**Introduction**

The elderly often seek medical attention because of gastroduodenal diseases. *Helicobacter pylori* (*H. pylori*) infection is associated with several gastroduodenal diseases and its prevalence increases with age worldwide. It is estimated that 10–15% of infected patients will have peptic ulcer disease and 1% of patients will have gastric cancer or mucosa-associated lymphoid tissue lymphoma. Notably, the most severe clinical outcomes, i.e., gastric cancer and complicated peptic ulcer diseases, usually occur in elderly patients. Thus the test-and-treatment strategy is not recommended for elderly patients with uninvestigated dyspepsia. However, biopsy specimens for the rapid urease test and histology should be taken from both the antrum and corpus to increase the detection rate in elderly patients, especially in those with atrophic gastritis. The urea breath test may increase the detection rate if the rapid urease test or histology are negative in elderly patients with atrophic gastritis. Standard triple therapy and sequential therapy can achieve satisfactory eradication rates for *H. pylori* in elderly patients. Elderly patients with peptic ulcers may have a similar benefit from treatment of *H. pylori* infection as non-elderly patients. Eradication of *H. pylori* infection may also lead to improvement in histologic grading of gastritis, but the risk of gastric cancer cannot be completely reduced, especially in patients with existing premalignant lesions.


Key Words: aged, gastrointestinal diseases, geriatrics, *Helicobacter pylori*
infected patients. Thus, we should pay more attention to the diagnosis and treatment of H. pylori infection in elderly patients. In this article, papers published in English were searched in PubMed using the key words “H. pylori”, “elderly”, “geriatrics”, “diagnosis”, and “treatment”. The similarities and differences in the diagnosis and treatment of H. pylori infection between elderly and non-elderly patients will be discussed.

H. pylori-associated Gastroduodenal Diseases in the Elderly with Gastritis

There are three major phenotypes of gastritis after prolonged H. pylori infection, including mild pangastritis, corpus-predominant gastritis, and antrum-predominant gastritis. The different phenotypes of gastritis are also associated with different clinical outcomes after H. pylori infection. While patients with corpus-predominant gastritis usually have gastric atrophy and hypochlorhydria and increased risk of developing gastric cancer, patients with antrum-predominant gastritis usually have a higher secretion of gastric acid and an increased risk of duodenal ulcer disease. In contrast, patients with mild pangastritis usually do not have clinically significant diseases. The different clinical outcomes are probably related to the interactions between bacterial virulence and host genetics after prolonged infection and inflammation. However, these three phenotypes of gastritis are not separate entities, as antrum-predominant gastritis may progress to corpus-predominant gastritis or pangastritis with time. Notably, both atrophic gastritis and intestinal metaplasia are strongly associated with H. pylori and not with age per se. Advancing age has no influence on gastric acid secretion in H. pylori-negative subjects. However, gastric acid secretion decreases with age in H. pylori-positive subjects. The grades of atrophy and intestinal metaplasia are also significantly higher in H. pylori-positive than in H. pylori-negative subjects. It has been reported that eradication of H. pylori infection in elderly patients can lead to a significant decrease in gastritis activity as compared with no change in histology in patients with continuing infection. Eradication of H. pylori infection in elderly patients with advanced atrophic gastritis may also lead to a significant improvement in the mean histologic scores of inflammation, atrophy and intestinal metaplasia, after a mean follow-up of 2.5 years after eradication therapy.

Altogether, evidence indicates that cure of H. pylori infection may lead to improvement of gastritis in elderly patients as it does in non-elderly adult patients.

Peptic Ulcer Disease

Peptic ulcer disease (PUD) is a common disease worldwide with a lifetime prevalence of about 10%. Most PUDs are related to H. pylori and NSAID use. Previous studies have shown that H. pylori infection is present in 90–100% of patients with duodenal ulcer and in 60–90% of patients with gastric ulcer. It is associated with at least a three- to fourfold increased risk of PUDs in elderly and non-elderly patients. In elderly patients, however, the proportion of NSAID-related peptic ulcer is higher than in non-elderly patients. Several studies have reported that the prevalence of H. pylori infection in elderly patients ranges from 58% to 78%. In a study conducted in 520 elderly patients with PUD, Pilotto et al. reported that 39% of patients with gastric ulcers and 24% of patients with duodenal ulcers had recent NSAID use (alone or in combination with H. pylori infection). Eradication of H. pylori infection in adult patients with a peptic ulcer can dramatically reduce the ulcer recurrence risk to 5–20% at 1 year. A recent meta-analysis also revealed that H. pylori eradication therapy was superior to no treatment in preventing duodenal ulcer recurrence (relative risk, 0.19) and gastric ulcer recurrence (relative risk, 0.31). This benefit was also observed in elderly patients. Pilotto et al. reported that eradication of H. pylori can reduce the ulcer recurrence rate from 41.6% to 2.2% among elderly patients with H. pylori-associated PUD. Symptom relief was also observed in over 85% of patients after treatment of this infection.

Whether eradication of H. pylori can prevent the occurrence of peptic ulcers in aspirin/NSAID users is also an important issue to be addressed in the elderly. H. pylori infection and aspirin/NSAID use have been reported to have synergistic effects in the development of peptic ulcers and ulcer bleeding in a meta-analysis. Eradication of H. pylori was also shown to reduce the incidence of peptic ulcers in patients receiving NSAIDs. In the eradicated group, Vergara et al. found that peptic ulcers occurred in 7.4% (34/459) patients, as compared with 13.3% (64/480) in the non-eradicated group. Sub-analyses further showed that the risk reduction was more significant (odds ratio, 0.26).
in NSAID-naïve patients than in previously treated patients. However, a study performed in elderly patients showed that maintenance proton pump inhibitor (PPI) therapy for preventing ulcers appeared to be more effective than *H. pylori* eradication therapy. In summary, *H. pylori* eradication may prevent peptic ulcers in naïve users of NSAID, but eradication therapy alone is not sufficient to prevent NSAID-related ulcer disease completely in chronic NSAID users. PPI maintenance therapy is helpful in the prevention of ulcer recurrence in chronic NSAID users who have already experienced peptic ulcer and/or ulcer bleeding.

**Gastric Cancer**

Gastric cancer is the second most common cause of cancer-related deaths worldwide. Several nested case control studies and meta-analyses have reported a two- to sevenfold increased risk of gastric cancer in *H. pylori*-infected patients. In animal models, Watanabe et al. demonstrated that 37% of Mongolian gerbils developed gastric cancer 62 weeks after oral inoculation of *H. pylori*. A prospective observational study in Japan revealed that 2.9% of the *H. pylori*-infected patients developed gastric cancer over 7.8 years, whereas none of the non-infected subjects developed gastric cancer. An interventional study in China has shown a 37% risk reduction after 7.5 years in patients who received *H. pylori* eradication therapy. However, the timing of eradication should be as early as possible before the development of premalignant lesions (e.g., in atrophic gastritis, intestinal metaplasia, and dysplasia) in which many types of molecular damage have become irreversible. This was supported by two recent animal model studies. Lee and colleagues reported that although the severity of dysplasia in *H. pylori*-infected transgenic mice overexpressing amidated gastrin (INS-GAS mice) could be reduced after *H. pylori* eradication at 8, 12 and 22 weeks postinfection (WPI), the development of gastric intraepithelial neoplasia was completely prevented only in mice that received *H. pylori* eradication at 8 WPI. Romero-Gallo et al. also found that eradication of *H. pylori* 8 WPI resulted in attenuation, but not in complete prevention of premalignant and malignant lesions, whereas none of the Mongolian gerbils treated with antibiotics at 4 WPI developed gastric cancer. A recent cost-effectiveness analysis also found that early *H. pylori* eradication once in a lifetime at age 30 years seemed more cost-effective than the surveillance strategy. Nevertheless, in a recent consensus meeting on gastric cancer prevention, most experts agreed that eradication of *H. pylori* to prevent gastric cancer should not be precluded in the elderly. However, further studies are warranted to support this viewpoint.

**Non-ulcer Dyspepsia**

The role of *H. pylori* in the pathogenesis of non-ulcer dyspepsia (NUD) remains controversial. Although some studies reported that *H. pylori*-infected patients were more likely to have ulcer-like dyspepsia, other studies failed to find such an association. Randomized controlled trials also met with conflicting results, probably related to the lack of a validated dyspepsia questionnaire in the outcome assessments, short follow-up periods, and inadequate *H. pylori* eradication regimens. However, a recent meta-analysis reported that there was a 10% relative risk reduction of NUD in an *H. pylori* eradication group as compared with placebo, and the number needed to treat to cure one case with NUD was 14. It was concluded that *H. pylori* eradication therapy has a small but statistically significant effect in *H. pylori*-positive NUD. In elderly patients, Pilotto et al. reported an improvement of dyspeptic symptoms in 70% of patients with chronic gastritis 2 months after treatment. Catalano et al. also reported a significant reduction in symptoms after eradication therapy in 126 patients with functional dyspepsia. However, it should be emphasized that endoscopy should be used instead of the test-and-treat strategy for elderly patients with dyspepsia, because the prevalence of gastroesophageal malignancy was higher in these patients.

**Gastroesophageal Reflux Disease**

The inverse relationships between *H. pylori* infection and gastroesophageal reflux disease (GERD) have been reported in adult patients, but their associations remain controversial. A meta-analysis examining 20 case-control studies evaluating the prevalence of *H. pylori* in patients with GERD showed that patients with reflux disease from the Far East, rather than those from Western countries, had a lower prevalence of *H. pylori*.
infection. Controversies also exist regarding whether eradication of H. pylori is likely to aggravate the severity of preexisting GERD or increase the risk of new-onset GERD. In an elderly population, Pilotto et al. reported that the clinical response to PPI therapy for GERD was not influenced by eradication therapy. The result was in agreement with a pH study where there was no significant change in the percentage of total time of esophageal pH < 4 after eradication of H. pylori. Therefore, the decision of whether to eradicate H. pylori infection or not should not be influenced by concerns about aggravation of GERD symptoms. On the other hand, it has been reported that long-term acid suppression with a PPI or H2 receptor blockers may affect the pattern and distribution of gastritis. This alteration may lead to the development of corpus-dominant gastritis, the acceleration of loss of specialized glands, and progression of atrophic gastritis. Therefore, it is recommended that H. pylori testing and treatment should be considered in patients receiving long-term PPI use.

**Diagnosis of H. pylori in the Elderly**

Diagnostic tests for H. pylori infection include invasive tests that require endoscopy and noninvasive tests that do not need endoscopy. Invasive tests include histologic examination, a rapid urease test, and cultures. Noninvasive tests include serology, a 13C-urea breath test (UBT), a stool antigen test (polyclonal or monoclonal antibody), and immunologic tests (laboratory- and office-based tests and tests on saliva and urine). Histologic examination provides an additional aid for assessing the severity of gastritis and the presence of malignancy or premalignant lesions. The rapid urease test is less expensive than histology and the result can be obtained within 1 hour. Cultures provide the chance to perform an antibiotic susceptibility test, but they are not available in many settings. A serology test is inexpensive and widely available, but its diagnostic accuracy is low (80–84%)2,38. It is helpful to assess H. pylori infection in patients with a bleeding ulcer and conditions associated with low bacterial density (extensive mucosal atrophy). The UBT is an accurate (accuracy > 95%) and readily available noninvasive test2,38. The sensitivity and specificity of the stool antigen test is 91% and 93%, respectively, if the stool sample is stored at −20°C before testing61. However, the sensitivity decreases to 69% if the specimen is stored at room temperature for 2–3 days. After eradication treatment, the UBT or stool antigen test should be employed for confirmation of eradication except in cases that require repeated endoscopy, such as in patients with a gastric ulcer.

There are some specific characteristics for the diagnosis of H. pylori infection in elderly patients. Because of the higher prevalence of gastroesophageal malignancy in elderly patients with dyspepsia, endoscopy is usually indicated in this population57,58. Therefore, the H. pylori test can be done by histologic examination, the rapid urease test or culture of biopsy specimens taken during endoscopy. However, the rapid urease test performed on antral biopsies has a lower sensitivity in patients aged 60 years and older because of the higher prevalence of atrophic gastritis in the elderly. In such conditions, a biopsy may be taken from both the antrum and corpus to increase the detection rate11,13. The sensitivity, specificity and diagnostic accuracy of serology in a study of elderly patients were 74.4%, 59%, and 67%, respectively. The false-negative rate for the stool antigen test is also high in hospitalized elderly patients, probably related to the high frequency of chronic constipation in these patients56. On the other hand, the UBT was reported to have a significantly higher sensitivity (94%), specificity (> 95%) and accuracy (98%) than other tests in the elderly. In a study comparing five diagnostic tests, the authors found that almost one-third of H. pylori infections would have been undetected if the UBT had not been used. Therefore, the UBT may provide the opportunity to detect H. pylori infection in elderly patients with atrophic gastritis who have a negative rapid urease test or histology for H. pylori.

After eradication treatment, it is recommended that elderly patients with a diagnosis of gastric ulcer or MALToma should be evaluated by endoscopy to confirm the healing of the underlying diseases11,13,38. However, elderly patients with mild or moderate gastritis may be assessed by UBT alone. The stool antigen test may be used if the UBT is not available.

**Treatment of H. pylori Infection in the Elderly**

Recommendations for H. pylori eradication in the Maastricht Consensus Report include patients with PUD,
MALToma, atrophic gastritis, post-gastric cancer resection, first-degree relatives of patients with gastric cancer, naive users of NSAIDs, patients receiving long-term maintenance treatment with PPIs, and patients who wish to be tested and treated for *H. pylori*38. The recommended first-line therapy regimens are dependent on the prevalence of antibiotic resistance (Figure)38. In areas with clarithromycin resistance rates less than 15–20% and a metronidazole resistance rate less than 40%, triple therapy with PPI, clarithromycin and metronidazole is recommended. In areas with clarithromycin resistance rates less than 15–20% and a metronidazole resistance rate greater than 40%, triple therapy with PPI, clarithromycin and amoxicillin is recommended. However, in areas with clarithromycin resistance rates greater than 20%, quadruple therapy is recommended as the first-line therapy. However, the eradication rate of the recommended first-line therapy is decreasing, probably related to increased antibiotic resistance rate. Therefore, several alternative first-line therapies, including sequential therapy, levofloxacin-based triple therapy, susceptibility and pharmacogenomic-based triple therapy, have been proposed38.

There are also some special considerations in the treatment of *H. pylori* infection for elderly patients. First, it should be clarified that the recommended regimens are equally effective in elderly patients. As it has been reported that the antibiotic resistance rate to metronidazole and clarithromycin were comparable among elderly and non-elderly patients69 and that most of the clinical trials assessing the efficacy of eradication therapy for *H. pylori* enrolled both elderly and non-elderly patients, it is expected that the results would be applicable to elderly patients. Several studies performed in elderly patients have also demonstrated that PPI-based triple therapy for 1 week is highly effective in geriatric patients11,11. Moshkowitz et al. reported that the eradication rate of a combination of omeprazole, clarithromycin and tinidazole was 92.9%70. Pilotto et al. also reported that the eradication rate of lansoprazole plus two of clarithromycin or metronidazole or amoxicillin were 80–86% in the intention-to-treat (ITT) group55. Dore et al. reported that the eradication rate of quadruple therapy including esomeprazole 20 mg, tetracycline 500 mg, metronidazole 500 mg and bismuth subcitrate tablets 240 mg twice daily for 10 days was 91% in ITT analysis. Zullo et al. reported that 10-day sequential therapy (rabeprazole 20 mg twice daily plus amoxicillin 1 g twice daily for the first 5 days, followed by rabeprazole 20 mg, clarithromycin 500 mg and tinidazole 500 mg, all twice daily, for the remaining 5 days) had a significantly higher eradication rate (94%) than the standard 7-day triple therapy regimen (rabeprazole 20 mg, clarithromycin 500 mg and amoxicillin 1 g, all twice daily) (80%) in elderly patients with peptic ulcer72. Both regimens had similar high compliance rates (>95%) and low adverse effect rates (<12%)72. Therefore, the recommended treatment strategy in the Maastricht Consensus Report is applicable to elderly patients.

Second, we need to look at whether the dosage or eradication regimens should be adjusted in elderly patients to reduce adverse effects and increase compliance in the elderly. It has been reported that age influences the disposition of clarithromycin and lansoprazole73. In contrast, the pharmacokinetics of amoxicillin is influenced by the age-dependent decline in renal function rather than by age per se73. Therefore, several studies have evaluated the effect of dosage of clarithromycin and PPIs on the eradication rate in the elderly74–76. Pilotto et al. compared the curative rate of low (250 mg twice daily) vs. high (500 mg twice daily) doses of clarithromycin in combination with amoxicillin and pantoprazole in elderly patients74. They found that the curative rates of *H. pylori* infection in the low-dose and high-dose groups were 83% and 79%, respectively, in the ITT analysis (*p* > 0.05)74. The adverse events were also not significantly different between the two groups, with 5% in the low-dose group and 9% in the high-dose group74. The effect of PPI dosage on the eradication rate in the elderly is also of importance. Pilotto et al. reported that the eradication rate of low-dose (20 mg daily) and high-dose (40 mg daily) omeprazole plus clarithromycin and metronidazole were 83.3% and 85.5%, respectively21. The eradication rates

---

**Figure.** Treatment strategies according to antibiotic resistance38.

- **C**larithromycin resistance rate
  - ≤ 15–20%
  - > 15–20%
  - + Amoxicillin
  - + Metronidazole
  - > 40%
  - ≤ 40%
  - Metronidazole resistance rate
  - PPI, clarithromycin and amoxicillin
  - PPI, clarithromycin and metronidazole
  - Quadruple therapy

---

International Journal of Gerontology | December 2008 | Vol 2 | No 4
of low-dosage pantoprazole (40 mg once daily) in combination with two of amoxicillin or metronidazole or clarithromycin were greater than 80%\textsuperscript{75}. Similarly, the eradication rates of low-dosage rabeprazole-based triple therapy (20 mg once daily) were also reported to be as high as 88.5%\textsuperscript{76}. These data suggest that low doses of PPI and low doses of clarithromycin may be sufficient to achieve an adequate eradication rate in elderly patients. However, more studies in different ethnic groups are warranted before a recommendation can be made.

**Conclusion**

The similarities and differences of *H. pylori* infection in elderly and non-elderly patients are summarized in the Table. The prevalence of *H. pylori* infection increases with age worldwide. However, the prevalence of *H. pylori* infection in patients with a peptic ulcer is lower in elderly than in non-elderly patients, probably related to the higher prevalence of NSAID-related PUD in the elderly. Elderly patients with a peptic ulcer may gain a similar benefit from cure of an *H. pylori* infection as non-elderly patients in terms of improvement in symptoms and reduction in ulcer recurrence. Eradication of *H. pylori* infection may also lead to improvement in histologic grading of chronic gastritis, but the risk for gastric cancer cannot be completely prevented, especially in patients with existing premalignant lesions. The test-and-treatment strategy is not recommended for elderly patients with uninvestigated dyspepsia because of the higher incidence of gastroesophageal

<table>
<thead>
<tr>
<th>Prevalence of <em>H. pylori</em></th>
<th>Elderly</th>
<th>Non-elderly</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of gastric cancer</td>
<td>Higher</td>
<td>Lower</td>
<td>1–3</td>
</tr>
<tr>
<td>Prevalence of complicated PUD</td>
<td>Higher</td>
<td>Lower</td>
<td>14</td>
</tr>
<tr>
<td>Proportion of NSAID related peptic ulcer</td>
<td>Higher</td>
<td>Lower</td>
<td>11, 13, 29</td>
</tr>
<tr>
<td>Secretion of protective prostaglandins and hydrophobicity in NSAID users</td>
<td>Lower</td>
<td>Higher</td>
<td>11, 12</td>
</tr>
</tbody>
</table>

**Gastric acid secretion**

- *H. pylori* un-infected: Not affected by age
- *H. pylori* infected: Decrease with increasing age

<table>
<thead>
<tr>
<th>GU:DU</th>
<th>1.7:1</th>
<th>1:7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigation for dyspepsia</td>
<td>Endoscopy usually required</td>
<td>Test and treat in younger patients without alarm symptoms</td>
</tr>
<tr>
<td>Biopsy site for <em>H. pylori</em> test</td>
<td>From both antrum and body to increase detection rate</td>
<td>Antrum</td>
</tr>
<tr>
<td>Histologic change after eradication of <em>H. pylori</em></td>
<td>Improvement in gastritis grading</td>
<td></td>
</tr>
<tr>
<td>Prevention of gastric cancer after eradication therapy</td>
<td>Risk reduced, but not completely prevented</td>
<td>Risk markedly reduced, especially in the absence of premalignant lesions</td>
</tr>
<tr>
<td>Eradication rate of triple therapy</td>
<td>Lower dosage of PPI and clarithromycin may have equal eradication rate to standard dose regimens</td>
<td>Standard dose is recommended</td>
</tr>
</tbody>
</table>

*PUD = peptic ulcer disease; NSAID = nonsteroidal anti-inflammatory drugs; GU = gastric ulcer; DU = duodenal ulcer; PPI = proton pump inhibitor.*
malignancy. However, the rapid urease test and histology from the antrum may have lower sensitivity in elderly patients, especially in those with atrophic gastritis. It is recommended that the biopsy sites should include both the antrum and corpus to increase the detection rate. A UBT may be used in elderly patients with atrophic gastritis if the rapid urease test or histology fails to detect H. pylori infection. The treatment strategy recommended in the Maastricht Consensus Report is also applicable to elderly patients. Low doses of a PPI and clarithromycin may be sufficient to achieve an adequate eradication rate in elderly patients, but more data are needed before a recommendation can be made.

References

49. Andersson SI, Hovellius B, Molstad S, Wadstrom T. Dyspepsia in general practice: psychological findings in relation to *Helicobacter pylori* infection and inflam- 


