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# 7th EMIRATES FAMILY MEDICINE SOCIETY CONGRESS 2024

DUBAI | UAE | 22 to 24 APRIL

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# Gastrointestinal Update

## GERD, PUD,
## Acute Diarrhea, Pancreatitis

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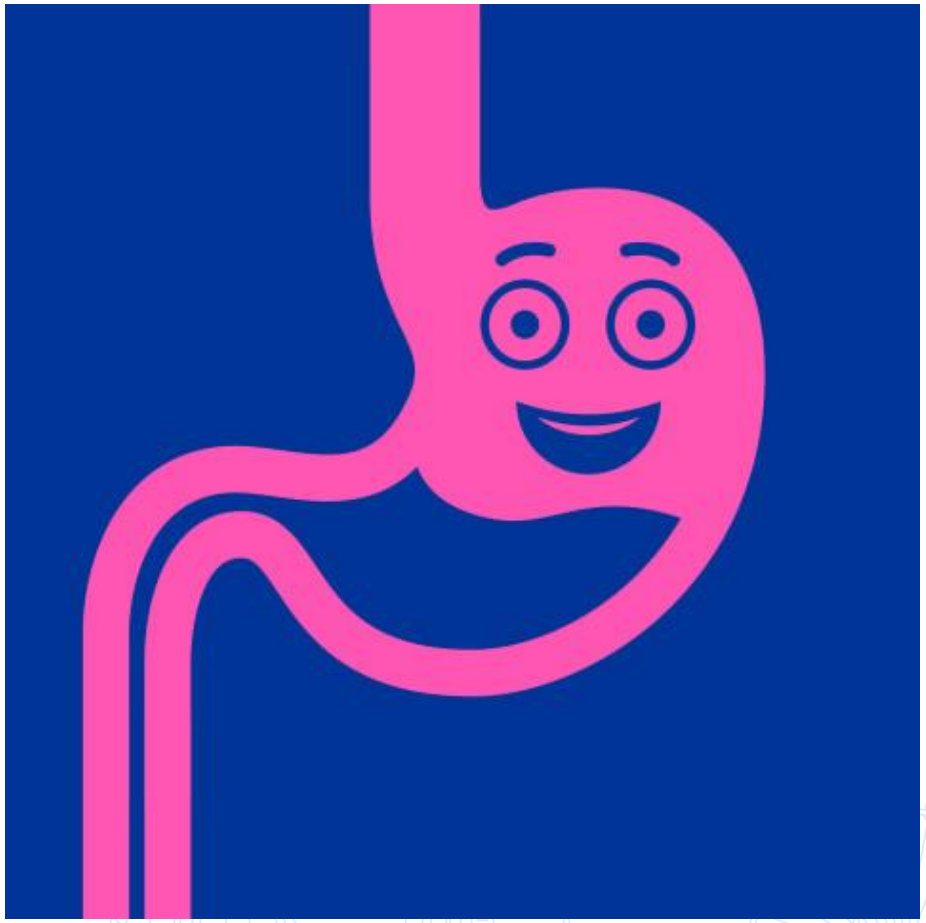
# Learning Objectives

Latest and greatest for

1. GERD
2. PUD
3. Acute Diarrhea
4. Acute Pancreatitis

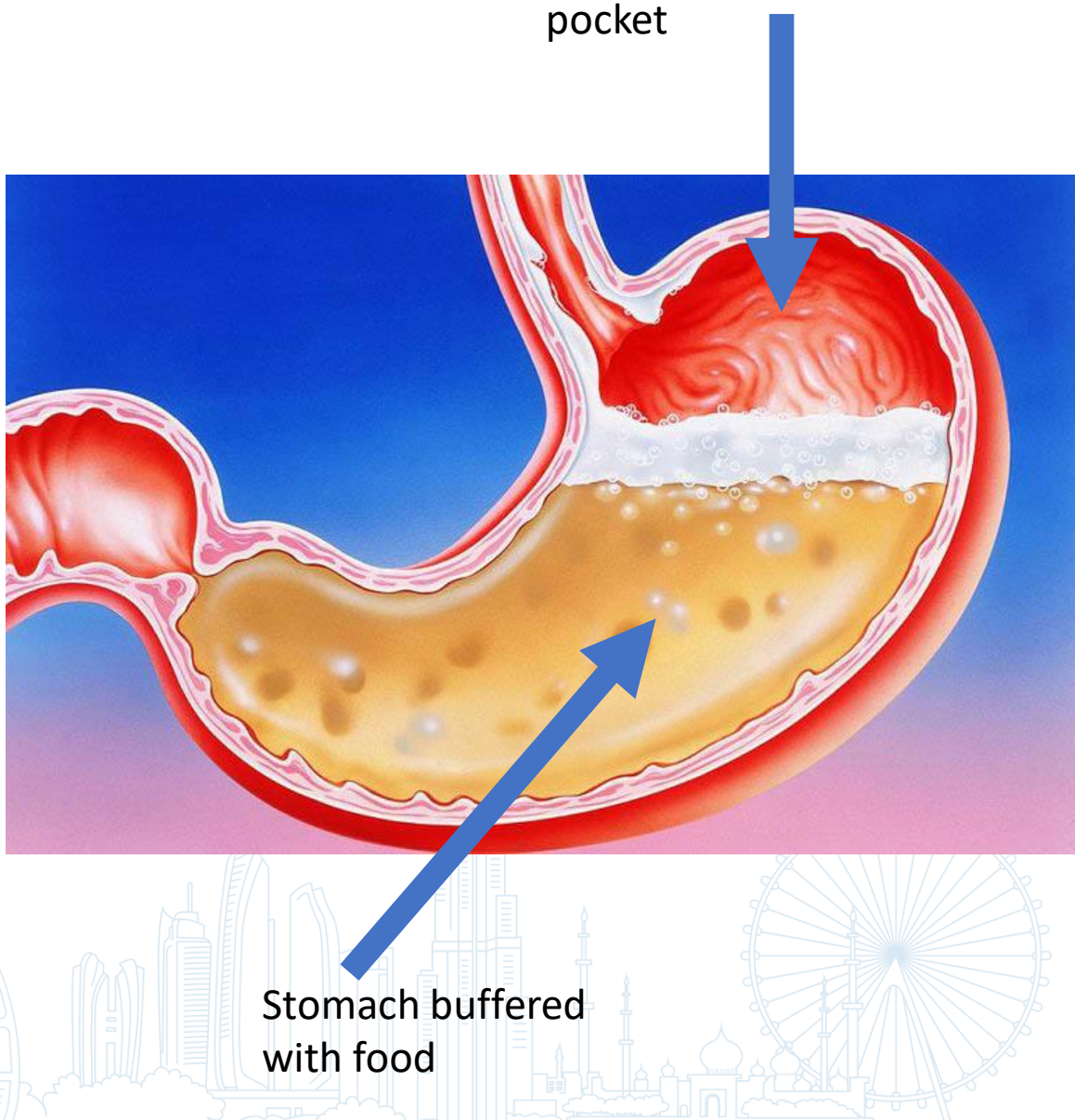
# Pathophysiology

- LES dysfunction
- Increased Intrabdominal Pressure
- Acid pocket-
  - Why is reflux most pronounced after eating?
  - Doesn’t the food buffer?



# Acid Pocket

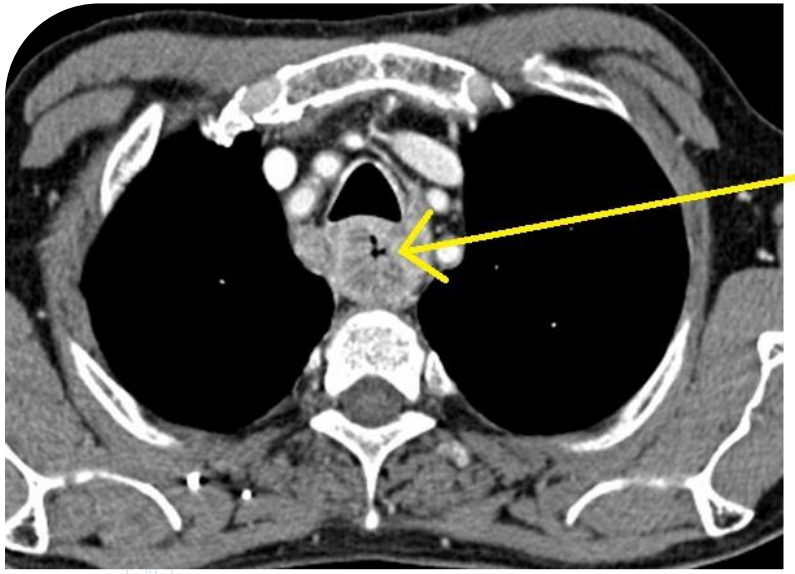
- Acid pocket-
  - Why is reflux most pronounced after eating?
  - Doesn't the food buffer?
    - Proximal stomach high acid sections + poor mixing
    - Regionally lower PH that refluxes into LES
    - Pt with GERD more likely to have measured acid pocket
    - Stomach PH and The PPI



# Barrett's and Esophageal Cancer

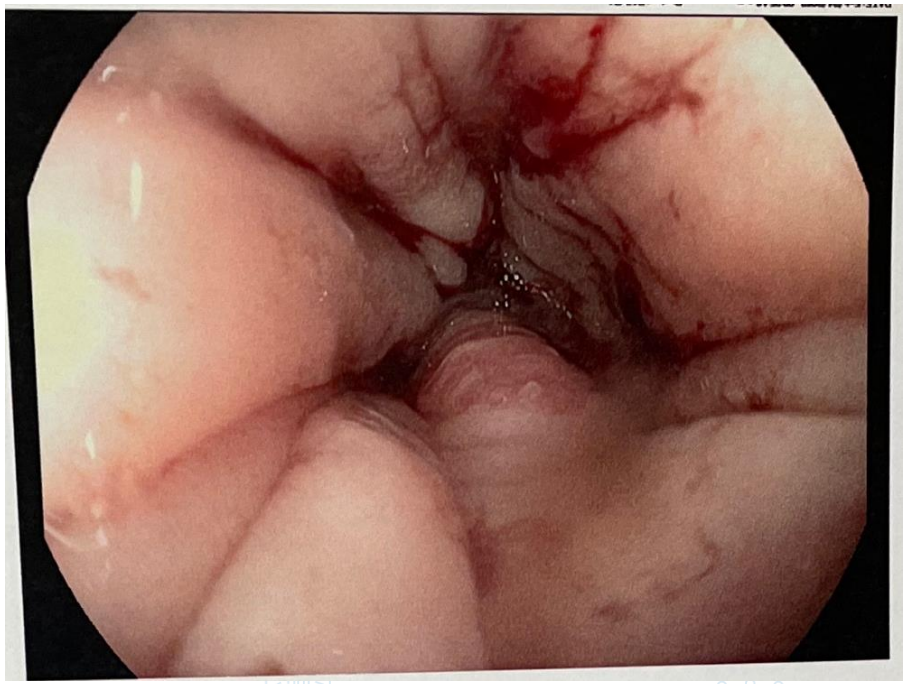
- Cancer
  - SCJ: Cervix vs anal vs esophageal mucosa
  - SCC unchanged in rate for years
  - Adenocarcinoma
    - fastest increasing incidence in western populations
    - >90% made at late stages
    - associated with inflammation and GE junction migration

- Can we screen effectively?
  - GERD 5-10x more likely to have Barrett's. Of those, 0.1-0.3% go on to develop cancer. Or over a 10-year period, 1-3% with Barrett's will progress to esophageal cancer
  - Low rate of progression in a very common cancer makes hard to effectively screen
  - Fhx?, long segment Barrett's?
  - Routine surveillance in those with endoscopic and pathologic changes consistent with dysplasia due to higher rate of cancer



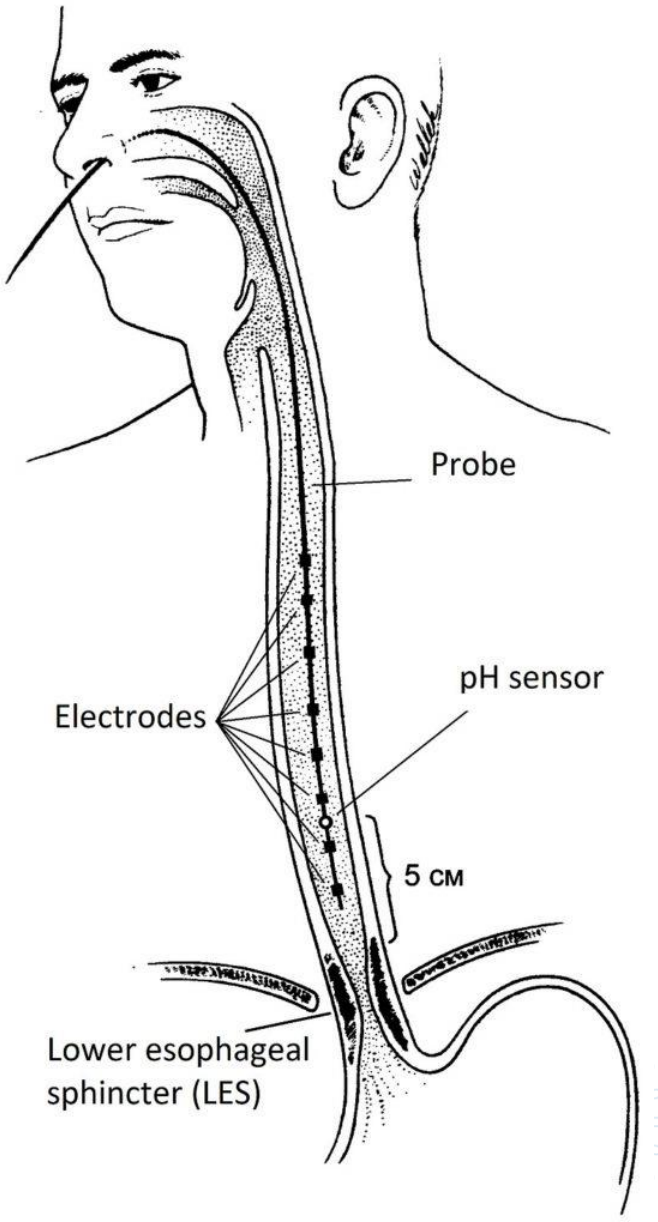
# So, Who Gets An EGD?

- Alarm Symptoms –
  - dysphagia, odynophagia, anemia, bleeding, weight loss
- Atypical symptoms-
  - chest pain, globus sensation, chronic cough, hoarseness, wheezing
- Lack of response to anti-secretory therapy
- Abnormal imaging
- High risk factors for Barrett's
- Allows visual and pathologic exam of tissue
- 80% of Pt with GERD have no endoscopic evidence



# PH/Impedance/Manometry

- Can be used in patients with typical symptoms that don’t respond to typical anti-secretory therapy
  - Measure total time pH below 4
- Impedance test measure liquids, solids, and gas that go past the LES
  - Good for looking at non-acid exposure in esophagus
- Manometry
  - How well is it closing?
  - Often used on surgical staging



# Management

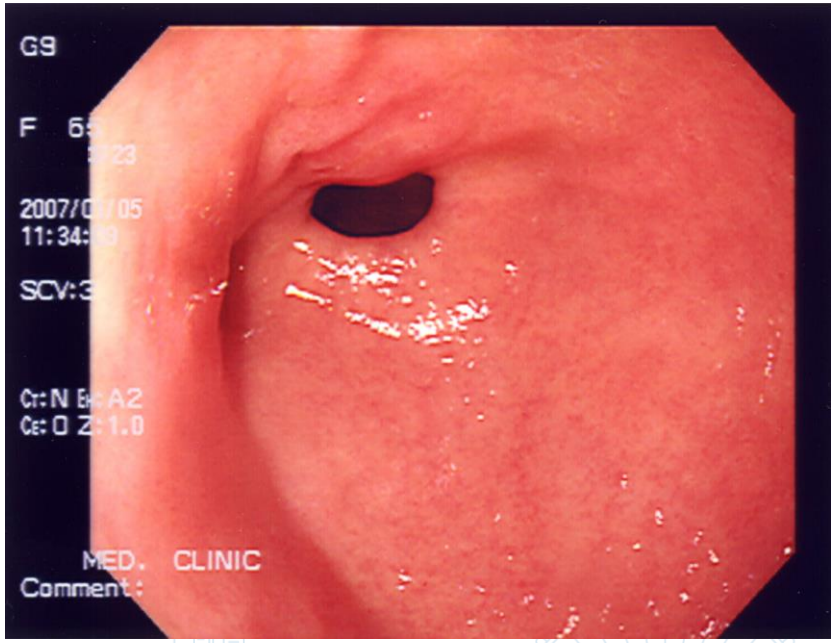
- Acid suppression main stay of treatment
  - PPI
  - H2RA
  - K Competitive blocker?
  - Alginates
  - Antacids
  - Cytoprotectants
  - Prokinetics ?
  - Muscle Relaxants
- 50% of patients don’t symptomatically respond to acid suppression
  - AGA 2022 update suggests EGD and/or pH, Imp testing if no response to antisecretory therapy

# Lifestyle

- Weight loss consistently shows benefit
- Quitting tobacco OR 5.67 of improved symptoms
- Head of the bed elevation came from a study of 15 patients- reduced esophageal pH time <4 from 21%-15%

# AGA 2022 Guideline

- Typical symptoms (heartburn, regurgitation, non-cardiac chest pain) without alarm
  - How long should I treat?
    - 4-8 weeks without alarm symptoms should be tried on single-dose PPI
  - No improvement?
    - Increase dose to BID
  - No improvement?
    - Switch agents (HSRA)
  - Still no improvement, acid probably isn't your problem.
  - Patient improves
    - PPI tapered to lowest effective dose.
- Personalization of pharmacotherapy should be based on GERD phenotype
  - Alginate antacids for breakthrough symptoms
  - Nighttime H2 receptor antagonist for nocturnal symptoms
  - Baclofen for regurgitation or belch predominant symptoms
  - Prokinetics for coexistent gastroparesis



# PPI- Is Chronic Use Ever OK?

- AGA guidelines
  - Erosive Esophagitis
  - Barrett's Esophagus
  - Chronic NSAIDS
  - Persistent symptoms control
- After 12 months on PPI's is there another cause we can reverse?
  - "In patients on PPIs for >12 months in unproven GERD, reevaluation of dosing should be done, and consideration of endoscopy or wireless reflex monitor off PPI therapy to confirm diagnosis."

# What About the PPI Side Effects?

- Associated vs Caused
- Superior to so many other antisecretory meds
  - Esophagitis (80% vs 49% H2RA)
  - Esophageal stricture (46% vs 30%)
- What have the RCT's shown
  - Cardiac disease n= 18k no difference
  - Pneumonia 2,500= no effect
  - AsPECT- large RCT showed no difference in all-cause mortality
- Guidelines recommend not treating to presumed possible effects

# PPI- How They Work
# To Understand When They Don't Work

- How important is the fasting to prodrug activation?
- BID?
- Is your diagnosis correct?
  - If acid isn't your problem, then acid suppression is not going to be your solution

# PPI Reduction Strategies

- PPI ingested
  - Decreased acid
  - Increase gastrin
  - Hypertrophy enterochromaffin
  - PPI stops = dramatic acid increase
- On Demand vs placebo
  - 83% vs 56% Placebo symptom control at 6 months
- 50% reduction in dose/week to lowest tolerated dose
  - 6 months 44% decreased or discontinued
- 79% able to reduce dose with concomitate used of H2 blocker

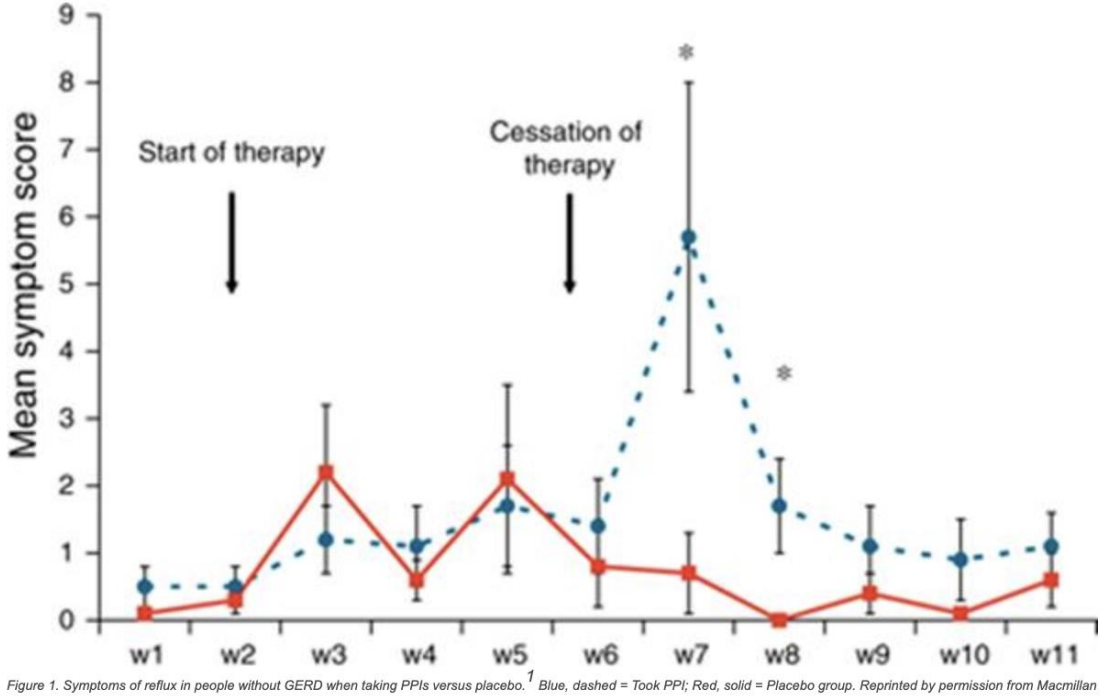



*Figure 1. Symptoms of reflux in people without GERD when taking PPIs versus placebo.*[1] *Blue, dashed = Took PPI; Red, solid = Placebo group. Reprinted by permission from Macmillan Publishers LTD: American Journal of Gastroenterology, copyright 2010.*

# New Kid on the Block Approved Nov 1, 2023!!!

- Vonoprazan –
  - Potassium competitive acid blocker
  - Able to keep more even acid suppression
  - Wider pH activation of prodrug so able to keep more even acid suppression
- 10-year track record in Japan, Korea, and Russia
- Superiority to PPI in healing
- Severe esophagitis (97% vs 93%)
- Peptic Ulcer Treatment (95% vs 78%)
- H. pylori eradication (95.8% vs 69.6%)
- Gastric and duodenal ulcer therapy (92% vs 75.9%)
- Less side effects then PPI (32% vs 40% most SE GI related, nausea and diarrhea)

# Management in Pregnancy

- Antacids- RCTs NNT-3.7
- Antacid + H2 vs antacid= No superiority
- Mag OH, Al OH superior to placebo
- No PPI RCT but cohort with 2.3 million showed no difference in safety
  - All are category B except omeprazole category C (harm in animals)

# Infants

- 50% are happy spitters
  - 90% resolved by 12 months
- Treatment not needed unless alarm features
  - FTT, irritability, feeding difficulties, sleeping difficulties, prolonged crying, anemia, bile or blood in the emesis, choking or coughing with feeding
- Reassurance
- 1st Interventions
  - Hypoallergenic formula or removed dairy products from Mom's diet
- PPI recommend in some guidelines but RCT's failed to show improvement of symptoms in studies

# Adolescents

- They’re just baby adults!
- Short trial of PPI to start
  - 2-4 weeks
- Lifestyle
  - Avoidance of caffeine, chocolate, abstinence for alcohol and tobacco
- Wean after 12 weeks

# Surgery

- Best patients
  - Responded well to PPI
  - Known hiatal hernia
  - Erosive esophagitis
  - Can’t wean from acid suppression
  - Barrett's esophagus
  - Poor PPI response means probably not an acid problem so stopping is not a good solution
- Laparoscopic
  - 5-year outcomes with laparoscopic fundoplication, in which
    - 29% of patients still use daily PPIs
    - 41% have persistent heartburn
    - 24.5% have other reflux symptoms, plus a higher side effect rate of 14-23%.[70]
- Endoscopic (TIF)
  - Short-term 99% success 2% reporting adverse events.
  - 5-10 years 74%-86% Patients satisfied with procedures
  - 75% of PPI
- No guarantee of long-term effectiveness
  - One Danish study n=3456 >50% patient back on PPI at 10 years]
  - The 5-year PPI cessation rate for magnetic sphincter augmentation is 85%, and 6-12 year data indicates a 79% cessation rate

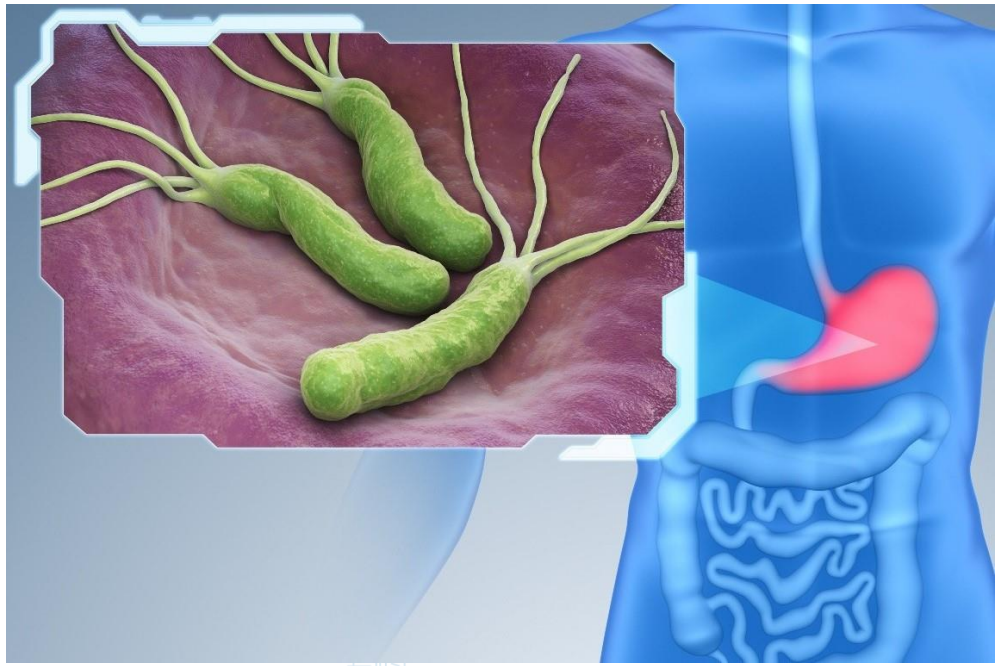
# Peptic Ulcer Disease

# Case Rate

- Greater than 50% decrease in the last 20 years!!!
- PPI's, effective H. pylori treatment, more judicial NSAID use
- Seen in low and high socioeconomic countries, so may not be just access to meds

# Cause

- H. pylori
  - Urease creates an alkaline environment, allowing bacteria to live in mucosal barrier
  - Inflammatory cascade creates ulcer, wide variety of inflammatory protein expression creates wide variety of symptoms in patients
- NSAID
  - Cycloxygenase-1 limited by NSAID
  - Decreased mucosal production
  - Decrease bicarbonate secretion
  - Reduced cell proliferation
  - Decreased blood flow to mucosa



| Test | Sen/ Spec | When to consider |
|---|---|---|
| **Noninvasive tests** | | |
| Urease Breath Test | 95.9%/95.7%<br>Can be affected by PPI within 2 weeks, antibiotics within 4 weeks, any active bleeding can decrease specificity | Good test for pretreatment diagnosis and post treatment test of cure.<br>May be less accurate in a pediatric population. |
| Fecal Antigen | 94% / 97%<br>Stool sample needs to be refrigerated<br>Decrease accuracy with PPI, antibiotics, bismuth, bleeding, and N-acetylcysteine treatments | Good test to diagnose initial infection.<br>If using to test for cure, should wait 3 months before repeat testing.<br>Good test to use in children. |
| Serum antigen | 74-84% / 79=90%<br>High negative predictive value | IgG only reliable test measure of IgG, IgM, and IgA<br>Less affected by patients on or unable to stop antibiotics, PPIs, or bismuth, active gastric bleeding or carcinoma, MALT lymphoma, or atrophic gastritis.<br>Inexpensive, Good Negative predictive value.<br>Unable to use as a test of cure since IgG antibodies will likely stay positive for a prolonged period after eradication. |
| **Invasive/ Endoscopic Testing** | | |
| Rapid Urease Test | >90%/ >90%<br>Results usually available in a few hours<br>PPI, bismuth, antibiotics may cause false negative results | Biopsies placed in urea-containing solution and pH indicator.<br>Best results if biopsies taken from gastric antrum and corpus.<br>Bacteria from mouth and stomach can cause false positive (*K. pneumoniae, S. aureus, P. mirabilis, E. cloacae, C. freundii)* |
| Mucosal Pathology Biopsy | 80-95% / 99-100% based on number of biopsies and location of biopsies | Considered the gold standard for diagnosis. |
| Culture | 65% | Not routinely done. Need specialized conditions to allow growth, used to help guide management in failed treatment |
| PCR | >95% >95% | Accurate in patients with gastric bleeding<br>Expensive, Used in research settings, not routinely in clinical practice. |
| | | |

# Find and Treat-
# Don’t Look In Asymptomatic Individuals

- Find and treat- no specific 1st line
- Retest for cure after 6 weeks (breath test, vs endoscopy)
- Long term NSAIDS should combine PPI with use
- Failed treatments
  - Should we go to vonoprazan treatment?

- Why should effective acid suppression be the key to kill a bacteria that thrives in acid?

# Lifestyle

- Stop
  - Alcohol
  - Tobacco
- Sleep apnea doubles risk of developing

# Integrative

- Probiotics
  - May help reduce side effects of eradication therapies
- H. pylori vaccination?
  - One Chinese study showed 71.8% effectiveness at 3 years

| Name of Therapy | Drugs | Length of Therapy/Notes |
|---|---|---|
| Triple therapy | PPI standard or high dose q12hr, Amoxicillin 1000mg q12hr, Clarithromycin 500 q12hr | 14 days, FDA approved. 1st line therapy |
| Triple therapy #2 | PPI high dose q12hr, Amoxicillin 1000mg q12hr, Metronidazole 500 mg q12hr | |
| Triple therapy #3 | PPI high dose q12hr, Clarithromycin 500mg q12hr, Metronidazole 500 mg q12hr | |
| Vonoprazan Triple therapy | Vonoprazan 20 mg po bid, Amoxicillin 1000mg po bid, Clarithromycin 500 mg po bid | 14 days |
| Sequential Quadruple Therapy | PPI standard dose q12hr days 1-10, Amoxicillin 1000mg q12hr days 1-5, Clarithromycin 500mg q12hr Day 6-10 +metronidazole 500 mg q12hr or tinidazole 500 mg q 2hr days 6-10 or Nitroimidazole 500 mg BID | 10-14 days<br>1st line therapy |
| Quadruple Therapy #1 | PPI standard dose q12hr, Amoxicillin 1000mg q12hr, Clarithromycin 500mg q12hr Metronidazole 500 mg q12hr | 14 days |
| Quadruple Therapy #2 | PPI standard dose q12hr, 120 mg bismuth subcitrate or bismuth subsalicylate 300mg q6hr, Tetracycline 500mg q6hr, Metronidazole 500 mg q12hr | 10-14 days<br>1st line therapy |
| Fluroquinolone Therapy | PPI standard dose Q12hr, Amoxicillin 1000mg q12hr, Levofloxin 500mg q24hr +/-Bismuth 240 mg q12hr | 10-14 days |
| Fluroquinolone Sequential Therapy | PPI standard dose or double dose q12hr + Amoxicillin 1000mg q12hr x for the 1st 5-7 days then<br>PPI standard dose q12hr or double dose + Amoxicillin 1000mg q12hr x Levofloxin 500mg q24hr + Nitroimidazole (500mg) BID for the second 5-7 days | 10-14 days<br>1st line therapy |
| Fluroquinolone LOAD Therapy | PPI double dose q12hr, Amoxicillin 1000mg q12hr, Levofloxin 250 mg q24hr, Nitroimidazole (500mg) BID, Doxycycline 100 mg QD | 7-10 days<br>1st line therapy |
| Triple Therapy- Rifabutin | PPI standard dose q12hr, Amoxicillin 1000mg q12hr, Rifabutin 150 mg q12hr | |

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# G6PD deficiency

11.4% of males and 11.9% of females have G6PD deficiency in UAE

1. **Nitroimidazoles:** Medications such as metronidazole and tinidazole, which are commonly used in H. pylori treatment regimens, can trigger hemolysis in individuals with G6PD deficiency. It's important to note that metronidazole is often part of the standard treatment for H. pylori, so alternatives may need to be considered.
2. **Sulfonamides:** Sulfamethoxazole, which is sometimes used in combination with trimethoprim (e.g., Bactrim, Septra), is another class of medications that may trigger hemolysis in G6PD-deficient individuals.
3. **Quinolones:** Ciprofloxacin, levofloxacin, and other fluoroquinolone antibiotics have been associated with hemolysis in individuals with G6PD deficiency.

Regiments safe

1. **Clarithromycin:** This macrolide antibiotic is commonly used in H. pylori treatment regimens and is generally considered safe for individuals with G6PD deficiency.
2. **Amoxicillin:** A penicillin antibiotic, amoxicillin is often included in H. pylori treatment and is generally safe for individuals with G6PD deficiency.

# Acute Diarrhea

# Post Infection Complications

- 9% of patients with infections will go onto develop IBS from it
- This accounts for 50% of current cases
- Increase diarrhea predominance by 5% and pain rates by 38%

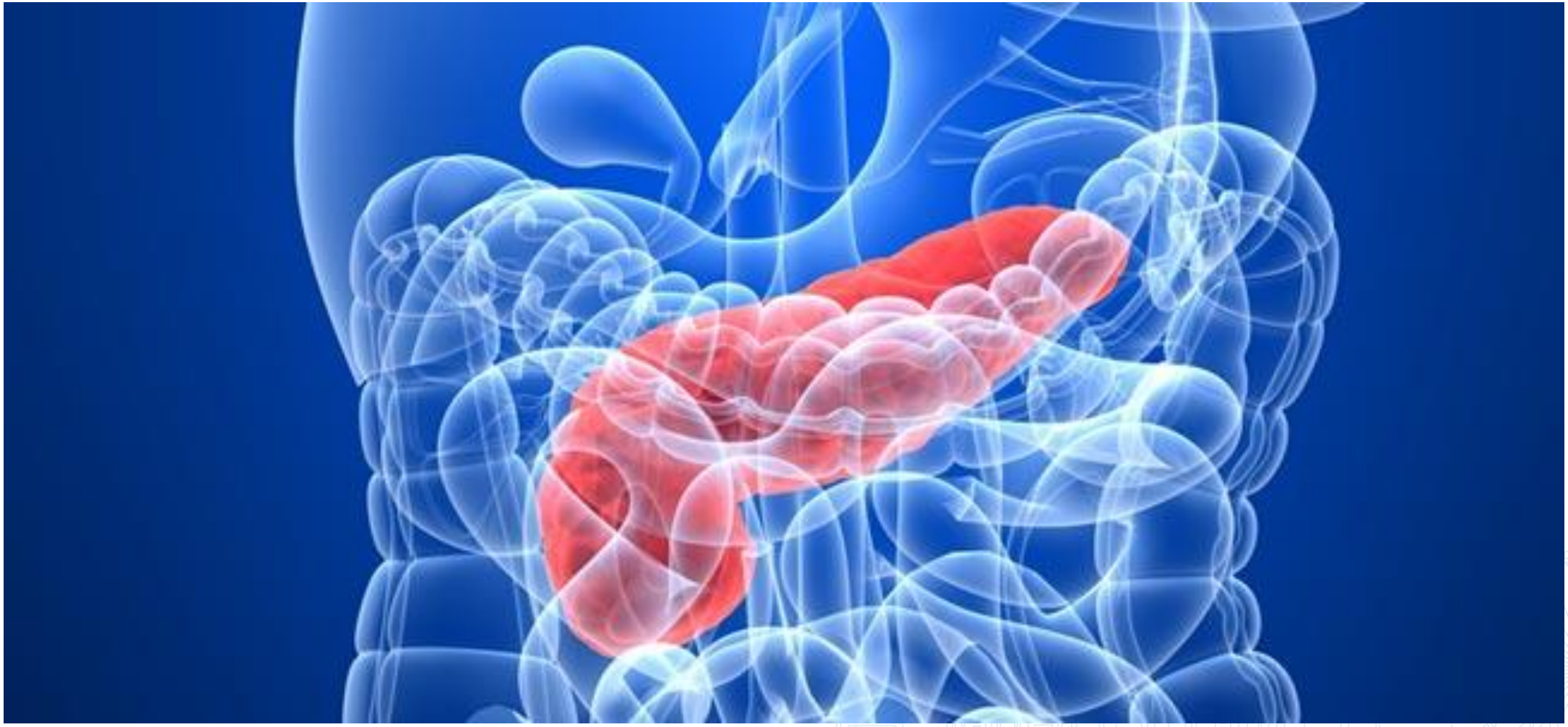
# Has Your Lab Changed Testing?

- Culture/Ova and parasites are out
- PCR nucleic acid amplification test/ toxin multi bug tests are in
- Speed to diagnosis, sensitivity and specificity improved (1-2 hours sn 75-85%, sp 95-100%)
- Increased number of bugs found that may not have pathologic problems
- No need to test of cure in patients with improvement of symptoms
  - (high false negatives due to residual proteins left)
- Fecal Leukocytes, calprotectin are not useful in an acute diarrhea setting

# Treatment

- No diet is superior
- Oral rehydration for mild to moderated, IV for severe
- Antibiotics for traveler's diarrhea.
  - Azithromycin, ciprofloxacin, Levofloxin, ofloxacin, rifaximin
  - Most have 1-day vs 3-day dosing
- C. diff
  - Fidaxomicin 1st line, 2nd vancomycin, 3rd metronidazole
- Fecal Transplants for abx resistant conditions
  - National registry shows 96% effectiveness with enema and capsule group

# Pancreatitis



# Acute Pancreatitis

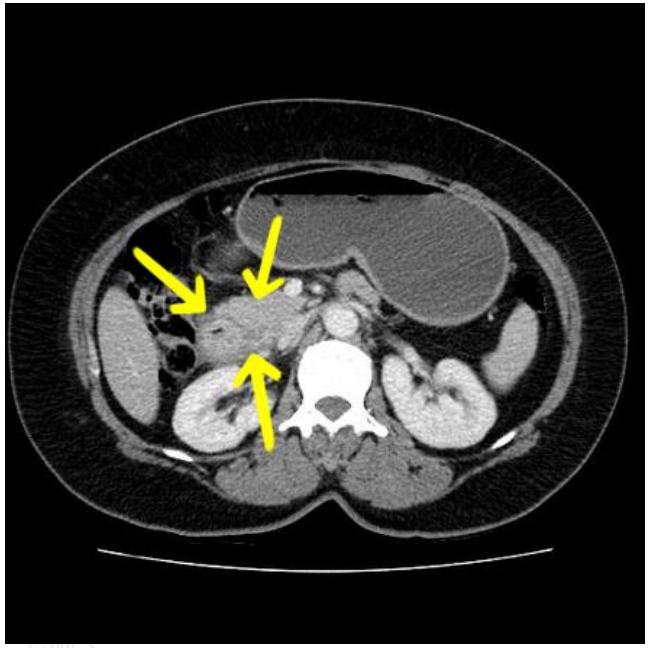
- Management
  - Fluid resuscitation
  - Pain management
  - Nutrition
- Chronic pancreatitis
- Pancreatic insufficiency
- Prevention
- Surgery

# Fluid Resuscitation

- Lactated Ringer is superior to Normal Saline
- 2018 meta-analysis, n=428,
  - Significant decreased odds of developing SIRS
    - OR 0.38 95% CI, 0.15-0.9 at 24 hours
  - Nonsignificant trend towards decreased mortality
    - OR=0.61; 95% CI 0.28-1.29.

# Moderate vs Aggressive Fluid Hydration

- RCT, N= 249
  - Moderate 10ml/kg of LR bolus in hypovolemic + no bolus without hypovolemia + 1.5ml/kg/hr
  - Aggressive 20 ml/kg in hypovolemia, No hypovolemia 3 ml/kg/hr
    - 20.5% vs 6.3% of aggressively hydrated patients developed fluid overload
    - 6 vs 5 days mean hospitalization (NNH 7)
- RCT, n= 76, China
  - Severe pancreatitis mod (5-10 ml/kg/hr) vs agg (10-15ml/kg/hr)
- Moderate =
  - less fluid sequestration (4215 ml vs 5378ml)
  - lower rate of mechanical ventilation (65% vs 94.4%)
  - lower abdominal compartment syndrome (32% vs 72%)
  - sepsis (37% vs 64)
  - lower mortality rate (69.4 vs 90%)



# Pain

- No specific pain management is superior in most pancreatitis

- What's on the horizon
  - Epidural anesthesia in severe pancreatitis?
    - Retrospective cohort (n=1003)
    - Reduced 30-day mortality (2% versus 17%) in those who received epidural vs parental opioids for pain management in the ICU

# To Eat or Not To Eat, That Is the Question

- Eating is the new NPO for pancreatitis!
  - Guidelines suggest starting feeds in the 1st 24 hours, if unable to tolerate starting even in severe or necrotizing pancreatitis.

- Metanalysis of 9 RCTs, n=500,
  - Total enteral nutrition vs total parental nutrition has a lower mortality rate
    - (OR 0.31 95%CI 0.18-0.54).
  - Shorter hospital stay
  - Lower risk of infection
  - Organ failure
  - Surgical intervention

- Meta-analysis, 10 RCT's n=1051 of early vs late enteral feeding (<48hrs vs >48hrs)
  - Decreased mortality (OR 0.53 95% CI 0.35 to 0.81)
  - Reduced multi-organ failure
  - Operative intervention
  - Systemic infection and septic complications

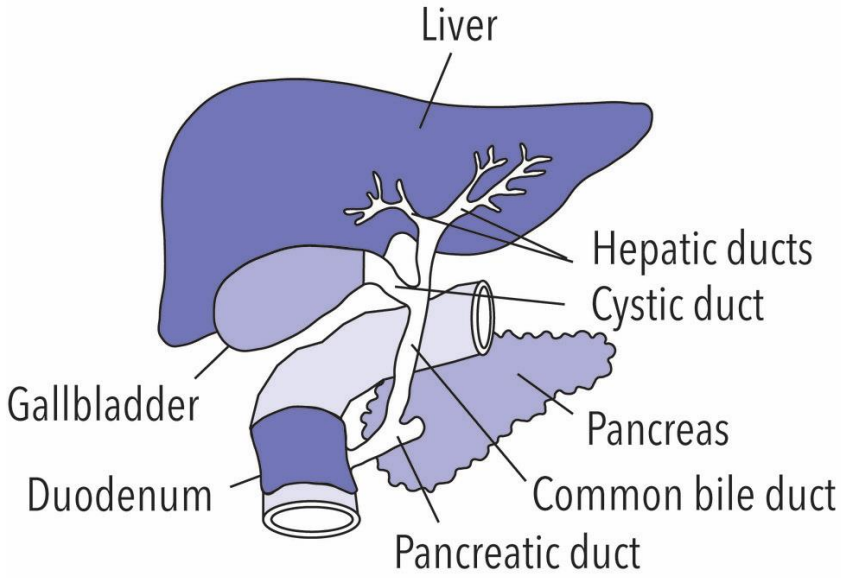
# “Biotics”

- Antibiotics?
  - No longer for pancreatitis, pancreatic necrosis unless image proven to be infectious pancreatitis

- Probiotics-
  - RCT n=298
  - Severe pancreatitis- probiotics increased complications
    - Bowel ischemia (9% vs 0% NNH=11)
    - Mortality (16% vs 6%, NNH=10)

# Surgery

- If pancreatitis is secondary to biliary pancreatitis, consider a surgical consult for cholecystectomy.
- Most mortality in recurrent pancreatitis comes from patients with biliary pancreatitis.
- If the cholecystectomy on the same admission mortality is lowered (5% vs 17%)
- If necrotizing pancreatitis, wait to remove gallbladder until resolved.
- Obstructive pancreatitis with cholangitis should be considered for ERCP with sphincterotomy to decompress.



# Practice Recommendations

GERD- Long-term PPIs for confirmed GERD, for patients taking long-term NSAIDS, erosive and Barrett's esophagitis
Take your PPI's correctly
Taper as able

PUD -H. pylori Test and treat, then retest 6 weeks later

Diarrhea- NAAT testing in pts with alarm symptoms

Pancreatitis- Oral feeding early

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