Should *H. pylori* infection be eradicated in most infected patients?

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H. pylori

Associated with:

- chronic gastritis
- peptic ulcer
- gastric mucosa associated lymphoid tissue (MALT) lymphoma
- associated with increased risk of cancer
- Majority of infected population remains asymptomatic
Indications for *H. pylori* testing

- Documented gastric and duodenal ulcer.
- History of peptic ulcer.
- Gastric Mucosa-Associated Lymphoma.
- After resection of early gastric adenocarcinoma.
- First-degree relative of a patient with gastric cancer.
- Dyspepsia in primary care setting.
Dyspepsia

Statement 1: A test-and-treat strategy is appropriate for uninvestigated dyspepsia in populations where the \textit{H pylori} prevalence is high (≥20%).

Evidence level: 1a  Grade of recommendation: A

Statement 3: \textit{H pylori} eradication produces long-term relief of dyspepsia in one of 12 patients with \textit{H pylori} and functional dyspepsia; this is better than any other treatment.

Evidence level: 1a  Grade of recommendation: A
Dyspepsia: Epidemiology

- Prevalence is 25% - 40% per year
- Accounts for 5% of all PCP referrals
- Accounts for 50% of gastroenterologists workload

Penston et al. 1996
### Long term PPIs Users

**Statement 10a:** Long-term treatment with PPIs in *H pylori*-positive patients is associated with the development of a corpus-predominant gastritis. This accelerates the process of loss of specialized glands, leading to atrophic gastritis.

| Evidence level: 1c | Grade of recommendation: A |

**Statement 10b:** Eradication of *H pylori* in patients receiving long-term PPIs heals gastritis and prevents the progression to atrophic gastritis. However, there is no evidence that this reduces the risk of gastric cancer.

| Evidence level: 1b | Grade of recommendation: A |
Long term PPIs Users

- Proton pump inhibitors (PPIs) are among the most widely used agents in the world
- Between 0.5% and 5.0% of the population used antisecretory medications on a long-term basis.

Aliment Pharmacol Ther. 2009 Oct;30(7):725-32
Do NSAID and H pylori infection induce ulcers by independent mechanisms?

- **H. Pylori**
  - Cytotoxins LPS, HSP Enzymes, etc.
  - Inflammatory cascade
  - Neutrophils
  - Lymphocytes Cytokines, etc.

- **NSAIDs**
  - Topical effect +
  - Systemic effect
  - Mucus
  - Bicarbonate
  - Blood flow
  - Cell restitution
  - Neutrophils

- Mucosal damage and ulceration
<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted OR (95% CI)</th>
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<tbody>
<tr>
<td>H. Pylori infection</td>
<td>4.69 (2.02 –10.91)</td>
</tr>
<tr>
<td>Ulcer history</td>
<td>15.2 ( 3.8 – 60.1 )</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>4.26 (1.79–10.40)</td>
</tr>
<tr>
<td>Antisecretory therapy</td>
<td>0.10 (0.02 – 0.31)</td>
</tr>
<tr>
<td>Nitrovasodilator therapy</td>
<td>0.26 (0.11 – 0.56 )</td>
</tr>
<tr>
<td>Calcium channel blocker therapy</td>
<td>2.54 (1.25 – 5.14 )</td>
</tr>
</tbody>
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Adjusted odds ratios (OR) of bleeding peptic ulcers among low-dose aspirin users with potential risk factors

*Aliment Pharmacol Ther 2002*
**Statement 7:** *H pylori* infection is associated with an increased risk of uncomplicated and complicated gastroduodenal ulcers in NSAID and low-dose aspirin (acetosalicylic acid (ASA)) users.

<table>
<thead>
<tr>
<th>Evidence level: 2a</th>
<th>Grade of recommendation: B</th>
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</table>

**Statement 8:** *H pylori* eradication is **beneficial** before starting NSAID treatment. It is mandatory in patients with a peptic ulcer history.

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<thead>
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<th>Evidence level: 1b</th>
<th>Grade of recommendation: A</th>
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However, *H pylori* eradication alone does not reduce the incidence of gastroduodenal ulcers in patients already receiving long-term NSAID treatment. They require continued PPI treatment as well as eradication treatment.

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<th>Grade of recommendation: A</th>
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**Statement 9:** Testing for *H pylori* should be performed in ASA users **with a history of gastroduodenal ulcer**. The long-term incidence of peptic ulcer bleeding is low in these patients after receiving eradication even in the absence of gastroprotective treatment.

<table>
<thead>
<tr>
<th>Evidence level: 2b</th>
<th>Grade of recommendation: B</th>
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Data from the Nurses Health Study showed that:
42% of women age 51 years or older used NSAID at least weekly.

4799 people surveyed.
807 (17%) reported NSAID use

Of the 258 exclusive OTC NSAID users, the median duration of use was 5 years,
18 (7%) reported using these agents for less than 2 years, 40 (16%) were reported using agents for 15 or more years. Sixty-nine respondents (27%) used OTC NSAID daily

Patterns of Use and Public Perception of Over-the-Counter Pain Relievers:
Focus on NSAIDs

J Rheumatol 2005;32:2218–24
Aspirin use among adults aged 40 and older in the United States: results of a national survey.

1299 adults aged 40 or older
Mean age: 55.9

Current regular aspirin use for CVD prevention was reported by 41% of respondents.


Daily or every-other-day aspirin use was reported by 36.2% of participants. Aspirin intake among those with CVD and diabetes was 82.8% and 62.6%, respectively.

Family practice patients' use of acetylsalicylic acid for cardiovascular disease prevention

Overall, 39.8% of patients reported taking ASA regularly.

Multistep Pathway in the Pathogenesis of Gastric Cancer
Statement 1: *H pylori* infection is the most consistent risk factor for gastric cancer. Its elimination is therefore the most promising strategy to reduce the incidence of gastric cancer.

Evidence level: 1a  
Grade of recommendation: A

Statement 8: *H pylori* eradication abolishes the inflammatory response and slows or may arrest the progression of atrophy. In some cases it may reverse atrophy.

Evidence level: 1a  
Grade of recommendation: A

Statement 9: There is strong evidence that *H pylori* eradication reduces the risk of gastric cancer development.

Evidence level: 1c  
Grade of recommendation: A
Relationship between gastric cancer and *H. pylori* infection: A prospective study

*Helicobacter pylori* eradication to prevent gastric cancer in a high-risk region of China.

Kaplan-Meier Analysis of Gastric Cancer Development With Respect to Treatment in Participants With No Atrophy, Intestinal Metaplasia, or Dysplasia

Wong et al (JAMA 2004;291:187)
Reduction of gastric cancer incidence: 25%
rate ratio: 0.753, 0.372-1.524

Lee, GUT 2012
# Gastric cancer prevention

**Statement 13:** A screen-and-treat strategy of *H pylori* should be explored in communities with a significant burden of gastric cancer

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<th>Evidence level: 2c</th>
<th>Grade of recommendation: A</th>
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**Statement 16:** *H pylori* eradication to prevent gastric cancer should be considered in the following:

- first-degree relatives of family members with a diagnosis of gastric cancer;
- patients with previous gastric neoplasia already treated by endoscopic or subtotal gastric resection;
- patients with a risk of gastritis: severe pan-gastritis, corpus-predominant gastritis, severe atrophy;
- patients with chronic gastric acid inhibition for more than 1 year;
- patients with strong environmental risk factors for gastric cancer (*heavy smoking*, high exposure to dust, coal, quartz, cement and/or work in quarries);
- *H pylori*-positive patients with a fear of gastric cancer.

| Evidence level: 1a to 4 | Grade of recommendation: A |
Statement 17: *H pylori* eradication to prevent gastric cancer should be undertaken in populations at high risk.

Evidence level: 1c

Grade of recommendation: A

Incidence of Stomach cancer: ASR (World)-Male (All ages)

<table>
<thead>
<tr>
<th>Incidence Range</th>
<th>Color</th>
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<tbody>
<tr>
<td>&lt; 14.9</td>
<td>Green</td>
</tr>
<tr>
<td>&lt; 28.7</td>
<td>Light Blue</td>
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<tr>
<td>&lt; 42.5</td>
<td>Red</td>
</tr>
<tr>
<td>&lt; 56.3</td>
<td>Light Red</td>
</tr>
<tr>
<td>&lt; 70.0</td>
<td>Black</td>
</tr>
</tbody>
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GLOBOCAN 2000
Asia-Pacific consensus guidelines on gastric cancer prevention.

**Pockets with a high or intermediate risk of gastric cancer**

- **Patients with dyspepsia**
  - Investigate dyspepsia
  - Qualified reassurance; perform 2nd test on individualized basis.

- **Asymptomatic individuals (18–60 years)**
  - One-off screening with locally validated serology test for *H. pylori*
    - Positive: Eradicate *H. pylori*
      - One-off treatment according to local guideline; e.g. 1-week triple therapy.
    - Negative: Continue program of gastric cancer surveillance based on national guidelines.

On a case-by-case basis, one may assess the success of *H. pylori* eradication by using non-serological tests at least 4 weeks post-therapy and institute a second-line therapy in the event of treatment failure.
Summary: populations with indication for *H. pylori* eradication

- Dyspepsia: 25-40%
- Long term PPI users
- Low-dose aspirin users: 40%
- NSAIDs Users: 20%
- Communities with high risk of gastric cancer
Conclusion: Globally, *H. pylori* infection should be eradicated in most infected patients.

Thank You