



**Brigham and Women's Hospital**  
Founding Member, Mass General Brigham

# Peptic Ulcer Disease

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# Molly Perencevich, MD



- Harvard Medical School
- Internal medicine residency @ Brigham and Women's Hospital (chief resident)
- GI fellowship @ Brigham and Women's Hospital
- Associate Physician @ BWH
- Assistant professor @ Harvard Medical School
- Clinical focus: general GI, *H. pylori*, celiac
- Program Director for fellowship in gastroenterology, hepatology & endoscopy
- Research focus: education, QI, CRC screening



# Disclosures

I have no disclosures to report

I will discuss the use of medications for non-FDA approved indications



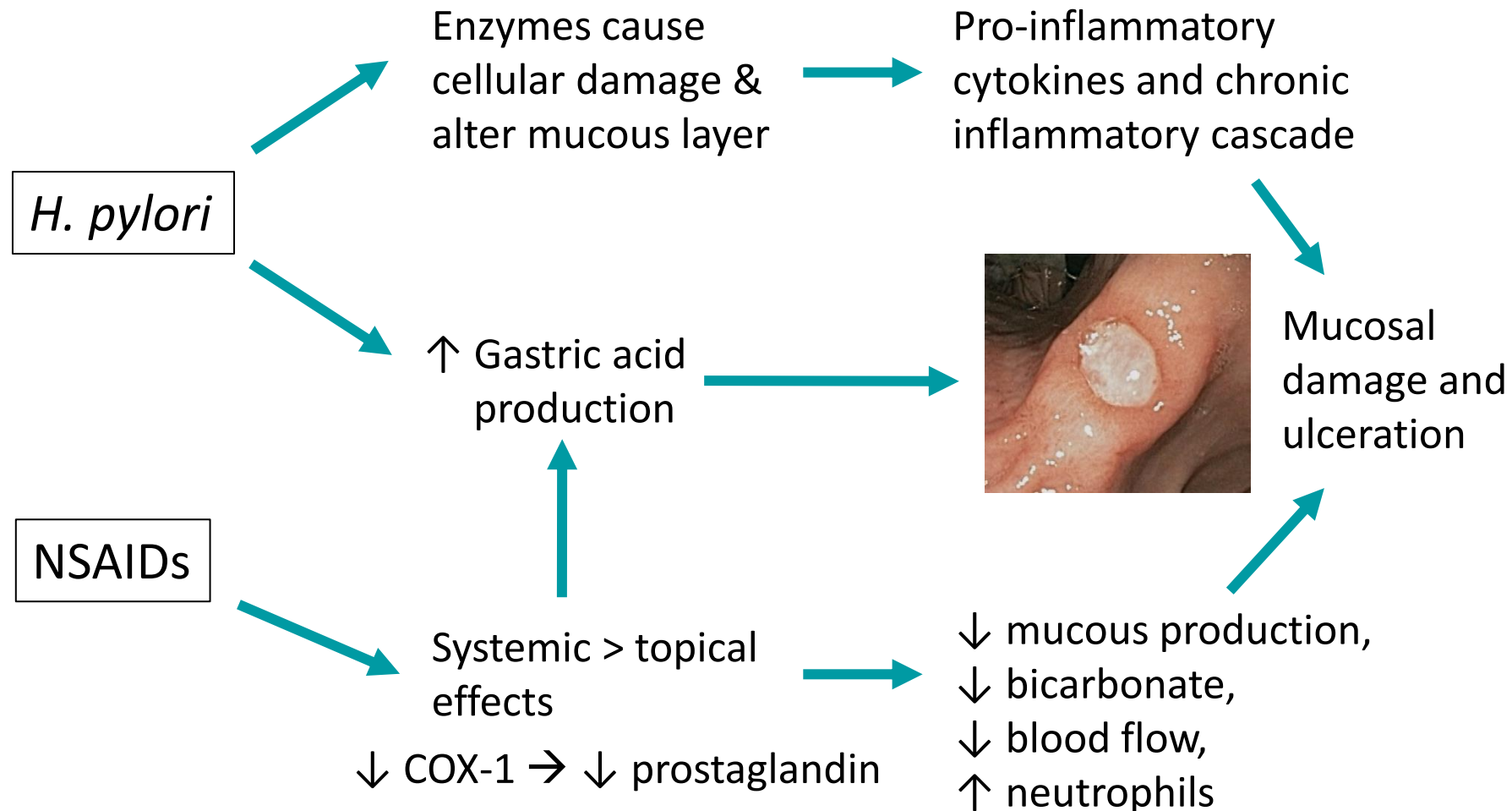
# Objectives

- Recognize the causes of peptic ulcer disease (PUD)
- Review the patient presentation of uncomplicated and complicated PUD
- Discuss the diagnoses and treatment of PUD, including medical and endoscopic management
- Explain current treatment recommendations for testing and treatment of *H. pylori* infection in the context of PUD



# Risk Factors for PUD

90% due to *Helicobacter pylori* and/or NSAIDs



# Risk Factors for NSAID-Induced PUD

- Older age
- Prior history of PUD
- Smoking – proportional to amount smoked
- Medications in combination with NSAIDs
  - Corticosteroids, anticoagulants, anti-platelets, SSRIs, bisphosphonates
- Systemic diseases – COPD, cirrhosis, mastocytosis, uremia



# *H. Pylori* and PUD

<i>H. pylori</i> gastritis location	Gastrin	Acid	Atrophy	Ulcer location	Gastric cancer risk
Antrum	↑	↑	Little/no	Duodenum	Low
Corpus/body	↑	↓	↑	Gastric	High

*H. pylori* testing for all PUD

- Ideally 2 negative tests
- Bleeding and PPI therapy may limit test sensitivity (more coming on this)

Treatment of *H. pylori* helps heal ulcers and prevents recurrent ulcers



# Other Causes of Upper GI Ulcers

- Malignancy (gastric > duodenal ulcers)
- Gastrinoma (Zollinger-Ellison syndrome)
- Infiltrative: Crohn disease, mastocytosis, sarcoid
- Viral infections: CMV, HSV
- Vascular: vasculitis, cocaine
- Roux-en-Y gastric bypass (marginal ulcer)
- Radiation therapy
- Stress ulcers (ICU)





# Gastrinoma (Zollinger-Ellison Syndrome)

- Neuroendocrine tumor (duodenum, pancreas)
- Hypergastrinemia → ↑ acid secretion
- PUD (duodenum, jejunum), diarrhea, GERD
  - Usually sporadic
- MEN1 syndrome in 25% of cases
- Diagnosis – gastrin level, cross-sectional imaging
  - Ddx hypergastrinemia – hypochlorhydria from PPI or atrophic gastritis



# PUD Patient Presentation

## Uncomplicated – dyspepsia, asymptomatic

- Gastric – worse with food – patients eat less, lose weight
- Duodenal – better with food, worse 2-3 hrs later – patients eat more, gain weight

## Complicated

- Bleeding (10-15% of patients)
  - Overt – coffee-ground emesis, hematemesis, melena, hematochezia
  - Occult – heme + stool, Fe deficiency
- Perforation – peritonitis, shock
- Penetration – depends on the associated site
  - Pancreas, duodenum (gastroduodenal fistula), vascular structures



- Obstruction – N/V, early satiety

# Diagnosis

## Endoscopy

- Most sensitive
- Biopsy ulcer – if malignant features and to potentially avoid f/u EGD (gastric > duodenal)
- Biopsy gastric mucosa – for *H. pylori* or other predisposing conditions



## Imaging

- CT if concern for perforation, penetration, or obstruction
- UGIS/barium studies less frequently performed



# Endoscopic Classification & Treatment

## PUD Classification

- a) Active bleeding
- b) Non-bleeding visible vessel
- c) Non-bleeding adherent clot
- d) Oozing
- e) Flat spot
- f) Clean base

## Ulcer Treatment

Combo therapy (epi + clip or coag)  
Clips or coag (both if high risk)  
Epi → remove clot → clips or coag  
Clips or coag  
No endoscopic therapy  
No endoscopic therapy

## PPI Treatment

IV high-dose PPI x 72 hours → PO high-dose PPI BID x2 weeks → standard dose PPI daily (total of 8-12 weeks)

PO standard dose PPI daily (8-12 weeks)  
(more if on PPI before)



# Endoscopic Classification & Treatment

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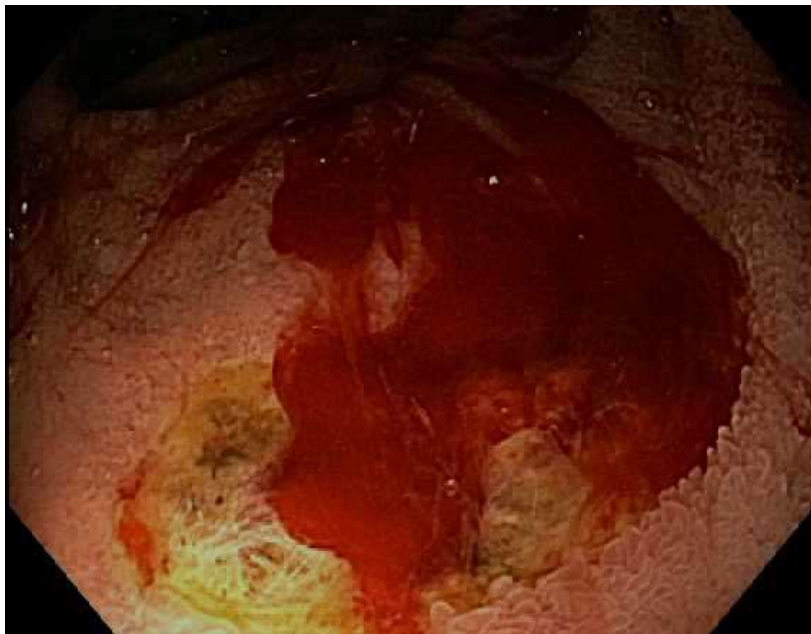
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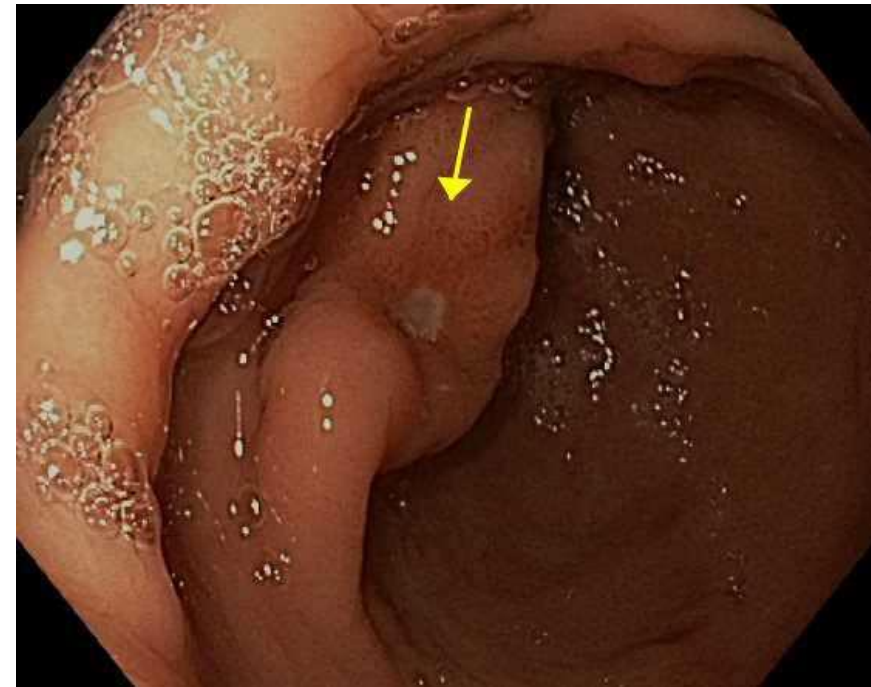
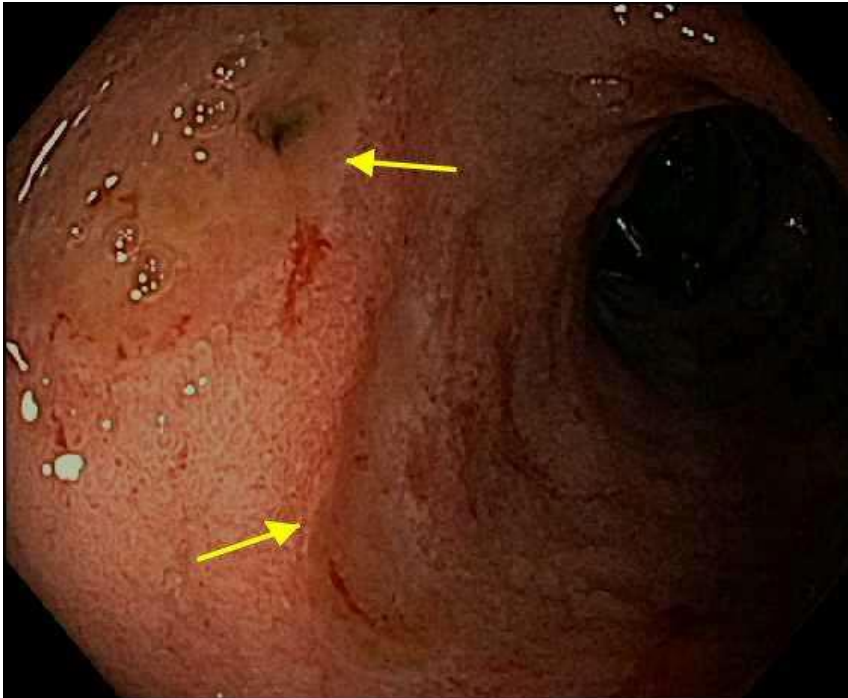
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# *H. pylori* – Noninvasive Tests

Test	Infection	Sensitivity	Specificity	Overview
Blood serology (IgG)	Past & active <i>H. pylori</i>	90-100%	75-95%	<p>False negatives: esp. in elderly, cirrhosis Not affected by antibiotics/bismuth/H2B/PPI</p> <p>False positives: PPV 50% in much of the US (prevalence &lt;20%) → treating some unnecessarily</p> <p>Can't use to test for eradication Easy, cheap Use limited given lower specificity</p>
Urea breath test	Active Helicobacter	88-95%	95-100%	<p>False negatives: antibiotics/bismuth (off for 4 weeks), PPI (off for 2 weeks), ? H2B (off for 48 hours), ? active GI bleeding</p> <p>Can use to test for eradication May not be easily available</p>
Stool antigen	Active <i>H. pylori</i>	91-94%	97%	<p>False negatives: antibiotics/bismuth (off for 4 weeks), PPI (off for 2 weeks), ? H2B (off for 48 hours)</p> <p>False positive: active GI bleeding ?</p> <p>Can use to test for eradication Requires stool sample</p>

# *H. pylori* – Endoscopic Tests

Test	Infection	Sensitivity	Specificity	Overview
Biopsy urease test	Active  Helicobacter	90-95%	95-100%	False negatives: same as urea breath test
Histology +/- immunostain	Active  <i>H. pylori</i>	95-100%	95-100%	<p>Most sensitive &amp; specific (considered gold standard)</p> <p>↓ sensitivity with antibiotics/bismuth and PPI/H2B, ? active GI bleeding</p> <p>Can test for eradication (if endoscopy indicated)</p>

- Ideally 2 negative *H. pylori* tests in PUD
  - Gastric biopsy may be most sensitivity and specific
  - PPI may decrease sensitivity of stool Ag/breath test
  - GI bleeding may cause false positive stool Ag



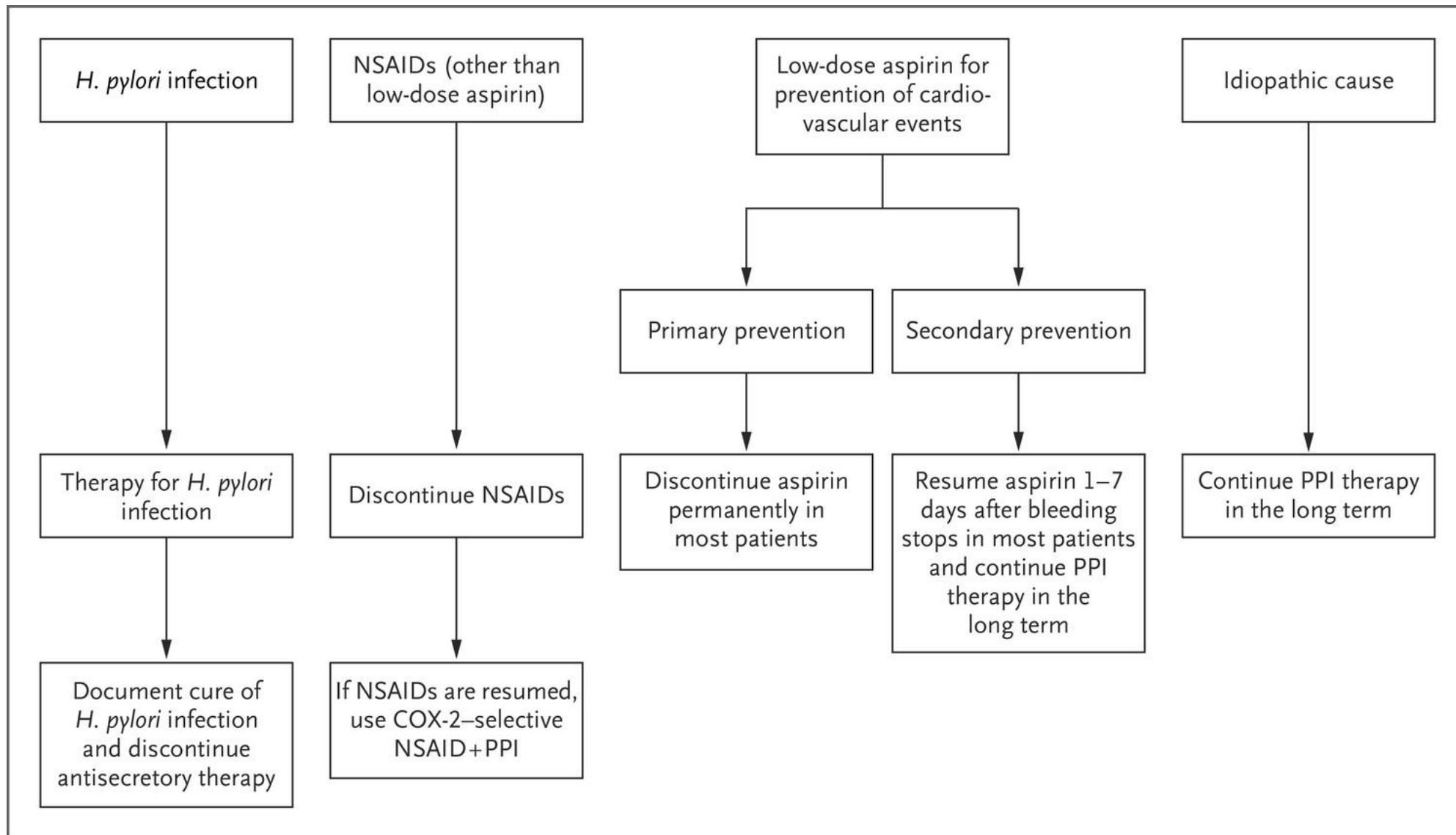


# Medical Treatment of PUD

- PPI > H2B
- Dose
  - Standard dose (ex. omeprazole 20-40mg daily)
  - Higher dose if patient previously on PPI or needs to stay on precipitating medications
- Duration – gastric ulcer 8 weeks, duodenal ulcer 4 weeks
  - Longer if can't remove precipitating factor or idiopathic
- Avoid NSAIDs/ASA (if possible)



# Long-Term Management of PUD



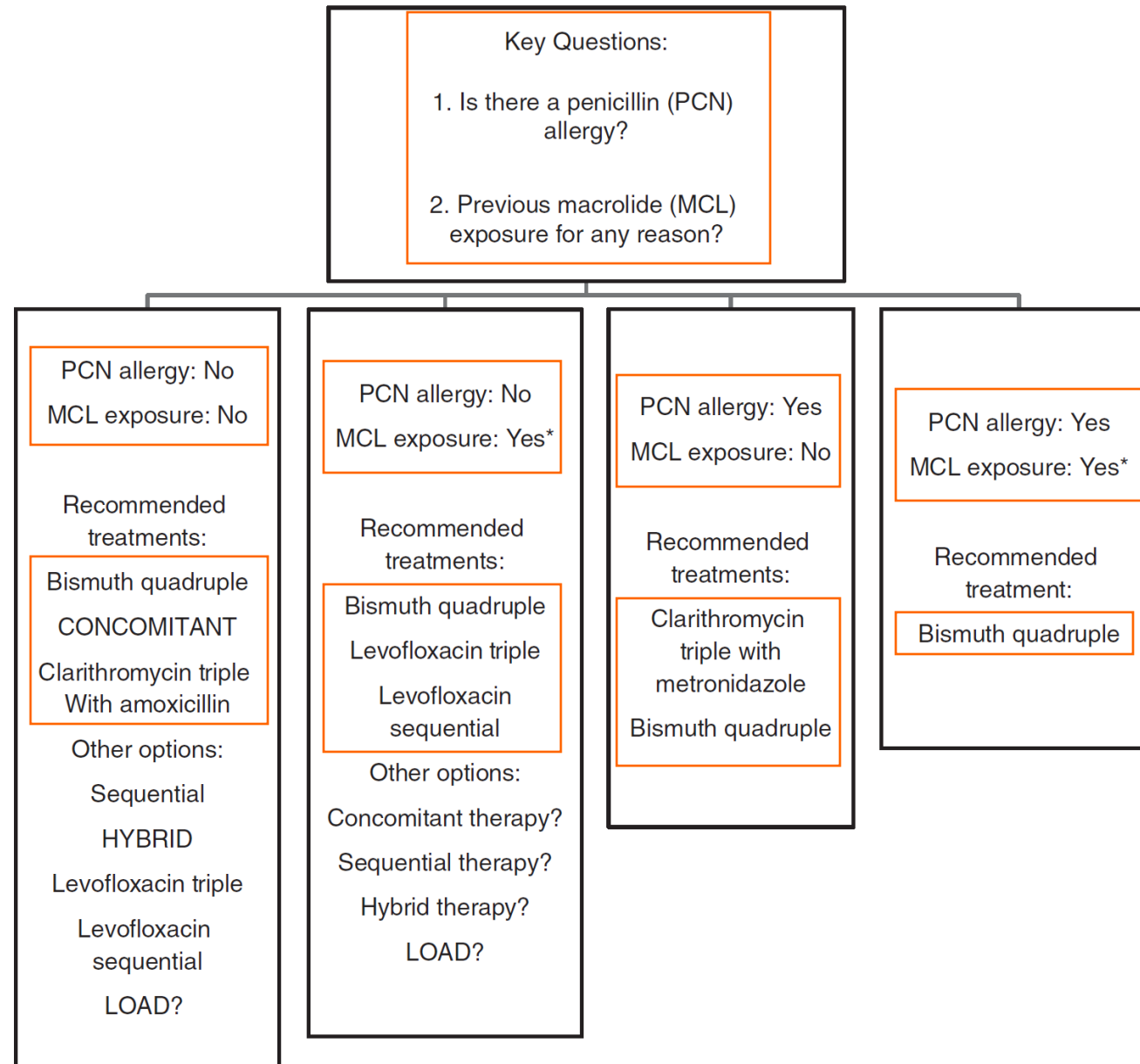
# *H. pylori* Treatment Guidelines

American College of Gastroenterology  
(ACG) 2017

“Triple therapy” – amoxicillin,  
clarithromycin, PPI

Bismuth “quad therapy” –  
tetracycline, metronidazole,  
bismuth, PPI

Concomitant – PPI, amoxicillin,  
clarithromycin, metronidazole



\*In regions where clarithromycin resistance is known to be >15% utilize recommendations for patients with a history of macrolide exposure

For drugs, doses, and durations of specific first-line regimens, see Table 2.



# First Line Treatment Summary

- Limited information on *H. pylori* resistance in the US → assume clarithromycin resistance is > 15% unless local resistance is known
- Macrolide use is common and patients don't remember if they have taken it in their lives



- Generally avoid “triple therapy”
- Bismuth “quad therapy” increasingly used as 1<sup>st</sup> line



# Consider Penicillin Allergy Testing

- Most patients with a history of penicillin (PCN) allergy do not have true PCN hypersensitivity
  - 5-10% of US population report PCN allergy →
  - 90% have negative skin testing and can tolerate PCN
- Consider referral for allergy testing after failure of a 1<sup>st</sup> line treatment to see if an amoxicillin-containing regimen can be given



# Follow-up of PUD

EGD to ensure healing (and not malignant)

- Gastric ulcers – consider for most 8-12 weeks later
- Duodenal ulcers – not generally needed unless unusual

Test for *H. pylori* eradication

- Biopsy gastric mucosa during f/u EGD
- If no repeat EGD needed – stool Ag or breath test
  - 4-8 weeks after treatment
  - Off PPI for 2 weeks



# Question #1

A 24-year-old woman presents with melena and is found to have anemia with a hematocrit of 31%. She had been taking NSAID 2-3 times per day for recent knee pain. She is treated with PPI and upper endoscopy shows a clean-based ulcer in the stomach. *H. pylori* testing is pending.

In addition to stopping NSAIDs, what treatment do you recommend?

- A. Omeprazole 20mg BID for 8 weeks, then continue 20mg daily
- B. Omeprazole 20mg daily for 4 weeks, then stop PPI
- C. Omeprazole 20mg daily for 8 weeks, then stop PPI
- D. Omeprazole 40mg BID for 8 weeks, then continue 20mg daily
- E. Omeprazole 40mg BID for 8 weeks, then stop PPI




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In a patient with a gastric ulcer likely due to NSAIDs, the recommended treatment is standard dose PPI (not high dose) for 8-12 weeks. The PPI should then be stopped if the NSAIDs are  also stopped.



## Question #2

A 37-year old woman with a gastric ulcer has an *H. pylori* Ab and gastric biopsies positive for *H. pylori*. She has a history of endometriosis and pneumonia last year for which she was treated with azithromycin. She is taking an OCP and has no medication allergies.

What regimen do you recommend for treatment?

- A. Amoxicillin, clarithromycin, PPI x 14 days
- B. Amoxicillin, metronidazole, PPI x 14 days
- C. Metronidazole, tetracycline, bismuth, PPI x 14 days
- D. Amoxicillin, levofloxacin, PPI x 14 days
- E. Amoxicillin, rifabutin, PPI x 14 days




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Guidelines for treatment of *H. pylori* infection changed due to concern for antibiotic resistance, especially to macrolides (clarithromycin). If a patient has clear macrolide exposure, clarithromycin-based triple therapy should be avoided and quadruple therapy is  recommended.

# MOC Reflective Statement (Brief Take Home Notes for Reference)

- NSAIDs and *H. pylori* are the primary causes of PUD
  - Others to consider (ex. gastrinoma/ZES)
- Symptoms – pain, bleeding (overt/occult); perforation, obstruction
- Diagnosis – usually EGD, sometimes UGIS/CT
- Endoscopic treatment of high-risk ulcers
- Treat with standard-dose PPI for 8-12 weeks
  - Stop PPI if the inciting factor (NSAIDs, *H. pylori*) is removed
  - Continue PPI if unclear etiology, patient needs to remain on NSAIDs/ASA
- Restart ASA (for secondary prophylaxis) within 7 days
- *H. pylori*
  - Evolving guidelines for first-line regimen: review prior antibiotic exposure, more commonly using quadruple therapy, consider penicillin allergy testing
- Follow-up EGD for most gastric ulcers in 8-12 weeks
  - *H. pylori* eradication testing (EGD; stool Ag/breath test off antibiotics for 4 weeks and PPI for 2 weeks)



# References

- Laine L. Upper gastrointestinal bleeding due to a peptic ulcer. N Engl J Med 2016;374:3267
- Lanza F, Chan F, Quigley E, et al. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol 2009;104:728
- McColl KEL. *Helicobacter pylori* infection. N Engl J Med 2010;362:1597
- Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of *Helicobacter pylori* infection. Am J Gastroenterol 2017;112:212
- Shah SC, Iyer PG, Moss SF. AGA Clinical Practice Update on the Management of Refractory *Helicobacter pylori* infection: Expert Review. Gastroenterology 2021;160:1831

