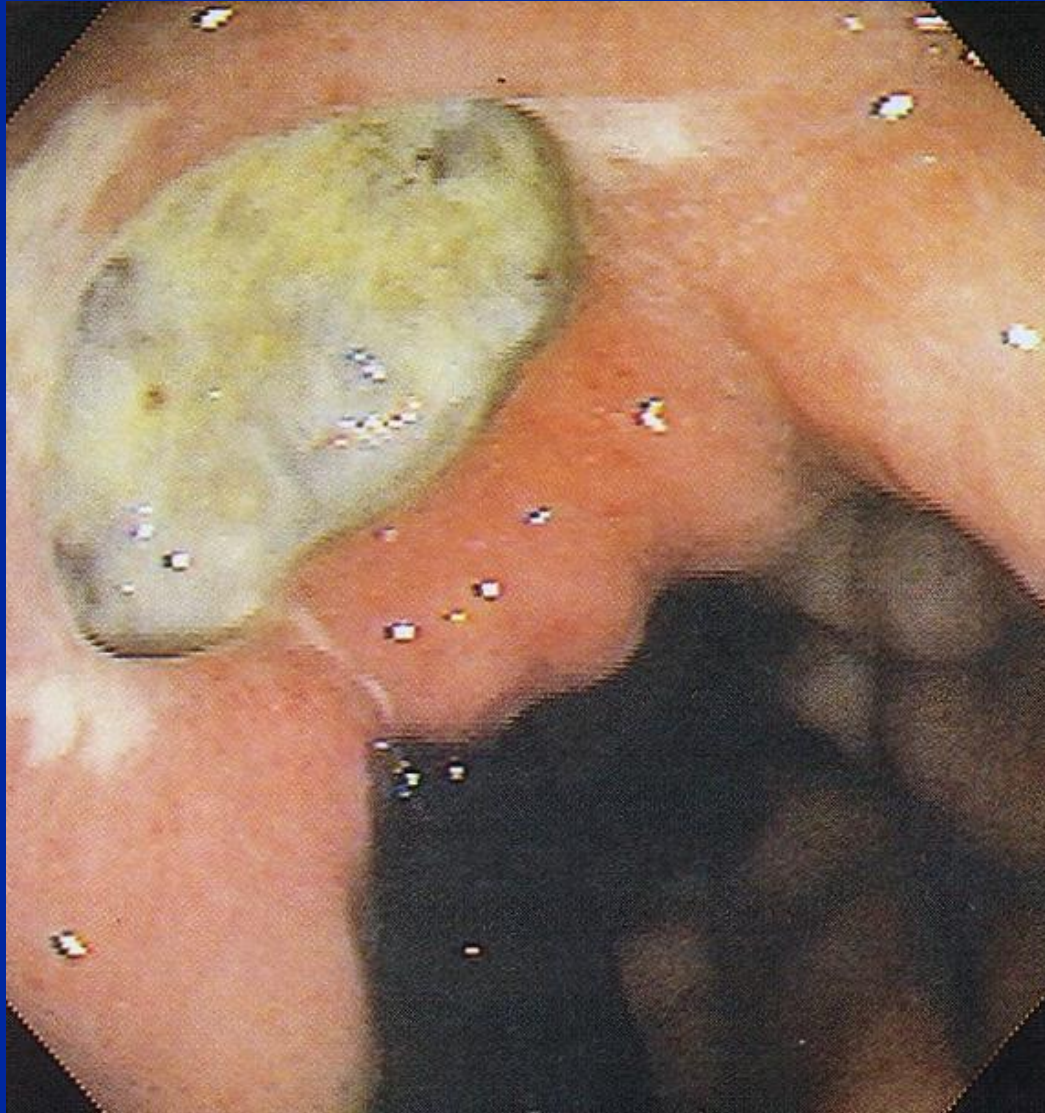


# *Helicobacter pylori* and gastritis treatment

**John Atherton**

**University of Nottingham and  
Nottingham University Hospitals NHS Trust**

# 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

Management of *Helicobacter pylori* infection – the Maastricht V / Florence Consensus Report. Gut 2017;66:6-30

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

Test and treat for *Helicobacter pylori* (HP) in dyspepsia. Public Health England 2017 [www.gov.uk/phe](http://www.gov.uk/phe)

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

Suspected cancer: recognition and referral. NICE 2015 and 2019 [nice.org.uk/guidelines/ng12](http://nice.org.uk/guidelines/ng12)

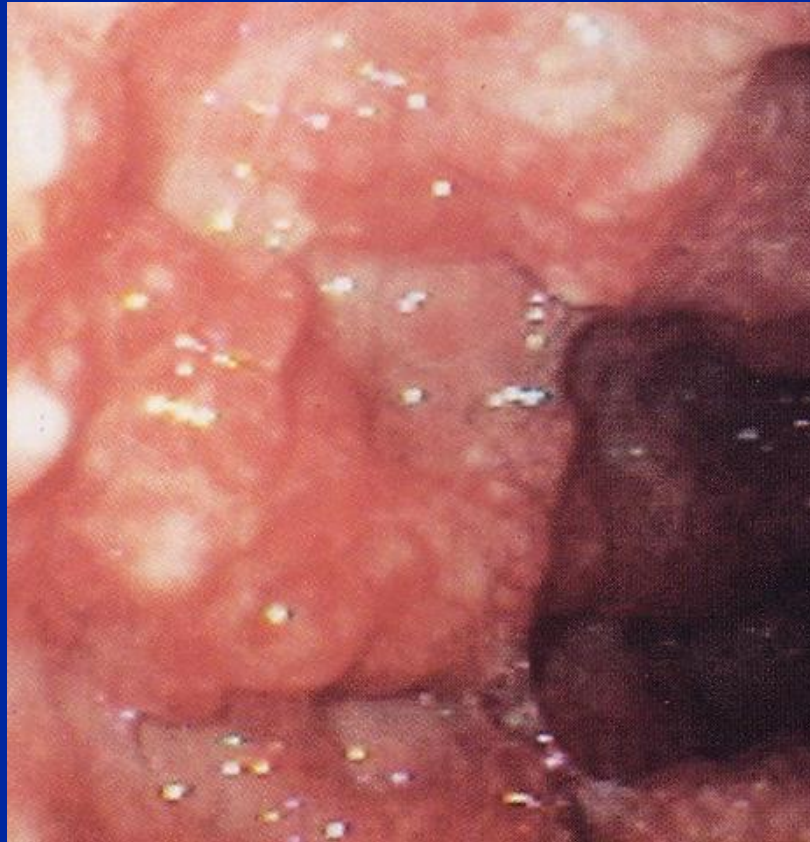
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- **Gastric ulcer**

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# Gastric MALT lymphoma



Isaacson and Wright, Cancer 1983;52:1410

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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 thrombocytopaenic 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**

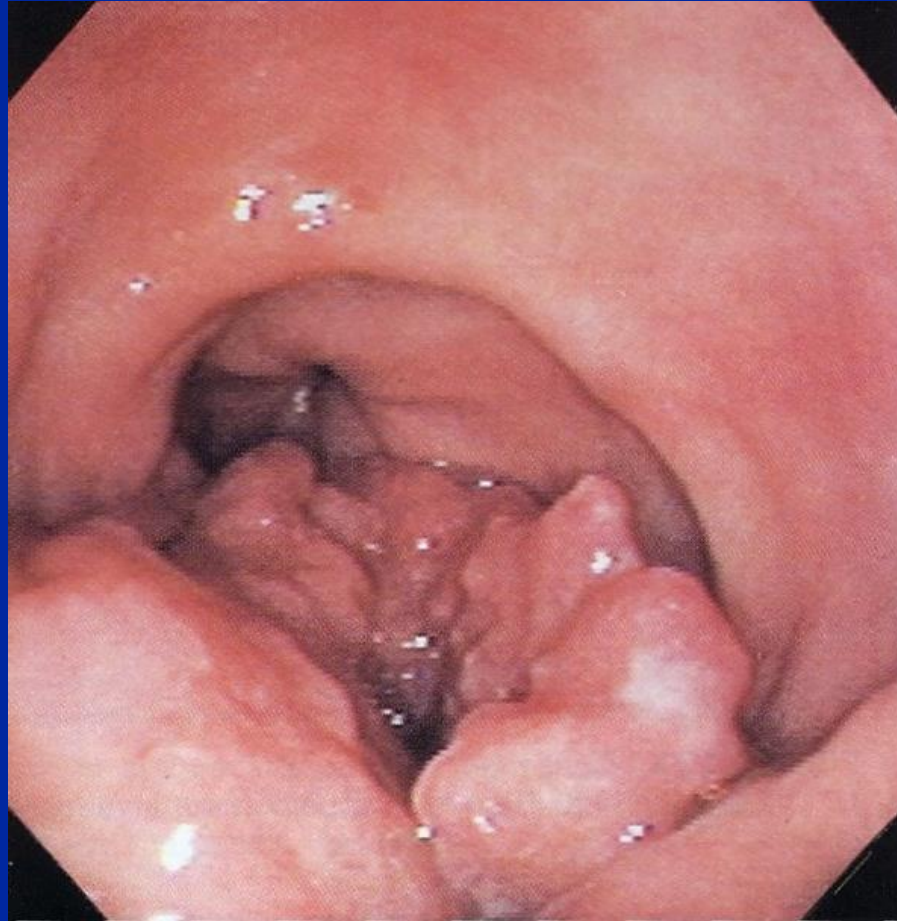
***SO* Test for and treat *H. pylori* in aspirin/NSAID users with a history of peptic ulceration (or dyspepsia)**

# **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)



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# 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* ?**

# **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* ?**

- 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 *H. pylori* until last 3-4 years

## One or two week triple therapy

PPI (e.g. omeprazole 20 mg bd)

+ clarithromycin 500 mg bd

+ amoxicillin 1g bd OR metronidazole 400mg bd



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Two weeks better (5-10%)

High dose PPI better (6-10%) or esomeprazole  
or rabeprazole

**Antibiotic-resistant *H. pylori* is  
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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**
    - **Amoxicillin 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)

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# 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

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# 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 + amoxicillin + metronidazole for 14 days**

# Second or third-line treatment

- **Levofloxacin, 500mg bd**
- **Amoxicillin, 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**

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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](http://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

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- **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**                    }  
**Stool antigen test**                } interchangeable

**Serology (not near patient kits)**