H. pylori Treatment Updates

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All relevant financial relationships have been mitigated

Outline

- H. pylori epi
- Why H. pylori is challenging to manage
- Updated treatment options
- Practical scenarios

I have experienced and/or known someone requiring H. pylori treatment

a) Yes
b) No

I feel comfortable when providing recommendations for H. pylori treatment

a) Yes
b) No

Epidemiology

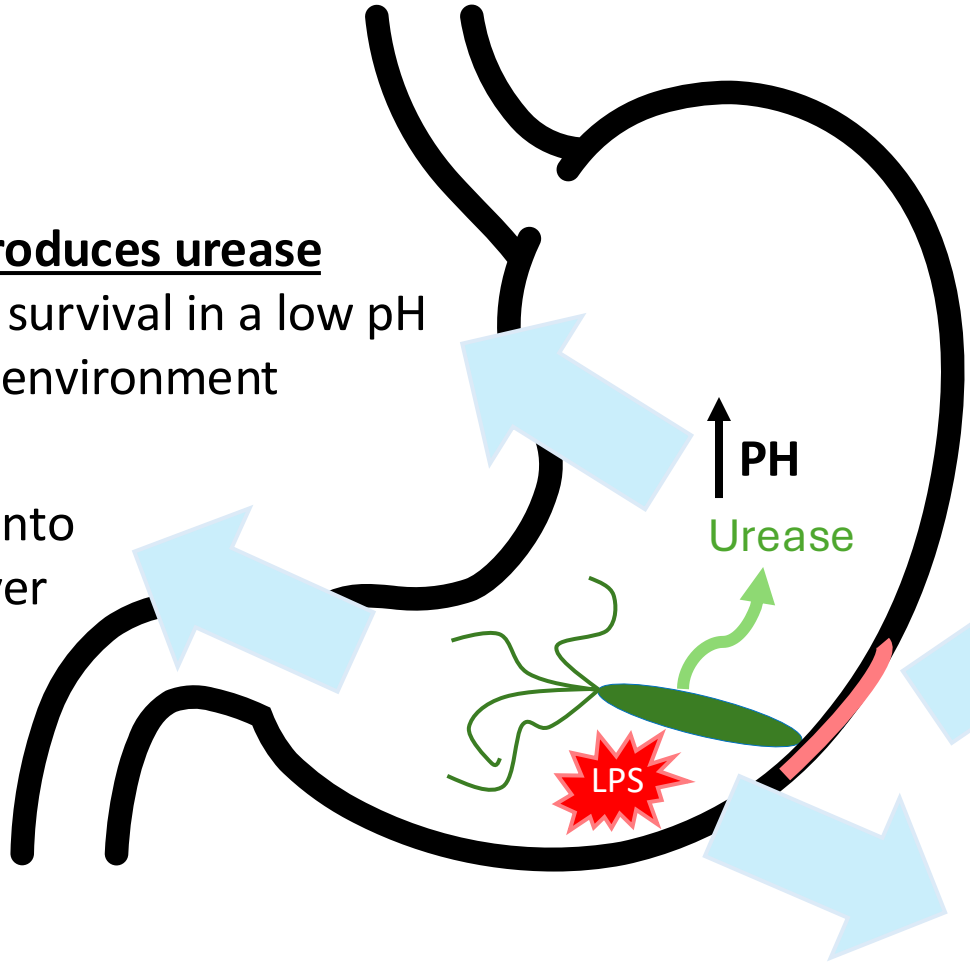
- Not much is known despite being the most common chronic bacterial infection worldwide
  - North America 30-40%
- Likely acquired via childhood and persists asymptomatically
- Spread via person-person/food-sharing
- Outcomes:
  - Asymptomatic/simple gastritis – majority of population
  - Duodenal/peptic ulcer – 10-15%
  - Gastric cancer – 1%

Chey WD, Howden CW, Moss SF, Morgan DR, Greer KB, Grover S, Shah SC. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2024 Sep 1;119(9):1730-1753.
Malfertheiner P, Camargo MC, El-Omar E, et al. Helicobacter pylori infection. Nat Rev Dis Primers. 2023 Apr 20;9(1):19.

Pathophysiology

Produces urease
Allows survival in a low pH environment

Flagella
Help with movement into the gastric mucus layer



Adhesion to gastric epithelial cells
Increases colonization despite gastric epithelial shedding/emptying

Elicits low level inflammation
Causes chronic inflammation without activating immune system

Amieva MR, El-Omar EM. Host-bacterial interactions in Helicobacter pylori infection. Gastroenterology. 2008 Jan;134(1):306-23.

Problem: H. Pylori is difficult to steward

- Poor lab stewardship
- Difficult regimens + longer durations encouraged
- Unpredictable cost of therapies
- Guidelines not reflective of real-world practices

Pitfalls of therapy

- Lack of understanding of therapy options
- Patients not taking medications as prescribed
- Starting incomplete regimens due to cost
- Success rates impacted by several factors

Solution: Treat as few times as possible

- Optimize understanding of existing regimens
- Select and recommend an option that will increase successful treatment the first time
- Provide practical counseling for patients

Updated ACG 2024 recommendations

AJG The American Journal of GASTROENTEROLOGY

1. Bismuth quadruple therapy (BQT)
2. Alternatives
   - Rifabutin triple therapy (RTT)
   - Vonoprazan therapy (PCAB) – dual therapy

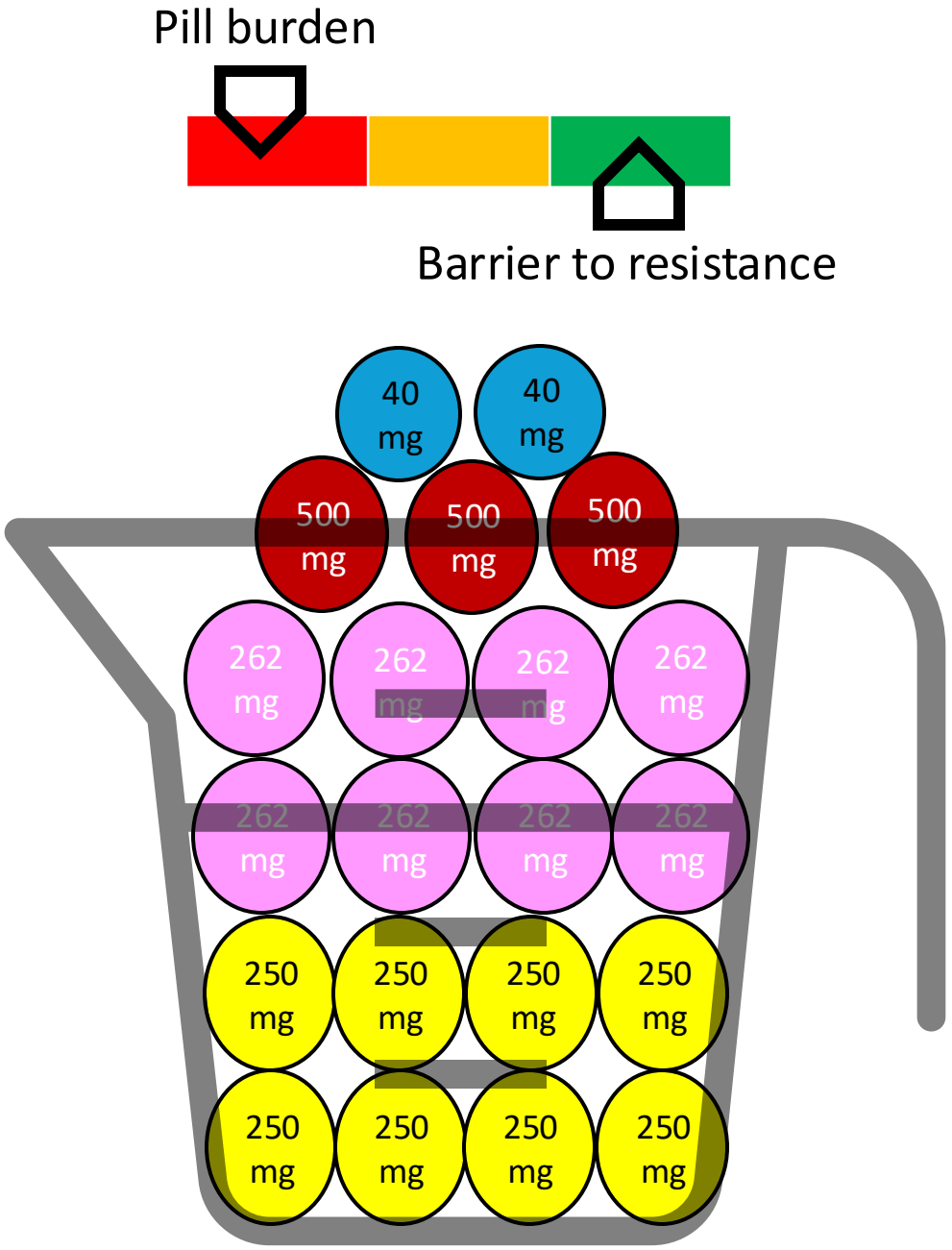
Chey WD, Howden CW, Moss SF, Morgan DR, Greer KB, Grover S, Shah SC. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2024 Sep 1;119(9):1730-1753.

How do these therapies work?

Ierardi E, Losurdo G, Fortezza RF, et al. Optimizing proton pump inhibitors in *Helicobacter pylori* treatment: Old and new tricks to improve effectiveness. World J Gastroenterol. 2019 Sep 14;25(34):5097-5104.
Chey WD, Howden CW, Moss SF, Morgan DR, Greer KB, Grover S, Shah SC. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2024 Sep 1;119(9):1730-1753.

BQT

- Pylera®: 3 capsules + PPI 4 times daily
- Each capsule:
  - Tetracycline 125mg
  - Bismuth subcitrate 140mg
  - Metronidazole 125mg
  - Packs built for 10 days only
- Individual drugs:
  - Tetracycline: 500mg 4 times daily
  - Bismuth subsalicylate (Pepto Bismol®): 262-525mg 4 times daily
  - Metronidazole: 500mg 3 times daily
  - PPI standard dosing: omeprazole 40mg 2 times daily
- Treatment duration: 14 days
- Success rate: 85%



Metronidazole (MTZ) resistance

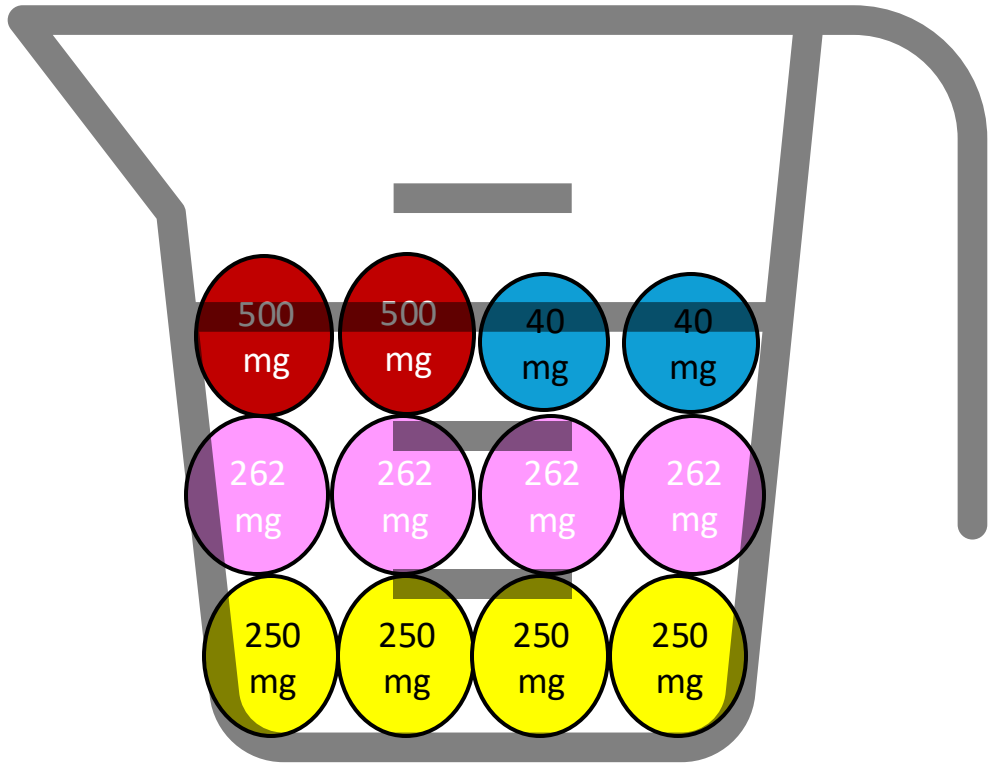
Study	Location	MTZ-R	Doses studied	Success w/ ANY dose + LOW MTZ-R	Success w/ LOW dose + HIGH MTZ-R	Success w/ HIGH dose + HIGH MTZ-R
PLOS ONE RESEARCH ARTICLE Meta-analysis: High-dose vs. low-dose metronidazole-containing therapies for *Helicobacter pylori* eradication treatment	Iran Europe Japan	Low-R: 5-35% High-R: 60%	120mg BID to 500mg TID	85%	50%	70-74%
Helicobacter **The HOMER Study: The Effect of Increasing the Dose of Metronidazole When Given with Omeprazole and Amoxicillin to Cure *Helicobacter pylori* Infection**	Europe	21%	400mg BID 400mg TID 800mg BID	85%	54%	75%

Increasing the dose or duration of metronidazole treatment may lead to improved activity against H. pylori.

Ji Y, Lu H. Meta-analysis: High-dose vs. low-dose metronidazole-containing therapies for Helicobacter pylori eradication treatment. PLoS One. 2018 Jan 25;13(1):e0189888.
Bardhan K, Bayerdörffer E, Veldhuyzen Van Zanten SJ, et al. The HOMER Study: the effect of increasing the dose of metronidazole when given with omeprazole and amoxicillin to cure Helicobacter pylori infection. Helicobacter. 2000 Dec;5(4):196-201.

BQT BID vs QID

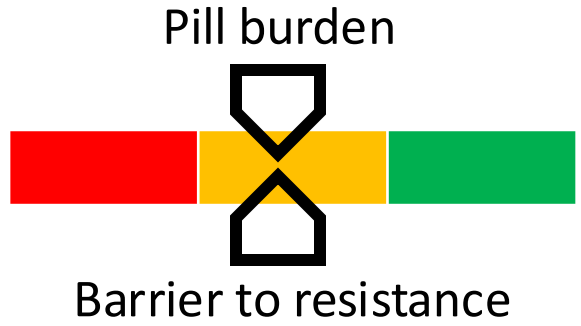
- BQT BID success rates up to 95% but poorly understood
- Lower success with metronidazole resistance
- Excellent adherence improves success
- Not routinely recommended

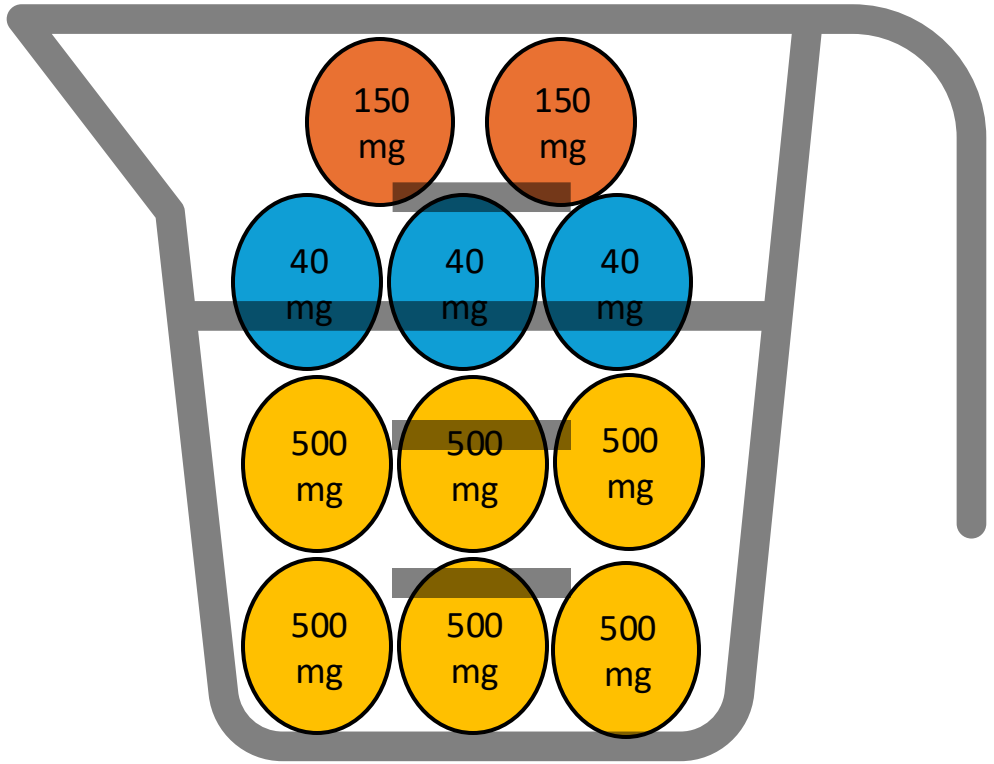


Graham DY, Hoffman J, el-Zimaity HM, et al. Twice a day quadruple therapy (bismuth subsalicylate, tetracycline, metronidazole plus lansoprazole) for treatment of Helicobacter pylori infection.
Graham DY, Belson G, Abudayyeh S, et al. Twice daily (mid-day and evening) quadruple therapy for H. pylori infection in the United States. Dig Liver Dis. 2004 Jun;36(6):384-7. Aliment Pharmacol Ther. 1997 Oct;11(5):935-8.
Dore MP, Farina V, Cuccu M, et al. Twice-a-day bismuth-containing quadruple therapy for Helicobacter pylori eradication: a randomized trial of 10 and 14 days. Helicobacter. 2011 Aug;16(4):295-300.

RTT

- Talicia®: 4 capsules three times daily
- Each capsule:
  - Amoxicillin 250mg
  - Omeprazole 10mg
  - Rifabutin 12.5mg
- Individual drugs:
  - Amoxicillin 1000mg 3 times daily
  - Omeprazole 40mg 2-3 times daily
  - Rifabutin 150mg 2 times daily
- Treatment duration: 14 days
- Success rate: 84%
- Improved success rate w/ RBT QD-BID:
  - Higher dosing (BID)
  - Longer durations (>10 days)

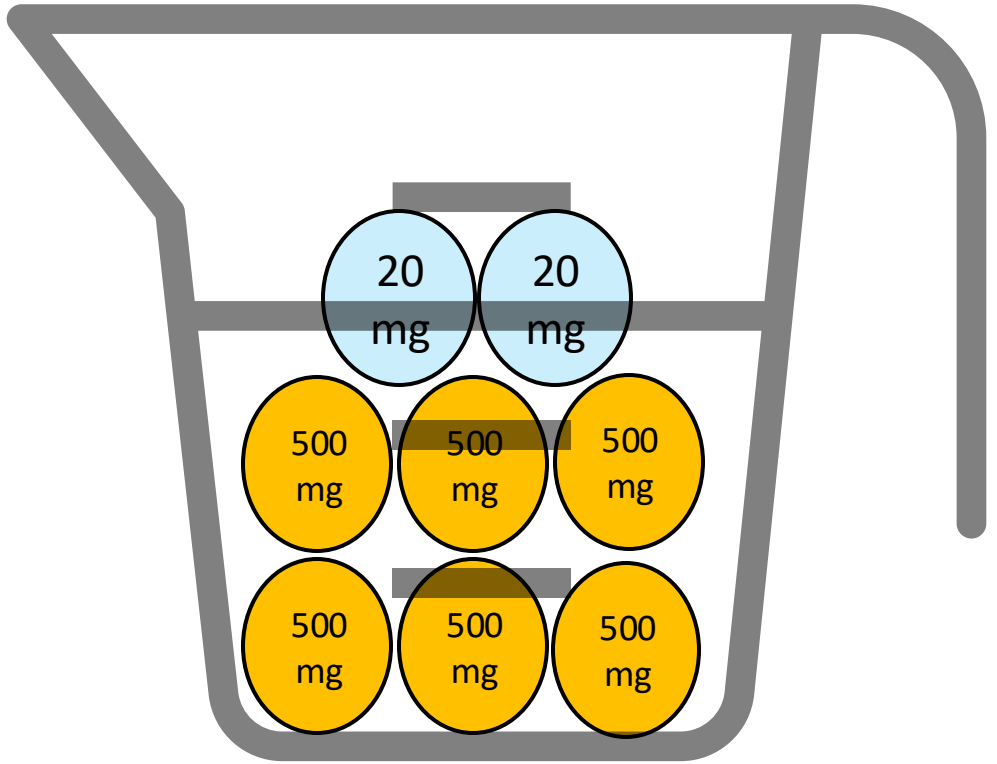




Borraccino AV, Celiberto F, Pricci M, et al. Rifabutin as salvage therapy for *Helicobacter pylori* eradication: Cornerstones and novelties. World J Gastroenterol. 2022 Dec 7;28(45):6356-6362.
Howden CW, Shah S, Pendse SN, et al. Physiologically-based pharmacokinetic modelling to predict intragastric rifabutin concentrations in the treatment of Helicobacter pylori infection. Aliment Pharmacol Ther. 2023 Jul;58(2):159-167.

PCAB dual therapy

- Voquezna DualPak®: 3 capsules 3 times daily
  - Each capsule:
  - Amoxicillin 500mg
  - Vonoprazan 20mg
- Individual drugs:
  - Amoxicillin 1000mg 3 times daily
  - Vonoprazan 20mg 2 times daily
- Treatment duration: 14 days
- Success rate: 77%



Why combo therapy?

- Susceptibilities not routinely performed
- Multiple agents with assumed activity are added to increased likelihood of active therapy
  - BQT>RTT>PCAB
- Clarithromycin or levofloxacin triple therapy no longer recommended for empiric treatment

Chey WD, Howden CW, Moss SF, Morgan DR, Greer KB, Grover S, Shah SC. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2024 Sep 1;119(9):1730-1753.

Why is 14 days preferred?

- 14 days is recommended OVER 10 days for both treatment-naïve or treatment-experienced patients
- Shortening courses may lead to decreased efficacy
  - ≥10% depending on therapy
- Assume suboptimal exposure – variability in dosing, adherence, and resistance

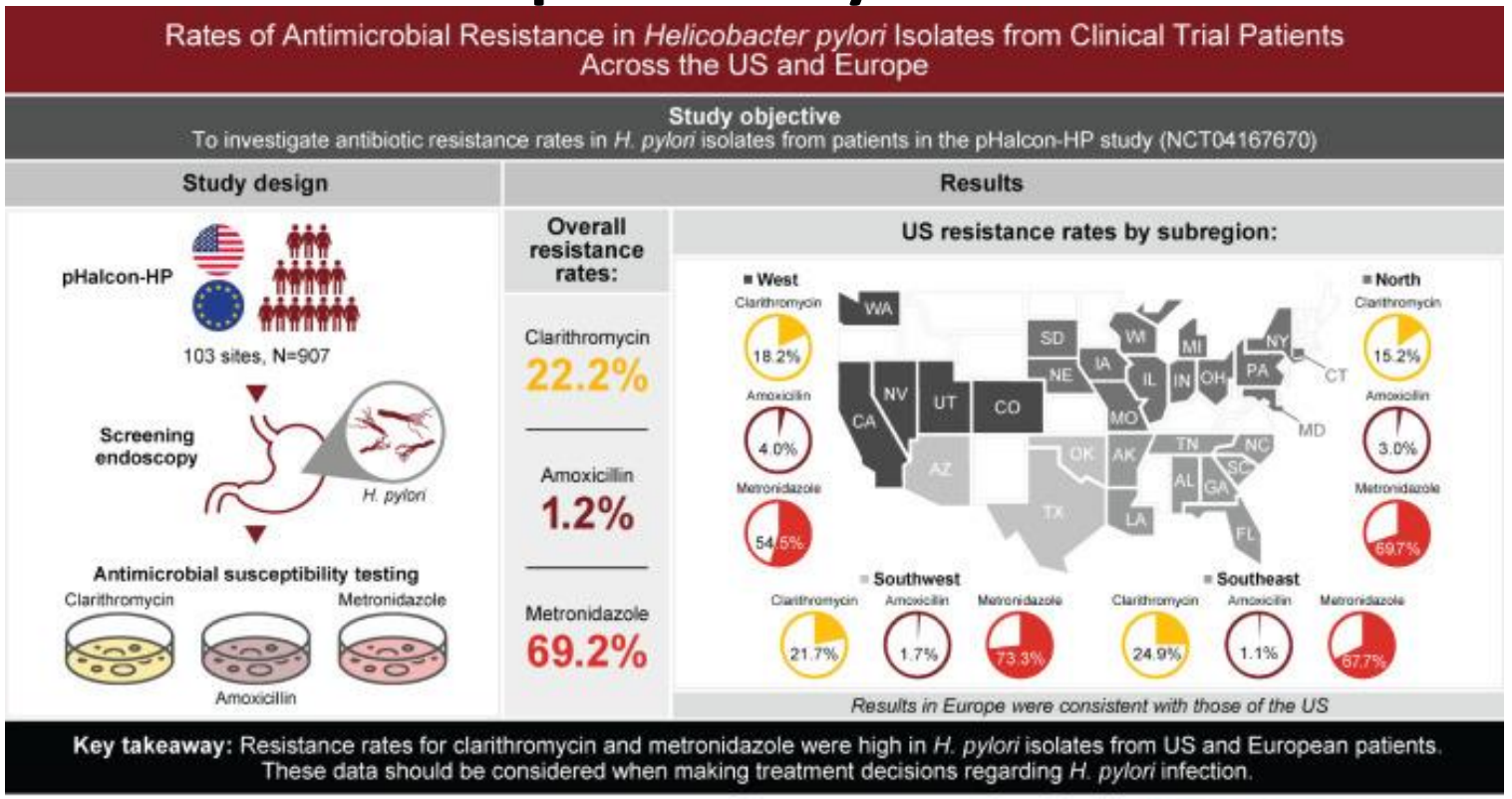
Chey WD, Howden CW, Moss SF, Morgan DR, Greer KB, Grover S, Shah SC. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2024 Sep 1;119(9):1730-1753.

Why is clarithromycin triple therapy no longer recommended?

- Increased resistance and higher risk of treatment failure
- Exception: susceptibilities confirmed prior to starting therapy
- Seattle: clarithromycin resistance >20%

Talarico S, Korson AS, Leverich CK, et al. High prevalence of Helicobacter pylori clarithromycin resistance mutations among Seattle patients measured by droplet digital PCR. Helicobacter. 2018 Apr;23(2):e12472.

Amoxicillin susceptibility remains excellent



Mégraud et al. *Am J Gastroenterol.* [2022]. [doi:10.14309/ajg.0000000000002045]

AJG The American Journal of GASTROENTEROLOGY

West coast	Amoxicillin	Clarithromycin	Levofloxacin	Metronidazole	Rifabutin	Tetracycline
H. pylori	95	77	42	56	100	98

BQT: swapping tetracycline for doxycycline

- Doxycycline is an option but not recommended by ACG due to decreased efficacy
- Use doxycycline in place of tetracycline if therapy cannot be initiated in a timely manner or is cost prohibitive

Junga ZC, Mertz A, Pak K, et al. Helicobacter pylori Treatment Regimen Selection and Eradication Rates Across Department of Defense Patients for Fiscal Years 2016-2018. Mil Med. 2023 Jul 22;188(7-8):e2089-e2095.

Would IV antibiotics work for H. pylori?

- Not addressed by guidelines
- PO is in theory preferred since achieves high concentrations in gastric mucosa
- Limited data supporting this practice – holding treatment preferred while patients are on broad spectrum for other indications
- If IV therapy is needed for H. pylori
  - PPI
  - Ampicillin
  - Doxycycline/levofloxacin
  - Metronidazole

How to handle persistent/MDRO H. pylori if no recommended regimen will work?

- Hold therapy while further workup ongoing
- Send susceptibilities – tailor regimen based on susceptible antibiotics
- Mix and match agents
- Pursue newer therapies: PCAB or RTT

Takeaways

- BQT remains first line
- 14 days is preferred over 10 days
- Do not use clarithromycin-based therapies empirically
- Increasing practicality of a regimen may compromise efficacy
  - Stick to guidelines when you can
  - Deviate when in the patient’s best interest

Questions?

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