Case

- 48-year-old, white female presents for the evaluation of cough.
  - Present for 12 months
  - Feeling of a “lump” in throat followed by spasms of cough
  - Occurs on a daily basis
  - Occurs anytime, but frequently after meals
  - Does not awaken her at night.
Case

- Mild heartburn after meals that is controlled with omeprazole 20 mg that she takes 3-5 mornings a week.
- No other gastrointestinal symptoms
- Recent 15 pound weight gain after changing jobs.
- Non smoker
- No other significant PMH, FH or SH

Case

- CXR and EKG normal
- ENT exam of vocal cords showed posterior erythema
- PFT’s with methacholine challenge normal
- Thyroid tests and ultrasound negative
- Trials of antihistamines and decongestants were not effective.

WHAT NEXT?
Extraesophageal GERD

- **ENT**
  - Laryngitis
  - Sinusitis
  - Otitis
  - Ulcers
  - Granuloma
  - Polyps
  - Laryngeal CA
    - (hoarseness, throat clearing, globus, sore or burning throat)

- **Pulmonary**
  - Asthma
  - Chronic cough
  - Pneumonia
  - Bronchitis
  - Interstitial fibrosis

- **Cardiac**
  - Chest pain
  - Sinus arrhythmia

- **Other**
  - Dental erosions
  - Halitosis

(Otitis) Enamel decay
(Laryngitis and dysphonia)
(Aspiration of gastric contents with lung injury
(chronic cough, pulmonary fibrosis)
Does the patient have gastroesophageal reflux?

- Do they have a history of esophagitis (LA-B or greater) or long segment Barrett’s?

- Laryngeal findings (including the calculated reflux finding score (RFS)) are not sufficiently specific to make a dx of GER.
  - Does not seem to distinguish normal from controls
  - Does not correlate well with traditional pH testing
  - Does not predict response to PPI therapy compared to placebo

- Do they have a positive ambulatory pH test?
Kenneth R. DeVault, MD, FACG

Proximal Reflux

Impedance-pH Monitoring Catheter

- Allows measurement of acid and nonacid reflux
- Reasonable choice for monitoring patients on therapy
- Values and interpretation of nonacid reflux not as well characterized and difficult to interpret

Reflux Events

A-Acid
B-Weakly acid
C-NonAcid

Hila et al CGH 2007;5:172-7

Symptom Association?

(1) Symptom Index (SI)

\[
SI = \left( \frac{\text{no. of reflux and cough events}}{\text{no. of cough events}} \right) \times 100
\]

• SI/SSI: Value ≥ 50% represents +ve association

(2) Symptom Severity Index (SSI)

\[
SSI = \left( \frac{\text{no. of reflux and cough events}}{\text{no. of reflux events}} \right) \times 100
\]

(3) Symptom Association Probability (SAP)

• SAP: calculates whether cough follows reflux more frequently than would be expected by chance alone, using Fisher’s Exact Test

\[
SAP = (1 - P \text{ value}) \times 100, \text{ where value} \geq 95\% \text{ represents +ve association}
\]
Simultaneous Cough and Reflux Recording

Cough Sounds

Oesophageal Impedance/pH

Reducing to 10-sec window, resulted in far fewer C-R associations, suggesting straining unlikely cause of cough induce reflux

Smith, Houghton et al Gastroenterology 2010; 139: 754-762
Approach to pH testing for proximal symptoms

- Dual channel (distal/proximal), impedance pH is the best tool
  - prolonged wireless ambulatory pH metry device if patient can’t tolerate
- Should be off PPI for at least 5 days
- Consider study “positive” if
  - Increased distal acid exposure
  - Increased proximal (?>3%) even if distal normal
- Possibly positive
  - Positive SAP with normal acid exposure
    - Acid events or nonacid impedance events
  - Proximal impedance events may be important

Airway Pepsin Levels

- Sputum pepsin inversely related to the frequency of coughing ($r=-0.52$, $p=0.04$).
  
Have other causes been excluded?

- Cough
  - Structural lesions
  - Asthma
  - Post Nasal Drip

- ENT
  - Structural lesions
  - Post Nasal Drip
  - Vocal use issues

- Chest pain
  - Cardiac
  - Musculoskeletal

Are the symptoms due to GER?

Response to PPI?
Effect of Omeprazole on Asthma Symptom Score

27% of patients required >20 mg/d of omeprazole to control reflux.


Chronic Cough and GERD: Placebo controlled RCT PPI trials

- After 8 weeks (esomeprazole 20 mg BID v placebo), no difference in
  - Cough frequency and severity
  - LCQ score
  - Citric acid challenge
  - RFS
  Respirology 2011;16:1150-6

- After 8 weeks (esomeprazole 40 mg BID v placebo), no difference in
  - QOL
  - Cough severity and frequency
  Aliment Pharmacol Ther 2011;33:225
Gastro-oesophageal reflux treatment for prolonged nonspecific cough in children and adults (Cochrane Review 2011)

- PPI is not efficacious for cough associated with GERD symptoms in very young children (including infants) and should not be used.
- There is insufficient data in older children to draw any valid conclusions.
- In adults, there is insufficient evidence to conclude definitely that GERD treatment with PPI is universally beneficial for cough associated with GERD.

Meta-analysis of PPI in LPR
AJG 2006;101:2646
Cough and Laryngopharyngeal Reflux (LPR): Gastroenterology Perspective!

- Laryngopharyngeal reflux (LPR) is frequently over and misdiagnosed
- Symptoms are not predictive of LPR perhaps with the exception of patients with both typical and proximal reflux symptoms.
- Laryngeal signs including the reflux finding score (RFS) are not specific for pathologic reflux.
- Well-designed, randomized trials of reflux therapy in patients with symptoms and positive RFS have not shown a benefit for PPI therapy when compared to placebo. There is no reason to suppose that surgery would do better in an appropriately designed trial.
Cough and LPR

- There is no physiological or trial based data to support the use of “mega” doses of PPI (greater than standard dose PPI BID).
  - Continuous infusion does not produce gastric achlorhydria

- In the rare cases that GERD is a cause, it is more commonly a multifactorial a cause of the symptoms, rather than GERD alone.

### PPI Efficacy: Randomized Controlled Trials

![Diagram showing PPI efficacy in randomized controlled trials]

- Placebo
- Therapeutic gain
- Esophagitis healing
  - Mild
  - Severe
- Heartburn relief
- Esophagitis
- NERD
- Regurgitation relief
- Chest pain (50% relief)
  - GERD (+pH)
  - GERD (-pH)
- Hoarseness (improved)
- GERD (-)
- Chronic cough (improved)
# Use of pH test and Rx trial results

<table>
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<tr>
<th>pH</th>
<th>Rx trial</th>
<th>Chronic PPI</th>
<th>Surgery</th>
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## How do atypical symptoms respond to fundoplication?


![Graph showing response of atypical symptoms to fundoplication](chart.png)
Fundoplication in lung transplant recipients

- Rodent study demonstrated equal damage regardless of pH of gastric content aspirated into lungs
  - Journal of Surgical Research 2013;181:e31-8
- Reduction of lipid-laden macrophage index after laparoscopic Nissen fundoplication in cystic fibrosis patients after lung transplantation.
  - Clinical Transplantation 2013;27:121-5
- Multiple small series suggesting safety and improvement in lung function, immune markers and decreased risk of BOS post fundoplication
- Symptoms do not seem to predict severity

Approach to GERD in Lung Transplant and Severe Interstitial Lung Disease (ILD)

- All transplant patients ideally should have an off PPI, impedance pH test in the month after transplant
- Esophageal manometry should be done at same time
- In those with pathologic reflux, surgery should be planned in the next 6-12 months
- If not a surgical candidate should probably have BID PPI with azithromycin and/or domperidone
- If reflux is not found on pH, then the patient can be followed
  - Can PPIs cause increased bacterial exposure to lungs?
  - Should PPI at that point
Esophageal Motility and Transplant Rejection (submitted manuscript)

- Study of high resolution manometry and impedance/pH testing in post lung transplant
- Associations with BOS
  - Incomplete bolus transit on EMS
  - Poor EJG relaxation
  - Proximal, but not distal reflux
- Highest association was with poor EJG relaxation

Is there a role for motility in other extraesophageal GERD symptoms?

Weak peristalsis with large breaks in chronic cough: association with poor esophageal clearance

C. Almansa, *, J. A. Smith, †, † J. Morris, M. D. Crowell, § D. Valdradou, † A. S. Lee, § K. R. DeVault* & L. A. Houghton*, †
CASE OUTCOME

• pH test showed normal distal and proximal acid exposure

• Despite this, PCP suggested a 3 month trial of BID PPI which did not improve symptoms

• After consultation, cough was improved with a trial of trazodone to lower cough sensitivity