinus x-ray; P = paranasal x-ray; M = rhinoscopy; D = diagnosis

Note: Incidence of all these diagnoses are present.
UACS:
- Allergic rhinitis
- Perennial nonallergic rhinitis
- Postinfectious rhinitis
- Bacterial sinusitis
- Allergic fungal sinusitis
- Rhinitis due to physical/chemical irritants
- Occupational rhinitis
- Rhinitis medicamentosa
- Rhinitis of pregnancy

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UACS:
- Specific treatment if cause of UACS-induced cough is obvious
- Most patients should receive an empiric trial of therapy (antihistamine/decongestant)
- Nonresponders should have sinus imaging to evaluate for chronic sinusitis

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GERD:
- May be the second most common cause of chronic cough
- Esophageal-bronchial reflex (no aspiration) or direct irritation
- Endoscopy may show: laryngitis, red arytenoids, piled-up interarytenoid mucosa, subglottic stenosis, hemorrhagic tracheobronchitis, mucosal erythema of distal bronchi
- Endoscopy can be normal (if reflex mediated)

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GERD:
- If chronic cough and GERD symptoms then treat
- Previous antireflux surgery does not rule out reflux as cause of cough
- Best diagnostic test is resolution of cough with therapy
- 24 hour esophageal pH probe most sensitive and specific but often does not rule-out reflux as cause of cough (severity doesn't correlate)
- Nonacid GERD can be a cause (normal pH probe) – sometimes seen on barium swallow

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GERD:
- Normal EGD does not rule out GERD
- Empiric therapy in most cases:
  - Lifestyle/dietary changes
  - Acid suppression therapy
  - Prokinetic therapy
- If empiric therapy fails – objective testing for GERD recommended (GERD not ruled out)

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GERD:
- Lifestyle changes:
  - Elevate head of bed
  - Avoid supine position 3 hours after meals
  - Avoid coffee, tea, soda, chocolate, mints, citrus products, tomatoes, alcohol, smoking
  - Avoid vigorous exercise (that increases intrabdominal pressure)
- If lifestyle changes and maximal medical therapy fail – consider antireflux surgery

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NAEB:
- Described as cause of chronic cough in 1989
- Nonsmokers without asthma
- No airway hyperresponsiveness
- >3% non-squamous cell sputum eosinophilia (outside 90th percentile in healthy patients)
- Etiology unknown – maybe associated with inhaled allergen

ACE:
- Occurs in 0 – 3%
- Dry and tickling cough
- Not dose dependent
- Cough more common in women, nonsmokers, and Chinese
- May occur from increased bradykinin (degraded by ACE) accumulating in lung or airway

ACE-inhibitor:
- In chronic cough ACE should be stopped regardless of time interval from onset of cough and initiation of ACE
- Most improve 1 - 4 weeks (a few take 3 months)
- If ACE is required – repeat trial of ACE may be attempted
- If cough then persist – try theophylline, sulindac, indomethacin, amldipine, nifedipine, Fe to suppress cough
- Incidence of ARB cough similar to control drug

Other causes not discussed:
- Asthma
- Acute and chronic bronchitis
- Bronchiectasis
- Bronchiolitis
- Lung tumors
- Aspiration of food and liquids
- Habit, tic, or psychogenic cough
- Interstitial lung disease
- Infections
- Numerous other causes!
IDIOPATHIC COUGH

Complications:
- Quality of life
  - Family frustrations
  - Embarrassment
  - Impaired work or social activities
  - Impaired ability to talk
  - Self-consciousness

Case 1:
- 54-year-old female with cough X 7 months
- PMHX: HTN, hypercholesterolemia
- Dry cough with mild hoarseness
- No heartburn or rhinitis
- Normal CXR
- Previously treated with Allegra, Flonase, Advair
- Also treated with Nexium 40 mg daily X 1 month without improvement
- Other questions?
- Next step?

Case 2:
- 45-year-old female with dry cough X 10 weeks
- PMHX: HTN, GERD, Type 2 DM
- Medications include Nexium and lisinopril
- ACE inhibitor started > 1 year ago
- Mild GERD symptoms and no rhinorrhea
- Normal CXR
- Next step?

Case 3:
- 62-year-old male with cough X 10 months
- Previous treatments include Nexium 40 mg daily X 4 months and Allegra/flonase daily X 3 months without any improvement
- Dry cough without wheezing
- Normal CXR
- Next step?