Chronic cough:
After PPIs don’t work

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Chronic cough

• Persistent cough for at least 8 weeks (or 12)
  Post-viral cough can last 2 months.
  Frequency and severity of coughing can be variable.

• Unexplained, refractory, idiopathic, or intractable
  ➢ What is the diagnosis?
  ➢ How should we treat it?
Sub-acute cough evaluation

- Smoker?
  - Consider CXR
- Immunosuppressed?
  - Workup for active infection
- Purulent sputum?
  - Consider pneumonia, acute sinusitis
- ACE Inhibitor?
  - 10-15% of ACE-I patients cough
  - Angiotensin receptor blockers better
- Whooping / paroxysms / emesis?
  - Bordetella pertussis culture, PCR, serologies
### Initial medical management

#### Specific treatments
- Nasal steroids
- Antihistamines
- Anti-Leukotriene agents
  - (monteleukast, zileuton)
- Inhaled steroids, bronchodilators
- Anti-reflux regimen

#### Non-specific treatments
- Dextromethorphan
- Codeine (less effective)
- Guaifenesin
- Inhaled ipratropium
- Benzonatate
- GABA inhibitors
  - (gabapentin, pregabalin)
All chronic cough is not reflux.
Cochrane Review 2011

• PPI vs Placebo for cough
  • No difference in cough resolution
  • Possible improvement in patient cough scores
  • 8 weeks is adequate
  • Number needed to treat = 12

• Up to 85% placebo response
  • Placebo-responders may needlessly continue treatment.
Risks of chronic PPI use

- Community-acquired pneumonia (RR 1.2)
- C. difficile infection (RR 1.7)
- Hip fracture (RR 1.3)
- Hypomagnesemia (FDA alert)
- Possible clopidogrel impairment
- Rebound acid hypersecretion
Mechanical reflux prevention

• Laparoscopic Nissen fundoplication
  • 85% of patients improved, in uncontrolled study
  ➢ *Reserved for pH probe-positive non-responders*

• Device-based interventions
  • Magnetic LES
  • Endoscopic sutures
  • Radiofrequency ablation
  • External compression
So what am I supposed to do??
Symptom-based diagnostic algorithm

Laryngologist:
Nasal endoscopy, Stroboscopy, possible TNE

- Nasal/sinus complaints
- Dyspnea
- Globus
- Heartburn
- Dysphagia
- Dysphonia
- URI
- No Sx
- ACE-I
Symptom-based diagnostic algorithm

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- Dysphonia
- Dysphonia
- Paresis?
- URI
- No Sx
- Neurogenic cough
- Chronic unexplained cough
- ACE-I
Symptom-based diagnostic algorithm

Laryngologist:
Nasal endoscopy, Stroboscopy, possible TNE

Nasal/sinus complaints
- Treat rhinosinusitis
  - Hx COPD
  - Hx Smoking
  - Chest X-Ray
  - Laryngospasm
  - Tx for PVFM
  - Pulmonology
    - Spirometry
    - PFTs
    - Methacholine challenge

Dyspnea
- Hx COPD
- Hx Smoking
- Chest X-Ray
- Laryngospasm
- Tx for PVFM
- Pulmonology
- Spirometry
- PFTs
- Methacholine challenge
- GI manometry
- pH Probe
- CP myotomy
- MBSS
- Reflux therapy
- Dysphagia
- Dysphonia
- Paresis?
- Speech therapy
- Augmentation
- Neuro-modulators
- URI
- No Sx
- Neurogenic cough

No Sx
- Neurogenic cough

Neuro-modulators
Neurogenic or
Chronic unexplained cough
Neurogenic cough

• Aberrant laryngopharyngeal sensory nerve function

• Diagnosis of exclusion

• Supported by findings of motor nerve impairment

• More common with recent URI or diabetes
Neural pathways

- Irritant or stimulus
- Sensory receptors
- Brainstem Cough Inhibitors
- Brainstem Cough Effectors
Treatment of neurogenic cough

- Neuromodulators
  - GABA analogs (gabapentin, pregabalin, baclofen)
  - Amitryptyline
  - Botulinum

- Behavioral / speech therapy

- VF Augmentation
Behavioral therapy for chronic cough

• American College of Chest Physicians guideline:
  
  In adult patients with unexplained chronic cough, we suggest a therapeutic trial of *multimodality speech pathology therapy*.

• Details of therapy to come later!
Neuromodulators for chronic cough

• American College of Chest Physicians guideline:
  In adult patients with unexplained chronic cough, we suggest a therapeutic trial of *gabapentin*, as long as side effects and risk-benefit profile are discussed, and reassessed at 6 months.

• RCT: Improved QOL, cough frequency, severity while on drug. 31% adverse events

(Ryan et al, Lancet, 2012)
Neuromodulators for chronic cough

• Baclofen
  • GABA receptor agonist
  • Reduces lower esophageal sphincter relaxations

• Amitriptyline
  • Inhibits reuptake of norepinephrine and serotonin
  • RCT 10 mg daily, 13 of 15 improved

• Botulinum toxin
  • Neuromuscular acetylcholine inhibition: reduce glottic trauma and reactivity
  • Inhibits release of numerous other excitatory neurotransmitters
VF Augmentation for cough

• With co-existing paresis
• Unknown mechanism
Granulomas and cough

Voice abuse / laryngeal tension
Acid reflux
Glottal insufficiency
Conclusions

• Cough is multi-factorial, and will persist until all factors are treated.

• Long-term PPI is not risk-free.

• Consider neuromodulators, vocal fold augmentation, and speech therapy for neurogenic or chronic unexplained cough.