Helicobacter pylori and gastritis treatment

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Peptic ulceration
Management of chronic relapsing peptic ulceration - the past
Management of peptic ulceration - the past
Management of chronic peptic ulceration - the present

*H. pylori* eradication therapy

PPI (e.g. omeprazole 20 mg bd)

+ ANTIBIOTICS (2-3)
Management of chronic peptic ulceration - the present

Eradication of *H. pylori*

- Heals ulcers
  (Lam, 1997)
- Prevents recurrence
  (Marshall, 1988; Rauws 1989; Graham 1990)

Cures peptic ulcer disease
Management of chronic peptic ulceration - the present

The present is now the recent past!
Management of *H. pylori* infection in 2019

- Who to treat
- How to treat
Management of *H. pylori* infection


ACG Clinical Guideline: Treatment of *Helicobacter pylori* infection. Am J Gastro 2017;112:212-238


Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. NICE 2014 and 2019 nice.org.uk/guidance/cg184

Suspected cancer: recognition and referral. NICE 2015 and 2019 nice.org.uk/guidelines/ng12
Eradication of *Helicobacter pylori* is indicated to treat:

- Duodenal ulcer
- Gastric ulcer
Eradication of *Helicobacter pylori* is indicated to treat:

- Duodenal ulcer
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- Gastric MALT lymphoma
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Isaacson and Wright, Cancer 1983;52:1410
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- Functional dyspepsia
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So….sensible to test for *H. pylori* and treat in people with uninvestigated dyspepsia
Eradication of *Helicobacter pylori* is indicated to treat:

- Duodenal ulcer
- Gastric ulcer
- Gastric MALT lymphoma
- Functional dyspepsia
- Uninvestigated dyspepsia (If alarm symptoms or treatment-resistant dyspepsia and age >55 refer for endoscopy to exclude upper GI cancer)
Eradication of *Helicobacter pylori* is indicated to treat:

- Duodenal ulcer
- Gastric ulcer
- Gastric MALT lymphoma
- Functional dyspepsia
- Uninvestigated dyspepsia
- Some specialists will treat *H. pylori* in unexplained iron deficient anaemia, unexplained B12 deficiency or chronic idiopathic thrombocytopenic purpura
Eradication of *Helicobacter pylori* in aspirin and NSAID users:
Eradication of *Helicobacter pylori* in aspirin and NSAID users:

- *H. pylori* and aspirin/NSAIDs are independent causes of peptic ulceration

*SOL* Test for and treat *H. pylori* in aspirin/NSAID users with a history of peptic ulceration (or dyspepsia)
Eradication of *Helicobacter pylori* in intending aspirin and NSAID users:

- Treatment of *H. pylori* before starting NSAIDs reduces risk of NSAID ulcers. Unclear for low dose aspirin (HEAT trial ongoing)

- *BUT* co-prescribing PPIs with NSAIDs is much more effective at reducing risk of ulceration

**SO** Concentrate on co-prescribing PPIs to prevent NSAID ulcers (particularly if ulcer history) .... but test for and treat *H. pylori* too.
Eradication of *Helicobacter pylori* for prevention of gastric adenocarcinoma
GASTRIC CANCER IS CAUSED BY AN INFECTION
Eradication of *Helicobacter pylori* in prevention of gastric cancer

- *H. pylori* treatment reduces the risk of gastric cancer
- This is most effective if it is done before the development of gastric atrophy (for example in younger patients)
Eradication of *Helicobacter pylori* in prevention of gastric cancer

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- But it is also effective in other populations, for example to prevent recurrence in endoscopically resected early gastric cancer
Eradication of *Helicobacter pylori* in prevention of gastric cancer

- *H. pylori* treatment reduces the risk of gastric cancer
- This is most effective if it is done before the development of gastric atrophy
- But it is also effective in other populations, for example to prevent recurrence in endoscopically resected early gastric cancer
- *H. pylori* population treatment is recommended in countries with a high population risk of gastric cancer, for example Japan and north China (Sugano et al, Kyoto global consensus on *H. pylori* gastritis. Gut 2015;64:1353-67)
Eradication of *Helicobacter pylori* in prevention of gastric cancer in Europe - screen and treat individuals at increased risk of gastric cancer

- First degree relatives of gastric cancer patients
- Patients with treated gastric neoplasia
- Patients with high risk gastritis (e.g. atrophy, intestinal metaplasia, dysplasia)
- Patients coming from a high incidence area of gastric cancer
Eradication of *Helicobacter pylori* in prevention of gastric cancer in Europe - screen and treat individuals at increased risk of gastric cancer

What if a patient has already been tested by someone else and is known to have *H. pylori*?
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What if a patient has already been tested by someone else and is known to have *H. pylori*?

- In practice, have an informed discussion with the patient.....and most will end up being treated.
Treatment of H. pylori in 2019
First-line treatment of \textit{H. pylori} until last 3-4 years

One or two week triple therapy
PPI (e.g. omeprazole 20 mg bd)
+ clarithromycin 500 mg bd
+ amoxycillin 1g bd OR metronidazole 400mg bd
First-line treatment of *H. pylori* until last 3-4 years

**One or two week triple therapy**

- PPI (e.g. omeprazole 20 mg bd)
- + clarithromycin 500 mg bd
- + amoxycillin 1g bd OR metronidazole 400mg bd

**Two weeks better (5-10%)**

**High dose PPI better (6-10%)**

or esomeprazone
or rabeprazole
Antibiotic-resistant *H. pylori* is now on the WHO list of dangerous antibiotic-resistant pathogens
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Due to increasing clarithromycin resistance
Treatment of *H. pylori* – principles in 2019

• Success dependent on
  – Antibiotic resistance of *H. pylori* strain
    • Clarithromycin resistance rates 5-60% depending on country and this almost invariably leads to treatment failure for a clarithromycin containing regimen
    • Metronidazole “resistance” very common but this is only partial and metronidazole still useful
    • Levofloxacin resistance increasing
    • Amoxycillin and tetracycline resistance very rare
  – Careful patient compliance
    • If fail therapy, very commonly acquire resistance
First-line treatment of *H. pylori* in 2019

**Step 1**

What is the likelihood of clarithromycin resistance in the patient’s strain?

- Primary resistance rates of *H. pylori* in that community (*usually unknown!*)
- Personal exposure of patient to clarithromycin or other well-absorbed macrolide
First-line treatment of *H. pylori* in 2019

Where clarithromycin resistance rates <15% and no previous clarithromycin exposure (supposedly UK and some other north European countries)

One or two week triple therapy

PPI (e.g. omeprazole 20-40 mg bd)  
+ clarithromycin 500 mg bd  
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First-line treatment of *H. pylori* in 2019

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One or two week triple therapy

PPI (e.g. omeprazole 20-40 mg bd)

+ clarithromycin 500 mg bd

+ amoxycillin 1g bd OR metronidazole 400mg bd
First-line in other countries, second-line treatment in UK

- PPI and bismuth-based quadruple therapy for 2 weeks
  - PPI full dose bd
  - Bismuth subsalicylate ii qds
  - Tetracycline HCl 500mg qds
  - Metronidazole 400mg tds

Gene, APT 2003;17:1137
Malfertheiner, Gut 2007;56:772
Alternative first-line in countries with high prevalence of clarithromycin resistance

- Non bismuth quadruple therapy
  - PPI + clarithromycin + amoxycillin + metronidazole for 14 days
Second or third-line treatment

- Levofloxacin, 500mg bd
- Amoxycillin, 1g bd
- PPI, full dose bd
- (+ bismuth subsalicylate ii qds ?)

- 10-14 days
- 80% success

Gisbert, APT 2006;23:35
Third-line treatment or if reason to suspect multiple antibiotic resistance

• Endoscopy with gastric mucosal biopsy, culture and antibiotic sensitivity testing
Third-line treatment or if reason to suspect multiple antibiotic resistance

- Endoscopy with gastric mucosal biopsy, culture and antibiotic sensitivity testing

National Infection Service Reference Laboratories Colindale; Bacteriology Reference Department User Manual, Version 9, 2018
Q-Pulse BRDW0078
GBRU@phe.gov.uk
www.gov.uk/phe
Options in difficult to treat patients

- Refer (endoscopy and sensitivity testing and/or other treatment regimens available)

- Maintain on PPIs (will suppress symptoms due to *H. pylori* and reduce risk of ulceration)
Close compliance is KEY

• Clear instructions to patient, importance stressed by prescriber and written if possible

• Patient should continue despite side-effects (stop if severe diarrhoea or true allergic reaction)
Checking treatment success
Checking treatment success

• Stop PPIs for two weeks before testing, preferably 4 weeks
• No antibiotics or bismuth for 4 weeks
• H2 receptor antagonists acceptable, but better without
Checking treatment success

- Urea breath test or stool antigen test
- Or endoscopy-based test if needs endoscopy anyway, for example GU follow-up (but often on PPI so still need non-invasive test after this)
- NOT serology
Special cases

• Simple uncomplicated dyspepsia
  – Most doctors do not check for success of treatment

• Where you REALLY need to succeed (ulcer bleeds and perforations, MALT lymphoma)
  – Always check
Conclusions

- Treatment indications for *H. pylori* treatment are widening
- In many countries everyone with *H. pylori* is treated
- Treatment should be based on personal risk of antibiotic resistance (especially clarithromycin)
- PPI and bismuth based quadruple therapy is the recommended first-line in most of the world
- Close compliance of the patient with treatment is vital
Use of tests: when and how?

At endoscopy
- Biopsy urease (CLO) test
- Histology (needs special stains)
- Culture (only if need antibiotic sens)

Non-invasive
- Urea breath test } interchangeable
- Stool antigen test } 
- Serology (not near patient kits)