Chronic Cough – Updates in Diagnosis and Management

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Why do we cough?

- Occasional cough is normal
- Allows us to clear irritants, foreign materials, and secretions from the airway
- 3 phases:
  - Inspiratory phase
  - Compressive phase (forced expiratory effort against closed glottis)
  - Expulsive phase (glottis opens, rapid expiratory airflow)
- Chronic cough
  - $\geq 8$ weeks in Adults
  - $\geq 4$ weeks in Children
Impact of chronic cough

* 10-12% prevalence in general population
* Up to 40% of practice volume for pulmonologist
* 2013 CHEST survey: $6.8 billion spent by U.S. consumers in 1 year
* Greatly underestimates total economic burden:
  * Direct costs: physician fees, imaging, laboratory testing, procedures
  * Indirect costs: time missed from work, school
Earlier Remedies

Dr. Batty's
For Your Health
Asthma Cigarettes
Since 1892
For the temporary relief of paroxysms of asthma
Effectively treats:
Asthma, Hay Fever, Foul Breath
All Diseases of the Throat,
Head Colds, Canker Sours
Bronchial Irritations
Not Recommended for Children under 6.

Cough
The problem
Has been solved by
the pharmaceutical compound known as
Glyco-Heroin (Smith)

One Night
Trade Mark
Cough Syrup
Each ounce contains
Alcohol, (less than 1%) 4.4
Cannabis Indica, F.E. 4.5
Chloroform, Morphia, Sulph.

Skillfully combined with a number of other ingredients

DIRECTIONS
Dose: One half teaspoonful three
Complications

- Headache
- Dizziness
- Sweating
- Urinary incontinence
- Social stigma
- Decreased QOL, work productivity
- Rib fracture
- Syncope
## Cough Reflex

<table>
<thead>
<tr>
<th>Receptors</th>
<th>Afferent pathways</th>
<th>Cough center</th>
<th>Efferent pathways</th>
<th>Effectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larynx</td>
<td>Branches of vagus nerve</td>
<td>Diffusely located in medulla near respiratory center; under control of higher brain centers</td>
<td>Vagus nerve</td>
<td>Muscles of larynx, trachea, and bronchi</td>
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<tr>
<td>Trachea</td>
<td></td>
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<td>Phrenic nerve Intercostal and lumbar nerves</td>
<td>Diaphragm, intercostal, abdominal, and lumbar muscles</td>
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<tr>
<td>Bronchi</td>
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<tr>
<td>Ear canal</td>
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<td>Pleura</td>
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<tr>
<td>Stomach</td>
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<tr>
<td>Nose</td>
<td>Trigeminal nerve</td>
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<tr>
<td>Paranasal sinuses</td>
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<tr>
<td>Pharynx</td>
<td>Glossopharyngeal nerve</td>
<td></td>
<td>Trigeminal, facial, hypoglossal, and accessory nerves</td>
<td>Upper airways and accessory respiratory muscles</td>
</tr>
<tr>
<td>Pericardium</td>
<td>Phrenic nerve</td>
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<tr>
<td>Diaphragm</td>
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<table>
<thead>
<tr>
<th>From above</th>
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<tbody>
<tr>
<td>* Allergic rhinitis</td>
<td>* Asthma</td>
</tr>
<tr>
<td>* Rhinosinusitis</td>
<td>* Lung/airway infection</td>
</tr>
<tr>
<td>* PND</td>
<td>* Lung inflammation</td>
</tr>
<tr>
<td>* Reflux/aspiration</td>
<td>* Chemical irritants</td>
</tr>
<tr>
<td>* Inhaled foreign body</td>
<td>* COPD</td>
</tr>
<tr>
<td>* Tumor</td>
<td>* Smoking</td>
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<tr>
<td></td>
<td>* Tumor</td>
</tr>
</tbody>
</table>
Threshold Stimulants

Neuropathy
Anxiety
Asthma
ACE-I ?

Cough Triggered

Stimulants

Infection
Inflammation
Allergic rhinitis
Rhinosinusitis
Hot/Cold
Dry
Smoking
Pollution
Chronic Cough

History to include:
- Red flags
- Occupational / Environmental Issues
- Travel Exposures
- Physical Exam
- Chest radiograph

Smoking ACEI Sitagliptin

Discontinue for at least 4 weeks

4 Most Common Causes to Consider:

Upper Airway Cough Syndrome (UACS) secondary to rhinosinus diseases
Consider:
- Sinus imaging
- Nasopharyngoscopy
- Allergy evaluation or empiric treatment

Asthma
Ideally evaluate:
- Spirometry
- Bronchodilator reversibility
- Bronchoprovocation challenge
- Allergy evaluation or empiric treatment

Non-asthmatic Eosinophilic Bronchitis (NAEB)
Ideally evaluate:
- Sputum eosinophilia
- Fraction exhaled nitric oxide (FENO)
- Allergy evaluation or empiric treatment

Gastroesophageal Reflux Disease (GERD)
Physiologic testing for refractory patients
Initial treatment to include:
- More than acid suppression

Investigate and treat

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

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

No response at 4-6 week follow up

Initial Treatments
- UACS – A/D
- Asthma – ICS, BD, LTRA, trigger avoidance
- NAEB – ICS, Trigger avoidance
- GERD – PPI, diet/lifestyle changes (Treatment of GERD should not be limited to acid suppression)
Inadequate response to optimal treatment, follow up 4-6 weeks

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

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

Red Flags
- Hemoptysis
- Smoker > 45 years of age with a new cough, change in cough, or coexisting voice disturbance
- Adults aged 55-80 years who have a 30 pack-year smoking history and currently smoke or who have quit within the past 15 years
- Prominent dyspnea, especially at rest or at night
- Hoarseness
- Systemic symptoms
  - Fever
  - Weight loss
  - Peripheral Edema with weight gain
- Trouble swallowing when eating or drinking
- Vomiting
- Recurrent pneumonia
- Abnormal respiratory exam and/or abnormal chest radiograph coinciding with duration of cough
Case #1

- 72 year old male
- Cough and throat clearing for several years. Now worse.
- Slightly hoarse when clears more often.
- Failed steroid inhalers.
- Reflux considered. Tried on omeprazole without improvement.
- No history of asthma nor smoking.
- Denies seasonal allergies
- Occasional sinus infection
Case #1

Exam:

* Mild nasal mucosal edema
* Wet nasal mucosa
* Hydrated oral mucosa
* Normal neck exam
Case #1

Transnasal flexible fiberoptic laryngoscopy

* Edematous, wet nasal mucosa
* Mucoid drainage from middle meati posteriorly
* Moderate vocal fold and mild post-arytenoid edema
* Normal vocal fold mobility
Case #1

Factors contributing to cough:

* Allergic rhinitis?
* Chronic sinusitis?
* Laryngopharyngeal reflux?
Case #1

* Nasal saline sprays or irrigations
* Fluticasone bid
* Azelastine bid
* 3 week course amoxicillin
* Omeprazole 20mg bid
* Allergy testing
Case #1

* Clearing the throat less
* Less coughing
* Negative allergy testing
* CT sinus
Case #1
Chronic Rhinosinusitis

- Sinusitis >12 weeks
- Affects 14%-16% of U.S. citizens
- Approximately ¼ have polyps
- Treatment
  1. Topical nasal steroid sprays
  2. Nasal saline irrigation
  3. Topical decongestants better than systemic
  4. Antihistamines for atopic patients
     - May worsen clearance due to drying effects
  5. Guaifenesin
     - Insufficient evidence to support use
Functional Endoscopic Sinus Surgery
Case #1

- Improved with FESS
- Weaned off azelastine
- Continues with fluticasone. Recurs if stops.
- Weaned off omeprazole.
- Taking ranitidine PRN
- Anti-reflux diet modifications
Case #2

* 54 year old female with 3 - 4 months of cough, minimally productive
* No wheezing or shortness of breath, no GERD symptoms
* Cough worse at night, especially with ambient humidity or heat
* Tried Robitussin without success
* No new environmental changes except daughter has moved in with dog
Case #2

- No throat clearing on exam, lungs clear without wheeze or crackles
- Mild posterior oropharyngeal erythema
- Spirometry shows FEV1 85% predicted, FVC 92% predicted, FEV1/FVC 73%
- Trial of inhaled fluticasone, 110mcg BID and PRN albuterol
- Also advised GERD lifestyle changes
Case #2

* Returns 3 months later with persistent cough despite fluticasone, maybe somewhat improved; albuterol helps
* Did not try GERD modifications
* Daughter and dog still living with her
* Spirometry similar to prior, exam unchanged
* Methacholine challenge ordered, borderline response
Case #2

- RAST testing performed, showing responsiveness to dog dander
- Advised removing dog (daughter declined)
- Trial of omeprazole 20mg daily x 1 month
- Added montelukast to fluticasone
- CXR unremarkable
Case #2

- Returns 3 months later, cough much improved
- 50% better after trial of omeprazole
- 100% better after removal of dog
- De-escalated therapy to PRN albuterol
- Lifestyle modifications for GERD, PRN omeprazole
- Returned 3 months later, cough continues only when not adherent to GERD recommendations
Case #3

* 63 year old male with throat clearing and cough.
* Present for several years.
* Getting more frequent. Harder to sleep.
* Takes lorazepam for anxiety.
* Voice hoarse over the last several months.
Case #3

* Intermittent throat clearing during exam
* Dry mouth
* Normal nasal exam
* FOE: dry, foamy secretions, bilateral vocal nodules, mild vocal fold edema
Case #3

- Hydrate
- Nasal saline sprays and/or irrigation
- Ativan only when needed
- Ranitidine 150 mg BID
Case #3

- Returns with persistent throat clearing and hoarseness
- Mucosa is better hydrated
- He reports a sensation of something in the throat. Like a “tick” or “dryness”.
- In-office skin prick allergy testing is negative
- Repeat laryngoscopy showed decreased edema, persistent vocal nodules
- Started on fluticasone inhaler BID
Case #3

* CT neck: normal
* Feeling more anxiety, so back to taking lorazepam nightly and during the day PRN
* Oral mucosa appears more dry
* Cough persists
Laryngeal Sensorineuropathy

* Neuropathy of the sensory nerves of the larynx
* May cough hundreds of times a day
* Sensation of “Tickle” or “Dry patch”
* Diagnosis of exclusion
* Responds to anti-seizure medication (gabapentin) or tricyclic antidepressants (amitriptyline)
Threshold

Neuropathy
Anxiety
Asthma
ACE-I?

Cough Triggered

Stimulants

Infection
Inflammation
Allergic rhinitis
Rhinosinusitis
Hot/Cold
Dry
Smoking
Pollution
Case #3

- Gabapentin increased over several visits to 300mg TID
- Started therapy for his anxiety
- Able to decrease anti-anxiety meds
- Improved hydration of laryngeal mucosa
- Cough improved
- Ranitidine now PRN
Quality of Cough Matters!

- Dry quality
  - Hydration
  - Asthma

- Tickle in the throat
  - Allergy
  - Laryngeal Sensory Neuropathy (LSN)

- Productive
  - Infection
  - Inflammatory
Case #4

* 46 year old female with increasing cough for the last 9 months
* PMH notable for former tobacco use, quit 6 months ago
* Episode of pneumonia (no CXR) about 2 years ago, some residual cough since that time, sometimes with small amount of sputum
* Fatigue that seems to coincide with worsening cough
* Sensation of something stuck in chest
Case #4

* HEENT exam unremarkable
* Lungs with right sided rhonchi that clear with vigorous cough
* CXR performed
Case #4
Bronchiectasis

- Cystic fibrosis vs. non-CF etiologies
- Causes include prior infections, autoimmune, airway obstruction

- Lab testing:
  - IgG +/- subclasses
  - CFTR mutations
  - CBC with differential
  - Rheumatoid factor
  - Total IgE/aspergillus specific IgE
  - Alpha-1 antitrypsin

- Overlap with non-TB mycobacterial disease
  - Check sputum for Gram stain/culture, AFB culture
Non-CF Bronchiectasis

* Treatments:
  * Airway hygiene
    * Acapella/flutter valve
    * Inhaled bronchodilators (often nebulized)
  * Mucolytics i.e. 0.9% vs. higher concentrations inhaled NaCl
  * Minimal evidence for N-acetylcysteine

* Treat underlying infections, i.e. non-TB mycobacteria

* Appropriate immunizations; avoid dehydration, GERD

* Treat underlying conditions (RF, A1AT etc)

* Surgical resection for localized disease
Bronchiectasis - complications

- Exacerbations (increased sputum, SOB, etc)
  - Pseudomonas, S. aureus, H. influenzae, Moraxella, S. pneumo
  - Often lack fevers, treat with appropriate antibiotics
- Hemoptysis – can be life-threatening
- Progressive decline in lung function (average annual decrease of 50mL/year versus 20-30mL normally), potential need for lung transplant
- Pulmonary vascular disease
- Increased 5 year mortality
Case #4

- Laboratory testing unremarkable
- Started on airway hygiene therapies with Acapella valve, bronchodilator nebulizers
- Some improvement noted after 8 weeks, but still persistent cough
- Sputum obtained for Gram stain/culture, no evidence of AFB growth
- Added inhaled 0.9% saline nebulizer treatments BID
- Cough now controlled with regular airway hygiene
Case #5

- 54 year old female with 2 years of chronic cough
- Worse at night
- Associated with nasal congestion
- Denies seasonal allergies
- Intermittent smoker
- High-stress, high-level job
- Cough affects her sleep and work performance
- No ACE-I
Case #5

* Treated with:
  * Steroid inhaler
  * Albuterol inhaler
  * Several courses of antibiotics
  * Oral antihistamines
  * Nasal saline irrigations

* Continued efforts towards smoking cessation

* Therapy for stress

* Tried acupuncture
Case #5

- Physical exam:
  - Boggy nasal mucosa
  - Allergic shiners

- Fiberoptic laryngoscopy:
  - Nasal mucosal edema
  - Clear secretions
  - Mild Reinke’s edema
  - Mild post-arytenoid edema

- Allergy testing positive for dust mite and mold
Case #5
Case #5

- Nasal steroid sprays BID
- Azelastine BID
- Ranitidine 150 mg BID
- Nasal saline irrigations
- Encouraged to quit smoking
Case #5

* No improvement

* What next?
  * I need to sleep
  * I’m coughing at board meetings
Case #5

* Allergy testing positive for mold
* Leak found in condo, with large amount of mold
* Started on SLIT for mold
* Mold remediation

Sun in an Empty Room – Edward Hopper
Case #5

* Coughing nearly gone
* Still smoking and stressed
Case #6

* 68 year old female with cough for 3 months
* Had been seen 2 weeks after onset of cough, had sick contacts, attributed to URI, recommended OTC decongestants
* Returned 4 weeks later with persistent cough, some improvement with nebulizer treatment in office, attributed to COPD with recent illness
* Returns now with worsening cough and malaise
Case #6
Case #6
Case #6

- Imaging revealed right sided mass with airway collapse
- Bronchoscopy performed, returned with high grade adenocarcinoma with suspected lung primary
- Started on immunotherapy with pembrolizumab

- Don’t forget the CXR for red flags!
Take Home Points

* Chronic cough negatively affects quality of life and has significant economic impact on health care costs & utilization

* Chronic cough is often due to multiple contributing factors, and one should consider both upper and lower airway causes

* A standardized approach to diagnosis and management can be helpful, but each patient must be looked as individually and high risk features recognized

* Pulmonary, GI, and ENT providers can often provide useful testing and management, depending on the cause
Thank you!

Questions?