

“Literature Update in Integrative and Functional Medicine”

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Objectives

- ▶ Introduce Integrative and Functional Medicine
- ▶ Review key literature updates from 2018
- ▶ Share tools to help patients with GERD

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Integrative/Functional Medicine

- ▶ **Integrative:**
 - Whole-person care
 - Tools to help patient reach a balanced state

- Nutrition
- Acupuncture
- Biofeedback
- Neurofeedback
- Supplements
- Chiropractic
- Exercise
(and more)



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Integrative/Functional Medicine

► **Functional:**

- Another tool within the Integrative Umbrella
- Looks for underlying causes of symptoms or diagnosis



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Integrative/Functional Medicine



- Evidence-based, whole-person treatment of chronic disease
- Approach looks upstream for source of disease
- Focus: food as medicine, lifestyle support, nutrients
- Aims to bridge allopathic and CAM for best outcomes

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GERD – High Disease Burden

- Prevalence of GERD: 10-20% in Western world
- Evidence suggests prevalence ↑ since 1995
- Direct costs + indirect costs: \$15B-\$20B in USA

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• <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411011/>
• El-Morad H, Lereut S, Winchester CC, Sorel J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut*. 2014 Jun;63(6):871-80. doi: 10.1136/gut.2012.304209.

Proton Pump Inhibitors

► Most commonly used medication

- Dyspepsia, ulcer, GERD
- Prophylactic treatment NSAIDs/glucocorticoids
- High-risk of peptic ulcer
 - › Frequent smokers
 - › Chronic alcoholics
 - › Taking bisphosphonates

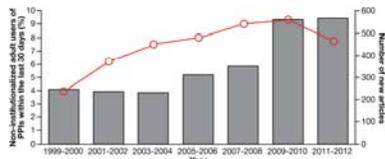
► Well-supported by evidence

Hassan, S., Siddiqui, A.N., Habib, A. et al (2018) Proton pump inhibitors' use and risk of hip fracture: a systematic review and meta-analysis. *Rheumatol Int* 38: 1999. <https://doi.org/10.1007/s00296-018-4142-x>

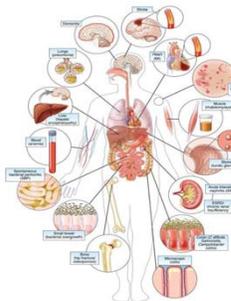
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Proton Pump Inhibitors

Most-commonly prescribed OTC medication (Global market value of \$13B)



- Freedberg DE, Kim LS, Yang YX (2017) The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American gastroenterological association. *Gastroenterology* 152:706-715
- Hassan, S., Siddiqui, A.N., Habib, A. et al (2018) Proton pump inhibitors' use and risk of hip fracture: a systematic review and meta-analysis. *Rheumatol Int* 38: 1999. <https://doi.org/10.1007/s00296-018-4142-x>



Potential Risks of PPIs

- Laura Targownik, MD, MSHS, FRCP(C) Discontinuing Long-Term PPI Therapy: Why, With Whom, and How? *Am J Gastroenterol* 2018; 113:1519-1526. doi: 10.1038/sj.ajg.121820

PPI use and hip fracture risk

- ▶ Systematic review and meta-analysis
- ▶ **Primary outcome** - quantify risk of hip fracture associated with PPI use
- ▶ **Secondary outcome** – subgroup analysis
 - calcium intake
 - duration of PPI use
 - study design

Husain, S., Siddiqui, A.N., Habib, A., et al (2018) Proton pump inhibitors' use and risk of hip fracture: a systematic review and meta-analysis. *Rheumatol Int* 38: 1999. <https://doi.org/10.1007/s00296-018-4142-x>

PPI use and hip fracture risk

- ▶ Hip fracture: A leading cause of substantial loss of healthy life-years in elderly adults
- ▶ PPI users: 26% increase risk of hip fracture as compared to non-PPI user



Husain, S., Siddiqui, A.N., Habib, A., et al (2018) Proton pump inhibitors' use and risk of hip fracture: a systematic review and meta-analysis. *Rheumatol Int* 38: 1999. <https://doi.org/10.1007/s00296-018-4142-x>

PPI use and hip fracture risk

- ▶ Risk persisted even when adjusted for calcium use and duration of PPI use ($p < 0.0001$)
- ▶ Higher risk if older age, several years of PPI intake, osteoporosis, post-menopausal woman



Husain, S., Siddiqui, A.N., Habib, A., et al (2018) Proton pump inhibitors' use and risk of hip fracture: a systematic review and meta-analysis. *Rheumatol Int* 38: 1999. <https://doi.org/10.1007/s00296-018-4142-x>

PPI use and hip fracture risk

Mechanism not fully understood

- ▶ Impaired calcium absorption in hypochlorhydric states
- ▶ Impaired magnesium absorption
- ▶ PPI-induced alterations in bone remodeling
- ▶ Impaired absorption of folate and B12
 - Connection with elevated homocysteine and altered bone remodeling

Hassan, S., Siddiqui, A.N., Haddad, A. et al. (2018) Proton pump inhibitors use and risk of hip fracture: a systematic review and meta-analysis. *Rheumatol Int* 38: 1999. <https://doi.org/proxy.kumc.edu/10.1007/s00296-018-4142-x>

PPI and Depression

- ▶ Use of PPIs associated with a higher Geriatric Depression Scale
- ▶ Higher PPIs dosages associated with increased probability of depression.
- ▶ No association found between use of H2-blockers or antacids and the GDS score



Laudisio A et al. Use of proton-pump inhibitors is associated with depression: a population-based study. *Volume 30, Issue 1, January 2018, 153-159.*

PPI and Depression

- ▶ Further analysis suggested 14% of depression cases could be avoided by withdrawal of PPIs
- ▶ Depression is the most common psychiatric disorder in the general population
 - Annual prevalence: 6.7%
 - Lifetime prevalence: 16.5%
 - Chronic medical illness -- annual prevalence: 25%



Laudisio A et al. Use of proton-pump inhibitors is associated with depression: a population-based study. *Volume 30, Issue 1, January 2018, 153-159.*
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6049349/> Accessed 3/2019

NERD

- Non-erosive reflux disease - heartburn with normal appearing mucosa on endoscopy;
- Most common form of GERD (70%)
- Less responsive to acid blockers
- But feel more impaired due to symptoms

• Lee-SW et al. Heartburn and regurgitation have different impacts on life quality of patients with gastroesophageal reflux disease. *World Journal of Gastroenterology*. WJG. 2014;20(34):12277-12282.

Current Best Practice Advice



- ▶ Patients with GERD and acid-related complications (erosive esophagitis or peptic stricture) should take a PPI for short-term healing, maintenance of healing and long-term symptom control.

• Freedberg DE, Kim LS, Yang YX (2017) The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. *Gastroenterology* 152:706-715

Current Best Practice Advice



- ▶ Patients with uncomplicated GERD who respond to short-term PPIs should subsequently attempt to stop or reduce them

• Freedberg DE, Kim LS, Yang YX (2017) The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. *Gastroenterology* 152:706-715

Current Best Practice Advice



- ▶ Patients with Barrett's esophagus should take a long-term PPI
- ▶ Severe esophagitis

* Freedberg DE, Kim LS, Yang YX (2017) The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. *Gastroenterology* 152:706-715

Current Best Practice Advice



- ▶ Patients at high risk for ulcer-related bleeding from NSAIDs should take a PPI if they continue to take NSAIDs.
- ▶ Documented history of bleeding GI ulcer

* Freedberg DE, Kim LS, Yang YX (2017) The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. *Gastroenterology* 152:706-715

How?



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How?

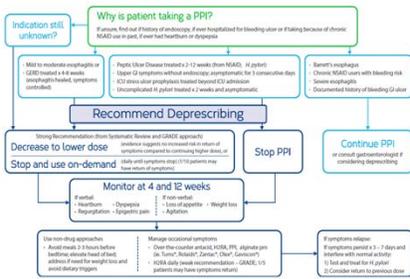
Rebound hyperacidity:

- ▶ Difficult to discontinue PPIs, even if underlying condition has resolved
- ▶ Gastrin

Approximately 2/3 of patients relapse

- ▶ Repeat acid-suppressing therapy
- ▶ Likely long-term

• uptodate.com/contents/medical-management-of-gastroesophageal-reflux-disease-in-adults Accessed 3/2019



• Farrell B, Poths K, Thompson W, et al. Deprescribing proton pump inhibitors: Evidence-based clinical practice guideline. Canadian Family Physician. 2017;63(3):354-364

Integrative/Functional Medicine

Stomach Acid: Protective and necessary in the right place at the right time

- ▶ Needed to properly digest proteins
- ▶ Impairment of gastric function is a documented risk factor for IgE food allergy

• Pali-Scho T, Jensen-Jarolim E. Anti-acid medication as a risk factor for food allergy. Allergy 2011; 66: 469-477.

• Hypochlorhydria shown to increase IgE rxns >10. Anti-ulcer drugs promote IgE formation toward dietary antigens in adult patients. FASEB J. 2009 Apr; 19(4): 656-6.

Integrative/Functional Medicine

Stomach Acid: Needed to liberalize minerals/vitamins, amino acids from our foods

Risk of:

- ▶ Bone loss
- ▶ Fracture
- ▶ Depression
- ▶ Low magnesium
- ▶ Low B12 (and more)

• Freedberg DE, Kim LS, Yang YX (2017) The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the american gastroenterological association. *Gastroenterology* 152:706-715
• Li W, Li W, W. Chan Proton pump inhibitor use and the risk of small intestinal bacterial overgrowth: a meta-analysis *Clin Gastroenterol Hepatol*. 11 (2013), pp. 483-490
• Chongsakorn W, Thongprayoon C, Kittanamongkolchai W, et al. Proton pump inhibitors linked to hypomagnesemia: a systematic review and meta-analysis of observational studies. *Ren Fail* 2015; 37:1237-1241.

Integrative/Functional Medicine

Stomach Acid: Helps prevent:

- ▶ C. diff
- ▶ Community-acquired pneumonia
- ▶ SIBO

(Bacterial overgrowth occurs during pH > 4.0)

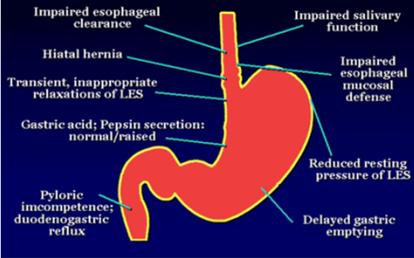
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Best of both worlds

How can we have adequate HCL for breakdown of our foods without heartburn symptoms?



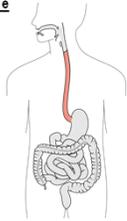
Pathophysiology of GERD



Why GERD?

Lower esophageal sphincter (LES) tone

- ▶ LES normally exists in a contracted state
 - Swallowing, burping
- ▶ With longer-term decreased tone, reflux
- ▶ Foods, beverages, smoking, medications
- ▶ AND low HCL



Rakel, D. (2012). Integrative Medicine (3rd ed.). Philadelphia, PA: Elsevier

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Associated with ↓LES Tone

Foods:

- ▶ Alcohol
- ▶ Chocolate
- ▶ Coffee
- ▶ Cow's milk
- ▶ High-fat foods
- ▶ Onions
- ▶ Garlic
- ▶ Citrus fruits (OJ)
- ▶ Spicy foods
- ▶ Tea
- ▶ Tomatoes
- ▶ Peppermint
- ▶ Carbonated drinks



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Associated with ↓ LES Tone

Smoking



Medications:

- ▶ Anticholinergics
- ▶ Beta-adrenergics
- ▶ CCB
- ▶ Nitrates
- ▶ Sildenafil



Associated with ↓ LES Tone

Other:

- ▶ Scleroderma-like diseases
- ▶ Gastric stasis



Other Causes

Stress

- ▶ Exacerbates GERD, particularly with high anxiety

Conditions that decrease saliva production

- ▶ Saliva has neutralizing effect on acid

Increased intra-abdominal & gastric pressure

- ▶ Obesity
- ▶ Ascites
- ▶ Pregnancy
- ▶ Tight clothing
- ▶ Recumbent position
- ▶ Bending over
- ▶ Hiatal Hernia

Other Causes

Decreased gastric emptying

- >4 hours suggests delay
- DM, impaired PNS

Hiatal Hernia

- Lose “pinch” from diaphragm, easier for reflux

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Prevention

- ▶ Reduce foods, drinks, lifestyle factors and medications that contribute to low LES tone
- ▶ Maintain ideal body weight
- ▶ Regular exercise
- ▶ Manage stress as much as possible
 - Focus on daily mind-body strategies
 - Practice mindful eating
- ▶ Avoid large meals
- ▶ Try to avoid food within 3 hours of sleep
- ▶ Walk 15-20 minutes after a meal

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Help tapering off PPI

- ▶ For those who may not need chronic acid suppression:
 - Stopping abruptly not recommended
- ▶ Lifestyle changes first
- Set yourself up for success
- ▶ Slowly start to taper:
 - Decrease PPI in small increments
 - Switch to H2B daily or alternate H2B/PPI

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Bridge therapy while tapering

- ▶ Reduce foods, drinks that can contribute to lowered LES tone
- ▶ Anti-inflammatory eating
- ▶ Lowered processed carbohydrates

• Rakel, D. (2012). Integrative Medicine (3rd ed.). Philadelphia, PA: Elsevier
• Bad food and GERD: Surita Bajaj T, Negrutu DE, Palaga M, Dumitrascu DL. Food and Gastroesophageal Reflux Disease. *Curr Med Chem*. 2017
• Wu KL, Kuo CM, Yao CC, Tai WC, Chuah SK, Lin CS, Chiu YC. The effect of dietary carbohydrate on gastroesophageal reflux disease. *J Formos Med Assoc*. 2018 Jan 12; pii: S0959-6646(17)30591-0.

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Bridge therapy while tapering

- ▶ Acupuncture 1-2x/week
- ▶ Stress management
- ▶ Raise Head of Bed
- ▶ Hiatal hernia
- ▶ Supportive supplements
- ▶ Gentle acid suppression - CaCO₃, MgOH

• Rakel, D. (2012). Integrative Medicine (3rd ed.). Philadelphia, PA: Elsevier
• Bad food and GERD: Surita Bajaj T, Negrutu DE, Palaga M, Dumitrascu DL. Food and Gastroesophageal Reflux Disease. *Curr Med Chem*. 2017
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Supplements - Demulcent

- ▶ Mucoprotection of esophageal mucosa
 - Soothes irritated tissues and promotes healing
- ▶ Deglycyrrhizinated licorice (2-4 380mg tablets pre-meal or PRN)
- ▶ &/or Sucralfate (Carafate) – 1g pre-meal
- ▶ &/or Slippery elm (1-2 tbsp of powdered root in water 3-4x/day)

• Rakel, D. (2012). Integrative Medicine (3rd ed.). Philadelphia, PA: Elsevier

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Supplements - LES tone

- ▶ **Melatonin**
 - Not only for circadian rhythm
- ▶ **Enterochromaffin cells of intestinal wall**
 - make 400-500x more melatonin than brain
 - Inhibit gastric acid secretion
 - Help stimulate contractile activity of LES
- ▶ **Omeprazole found to decrease day-time melatonin**
- ▶ **6 mg/night**

• Patrick, L. 2011; Brzozowski, T. 2011; de Oliveira Torres, JD; Madanaki, MH 2010.

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Supplements - LES tone

- ▶ **Value:**
 - Well-tolerated
 - Has been studies for safe use up to 2 years
 - Caution: long-term use in patients under 20 (Gonadal development)
- ▶ **AE:**
 - Headaches, dizziness, nausea, drowsiness
 - Case reports: Risk of blood-clotting if patient takes warfarin
 - Case reports: Risk of seizure with overdose

<https://pubmed.ncbi.nlm.nih.gov/23600000/> accessed 3/2019

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Supplements - Barrier

- ▶ **Alginate**
 - Gaviscon or other preparation
 - Soothes and coats the esophagus
 - Forms a floating barrier
 - Reduces reflux

• RohofW et al. An alginate-antacid formulation localizes to the acid pocket to reduce acid reflux in patients with gastroesophageal reflux disease. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2011;11(12):1958-61.
• Mariani KG, Daggly BP, Brodie DA, et al. Review article: alginate-raft formulations in the treatment of heartburn and acid reflux. Aliment Pharmacol Ther. 2000;14:659-60.

Supplements – Prokinetics

- ▶ Probiotic- helps with dysbiosis from PPI
- ▶ Ginger - 1500-2000mg/day
- ▶ Iberogast- 1mL three times/day
- ▶ D-Limonene from citrus peels-1000mg BID
- ▶ Acupuncture
- ▶ Stress management



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Help tapering off PPI

If taper is successful, slowly taper off supplements:

- Example: reduce dosage/frequency of supportive supplements
- Continue lifestyle support

If symptoms return:

- Re-introduce supplements for longer period of time
- Add H2B or
- Add back PPI (low dose)

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Cautions/Contraindications

- ▶ Remember to move slowly
- ▶ Stay in touch with PCP/ENT, repeat imaging
- ▶ Remember risks vs benefits
 - De-prescribing not connected with significant clinical harms

• Farrell B, Pottie K, Thompson W, et al. Deprescribing proton pump inhibitors: Evidence-based clinical practice guideline. Canadian Family Physician. 2017;63(5): 354-364

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