


## Management of *Helicobacter pylori* Infection



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## Prevalence of *H. pylori* infection in the United States

Race / ethnicity	<i>H. pylori</i> seropositivity (%)
Non-Hispanic white	18.4
Non-Hispanic black	46.2
Mexican-American	49.1
Other Hispanic	47.1
Other	34.5
Place of birth	
Outside United States	56.3
United States	21.9

Cardenas et al, Am J Epidemiol 2006; 163: 127

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## Whom Should We Test for *H. pylori* Infection?

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**Established Indications for  
Diagnosis and Treatment of H. pylori**

- Confirmed duodenal ulcer
- Confirmed gastric ulcer
- Patients taking antisecretory maintenance therapy for peptic ulcer
- Gastric MALT lymphoma (low grade)
- Uninvestigated Dyspepsia

Chey WD and Wong B. Am J Gastroenterol 2007

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**Controversial Indications for  
Diagnosis and Treatment of H. pylori**

- Functional dyspepsia
- Gastroesophageal reflux disease
- Iron deficiency anemia
- Patients taking NSAIDs
- Populations at high risk for gastric cancer
- Idiopathic thrombocytopenic purpura

Chey WD and Wong B. Am J Gastroenterol 2007

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**How Should We Test  
for H. pylori Infection?**

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### Diagnostic Tests

<b>Nonendoscopic</b>	<ul style="list-style-type: none"><li>• antibody detection</li><li>• urease tests</li><li>• fecal antigen detection</li></ul>
<b>Endoscopic</b>	<ul style="list-style-type: none"><li>• rapid urease test</li><li>• histology</li><li>• culture</li></ul>

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### ELISA Testing for *H. pylori*

- Meta-analysis of 21 studies
- No significant differences in accuracy between tests

Sensitivity	Specificity
85%	79%

Loy CT, et al. *Am J Gastroenterol.* 1996;91:1138-1144

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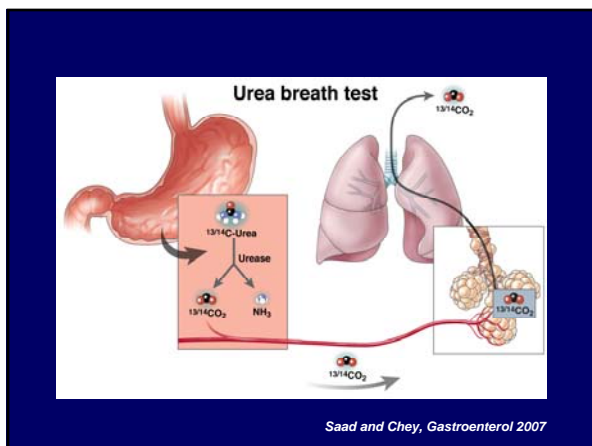
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### Nonendoscopic Urease Tests

- $^{13}\text{C}/^{14}\text{C}$ -urea breath tests
- $^{13}\text{C}$ -urea blood test
- Accurate for pre- or post-treatment testing
- FN results with
  - Antibiotics or bismuth within 2 to 4 weeks
  - PPIs within 1 to 2 weeks
  - High dose  $\text{H}_2\text{RAs}$

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### Fecal Antigen Test

- Fecal antigen detected by EIA
  - Monoclonal test more accurate than polyclonal test
- Stool can be stored at  $2-8^\circ\text{C}$  for 3d and at  $-20^\circ\text{C}$  indefinitely
- Accurate for pre- and post-treatment testing
- Timing of eradication testing controversial
- FN results occur with antibiotics, bismuth or PPIs

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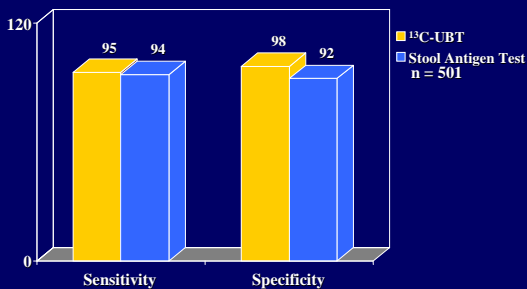
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### Urea Breath Test or Stool Antigen Test for *H. pylori* Infection



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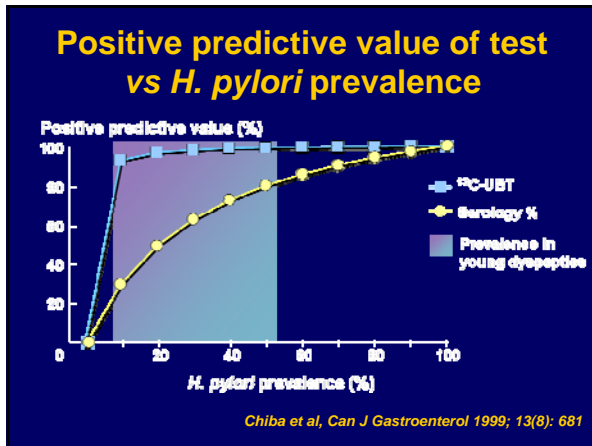
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- ### Endoscopic Tests for *H. pylori*
- Rapid urease tests
  - Histology
  - Culture
  - PCR

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- ### *H. pylori* testing in acute UGI bleeding from PUD
- The sensitivity of RUT in acute UGI bleeding is 70-80%
  - Consider antibody testing ± EGD tests in the acute setting
    - PPV of antibody testing in patients with an ulcer is good
  - If antibody testing negative, confirm with an active test at a later date
- Saad, Chey, Clev Clin Med J 2005*

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## Post-Treatment *H. pylori* Testing

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### *H. pylori* and PUD: Where are we falling short?

- Most patients with an ulcer are being tested for *Hp*
  - there remains confusion about testing in patients with ulcer bleeding
    - » sensitivity of endoscopic tests may be reduced
    - » serology? Delayed testing?
- All patients with an ulcer should undergo a test to prove *H. pylori* eradication
  - UBT or stool test more than 4 weeks after treatment
  - serology is only useful if it is negative
  - failure to test increases risk of recurrent ulcer bleeding

Chey and Wong, Am J Gastroenterol 2007;102:1808

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### Importance of confirming *H. pylori* cure in Peptic Ulcer Bleeding

- Retrospective analysis of 127 (mean age = 68 ± 11 years) patients admitted for acute ulcer bleeding
  - NSAID alone = 39%
  - *Hp* alone = 16%
  - Both = 29%
  - Neither = 16%
- 52 (91%) with *Hp* ulcer received antibiotics
- 19 (37%) underwent eradication testing
- 18 (14%) rebleeding
  - *Hp* cured - 13%
  - *Hp* not cured or not confirmed - 33%
- **Bottom line: Underutilization of eradication testing is common and leads to recurrent ulcer complications**

Gandolfo et al. DDW #T1043

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### Post-Therapy *H. pylori* Testing

- **Urea breath test**
  - Perform >4 wks after completion of therapy
  - May be accurate when done 2 weeks after therapy
- **Fecal antigen test**
  - Perform >4 wks after completion of therapy
  - Monoclonal test preferred
- **Biopsy-based testing**
  - histology ± RUT
  - requires multiple biopsies

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### Treatment of *H. pylori* Infection

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### Primary Therapy for *H. pylori*

Drugs	Frequency	Duration
PPI, Clarithromycin 500 mg Amoxicillin 1 gm or metronidazole 500 mg	BID	10-14 d.
PPI	QD	10-14 d
Tetracycline 500 mg	QID	
Pepto Bismol 2 tablets (525 mg)		
Metronidazole 250-500 mg		

Chey and Wong, Am J Gastroenterol 2007;102:1808

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### *H. pylori* Treatment Regimens: Shifting Sands

- Eradication rates with clari triple and bismuth quadruple therapy  $\leq 80\%$
- 14 days of therapy may be superior to 7 days of therapy
- Clari-R rates are rising
- Clari-R is absolute and affects eradication rates
- PPIs and increased metronidazole dose may overcome metronidazole-R

Saad & Chey. *Gastroenterol Hepatol Ann Rev* 2006

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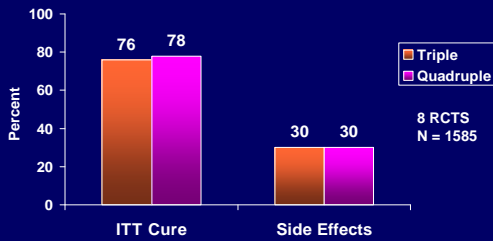
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### Triple vs. Quadruple therapy for *H. pylori* infection: A meta-analysis



Luther et al., *ACG* 2008

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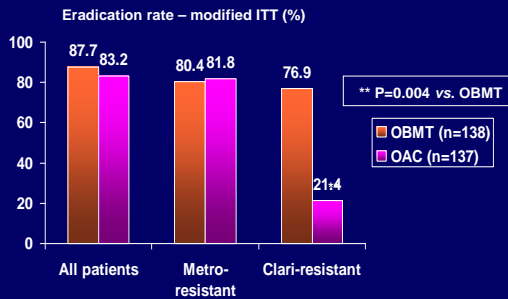
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### “Single-triple” capsule & PPI or triple therapy for *H. pylori* infection



Laine et al., *Am J Gastroenterol* 2003; 98: 562

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Session 1A: The Upper Gut: *H. pylori* 2009:  
When to Test, How to Test and How to  
Treat

**Clarithromycin and Metronidazole:  
Any previous exposure increases resistance**

- 125 pts infected with *Hp* from Alaska
  - 30% Clari-R, 66% Metro-R, 29% Dual-R
  - Clarithromycin resistance
    - › Previous macrolide 92% in those with Clari-R vs. 57% in those with Clari-S (p<0.001)
    - › Likelihood of resistance related to number of courses of macrolide
    - › Rx failed in 77% with Clari-R vs 13% with Clari-S strains
  - Metronidazole resistance
    - › Previous Rx 60% vs. no previous Rx 10% (p<0.001)
    - › Rx failed in 11% with Met-R vs 38% with Met-S strains

McMahon. Ann Intern Med 2003;139:463

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**What is Sequential Therapy?**

Drugs	Frequency	Duration
PPI + Amoxicillin 1 gm	BID	5 d.
PPI, Clarithromycin 500 mg, Tinidazole 500 mg	BID	5 d.

Zullo. et al. Aliment Pharmacol Ther 2003;17:719

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**Meta-analysis of Sequential vs. Triple therapy for *H. pylori***

- 10 RCTs
- Publication bias, only 1 DB, most Italian

Metric	Sequential Rx (n = 2747)	Triple Rx (n = 1363)
Cure Rate	94	77
Clari-R	82	41
Adherence	97	97

Jafri et al. Ann Int Med 2008;148.

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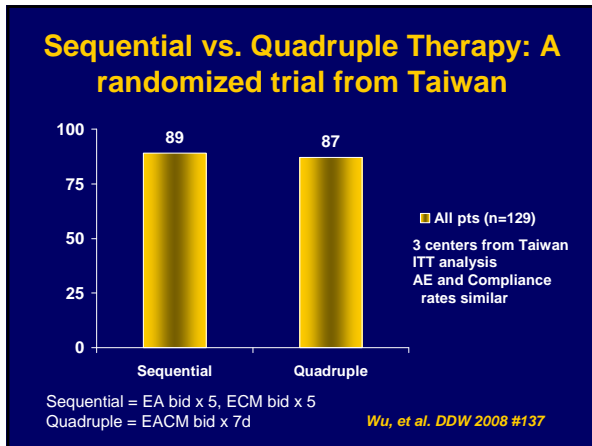
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Session 1A: The Upper Gut: *H. pylori* 2009:  
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- ### Sequential Therapy for *Helicobacter pylori*
- **Bottom line:** Sequential therapy is at least as good and may be superior to triple therapy.
  - Greatest benefit appears to be in those with Clari-R *Hp*
  - Not clear if drugs need to be given sequentially
  - Complexity is a concern
  - Sequential therapy requires validation in the US before it can be recommended as standard first-line therapy

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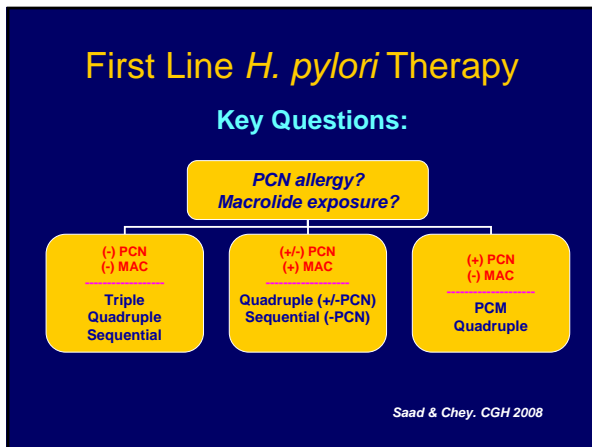
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## Rescue Therapy for *H. pylori*

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## Rescue Therapy for *H. pylori*

- Do not use the same antibiotics
- Treat for 10-14 days
- Role of culture and sensitivity testing?

Saad & Chey. Gastroenterol Hepatol Ann Rev 2006

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## Salvage Therapies for Persistent *H. pylori* infection

Bismuth Quadruple Therapy	Frequency	Duration
PPI	QD	7-14 d.
Tcn, bismuth subsalicylate, metronidazole	QID	

Levofloxacin Triple Therapy		
PPI, Amoxicillin 1 gm	BID	10-14 d.
Levofloxacin 500 mg	QD	

Chey and Wong, Am J Gastroenterol 2007;102:1808

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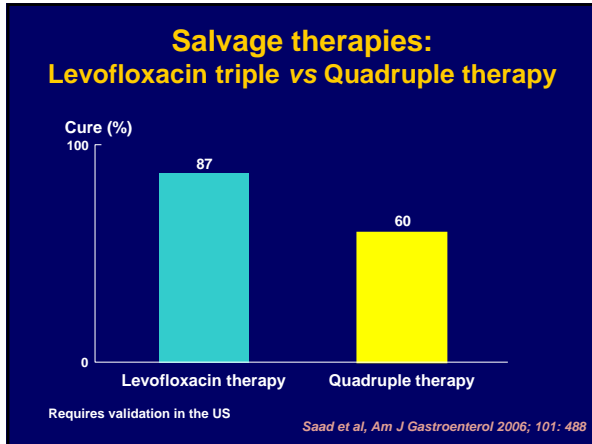
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Session 1A: The Upper Gut: *H. pylori* 2009:  
When to Test, How to Test and How to  
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- Key Management Points for *H. pylori***
- Only test if there is an indication for treatment
  - The choice of diagnostic test depends upon the need for EGD, performance and cost of specific tests, and the prevalence of *H. pylori*
  - Follow-up testing should be performed >4 weeks after therapy
  - Therapy should consist of 3 or 4 drugs given for 7-14 days
    - Potential role for probiotics?
  - Compliance and antibiotic resistance influence the success of therapy

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