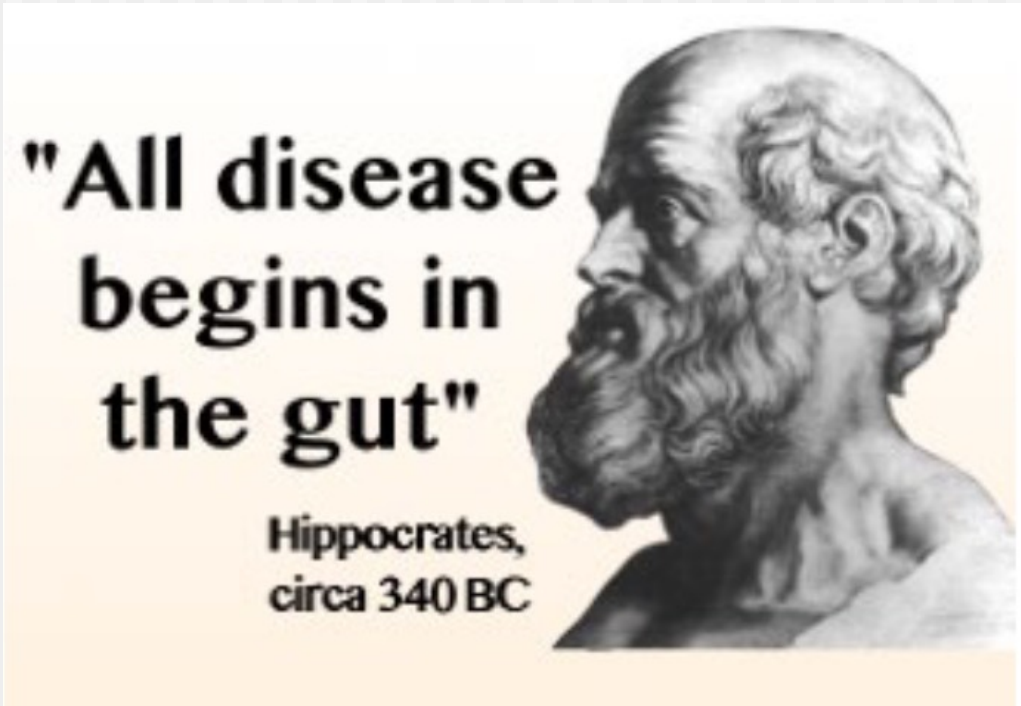
FAST 15!

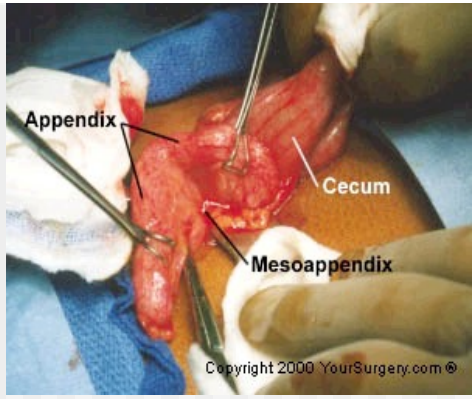
Introducing:

a new class of

acid reducing medications



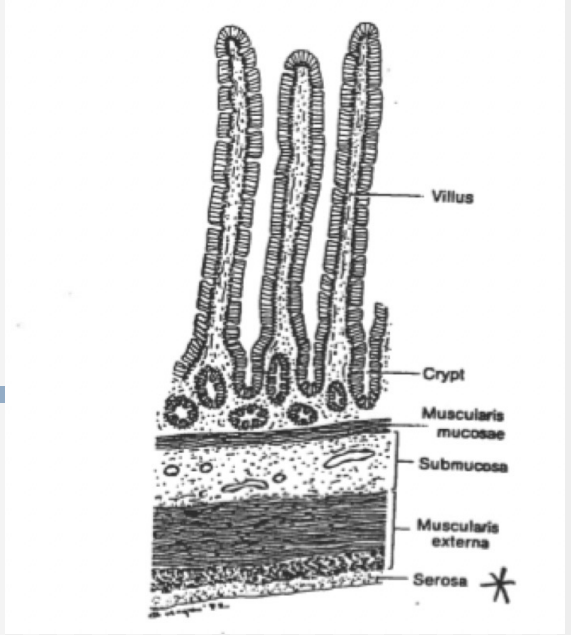
& a power review of GERD



- **Gerald T. Simons, PA-C**
- **Clinical Assistant Professor**
  - **Stony Brook PA Program**
- Surgical PA
  - Private practice GI focus
- AASPA
  - Past President
  - Wound Care Instructor
  - BOD

-NO DISCLOSURES
-I have no financial interest in any companies or products mentioned.

My interest



- I have a 25 year interest in the gut.
- It began simply as a technical interest- how to resect the bowel, staple, suture, and scope it. As time when on, I became more interested in its physiology, neurologic innervation, absorption etc.
- I've come to realize that the gut
  - is a key part of our immune system & overall ecosystem
  - oral medication can alter its function
  - nutrition can affect and is affected by its role.
  - Probiotics are an important prescription for many
  - FMT will be seen more often

Fast 15
Objectives

- Describe the mechanism of action of potassium-competitive acid inhibitors
- Compare and contrast PCABs with proton pump inhibitors
- Describe the typical patient that would benefit from a PCAB over other acid regulating medications

GERD: think GE Junction

Squamocolumnar junction

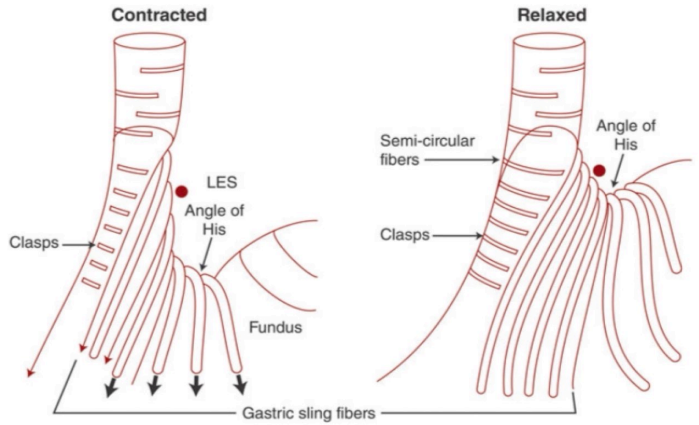


Fig. 1.1 The clasp and sling muscle fibers that make up the lower esophageal reflux barrier in the contracted and relaxed state

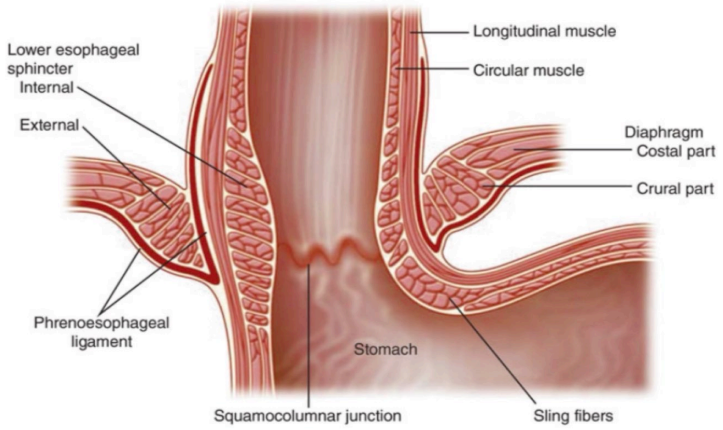
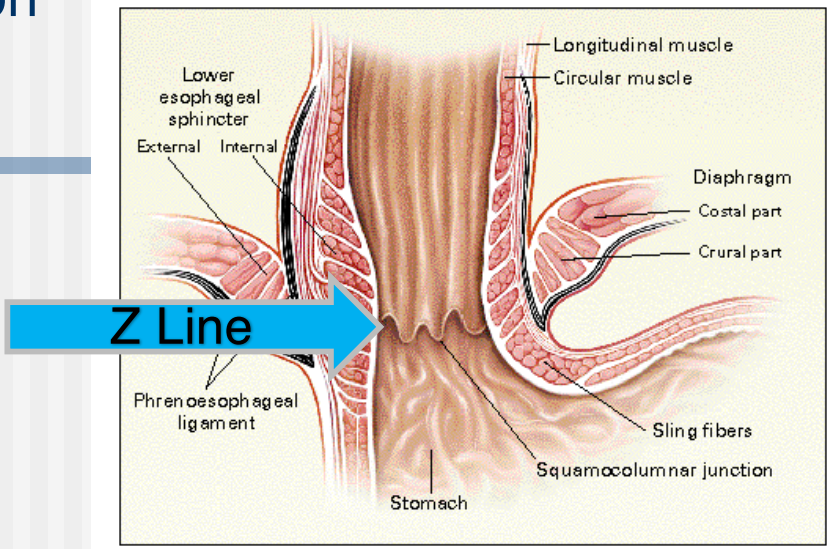
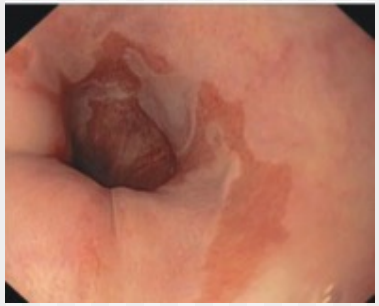


Fig. 1.2 The anatomic relationship of the gastroesophageal junction, the phrenoesophageal ligament, and the diaphragm at the esophageal hiatus



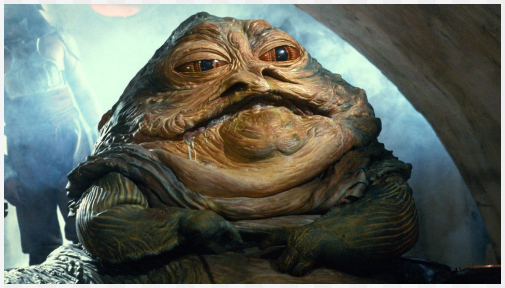


"I'm a PA &
I find the Z!"

GERD Tx

Everyone requires lifestyle changes!

- **GET PRESSURE OFF THE LES**
- Weight loss
- Elevate the head of the bed
  - use bricks
- GERD Pillow
- Chew and eat slowly, smaller meals
- Avoid eating 3 hours before laying down.
- Avoid foods that trigger symptoms:
  - Mint, milk, fried foods, tomato, coffee, carbonation, garlic, etc.

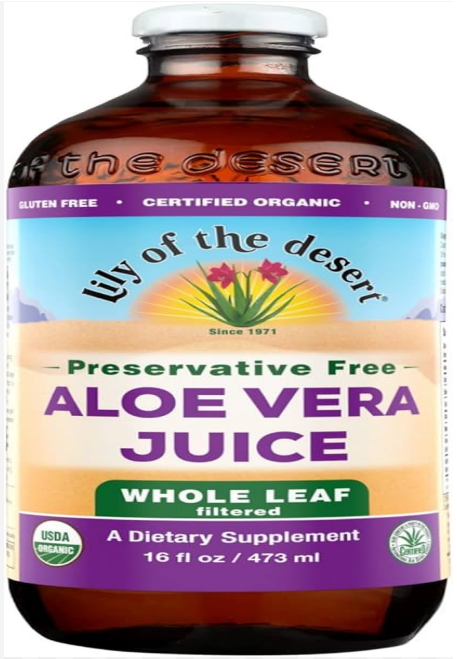


GERD Tx: Lifestyle

- Avoid constipation
- Improve saliva production
  - Saliva contains bicarbonate and epidermal growth factors
- Quit smoking
- Stop alcohol

Check every GERD patient for H Pylori!

Aloe Juice/capsules



- Aloe is known to be anti-inflammatory
- Helps with mucosal lining
- Drink 2 oz as a maintenance dose or as needed for reflux.
  - No added sugar products are best
- Great results with esophagitis & DU if combined with cryoprotection!

Glutamine
*All GERD patients should be on!

- Vital amino acid
  - Check serum IgA levels!
- Produces GABA
  - Vital for LES tone
- Vital for muscle function
- Intestines have highest demand
  - Especially when ill or under stress
  - More glutamine=more healthy gut mucosa

Look for increased use in surgical stress/ICU

Proton-Pump Inhibitors

KEEP PARIETAL CELLS CLOSED irreversibly during its effect!

Must be taken as a preventative BEFORE A MEAL

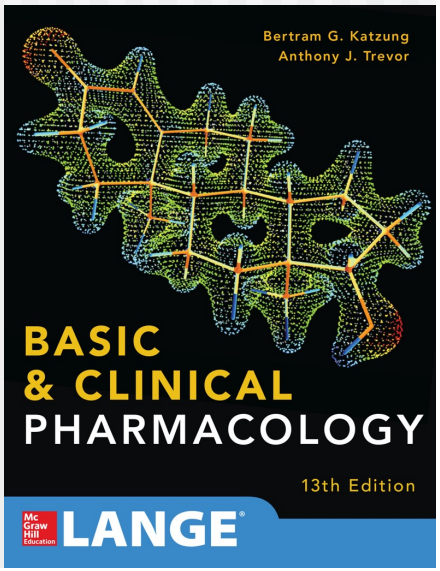
Not helpful when feeling pyrosis!

Dexlansoprazole-Dexilant *ultimate delay release*
Lansoprazole-Prevacid
Rabeprazole-Aciphex
Esomeprazole-Nexium
Pantoprazole-Protonix
Omeprazole- Prilosec

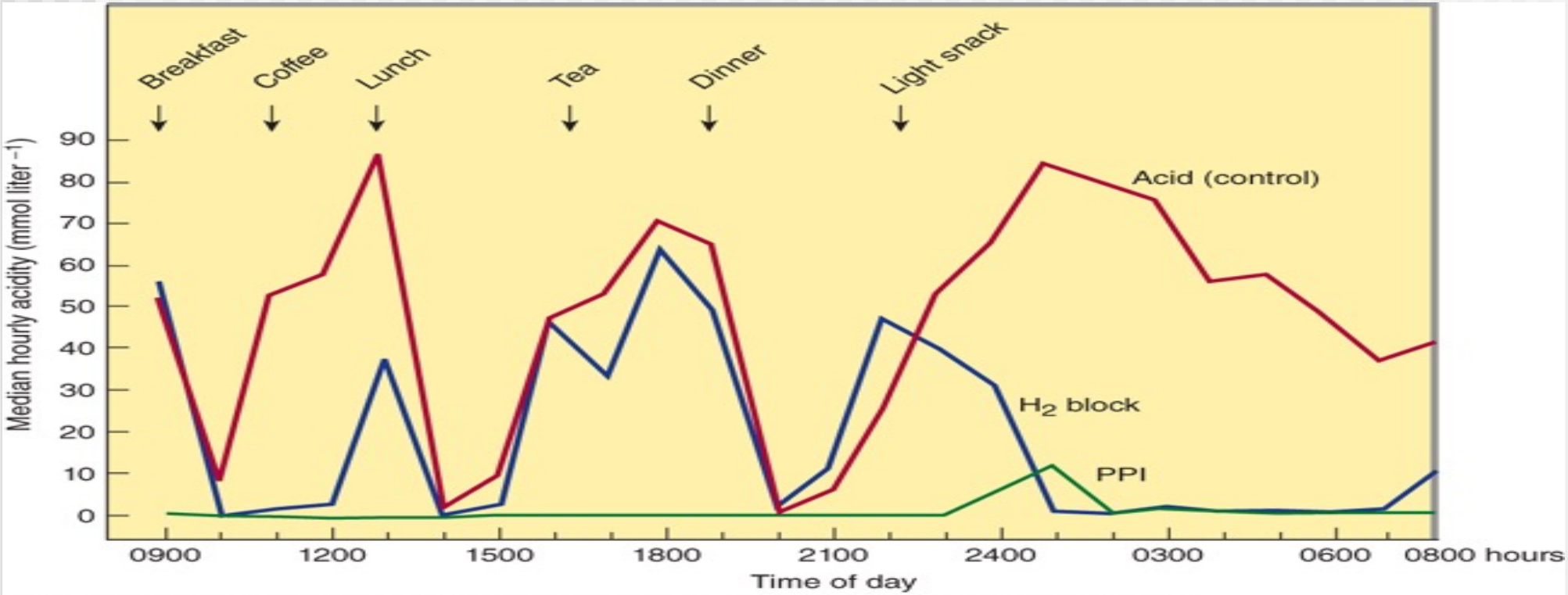
PATIENT ED:
-Takes 3-4 days to work
-Must be BEFORE YOU EAT
-Will not help pyrosis
-Not ideal taken long term

“PPIs are the most effective agents for the Tx of nonerosive and erosive reflux disease, esophageal complications of reflux disease (peptic stricture or Barrett’s esophagus), and extraesophageal manifestations of reflux disease.

Once-daily dosing provides relief and tissue healing in 85% of patients;
15% of patients require twice-daily dosing.
GERD symptoms recur in over 80% of patients within 6 months after discontinuation of a PPI.
Erosive esophagitis or esophageal complications, **long-term daily maintenance therapy with a full-dose or half-dose PPI is usually needed**. Many patients with nonerosive GERD may be treated successfully with intermittent courses of PPIs or H2 antagonists taken as needed (“on demand”) for recurrent symptoms.”



PPIs: Is this normal? (Wow H2's great at night)



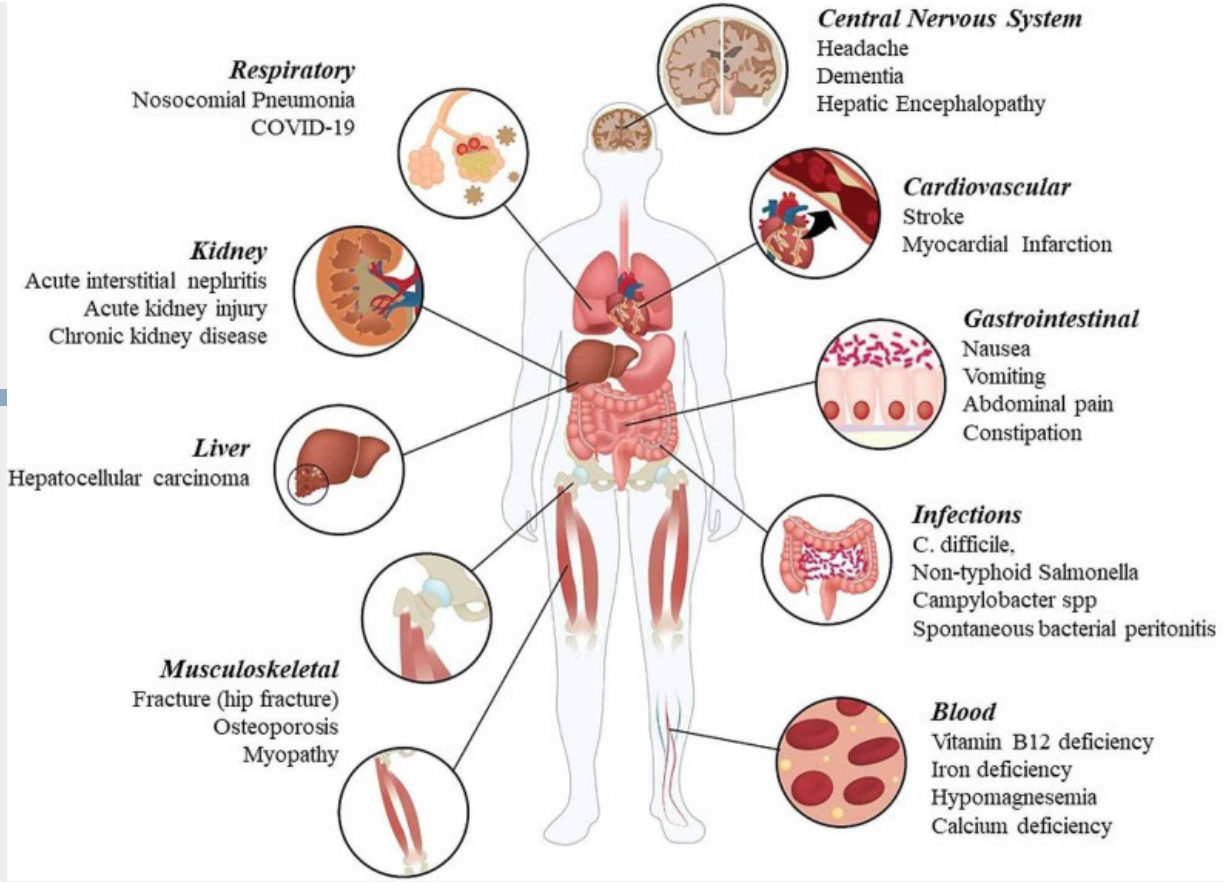
Source: Bertram G. Katzung, Anthony J. Trevor: Basic & Clinical Pharmacology, 13th Ed.
www.accesspharmacy.com

PPI's alter our gut microbiome

- PPIs alter the pH and affect the modulation of the immune response.
- SIBO and intestinal infections including *Salmonella* spp. and *C. difficile* are more common.
- "Indications are that probiotics may have an effect on inhibiting intestinal dysbiosis after PPIs and may help alleviate the side effects of PPIs therapy."
  - *Kiecka, A. et.al. Proton pump inhibitor-induced gut dysbiosis and immunomodulation: current knowledge and potential restoration by probiotics. Pharmacol. Rep (2023)*

ABIM:"More than half of the people who take PPIs probably do not need them."

REMINDER: PPI Problems



- COVID-19
- Less microbial diversity
- Low magnesium
- Bone loss/fractures
- Renal disease
- C.diff (*Significant risk*)
- Low B12
- Addiction! Rebound acid!

AGA Guideline warning &
>5 studies, most recent:
Yibirin M, De Oliveira D, Valera R, Plitt AE, Lutgen S. Adverse Effects Associated with Proton Pump Inhibitor 2021

PPI Problems

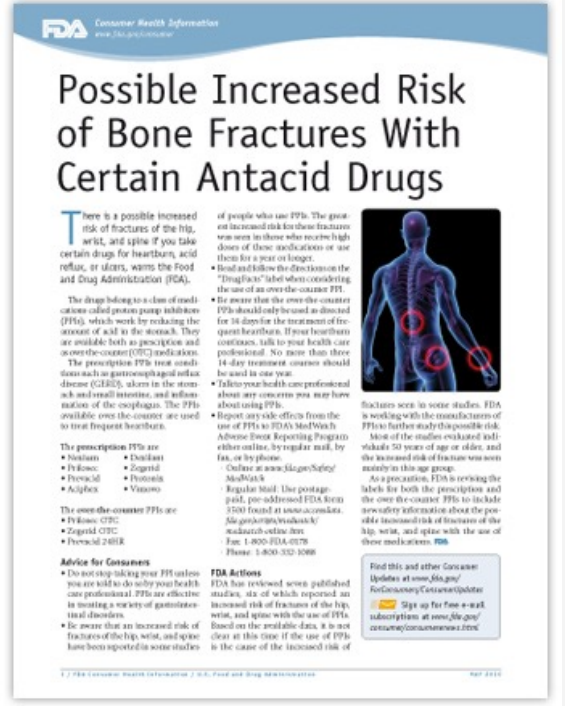
Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population

Nigam H. Shah, Paea LePendu, Anna Bauer-Mehren, Yohannes T. Ghebremariam, Srinivasan V. Iyer, Jake Marcus, Kevin T. Nead, John P. Cooke, Nicholas J. Leeper

Published: June 10, 2015 • https://doi.org/10.1371/journal.pone.0124653

PSYCH patient?

Ask about PPI
Check B12 & minerals.



FDA Consumer Health Information

Possible Increased Risk of Bone Fractures With Certain Antacid Drugs

There is a possible increased risk of fractures of the hip, wrist, and spine if you take certain drugs for heartburn, acid reflux, or ulcers, warns the Food and Drug Administration (FDA).

The drugs belong to a class of medications called proton pump inhibitors (PPIs), which work by reducing the amount of acid in the stomach. They are available both as prescription and as over-the-counter (OTC) medications.

The prescription PPIs treat conditions such as gastroesophageal reflux disease (GERD), ulcers in the stomach and small intestine, and inflammation of the esophagus. The PPIs available over the counter are used to treat frequent heartburn.

The prescription PPIs are
- Nexium
- Dexilant
- Prilosec
- Zegerid
- Prevacid
- Protonix
- Aciphex
- Vimovo

The over-the-counter PPIs are
- Prilosec OTC
- Zegerid OTC
- Prevacid 24HR

Advice for Consumers
- Do not stop taking your PPI unless you are told to do so by your health care professional. PPIs are effective in treating a variety of gastrointestinal disorders.
- Be aware that an increased risk of fractures of the hip, wrist, and spine have been reported in some studies of people who use PPIs. The greatest increased risk for these fractures was seen in those who receive high doses of these medications or use them for a year or longer.
- Read and follow the directions on the "Drug Facts" label when considering the use of an over-the-counter PPI.
- Be aware that the over-the-counter PPIs should only be used as directed for 14 days for the treatment of frequent heartburn. If your heartburn continues, talk to your health care professional. No more than three 14-day treatment courses should be used in one year.
- Talk to your health care professional about any concerns you may have about using PPIs.
- Report any side effects from the use of PPIs to FDA's MedWatch Adverse Event Reporting Program either online, by regular mail, by fax, or by phone:
  - Online at www.fda.gov/Safety/MedWatch
  - Regular Mail: Use postage-paid, pre-addressed FDA form 3500 found at www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
  - Fax: 1-800-FDA-0178
  - Phone: 1-800-332-1088

FDA Actions

FDA has reviewed seven published studies, six of which reported an increased risk of fractures of the hip, wrist, and spine with the use of PPIs. Based on the available data, it is not clear at this time if the use of PPIs is the cause of the increased risk of fractures seen in some studies. FDA is working with the manufacturers of PPIs to further study this possible risk.

Most of the studies evaluated individuals 50 years of age or older, and the increased risk of fracture was seen mainly in this age group.

As a precaution, FDA is revising the labels for both the prescription and the over-the-counter PPIs to include new safety information about the possible increased risk of fractures of the hip, wrist, and spine with the use of these medications. FDA

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PPI
best practices

- Use to diagnosis GERD
- Shortest course of therapy
- Lowest possible dose
- Take correctly
- Endoscopy for GERD >5 yrs.
- Close monitoring in chronic use
- Use a deprescribing protocol
  - Consider H2RA on weekends, or rotating PPI and H2RAs

And now!
After 30 years…

Potassium-competitive acid blockers

- "PCAB"
- New class of acid suppressant
  - Registered with WHO 2012
  - Japan approval 2015
  - USA November 2023
- **Inhibit gastric H + K + ATPase with a faster onset of action than PPI.**

Not yet recognized by many insurance companies, and usually highest co-pay tier.

PCAB

- Potassium-competitive acid blockers
- Characteristics distinct from PPIs:
  - Acid stability with dosing independent of food consumption
  - Rapid onset of action
  - Less variability with CYP2C19 polymorphisms
  - Extended half-lives
    - 6.8 hours (Omeprazole 1 hour)
  - Only PO (no IV approved)

Vonoprazan

- Initial US review 2022
  - Approval November 2023
- Decrease in gastric acid secretion 350 times greater than standard PPIs!
  - Too strong?

Indications

- Healing all grades of erosive esophagitis and heartburn associated w EE
- Maintain healing in all grades of EE and heartburn associated with healing EE
- H Pylori
  - Amoxil alone
  - Amoxil + Clarithromycin

Dosing: Erosive esophagitis

- Healing Erosive esophagitis
  - 20mg daily x 8 weeks
- Adults with endoscopically confirmed EE. One group took 20 mg daily, 2-8 weeks during the healing phase.
  - 93% experienced healing by 2 months (compared to 85% on PPI)

Dosing: Maintenance of healed EE

- Maintaining healed EE
  - 10mg daily for 6 months
  - In patients with healed esophagitis (by PCAB or PPI):
    - 10 mg daily for up to 6 months during the maintenance phase. 79% of those stayed healed for 6 months on PCAB maintenance treatment (compared to 72% PPI)

Dosing: H Pylori

- Healing Erosive esophagitis
  - 20mg daily x 8 weeks
- Maintaining healed EE
  - 10mg daily for 6 months
- H Pylori
  - Triple therapy: Vonoprazan 20mg + Amoxil 1000mg + Clarithromycin 500mg one each every 12 hours x 14 days
  - Dual therapy: Amoxil 1000mg 3x a day Vonoprazan 20mg twice a day x 14 days

Most common side effects

- >2%
  - Gastritis
  - Diarrhea
  - Abdominal distension
  - Nausea
  - Hypertension (in maintenance group)

Under research (looks promising)

- Eosinophilic esophagitis
- Peptic ulcer healing
- Secondary prophylaxis.

With the great power of PCABs

Comes great responsibility!

Limit 20mg to 2-8 weeks acute phase

Limit 10mg to 6 months max maintenance phase

Follow all lifestyle changes including diet, probiotics, aloe, and glutamine.

Precautions

- More intense side effects than PPIs?

WARNINGS AND PRECAUTIONS

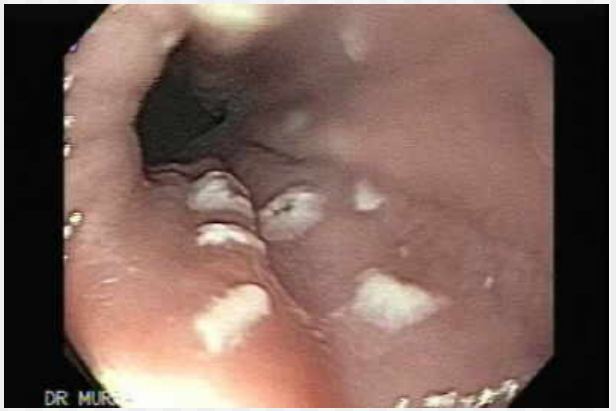
- Gastric Malignancy: Symptomatic response to treatment does not preclude the presence of gastric malignancy; consider additional follow-up and diagnostic testing. (5.1)
- Acute Tubulointerstitial Nephritis: Discontinue treatment and evaluate patients. (5.2)
- *Clostridioides difficile*-Associated Diarrhea (CDAD): May be associated with an increased risk; use the shortest duration of treatment appropriate to the condition. (5.3)

- Bone Fracture, including Osteoporosis-related Fracture: Use the shortest duration of treatment appropriate to the condition. (5.4)
- Severe Cutaneous Adverse Reactions: Discontinue at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation. (5.5)
- Vitamin B12 (Cobalamin) Deficiency: Long-term use may lead to malabsorption or deficiency; consider further workup if clinical symptoms are present. (5.6)
- Hypomagnesemia and Mineral Metabolism: Consider monitoring magnesium levels prior to starting treatment and periodically if prolonged treatment is expected, or if concomitant use of digoxin or other drugs that cause hypomagnesemia. (5.7)
- Interactions with Investigations for Neuroendocrine Tumors: Increased chromogranin A (CgA) levels may interfere with diagnostic investigations; temporarily stop VOQUEZNA at least 14 days before assessing CgA levels. (5.8, 7)
- Fundic Gland Polyps: Risk increases with long-term use; use the shortest duration of treatment appropriate to the condition. (5.9)

Voquenza
Package insert

Differential Diagnosis of GERD Not responding to therapy?

- Infectious esophagitis
  - Candida
  - Herpes
- Pill esophagitis
- Eosinophilic esophagitis
- Non ulcer dyspepsia
- Biliary tract disease
- Cardiac
- Esophageal motility disorder
- Stomach cancer



If the diagnosis of GERD is suspected but not clear, and endoscopy shows no objective evidence of GERD, use manometry & reflux monitoring off therapy to establish the diagnosis

Non-responder? Are they compliant with lifestyle and medication instructions?

Thank you!

- Remember all disease begins in the gut!
- Teach lifestyle changes and reinforce them
  - Use glutamine, aloe and probiotics
- For PCABs and PPIs, use the shortest dose possible
  - Give probiotics when on antibiotics!

@JerrythePA

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