

Navigating the Decisions in Diagnosis and Management of Gastroesophageal Reflux Disease

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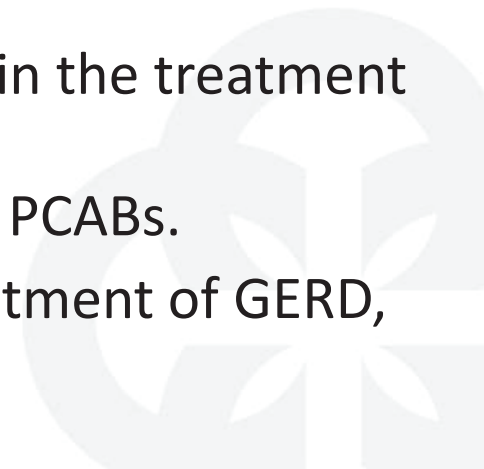
Disclosure

- We have nothing to disclose. No relationships with industry.



Objectives

1. Understand the increasing prevalence of GERD and the impact of GERD and related complications.
2. Review the definition of GERD.
3. Understand the spectrum of GERD, Esophagitis, and hiatal hernia.
4. The over diagnosis of laryngopharyngeal reflux and the role of ARS in LPR.
5. Review initial diagnostics and therapy for GERD.
6. Review the strengths, weakness and risks of PPI therapies in the treatment of GERD.
7. Discuss what's coming for the medical treatment of GERD, PCABs.
8. Understand the evolution of antireflux surgery for the treatment of GERD, hiatal hernia and PEH over the last decade.



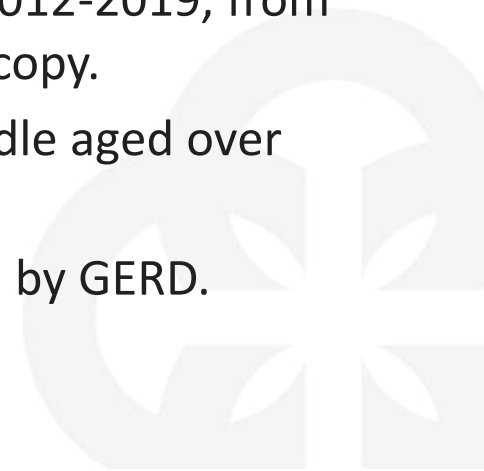
GERD: Situation and Background

Prevalence

- 18.6 million people afflicted in US.
- 10M annual office visits, 459K ER visits, 175K inpatient hospitalizations, 5.8B in drug costs, 3.5B in office and hospital cost, 14.6B in lost productivity.

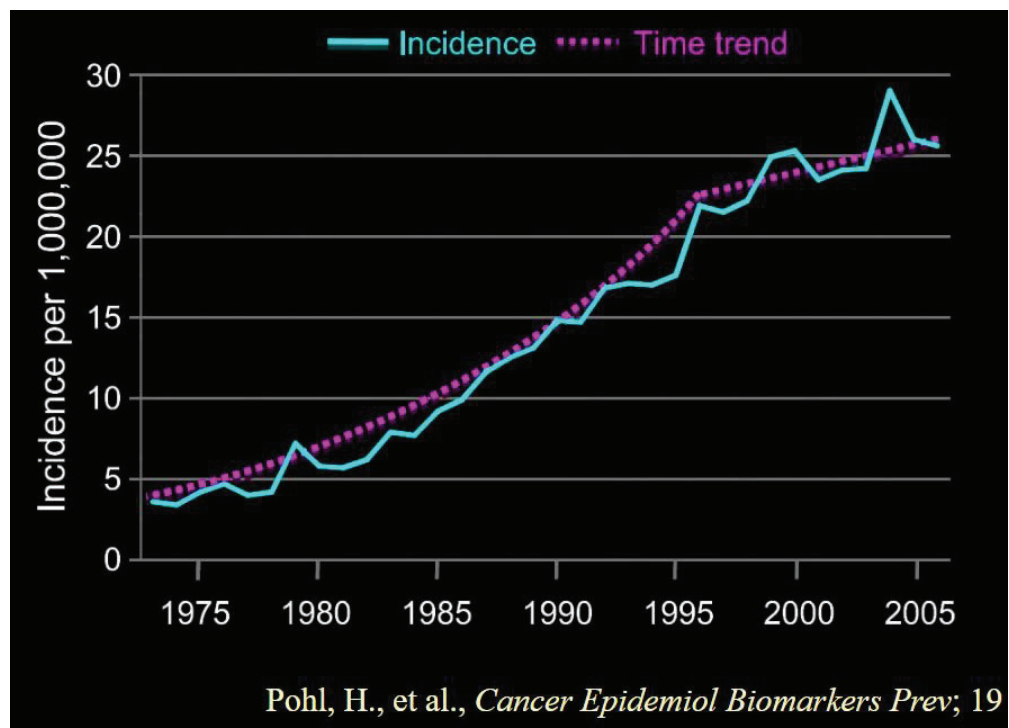
Impact of GERD

- Barrett's esophagus (BE) incidence has increase 54% in from 2012-2019, from 304/100,000 to 466/100,000 with no increase in upper endoscopy.
- Esophageal adenocarcinoma (EAC) has increased 200% in middle aged over the same time period.
- 103% increase in hospitalizations for treating disorders caused by GERD.

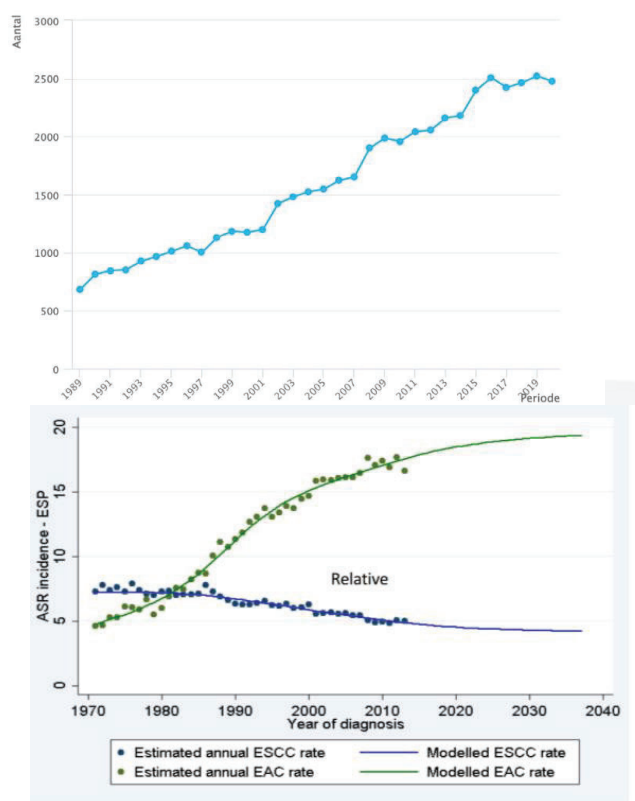


International Incidence of Esophageal Adenocarcinoma (EAC)

United States Incidence of EAC



Northern European Incidence of EAC



Offman J et al. *Br J Cancer* 2018.

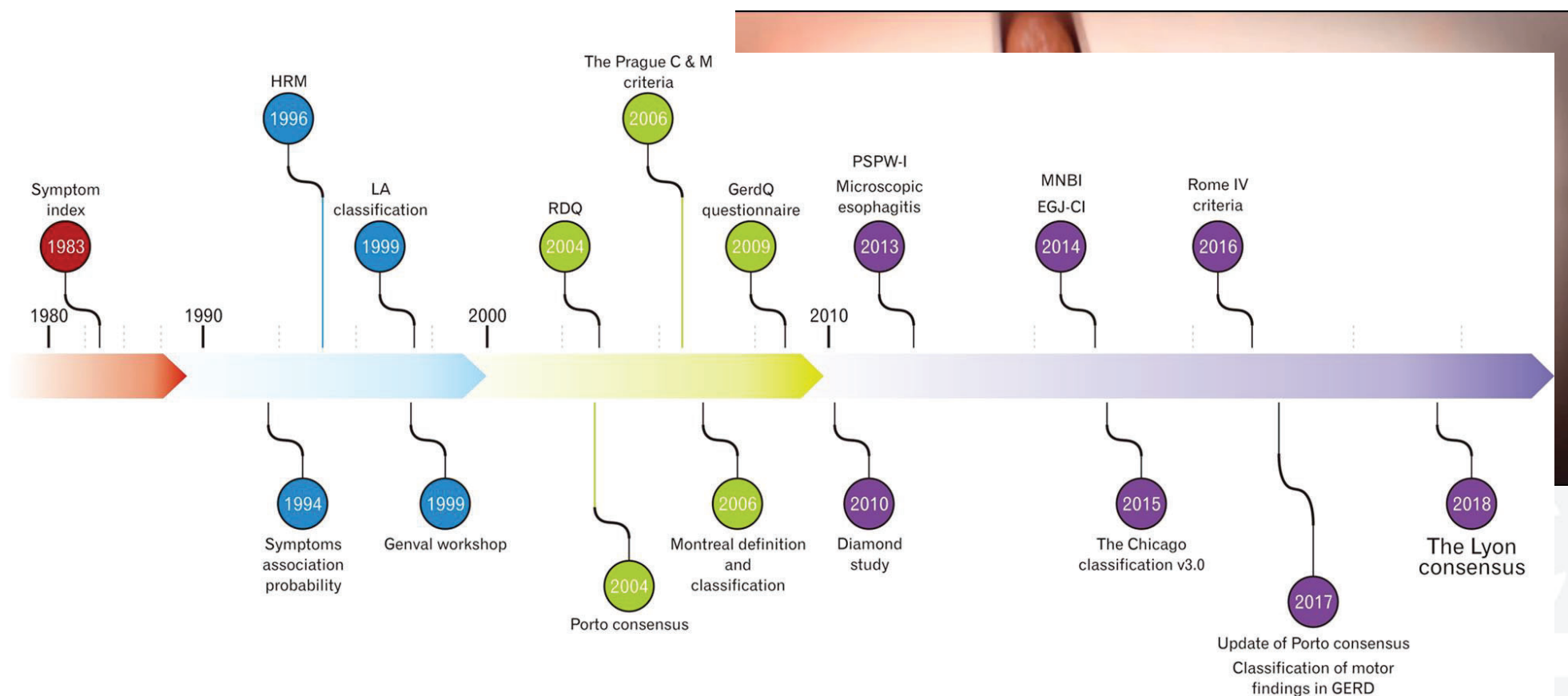
Assessment

- Our current approach to the prevention and management of gastroesophageal reflux disease is a failure.
- Despite seemingly efficacious treatment, all aspects of the disease including frequency, severity, cost, premalignant and malignant complications are rising exponentially.
- These facts beg for a reassessment of the current management paradigms addressing both risk factors and treatment approaches

*Jeffery Peters MD
University Hospitals COO
2023*

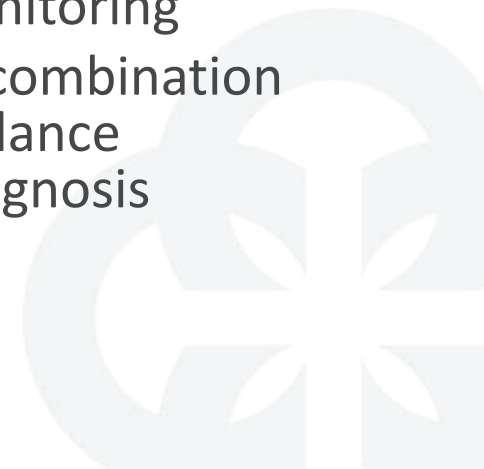


What is the Definition of Gastroesophageal Reflux Disease (GERD)?



The Definition of Gastroesophageal Reflux Disease

- GERD is defined as a disease associated with symptoms and/or complications due to the reflux of stomach contents into the esophagus with objective evidence of reflux:
 - Evidences for reflux include high-grade erosive esophagitis
 - Barrett's esophagus
 - peptic strictures at endoscopy as well as esophageal acid exposure time > 6% on pH-metry or combined pH-impedance monitoring
 - Even if a normal endoscopy does not exclude GERD, its combination with distal acid exposure time < 4% on off-PPI pH-impedance monitoring provides sufficient evidence refuting this diagnosis

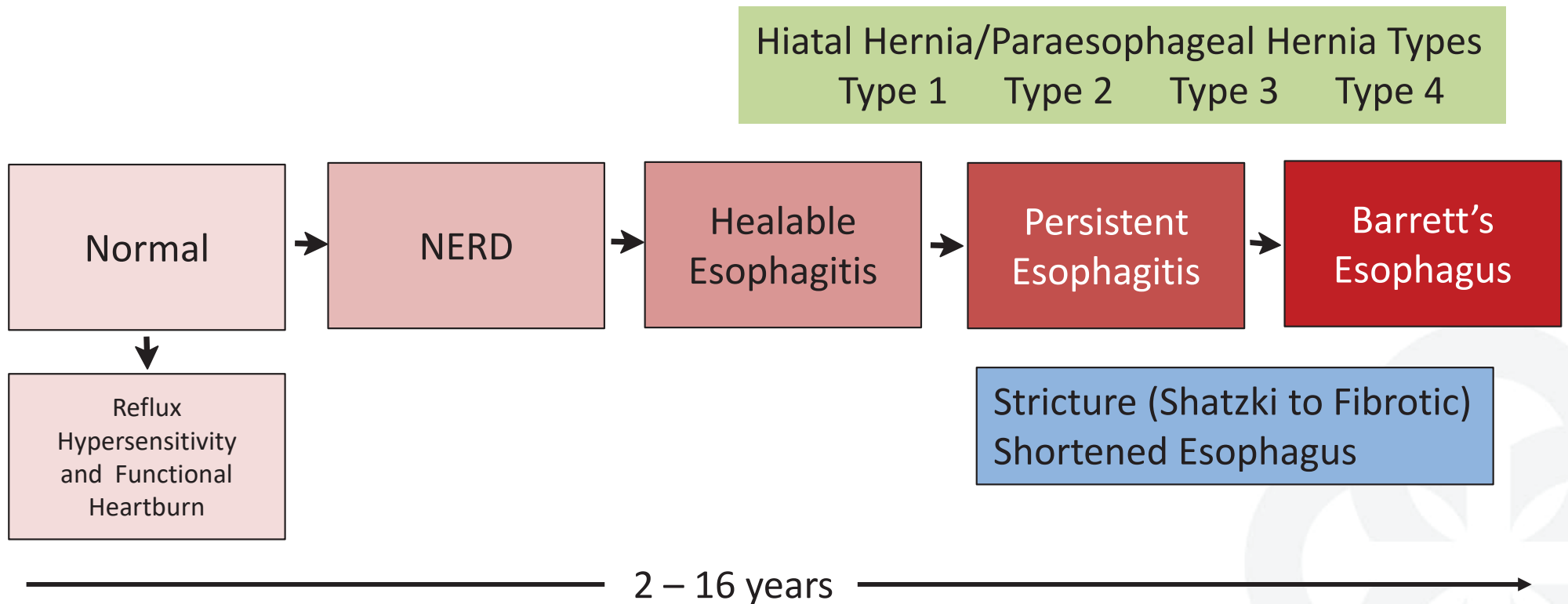


Nuances in the Diagnosis of GERD

- GERD symptoms can be diverse with similarities to many other disease processes.
- GERD is a chronic disease like osteoarthritis!
- Accuracy of diagnosis has an impact on response to therapy.
- Multimodal diagnostics are required to sort and define GERD patient symptoms



The Spectrum of GERD/Esophagitis and Hiatal Hernia



Spectrum of GERD Symptoms

Classic Symptoms

- Heartburn
- Regurgitation

Atypical Symptoms

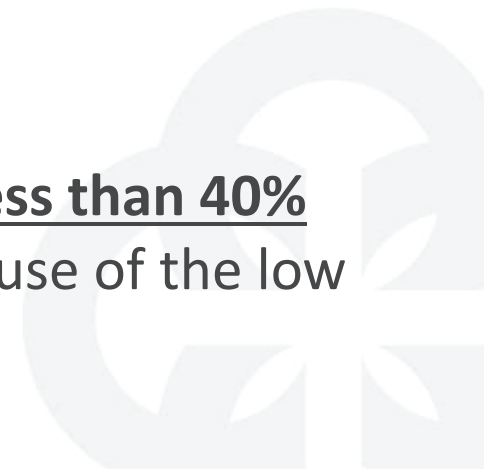
- Globus
- Cough
- Shortness of breath
- Exacerbation of RAD
- Hoarseness
- Odynophagia
- Dysphagia
- Chest pain



How many cases of laryngopharyngeal reflux suspected by laryngoscopy are gastroesophageal reflux disease-related?

Nicola de Bortoli¹, Andrea Nacci, Edoardo Savarino, Irene Martinucci, Massimo Bellini, Bruno Fattori, Linda Ceccarelli, Francesco Costa, Maria Gloria Mumolo, Angelo Ricchiuti, Vincenzo Savarino, Stefano Berrettini, Santino Marchi

Conclusion: MII-pH analysis confirmed GERD diagnosis in **less than 40%** of patients with previous diagnosis of LPR, most likely because of the low specificity of the laryngoscopic findings.



Is there a role for ARS in LPR?

- Yes. In carefully selected patients and only with objective data supporting the diagnosis of reflux as the cause.
- Confirmed reflux in the distal esophagus, usually with pH monitoring.



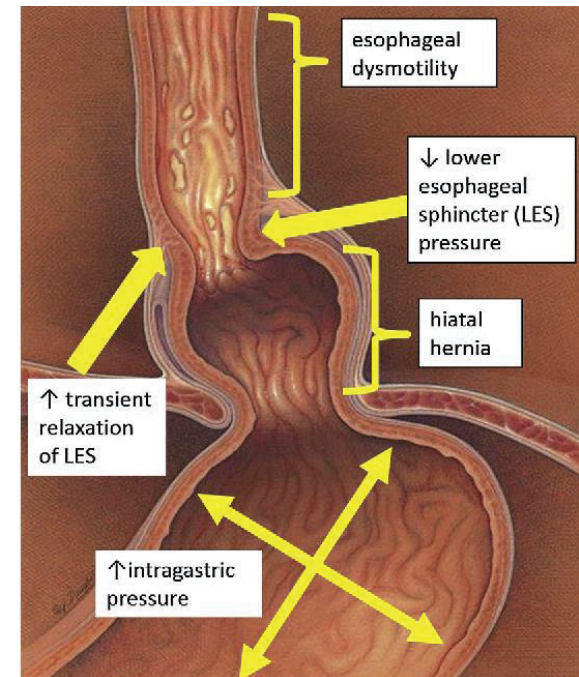
Initial Diagnostics and Therapy

Initial diagnostics

- Complete history and physical exam
- EGD with biopsy
- PPI trial

Advanced diagnostics:

- Esophagram
- pH study
- Manometry
- CT
- Nuclear medicine gastric emptying study



The Role and Controversy of PPIs in GERD Management

- Strengths of PPI
- Weaknesses of PPI therapy
- Potential harm of long-term PPI
- Statistics, relative vs absolute risk
- Guidelines for deprescribing



Strengths of PPIs

- The most potent daytime suppressor of gastric acid secretion.
- Outstanding at healing esophagitis LA Grade A-D and peptic ulcer disease.
- Best available treatment for GERD and reduce or eliminate symptoms in most patients.

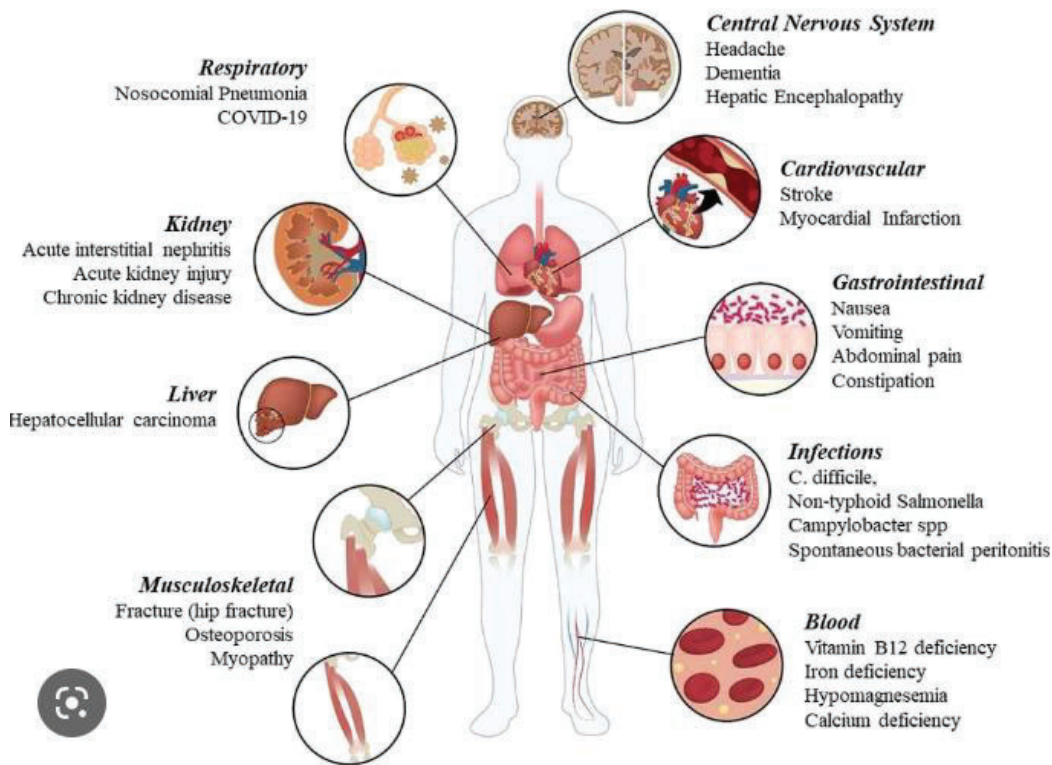


Weaknesses of PPI

- Variability in acid control makes once daily dosing for many inadequate
- On-demand or intermittent therapy ineffective
- Compliance with BID dosing is difficult
- Bedtime dosing not as effective as prior to evening meal.
- Dosing prior to meal required for optimal acid suppression
- Rebound, while not long lasting, makes dose reduction challenging
- Efficacy affected by CYP2C19 genetics
- Common side effects: headache and diarrhea



Reported Potential Side Effects of PPI Use



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What is the Risk, Really?

Absolute excess risk from PPI therapy is very low for nearly all reported effects.

Table 2. Absolute and Relative Risks for Adverse Effects Associated With Long-term PPIs

Potential adverse effect	Relative risk	Reference for risk estimate	Reference for incidence estimate	Absolute excess risk
Chronic kidney disease ¹	10% to 20% increase	Lazarus et al ⁹	Lazarus et al ⁹	0.1% to 0.3% per patient/year
Dementia ²	4% to 80% increase	Haenisch et al ¹²	Haenisch et al ¹²	.07% to 1.5% per patient/year
Bone Fracture ³	30% to 4-fold increase	Yang et al ¹⁴	Yang et al ¹⁴	0.1% to 0.5% per patient/year
Myocardial infarction	No association in RCTs	—	—	—
Small intestinal bacterial overgrowth	2-fold to 8-fold increase	Lo et al ²⁴	None available	Unable to calculate
<i>Campylobacter</i> or <i>Salmonella</i> infection	2-fold to 6-fold increase	Bavishi et al ²⁶	Crim et al ⁷⁸	.03% to 0.2% per patient/year
Spontaneous bacterial peritonitis ⁴	50% to 3-fold increase	Xu et al ²⁸	Fernandez et al ⁷⁹	3% to 16% per patient/year
<i>Clostridium difficile</i> infection ⁵	No risk to 3-fold increase	Furuya et al ³¹	Lessa et al ⁸⁰	0% to .09% per patient/year
Pneumonia	No association in RCTs	—	—	—
Micronutrient deficiencies ⁶	60% to 70% increase	Lam et al ⁴⁸	Bailey et al ⁸¹	0.3% to 0.4% per patient/year
Gastrointestinal malignancies	No association in RCTs	—	—	—

Freeberg et al. *The risks and Benefits of Long-term Use of Proton Pump Inhibitors: Expert review and Best Practice Advice From The American Gastroenterology Association. Gastroenterology* 2017; 152: 706-715

AGA Consensus statement for best practice advice (BPA) regarding PPI deprescribing

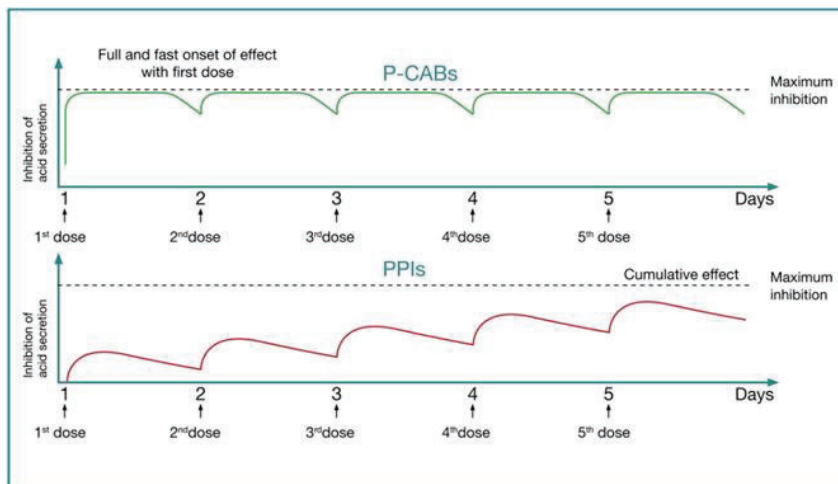
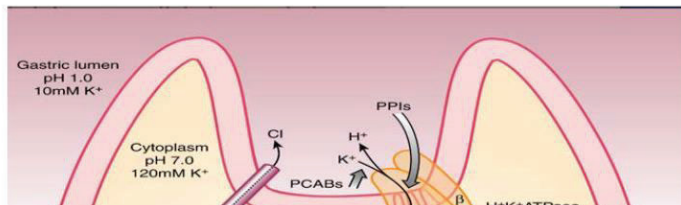
- BPA 1: All patients taking a PPI should have a regular review of the ongoing indications for use and documentation of that indication. This review should be the responsibility of the patient's primary care provider.
- BPA 2: All patients without a definitive indication for chronic PPI should be considered for trial of de-prescribing.
- BPA 3: Most patients with an indication for chronic PPI use who take twice-daily dosing should be considered for step down to once-daily PPI.
- BPA 4: Patients with complicated gastroesophageal reflux disease, such as those with a history of **severe erosive esophagitis, esophageal ulcer, or peptic stricture, should generally not be considered for PPI discontinuation.**
- BPA 5: Patients with **known Barrett's esophagus, eosinophilic esophagitis, or idiopathic pulmonary fibrosis should generally not be considered for a trial of de-prescribing.**
- BPA 6: PPI users should be assessed for upper gastrointestinal bleeding risk using an evidence-based strategy before de-prescribing.
- BPA 7: Patients at **high risk for upper gastrointestinal bleeding should not be considered for PPI de-prescribing.**
- BPA 8: Patients who discontinue long-term PPI therapy should be advised that they may develop transient upper gastrointestinal symptoms due to rebound acid hypersecretion.
- BPA 9: When de-prescribing PPIs, either dose tapering or abrupt discontinuation can be considered.
- BPA 10: The decision to discontinue PPIs should be **based solely on the lack of an indication for PPI use, and not because of concern for PPI associated adverse events (PAAE).** The presence of a PAAE or a history of a PAAE in a current PPI user is not an independent indication for PPI withdrawal. Similarly, the presence of underlying risk factors for the development of an adverse event associated with PPI use should also not be an independent indication for PPI withdrawal.

What's New on the Horizon for the Medical Management of GERD

- A **new class** of acid inhibitors is soon to be released called Potassium Competitive Acid Blockers (PCABS).
- They are **Not** a new version of PPIs, they are new class of acid inhibitors, and they are better than PPIs.



Potassium Competitive Acid Blocker (PCAB)

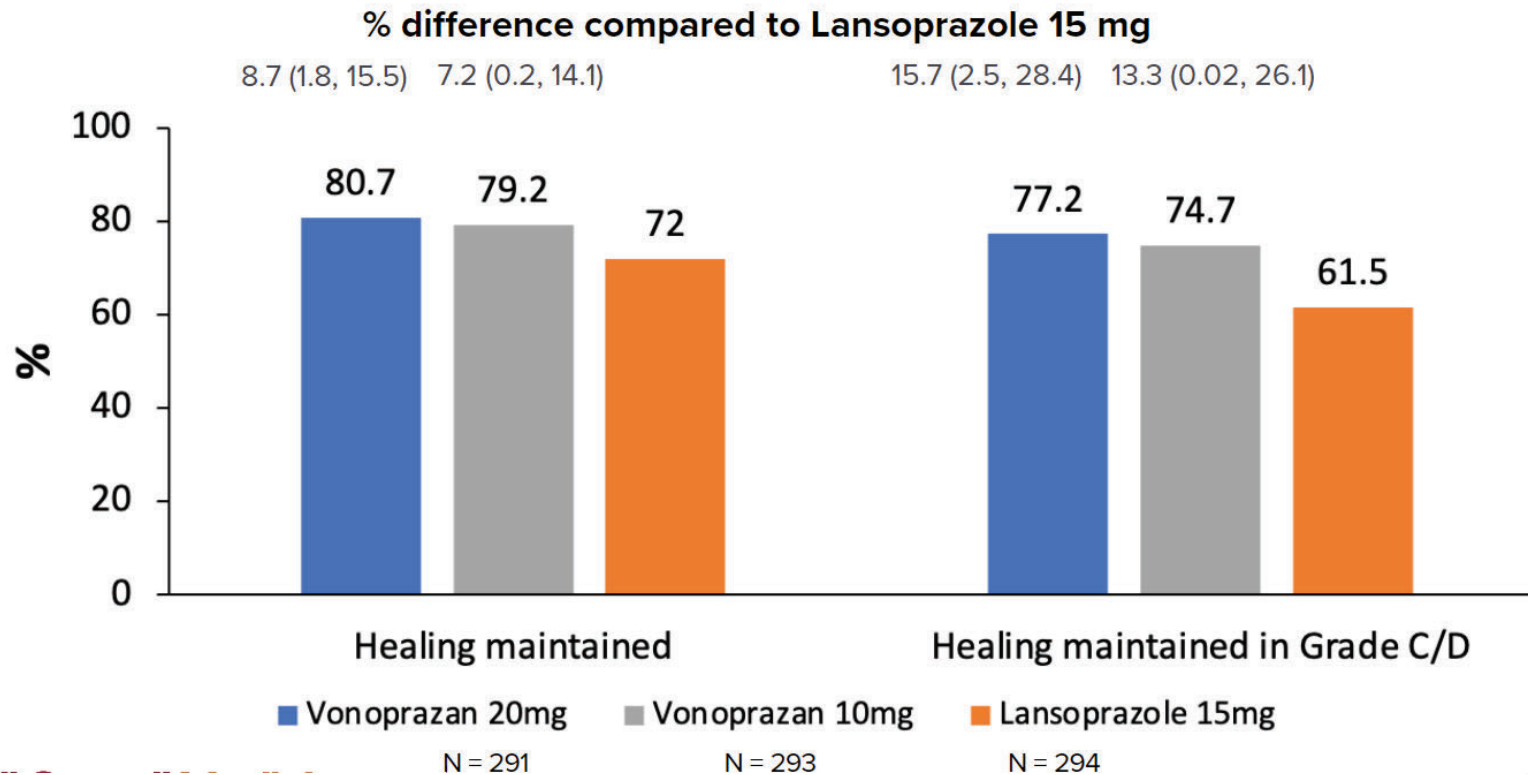


Mechanism of action and pharmacologic features

- Act on parietal cells
- Bind active and inactive proton pumps
- Inhibit H⁺,K⁺ ATPase
- Reversibly bind to proton pump
- Superconcentrates in parietal cell acid space, 100K higher than plasma
- Full effect after first dose
- Acid stable and do not require enteric coating
- Active drugs not prodrugs like PPIs
- No need to time drug around meal
- Not metabolized primarily by CYP2C19

PPI vs PCAB

Phase 3 Trial of Vonoprazan vs Lansoprazole in US and European Patients With EE: Maintenance Phase

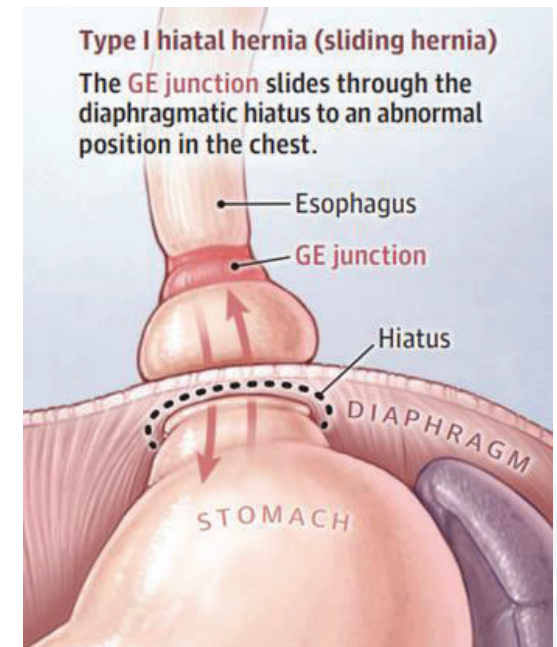


How has the Surgical Management of GERD and PEH Evolved over the last Decade?

GERD patient stratification and selection for surgery has been refined. We are making better choices. *Not everyone with reflux symptoms should have surgery.*

Predictors of success

- Typical GERD symptoms
- Good response to PPI therapy
- Documented abnormal acid exposure and/or esophagitis



How has the Surgical Management of GERD and PEH Evolved or the Last Decade?

- Surgical techniques have been refined.
- Focusing surgery at high volume centers dedicated to foregut surgery improves patient outcomes
- We have more tools in our tool belt
 - Robotics
 - Mesh reinforced hernia repairs
 - Variations in fundoplication based on motility
 - Magnetic sphincter augmentation
 - Transoral fundoplication (TIF)



GERD Presurgical Workup

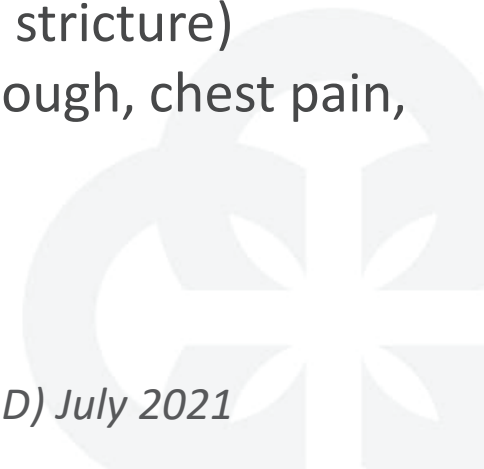
- GERD Health-Related Quality of Life (HRQL) symptom severity instrument
- PPI Trial*
- EGD with biopsy
- Ambulatory pH Study
- Esophagram
- Manometry
- Nuclear medicine gastric emptying study*



Who Gets Antireflux Surgery?

When the **diagnosis of reflux is objectively confirmed**, surgical therapy should be considered in individuals who:

- failed medical management (inadequate symptom control, severe regurgitation not controlled with acid suppression, or medication side effects)
- opt for surgery despite successful medical management (due to quality-of-life considerations, lifelong need for medication intake, expense of medications.)
- have complications of GERD (e.g., Barrett's esophagus, peptic stricture)
- have extra-esophageal manifestations (asthma, hoarseness, cough, chest pain, aspiration)*



Patient Selection for Surgery

Variable	Odds Ratio
Normal pH + Atypical Symptoms + Poor response to PPI	1.0
Normal pH + Typical Symptoms + Good response to PPI	16.7
Abnormal pH + Atypical Symptoms + Good response to PPI	17.7
Abnormal pH + Typical symptoms + Poor response to PPI	27.2
Abnormal pH + Typical symptoms + Good response to PPI	89.8

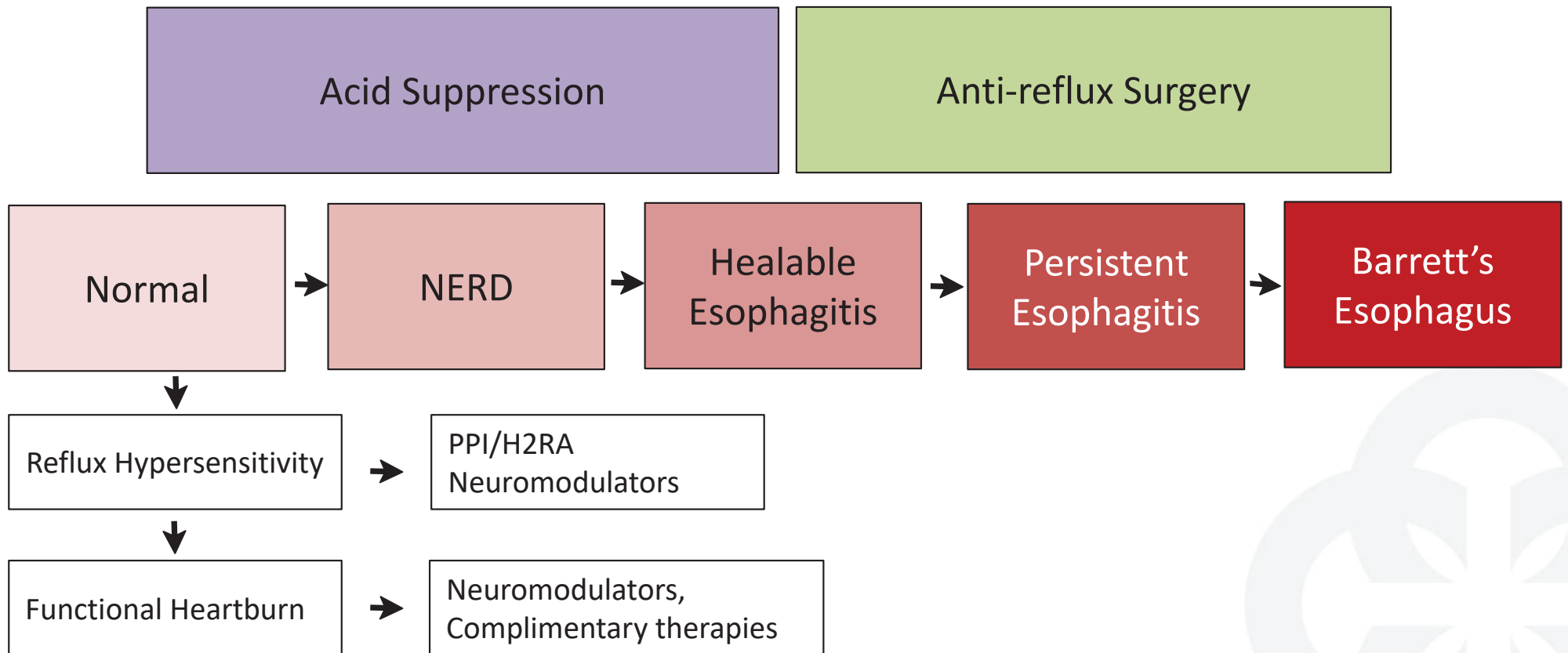
Campos, GMR. J Gastrointestinal Surgery 1999

Who doesn't get anti-reflux surgery?

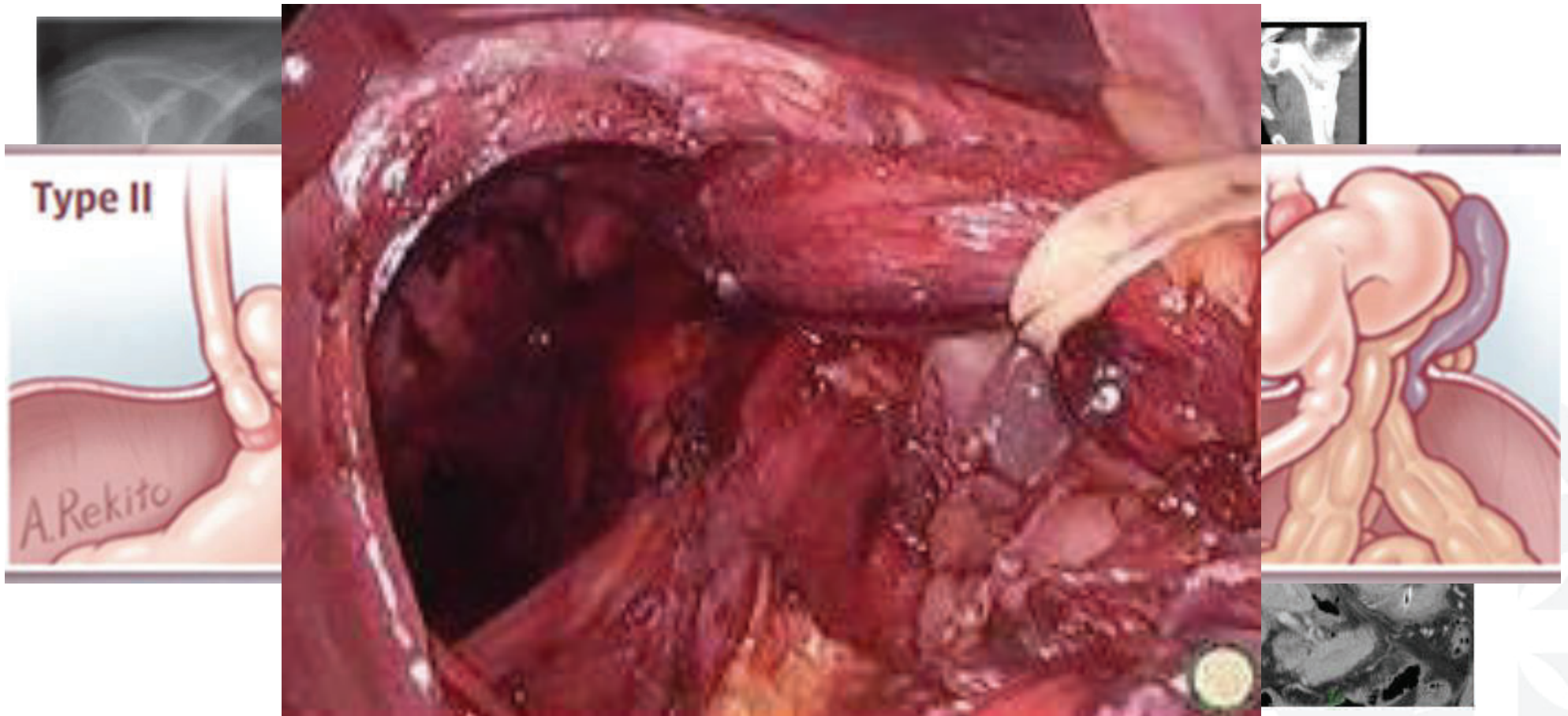
- Patients without objective evidence of reflux
- Patients who are better candidates for medical therapy
- Morbid obesity (BMI >35) or central obesity*
- Age > 80
- Significant cardiopulmonary disease
- Significant psychiatric disease
- Frailty



Individualized and Tailored Treatment



Paraesophageal Hernia (PEH)



Paraesophageal Hernias (PEH)

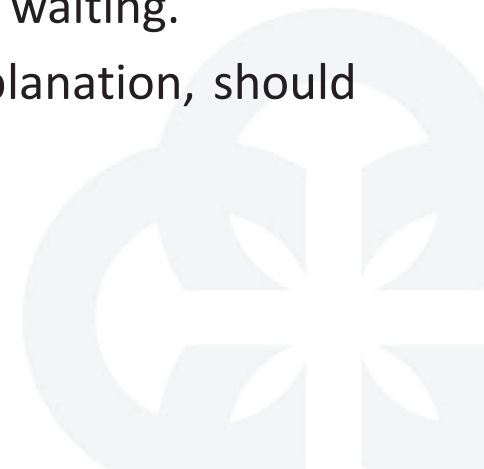
- We typically see these large hernias with intrathoracic stomach in advanced age patients.
- Dreaded complications of PEH include gastric volvulus with strangulation, ischemia and gastric necrosis. Immediate NG decompression.
- Associated symptoms include: dysphagia, heartburn, SOB, bloating, chest pain, anemia.
- Microcytic anemia in the absence of any other identifiable cause in a patient with a paraesophageal hernia is due to the PEH and should be offered surgery.
- These patients can be very frail and often have protein malnutrition. They may require extensive prehab to improve their protein nutrition to achieve an albumin level above 3.5 and improved cardiopulmonary performance in order to have the best outcomes.

Paraesophageal Hernia Repair Indications

- All patients under 65 should be evaluated for elective PEH repair.
- Patients over 65 years of age with type II/III PEH and minimal or no symptoms can be considered for watchful waiting and those with significant symptoms should be evaluated for surgery.
- All patients with a Type IV hernia should be evaluated for elective PEH repair regardless of age due to potential morbidity and mortality risk of non-elective, urgent/emergent surgical outcomes and the morbidity of watchful waiting.
- All patients with cameron erosions, or anemia without other explanation, should be evaluated for elective PEH repair.

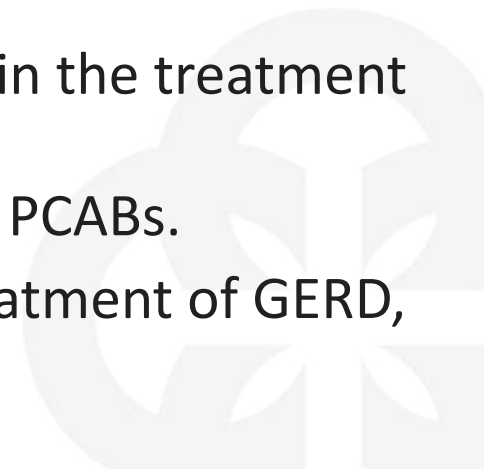
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Summary

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Saint Alphonsus Foregut and Reflux Surgery

- Nampa and Caldwell Outreach May 2023
- Manometry offered in clinic starting this summer
- POEM procedures for esophageal motility disorders this summer.



Thank you

- Questions?

