Treatment of *H. pylori*: What works and what doesn't

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Disclosures

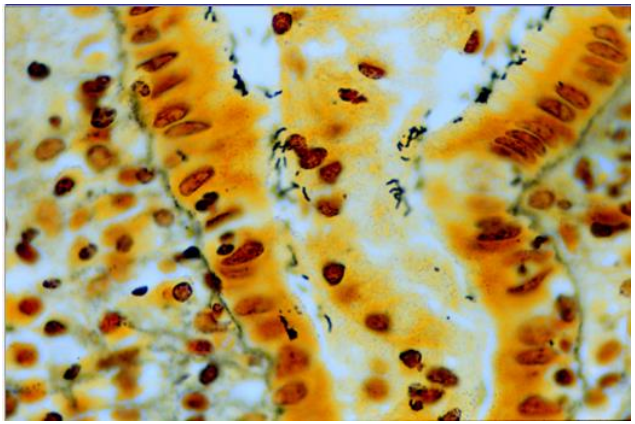
No relevant financial disclosures

Objectives

- Identify who to test and treat based on clinical presentation
- Select an appropriate evidence-based first-line regimen and duration
- Know how to confirm eradication correctly
- Choose an appropriate salvage regimen after treatment failure

What is *H. pylori* ?

- Helicobacter pylori
- Gram-negative, spiral-shaped bacterium adapted to survive in acidic stomach environment
- Co-evolved with humans, strain diversity varies by geography
- Produces enzymes including urease, which neutralizes stomach acid and allows bacteria to invade stomach lining
- Triggers inflammatory response that damages stomach surface and can lead to atrophic gastritis



A change in thinking...

In the mid 20th century, Dr. Hans Selye, popularized the idea of stress as a cause of illness.

- In 1982, Drs. Barry Marshall and Robin Warren identified H. pylori on gastric biopsies.
- In 1985, Dr. Marshall ingested H. pylori to give himself ulcers and prove the link.
- In 2005, both awarded the Nobel Prize in Medicine.

H. pylori - Epidemiology

- Global prevalence >40%, higher in low resource settings
- US prevalence ~30-40% overall, with important demographic variation
- Higher rates among many immigrant groups and certain US regions
- Spread through person-to-person contact (oral-oral, fecal-oral, gastric-oral)
- Usually acquired in childhood, but adult acquisition possible
- Often spread within families

H. pylori - Epidemiology

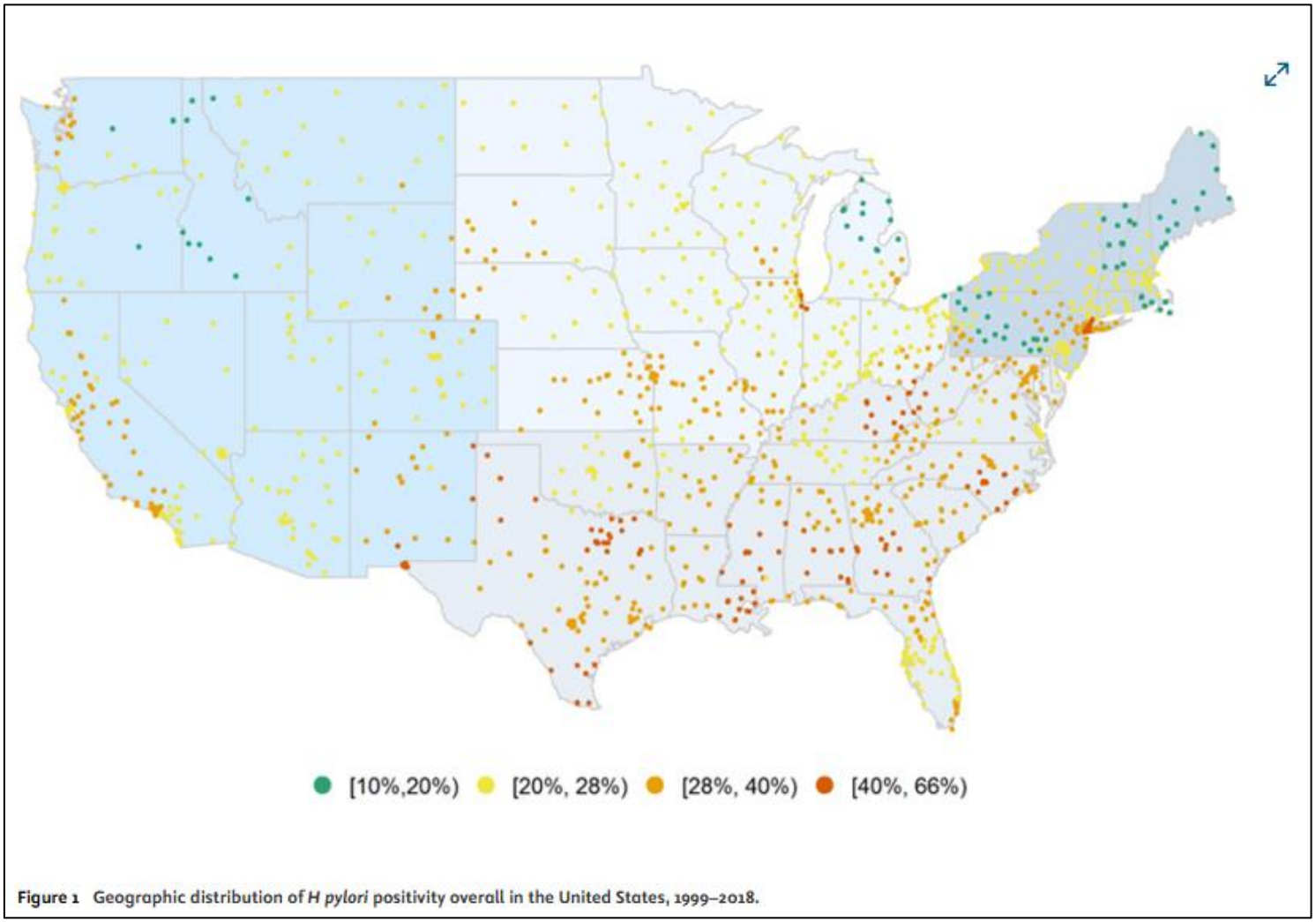


Figure 1 Geographic distribution of *H pylori* positivity overall in the United States, 1999–2018.

H. pylori - Epidemiology

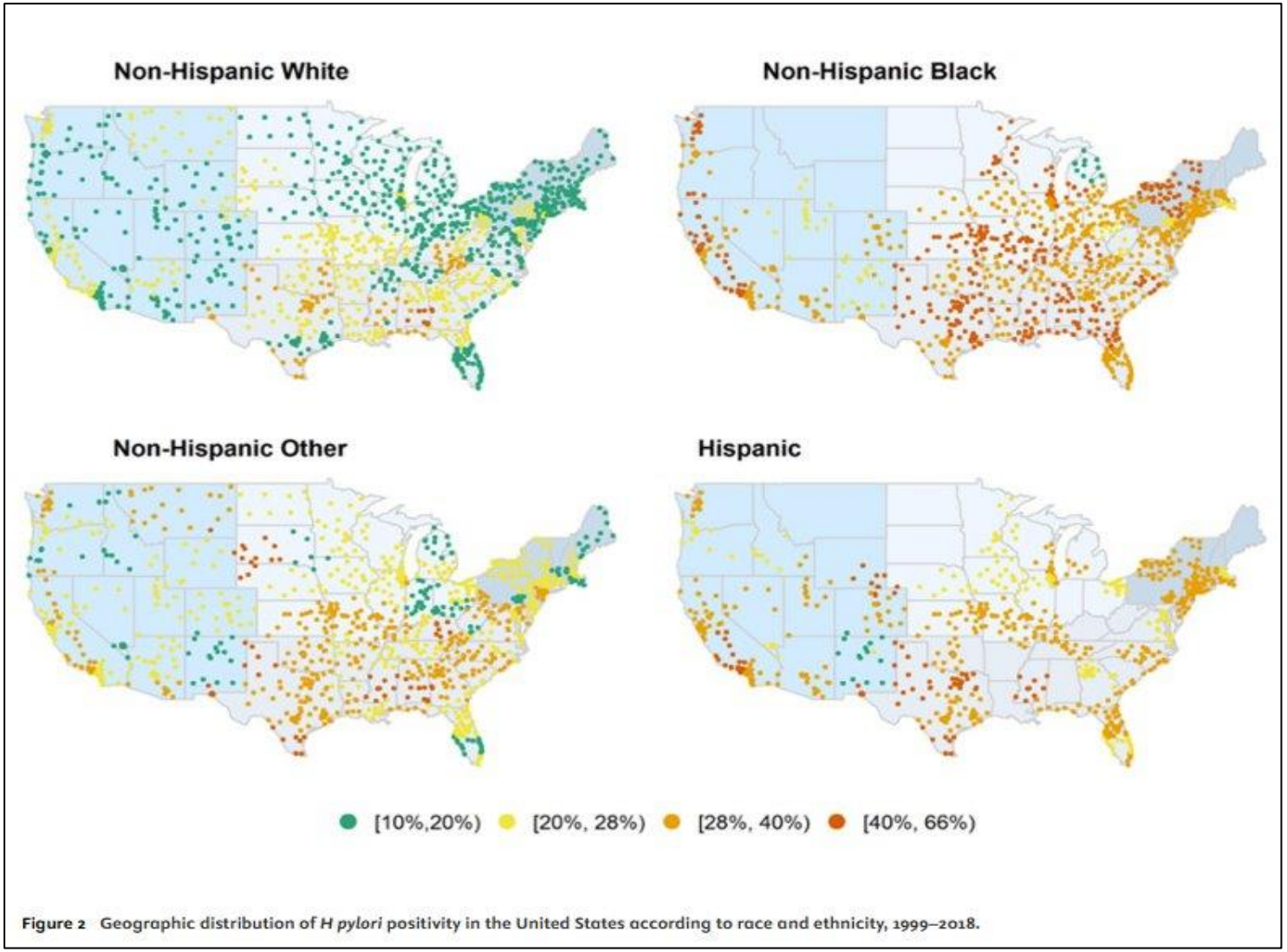
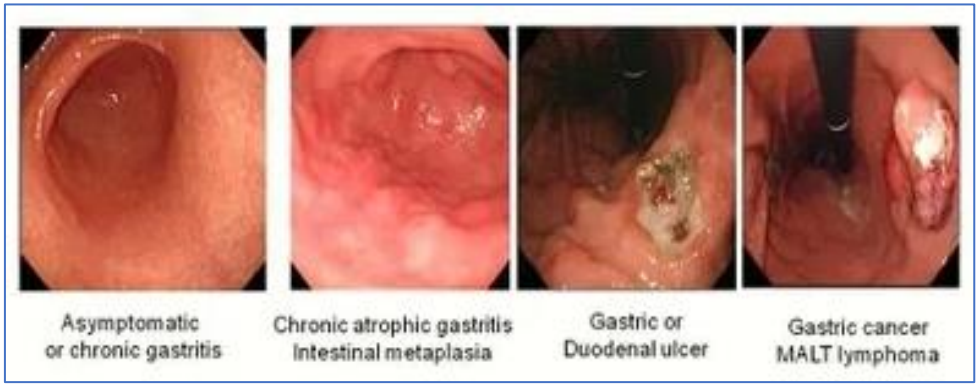


Figure 2 Geographic distribution of *H pylori* positivity in the United States according to race and ethnicity, 1999–2018.

Common clinical presentations

- Dyspepsia
- Peptic ulcer disease (duodenal or gastric)
- Gastric cancer (MALT lymphoma, adenocarcinoma)
- Unexplained iron deficiency anemia



Treating *H. pylori* – why is it important?

- Common chronic infection --> causes lifelong gastritis and symptoms unless treated
- Definite carcinogen
- By eradicating, we prevent:
  - Peptic ulcer disease recurrence / complications
  - Gastric cancer risk
  - Gastric MALT lymphoma response / remission in some cases

Question #1

A 55-year-old man with chronic dyspepsia comes to the office as a new patient and asks for a refill of his PPI prescription. He has never had testing for *H. pylori* and he seems annoyed when you propose testing instead of empiric treatment for his symptoms. Which of the following best explains the rationale for identifying and eradicating *H. pylori*?

A. *H. pylori* infection usually resolves spontaneously without treatment.

B. Eradication primarily improves dyspepsia but does not affect long-term outcomes.

C. *H. pylori* is a WHO Group 1 carcinogen and a major risk factor for gastric cancer.

D. Testing is recommended mainly to guide acid-suppression dosing.

E. Treatment is only indicated in patients with peptic ulcer disease.

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How to test

- Urea breath test (UBT)
  - Pros: Most accurate (sen ~95%, spec ~95%), detects active infection
  - Cons: Requires stopping PPI for minimum 2 weeks, availability, cost

- Stool antigen test (SAT)
  - Pros: High accuracy (sen ~93%, spec ~93%), widely available, less expensive
  - Cons: Requires stopping PPI for minimum 2 weeks, sample handling

- Serology, IgG antibody ??
  - Cannot distinguish active vs prior infection
  - Not recommended for diagnosis or test-of-cure

How to test

- Endoscopy with biopsy
  - Pros: Direct visualization to evaluate for gastritis, ulcers, malignancy, etc.; biopsy allows for histology and IHC +/- rapid urease testing (ie. CLO)
  - Cons: Invasive; still affected by PPI / antibiotic use; higher cost
  - Best for patients with alarm features, GI bleeding, age-based endoscopy indications

- Culture
  - Pros: Determines antibiotic susceptibility
  - Cons: Limited availability; low sensitivity
  - Not common in usual clinical practice.

Question #2

A 46-year-old woman with dyspepsia and no alarm features is being evaluated for *H. pylori*. She is currently taking omeprazole daily. Which of the following is the most appropriate initial diagnostic strategy?

A. Serum *H. pylori* IgG antibody testing.

B. Urea breath test while continuing omeprazole.

C. Stool antigen test after holding omeprazole for 2 weeks.

D. Endoscopic biopsy with culture and suspectibility testing.

E. Empiric clarithromycin triple therapy without testing.

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H. pylori positive! How to treat...

- Treatment involves a combination of acid suppression and antibiotics
- *H. pylori* normally uses acid to hide
- Acid suppression helps expose the bacteria, stabilizes antibiotic activity, also helps to heal the stomach lining
- Antibiotics kill the bacteria itself
  - Multiple antibiotics target different bacterial pathways

H. pylori positive! How to treat...

- For treatment duration, 14 days is best
- Important to pick initial treatment regimen wisely
- Considerations:
  - Local resistance patterns
  - Antibiotic allergy
  - Prior antibiotic exposure

Antimicrobial resistance has risen over time

Table 1. Geographic Distribution of Antimicrobial Resistance Patterns per US Region, 2017–2018

Antibiotic	All Isolates (N = 345)	West (n = 108)	Central (n = 86)	East (n = 151)	*P*
Amoxicillin	6.4 (22)	8.3 (9)	5.8 (5)	5.3 (8)	.6
Clarithromycin	17.4 (60)	11.1 (12)	15.1 (13)	23.2 (35)	.03
Metronidazole	43.6 (150)[a]	35.5 (38)[a]	43.0 (37)	49.7 (75)	.08
Rifabutin	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	ND
	Limited Analysis (n = 71)	(n = 19)	(n = 19)	(n = 33)	
Tetracycline	2.8 (2)	5.3 (1)	5.3 (1)	0.0 (0)	.3
Levofloxacin	57.8 (41)	57.8 (11)	68.4 (13)	17 (51.5)	.5

NOTE. Values are % (n). ND, not done.
[a]Metronidazole susceptibilities were available for 107 isolates from the West region and from 344 isolates in total.

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National and Regional US Antibiotic Resistance to *Helicobacter pylori*: Lessons From a Clinical Trial

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First-line treatment: Bismuth Quadruple Therapy (BQT)

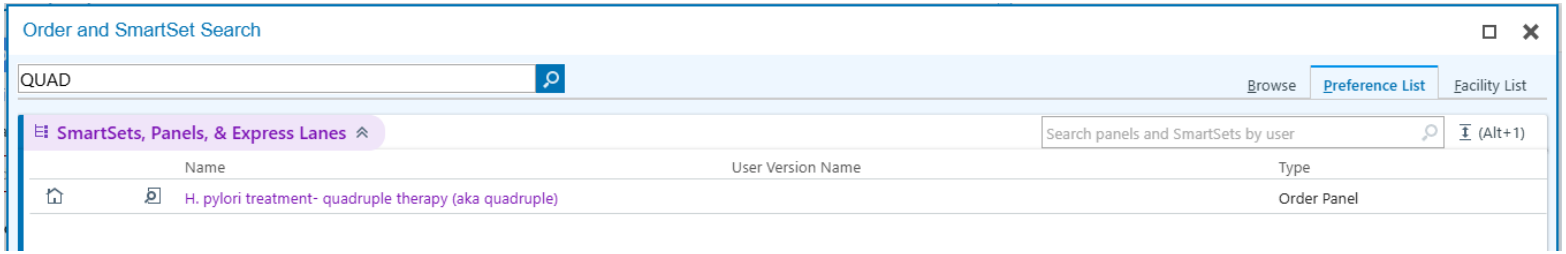
Regimen should include 14 days of:

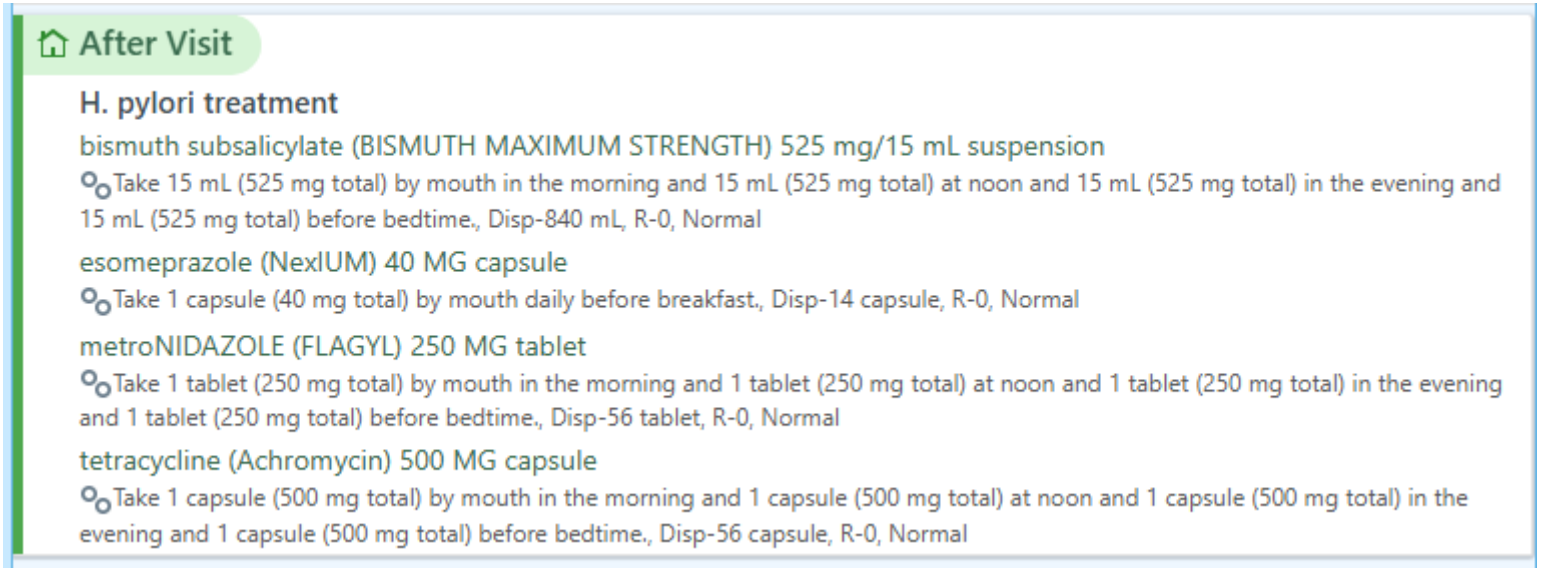
PPI + bismuth + tetracycline + metronidazole/tinidazole

- Pros:
  - Not impacted by clarithromycin resistance
  - Good real-world effectiveness

- Cons:
  - Adherence is a challenge
  - Number of pills
  - Duration
  - Side effects (ie nausea from metronidazole)

BQT Epic order panel





Alternative first-line treatment options

First-line treatment regimens for *H. pylori* infection in treatment-naïve adults

Regimen (United States brand names)	Drugs (doses)	Dosing frequency*	
Optimized bismuth quadruple (component therapy)	PPI standard dose¶	Twice daily	14
	Bismuth subsalicylate 300 or 524 mgΔ **or** Bismuth subcitrate 120 to 300 mg (not available in United States)	4 times daily	
	Tetracycline 500 mg◇		
	Metronidazole 500 mg	3 or 4 times (preferred) daily	
Bismuth quadruple (as Pylera combination capsules plus PPI)§	PPI standard dose¶	Twice daily	10
	Fixed-dose combination capsules; 3 capsules deliver bismuth subcitrate 420 mg, metronidazole 375 mg, and tetracycline 375 mg	4 times daily	
Rifabutin-amoxicillin-PPI triple (Talicia)	Fixed-dose combination capsules; 4 capsules deliver omeprazole 40 mg, rifabutin 50 mg, and amoxicillin 1 g	3 times daily	14
Vonoprazan-amoxicillin dual (Voquezna Dual Pak)	Vonoprazan 20 mg	Twice daily	14
	Amoxicillin 1 g	3 times daily	
Vonoprazan-amoxicillin-clarithromycin triple (Voquezna Triple Pak)¥	Vonoprazan 20 mg	Twice daily	14
	Amoxicillin 1 g		
	Clarithromycin 500 mg		

Question 3

A 60-year-old man from Massachusetts tests positive for *H. pylori* by stool antigen. He reports prior treatment with azithromycin for pneumonia. He has no known drug allergies but reports that metronidazole has made him nauseous in the past. Which is the best empiric first-line treatment?

A. Clarithromycin triple therapy for 7 days

B. Clarithromycin triple therapy for 14 days

C. Levofloxacin-based triple therapy

D. Bismuth quadruple therapy for 14 days

E. High-dose PPI monotherapy

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Test of cure – how to confirm eradication

- Urea breath test or stool antigen are recommended

- Timing is important:
  - At least 4 weeks after therapy
  - Off PPI for 2 weeks

- Proving eradication is particularly important for:
  - Persistent symptoms
  - History of peptic ulcer disease
  - Personal or family history of gastric cancer (MALT, adenocarcinoma)

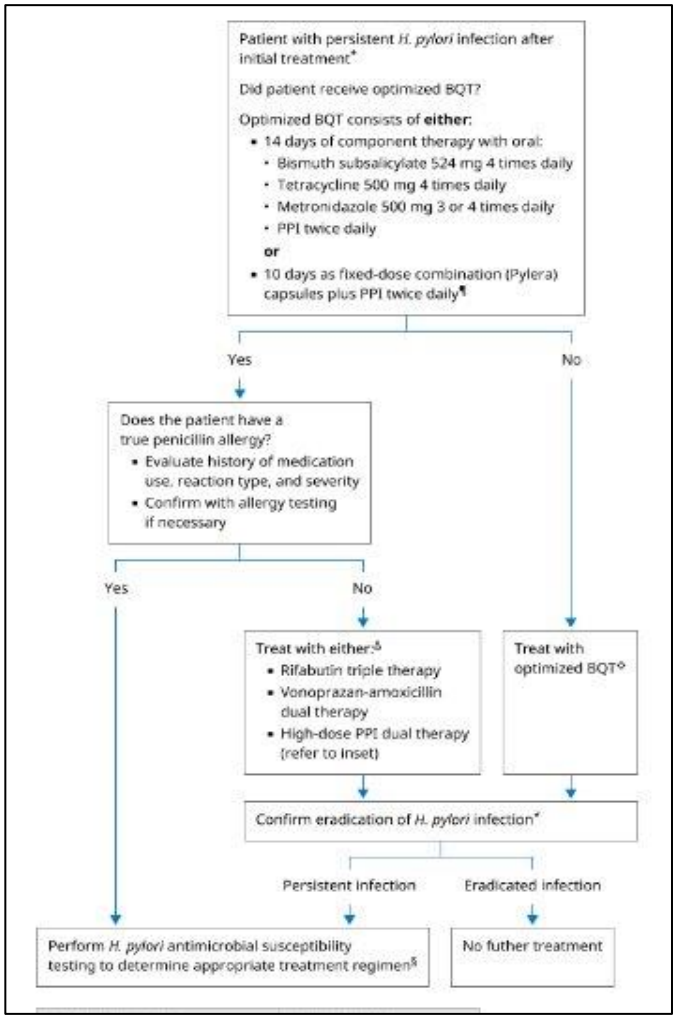
Persistent infection?

Was BQT optimized?

Is the patient PCN allergic?
If yes, needs confirmation.

Consider rifabutin triple therapy or vonoprazan regimen.

Susceptility testing only considered for true PCN-allergy or after multiple treatment failure



When to consider culture

- Consider culture with susceptibility testing when:
  - 2-3 failed eradication attempts
  - True PCN allergy limiting options
  - Other complexity in decision-making, ie. toxicity, adherence barriers, high-risk history

- How to culture:
  - Requires endoscopic gastric biopsies, antrum + body
  - Need to be off PPI for 2 weeks, off Abx for 4 weeks
  - Logistics are hard: fastidious organism, transport medium and timing are important, incubation may be prolonged.
  - Practically speaking, comfort and expertise with culture not widely available

Question #4

A 58-year-old woman from New Hampshire was diagnosed with *H. pylori* by urea breath test. She initially received 14 days of clarithromycin-amoxicillin-PPI triple therapy but eradication testing remained positive. Despite this, she says her dyspepsia is better. She has no known drug allergies. What is the most appropriate next step?

A. Repeat clarithromycin-based triple therapy for 14 days

B. Bismuth quadruple therapy for 14 days

C. Levofloxacin-based triple therapy for 14 days

D. High-dose PPI monotherapy if symptoms recur

E. Plan endoscopy for culture and susceptibility testing

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E. Plan endoscopy for culture and susceptibility testing

Take home points

- *H. pylori* is common
- Treatment is important for prevention of acute and chronic disease
- Testing is primarily done by urea breath test and stool antigen
- Important to choose first treatment regimen carefully. In the Northeast, bismuth quadruple therapy (BQT) is best.
- All patients should have test-of-cure.
- Rifabutin and vonoprazan-based regimens should be considered for alternative first-line treatment or initial treatment failure.
- Practically speaking, most patients can be treated empirically, even after treatment failure, and culture is not usually needed.

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Thank you

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