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NTM Lecture Series

for Patients and Families

April 27, 2024

NTM Lecture Series for Patients

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NATIONAL JEWISH HEALTH

Overview of GERD

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Disclosures

- I have no financial disclosures

- The off-label use of the medications baclofen and bethanechol will be discussed in this talk

Learning Objectives

I. Understand how GERD may effect NTM pulmonary disease

II. Understand options for reflux testing

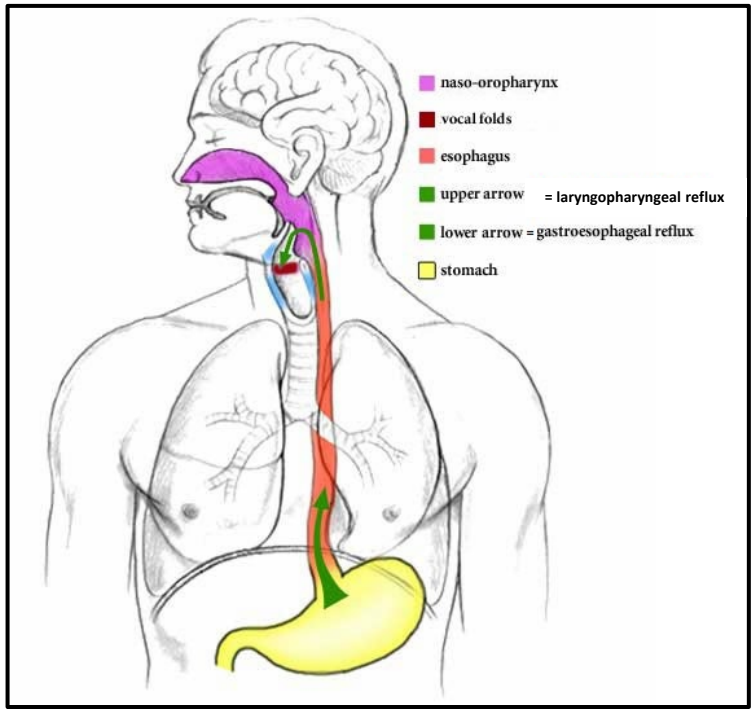
III. Understand how reflux management may differ when trying to prevent aspiration

Outline

I. Relationship Between GI Tract and Lungs
II. GERD and NTM
III. Reflux Testing
IV. Treatment of Reflux

Relationship Between GI Tract and Lungs

Location, Location, Location



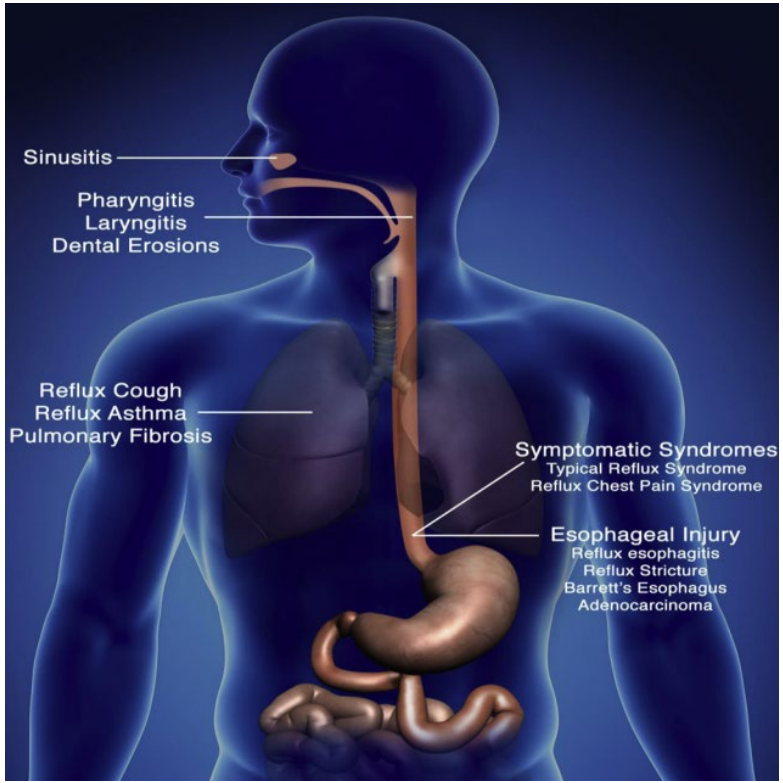
- **GERD (Gastroesophageal Reflux Disease):** symptoms or complications resulting from the reflux of gastric contents into the esophagus or beyond, including the oral cavity and/or lungs
- **Laryngopharyngeal Reflux (LPR):** retrograde movement of gastric contents into the larynx, pharynx, and upper aerodigestive tract
- **Aspiration:** entry of material from the oropharynx or GI tract into the larynx and lower respiratory tract (antegrade or retrograde)
- **GI-Related Aspiration (GRASP):** aspiration of material originating distal to the upper esophageal sphincter (retrograde only)

Am J Gastroenterol. 2013 Feb;108:308-28.

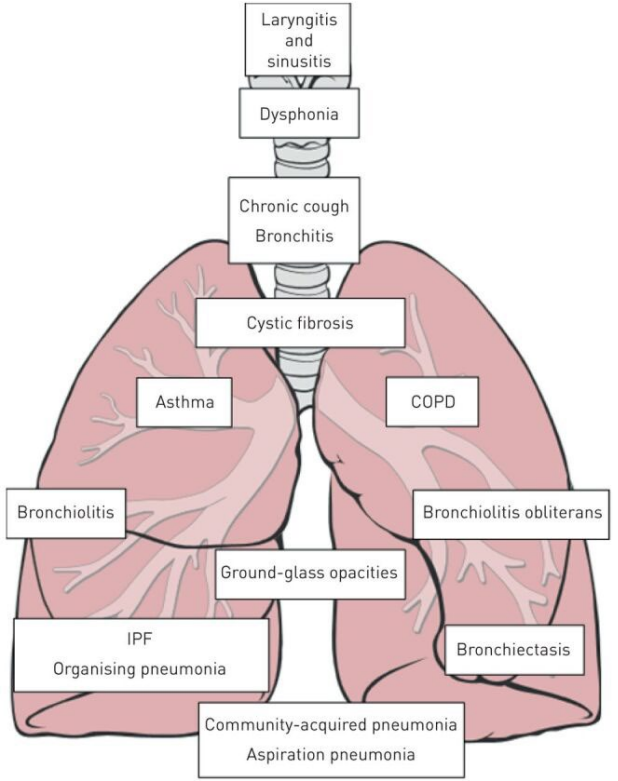
How Common is GERD?

- 60% of adults experience reflux symptoms over a 12 month period
- 30-40% had reflux symptoms in the last month
- 20-30% have weekly symptoms
- 10% have symptoms ≥ twice weekly

Manifestations of GERD



Best Pract Res Clin Gastroenterol. 2013 Jun;57(3):415-31.

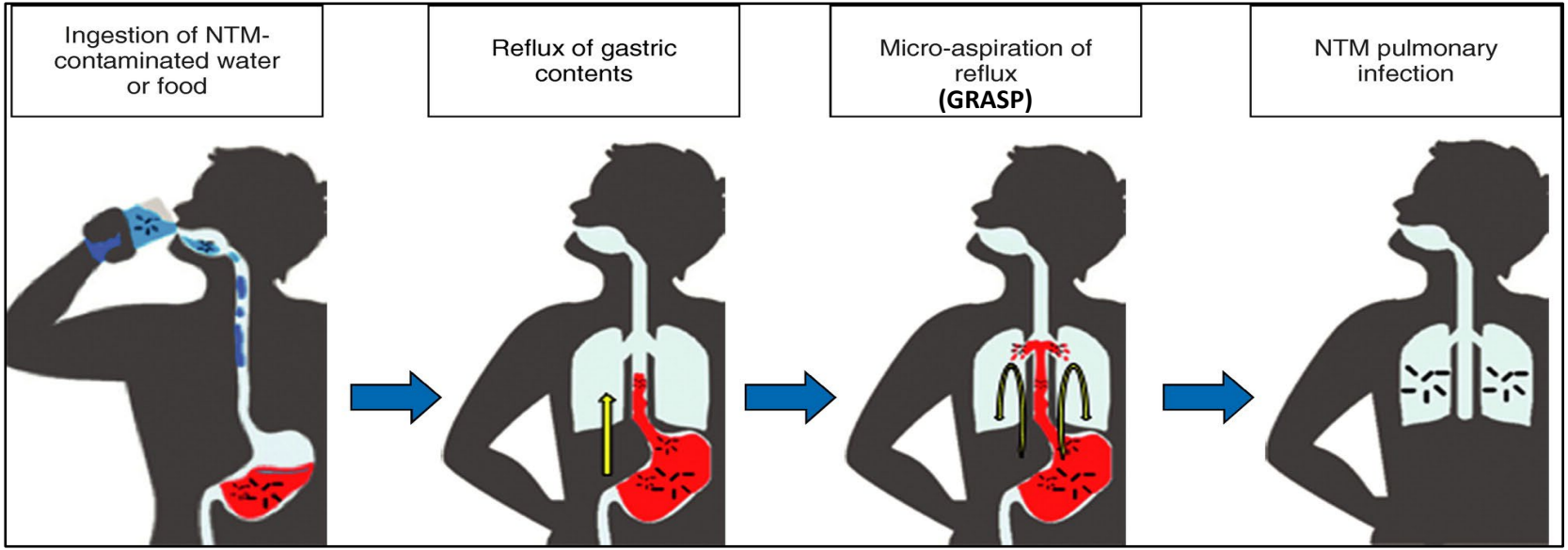


ERJ Open Res. 2020; 6: 00190-2019.

GERD and NTM

How Does GERD Relate to NTM?

- NTM are ubiquitous environmental organisms



Am J Respir Crit Care Med. 2020 Aug;202(3):466-469.

- In the proper host setting, this may cause chronic infection

GERD and NTM

Table 4—*Prevalence of GERD and Consumption of Acid-Suppressive Medication in Cases (MAC+) and Controls (MAC−)

Variables	MAC+	MAC−	p Value (Fisher Exact Test)
GERD	25 (43.1)	16 (27.6)	< 0.0001
Antacids	4 (6.9)	14 (24.1)	0.038
H2RAs	15 (25.9)	6 (10.3)	0.013
Proton-pump inhibitor	12 (20.7)	7 (12.1)	0.127
Prokinetic agents	4 (6.9)	0	0.039
Any acid suppression	27 (56.3)	26 (44.8)	0.165

*Data are presented as No. (%).

Chest. 2007 Apr;131(4):1166-72.

GERD and NTM

Table 3—*Demographic Characteristics of GERD-Positive and GERD-Negative Patients With the Nodular Bronchiectatic Form of NTM Lung Disease

Characteristics	GERD Positive (n = 15)	GERD Negative (n = 43)	p Value
Age, yr	56 (43–63.5)	57 (53–66.5)	0.320
Female gender	13 (87)	37 (86)	1.000
Body mass index, kg/m^2	20.0 (18.6–21.7)	20.6 (19.5–22.2)	0.316
Smoking status			
Non-smoker	14 (93)	40 (93)	1.000
Ex-smoker	1 (7)	3 (7)	
Etiology			
M avium complex	5 (33)	22 (51)	0.368
M abscessus	10 (67)	21 (49)	
AFB smear positive	12 (80)	19 (44)	0.033
Involved lobes on HRCT, No.			
Bronchiectasis	4 (3–4)	2 (2–3)	0.008
Bronchiolitis	4 (3–5)	2 (2–4)	0.005
Pulmonary function tests			
FVC, % of predicted	93.0 (83.0–102.0)	87.0 (77.5–93.5)	0.170
FEV_1, % of predicted	92.5 (76.5–107.0)	88.0 (72.5–102.0)	0.508
FEV_1/FVC, ratio	76.0 (67.0–84.0)	74.0 (71.0–80.0)	0.880
Peak expiratory flow, % of predicted	92.0 (80.0–111.5)	96.0 (74.5–99.0)	0.748

*Data are presented as the median (interquartile range) or No. (%). Bronchiolitis was defined as the presence of small centrilobular nodules (< 10 mm in diameter) or branching nodular structures (tree-in-bud pattern) on HRCT.

Chest. 2007 Jun;131(6):1825-30.

GERD and NTM

- U.S. Bronchiectasis Research Registry
- 1,826 patients with bronchiectasis
- 63% had history of NTM
- GERD: 51% NTM patients, 40% no NTM

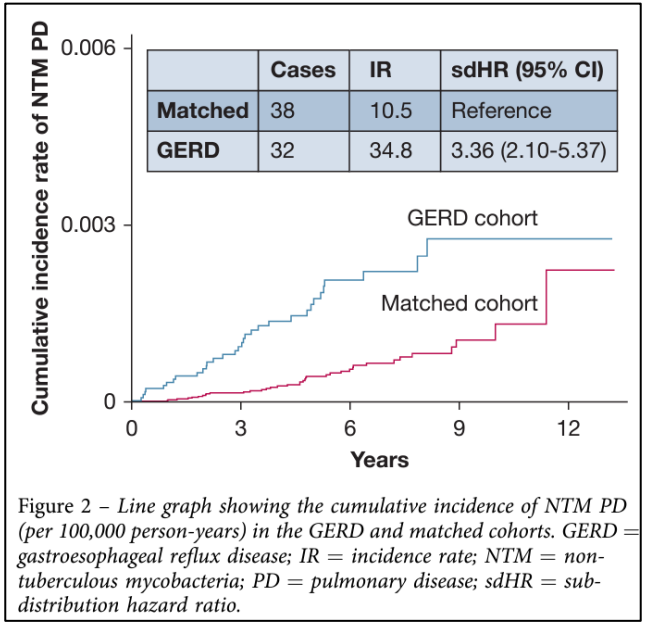
Chest. 2017 May;151(5):982-992.

GERD and NTM

- Korean National Health Insurance Service National Sample Cohort
- Matched GERD patients with non-GERD patients (1:4) from 2003-2014.
  - ICD-10 codes and PPI use > 3 months.
- Looked at who developed NTM.

Chest. 2023;163(2):270-280.

GERD and NTM



	Cases	IR	sdHR (95% CI)
Matched	38	10.5	Reference
GERD	32	34.8	3.36 (2.10-5.37)

Figure 2 – *Line graph showing the cumulative incidence of NTM PD (per 100,000 person-years) in the GERD and matched cohorts. GERD = gastroesophageal reflux disease; IR = incidence rate; NTM = nontuberculous mycobacteria; PD = pulmonary disease; sdHR = subdistribution hazard ratio.*

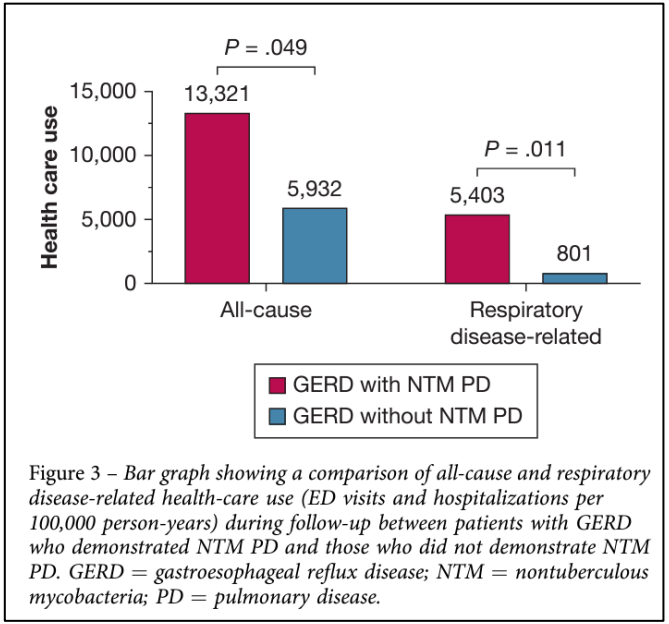


Figure 3 – *Bar graph showing a comparison of all-cause and respiratory disease-related health-care use (ED visits and hospitalizations per 100,000 person-years) during follow-up between patients with GERD who demonstrated NTM PD and those who did not demonstrate NTM PD. GERD = gastroesophageal reflux disease; NTM = nontuberculous mycobacteria; PD = pulmonary disease.*

Chest. 2023;163(2):270-280.

How Do We Detect/Measure GRASP?

- **WE CAN'T!!!**

- What can we measure?
  - Gastroesophageal reflux
  - Esophageal motility
  - Stomach motility
  - Sputum cultures
  - Lung inflammation/damage
  - Lung function

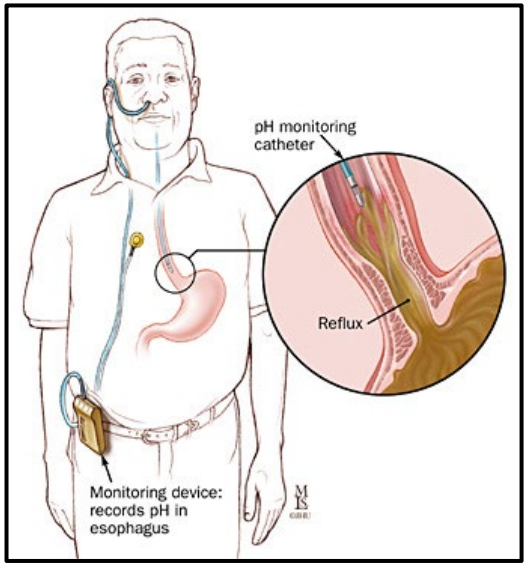
- There are no agreed-upon criteria for diagnosing GRASP

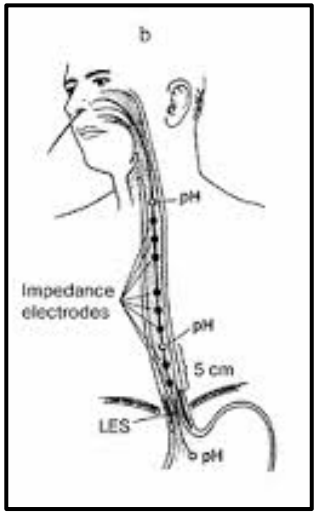
- Current testing may tell us how at-risk or not at-risk a patient is for GRASP

Reflux Testing

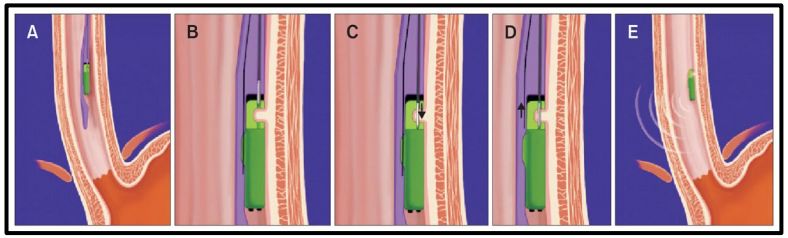
Reflux Testing

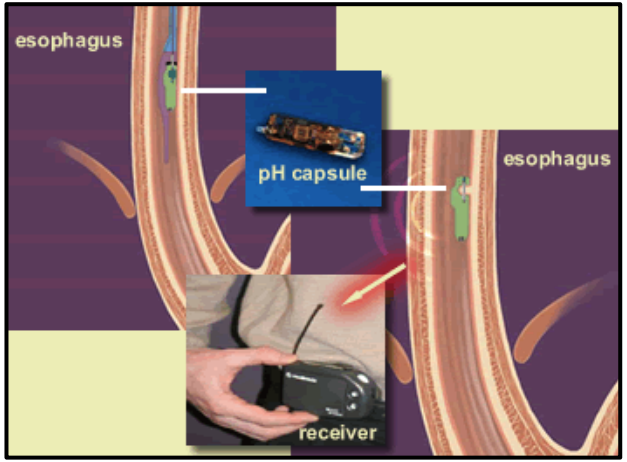
pH-Impedance Testing





Bravo pH Testing





pH-Impedance vs. Bravo

	pH-Impedance	Bravo
Time	22-24 hrs	48-96 hrs ✓
Where in Esophagus	Top and bottom ✓	Bottom
Discomfort	Yes	Minimal ✓
Detects Acid	Yes ✓	Yes ✓
Detects Non-acid	Yes ✓	No

Treatment of Reflux

How Can We Reduce Reflux?

1. Lifestyle modifications

2. Medications

3. Antireflux procedures

Lifestyle Modifications for GERD

Table 3. Efficacy of lifestyle interventions for GERD

Lifestyle intervention	Effect of intervention on GERD parameters	Sources of data	Recommendation
Weight loss (46,47,48)	Improvement of GERD symptoms and esophageal pH	Case–Control	Strong recommendation for patients with BMI>25 or patients with recent weight gain
Head of bed elevation (50–52)	Improved esophageal pH and symptoms	Randomized Controlled Trial	Head of bed elevation with foam wedge or blocks in patients with nocturnal GERD
Avoidance of late evening meals (180, 181)	Improved nocturnal gastric acidity but not symptoms	Case–Control	Avoid eating meals with high fat content within 2–3 h of reclining
Tobacco and alcohol cessation (182–184)	No change in symptoms or esophageal pH	Case–Control	Not recommended to improve GERD symptoms
Cessation of chocolate, caffeine, spicy foods, citrus, carbonated beverages	No studies performed	No evidence	Not routinely recommended for GERD patients. Selective elimination could be considered if patients note correlation with GERD symptoms and improvement with elimination

BMI, body mass index; GERD, gastroesophageal reflux disease.

Am J Gastroenterol. 2013 Feb;108:308-28.

Management of Suspected Extraesophageal Reflux – AGA Recs

Grade B: recommended with fair evidence that it improves important outcomes

I. Acute or maintenance therapy with once- or twice-daily PPIs (or H_2RAs) for patients with a suspected extra-esophageal GERD syndrome (laryngitis, asthma) with a concomitant esophageal GERD syndrome.

Grade D: recommend against, fair evidence that it is ineffective or harms outweigh benefits

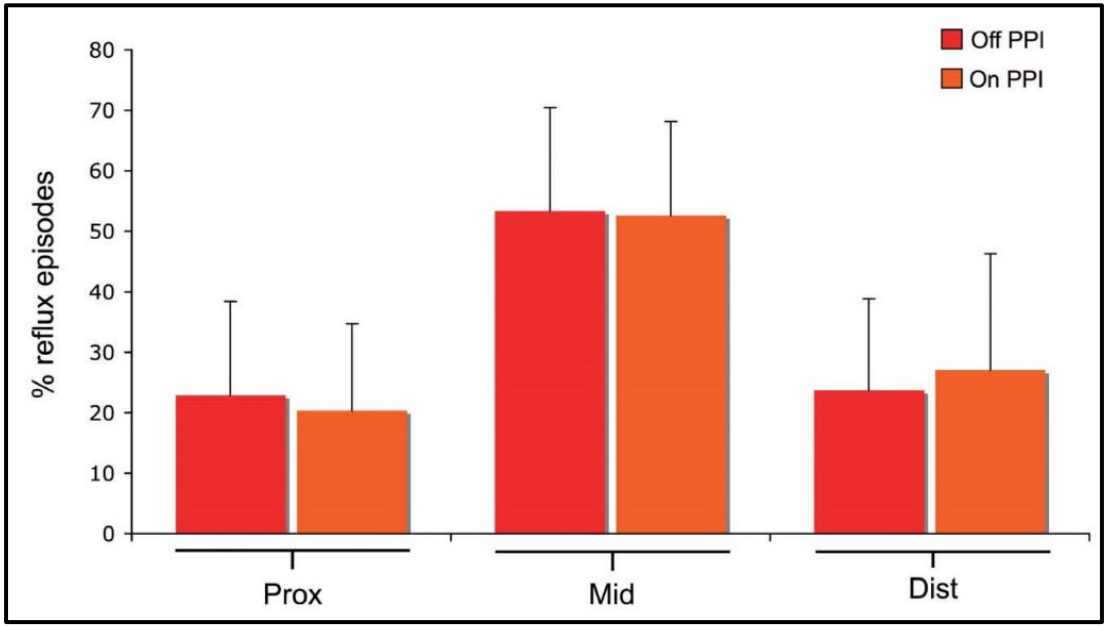
I. Once- or twice-daily PPIs (or H_2RAs) for acute treatment of patients with potential extraesophageal GERD syndromes (laryngitis, asthma) in the absence of a concomitant esophageal GERD syndrome.

Grade Insuff: no recommendation, insufficient evidence to recommend for or against

I. Once- or twice-daily PPIs for patients with suspected reflux cough syndrome.

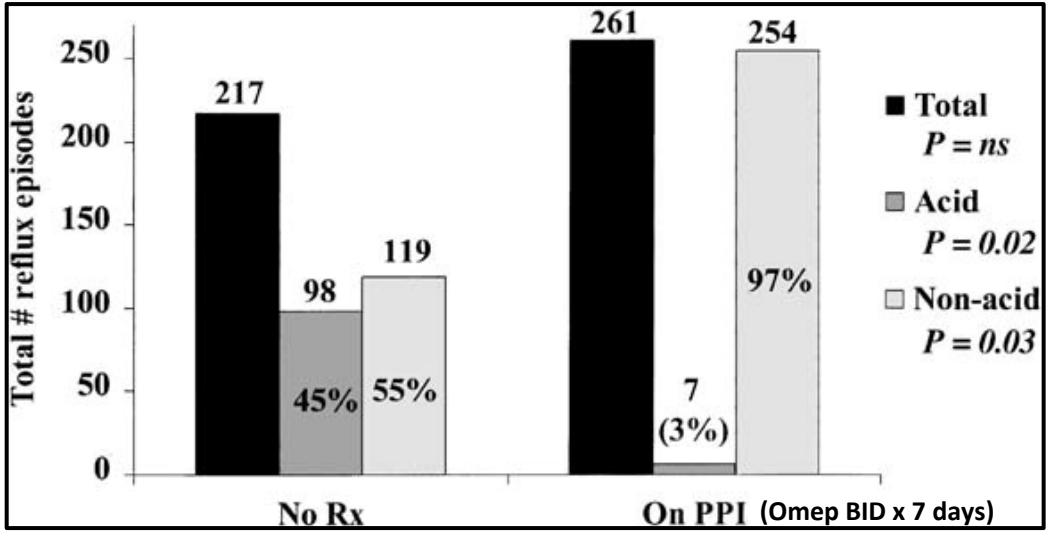
Gastroenterology. 2008;135:1383-91.

Why Aren't Acid Reducers the Right Choice?



Am J Gastroenterol. 2008 Oct;103(10):2446-53.

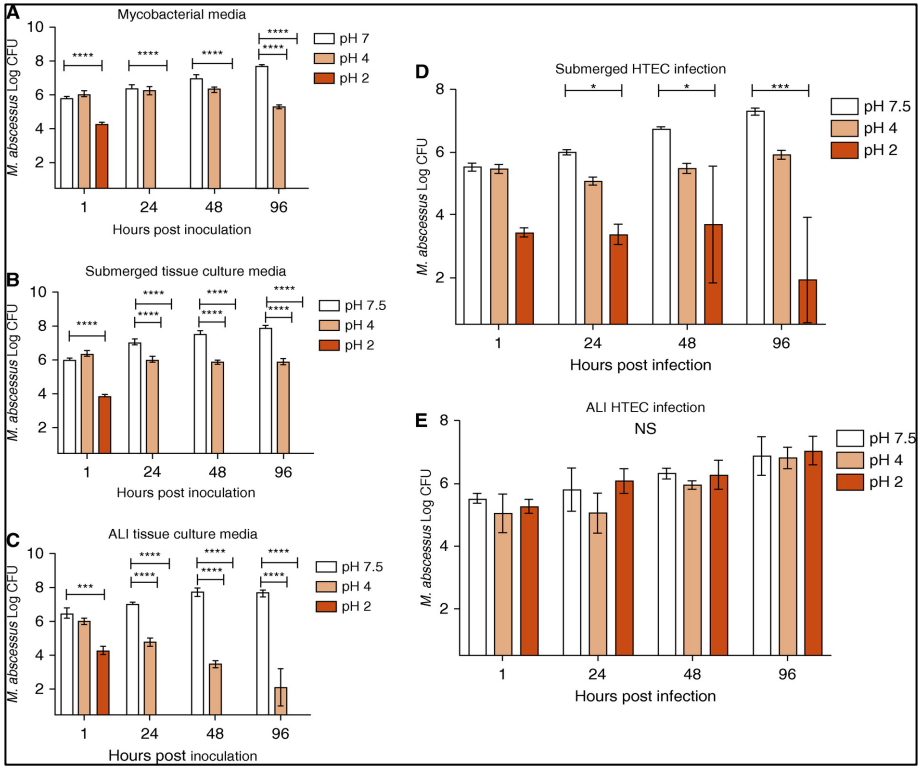
Why Aren't Acid Reducers the Right Choice?



** PPIs REDUCE ACID, NOT REFLUX **

Gastroenterology. 2001 Jun;120(7):1599-1606.

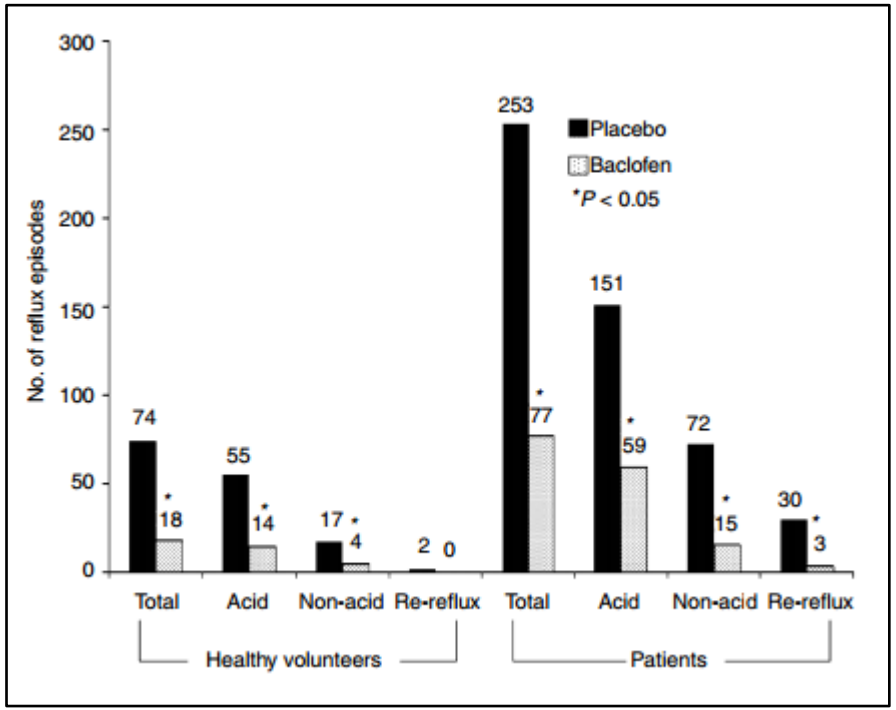
Can Acid Reducers Worsen NTM?



Am J Respir Crit Care Med. 2020 Aug;202(3):466-469.

Are There Medications That Reduce Reflux?

Baclofen



Aliment Pharmacol Ther. 2003 Jan;17(2):243-51.

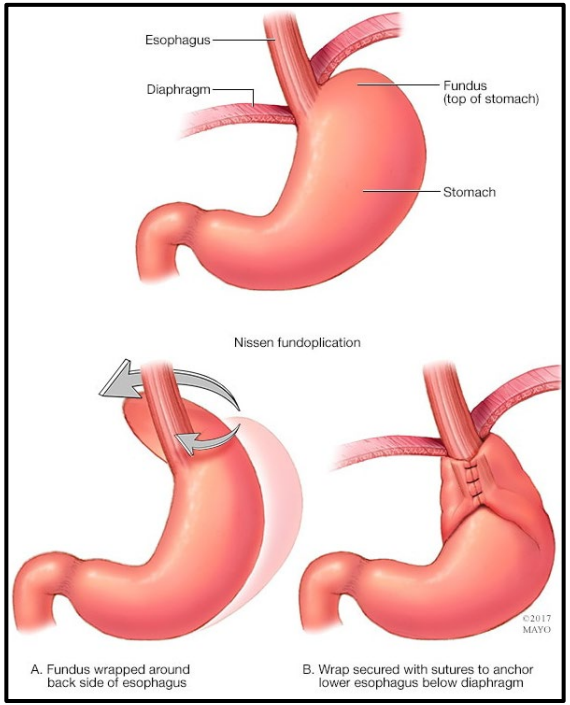
Bethanechol

- Improves esophageal motility/clearance
- Increases LES pressures
- Anecdotal evidence of reducing reflux
- ** No reflux studies **

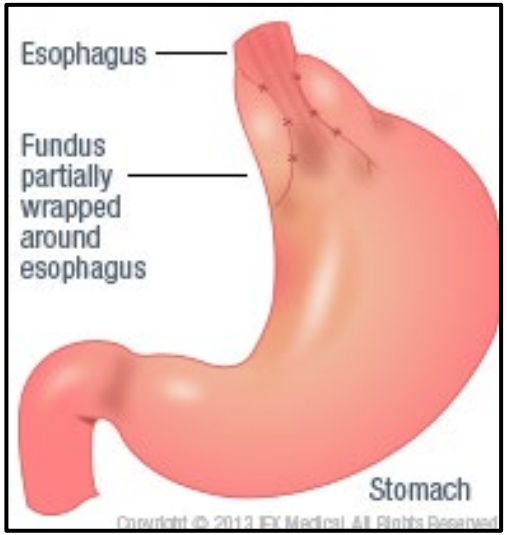
Yale J Biol Med. 1999 Mar-Jun;72(2-3)173-80.
J Clin Gastroenterol. 2007 Apr;41(4):366-70.
Gut. 1999 Sep;45:346-54.

Antireflux Surgeries

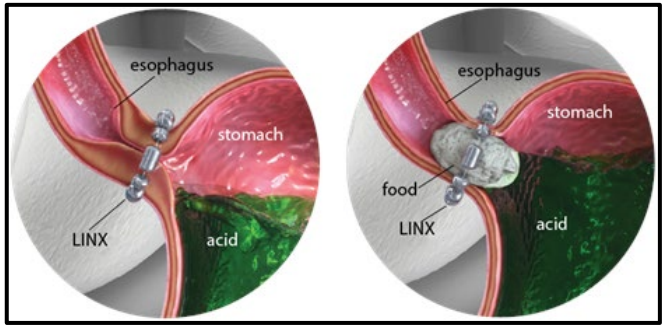
Nissen Fundoplication



Partial Fundoplication



LINX Procedure



Take Home Points

- The GI tract and airway are close together
- GRASP likely plays a role in NTM infection
- We cannot definitively diagnose GRASP
- Choose the proper reflux test and interpret properly
- Not all reflux is acid; acid reducers don’t reduce reflux
- Lifestyle mods, meds, and surgery can reduce reflux

Thank You

References

1) *Am J Gastroenterol*. 2013 Feb;108:308-28
2) *Best Pract Res Clin Gastroenterol*. 2013 Jun;57(3):415-31
3) *ERJ Open Res.* 2020; 6: 00190-2019
4) *Am J Respir Crit Care Med.* 2020 Aug;202(3):466-469
5) *Chest*. 2007 Jun;131(6):1825-30
6) *Chest*. 2007 Apr;131(4):1166-72
7) *Chest.* 2017 May;151(5):982-992
8) *Chest*. 2023;163(2):270-280
9) *Am J Gastroenterol*. 2008 Oct;103(10):2446-53
10) *Gastroenterology*. 2008;135:1383-91
11) *Gastroenterology*. 2001 Jun;120(7):1599-1606
12) *Aliment Pharmacol Ther*. 2003 Jan;17(2):243-51
13) *Yale J Biol Med*. 1999 Mar-Jun;72(2-3)173-80
14) *J Clin Gastroenterol*. 2007 Apr;41(4):366-70
15) *Gut*. 1999 Sep;45:346-54