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Care of Older Adult Populations Diagnosed With *Helicobacter pylori*

A Review of Current Literature

ABSTRACT

Helicobacter pylori has been linked to development of peptic ulcers and increases the risk of developing gastric carcinoma. Currently, about half of the world's population is infected with *H. pylori*, many of whom are older adults. Older adult populations often have multiple comorbidities that may mask dyspeptic signs and symptoms. The role of *H. pylori* and infective signs vary by age, and the confusing symptoms in older adult populations may delay detection and treatment of *H. pylori*. In addition, time of detection and appropriate treatment is paramount to prevent gastric pathology. Clinicians need to recognize and understand the importance of risk factors, screening, detection, and treatment of *H. pylori*, particularly in older adults. Earlier detection and more aggressive, proactive clinical recognition of dyspeptic signs and symptoms may lead to earlier screening and diagnosis of *H. pylori* in older adult populations and help decrease the frequency of gastric metaplasia.

Infection with *Helicobacter pylori* plays an important role in gastrointestinal (GI) disease and pathology. *H. pylori* is the cause of most peptic ulcer disease and is considered a primary risk factor in the development of gastric cancer (National Cancer Institute, 2006). Approximately 50% of the world's population is infected with *H. pylori*, which is considered a type I carcinogen, and should be a major concern for clinicians (Naja, Kreiger, & Sullivan, 2007). In the older adult population, reports of typical dyspeptic signs and symptoms linked to *H. pylori* infection may be masked by physical and functional status, cognitive abilities, current medication regimen, and other comorbid conditions (Pilotto et al., 2000).

One role of the GI healthcare provider is to assess risk factors that may contribute to *H. pylori* infection. In addition, clinicians need to be attentive to current screening recommendations, types of testing recommended, and treatment regimens. The purpose of this article is to reinforce the importance of detecting *H. pylori* through recommended screenings, examining reported signs and symptoms that may relate, and understanding the recommended treatment regimens to eradicate *H. pylori* bacteria in older adult populations.

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Helicobacter pylori

Previous to early beliefs that gastric ulcers were caused by stress and spicy foods, current literature sheds light on the fact that most stomach ulcers and gastritis are in fact caused by an infection by the *H. pylori* bacteria (Marshall & Warren, 1984). According to the World Health Organization (WHO), *H. pylori* is a small, spiral, gram-negative bacillus that inhabits the gastric mucosal layer after being ingested via fecal to fecal or fecal to oral route. The bacterium possesses flagella, which are used to drill into the stomach layers, in which it finds ways to inhabit the stomach mucosal lining (Shirotani, Okada, & Murayama, 1996).

H. pylori produces adhesions, which bind to the epithelial cells in the stomach wall, and produces potent urease, secretes ammonia, neutralizes gastric

acid, and makes the gastric lining favorable to irritants and ulcers. Because of the bacteria's potent ability to alter the natural, protective lining of the stomach, *H. pylori* causes inflammation, atrophy, and gastric metaplasia. In addition, according to the Centers for Disease Control and Prevention (CDC), *H. pylori* has been found to be contributory to 90% of duodenal ulcers and 80% of gastric ulcers (Kuipers, Thijs, & Festen, 1995). With chronic habitation of *H. pylori* undetected in the stomach lining, the CDC has concluded that infected individuals are at a two- to sixfold increased risk of developing gastric cancer (Helicobacter and Cancer Collaborative Group, 2001).

Older adult populations are at higher risk of the negative effects of *H. pylori*, secondary to large amounts of consumed nonsteroidal anti-inflammatory drugs (NSAIDs) coupled with a higher incidence of atrophic gastritis (Snyder, 2005). The mechanism of action and detrimental effects of *H. pylori* may be easy to understand, but prevalence and presentation may be conspicuous. In a study looking at dyspeptic presentation and links to *H. pylori* in older adults, the role of *H. pylori* infection and signs and symptoms were found to vary by age. The possible loss of symptoms in the older adult populations may delay detection and treatment, making detection a more intricate piece of work for clinicians (Bode, Brenner, Adler, & Rothenbacher, 2002). Despite the seriousness of a diagnosis of *H. pylori*, substantial noncompliance to national treatment and screening standards has been shown to be widespread among clinicians (Howden, Blume, & Lissovoy, 2007).

Prevalence and Presentation

Most individuals who test positive for *H. pylori* are asymptomatic, so a complete history and physical examination with particular attention to GI complaints is necessary to formulate a differential diagnosis (Meurer & Bower, 2002). In a 12-case meta-analysis, a strong link exists between long-term *H. pylori* infection and three to six times the risk of developing gastric cancer (Helicobacter and Cancer Collaborative Group, 2001). *H. pylori* is found to be directly associated with an increased risk of gastritis (Fennerty, 1994). Furthermore, individuals aged 60 years or older coupled with *H. pylori* are strongly associated with increased gastric atrophy and intestinal metaplasia (Ohkuma et al., 2000). Individuals can present with dyspeptic signs, and symptoms may include gastric burning, nausea, flatulence, bloating, and abdominal distention; however, an overwhelming majority of individuals infected with *H. pylori* are asymptomatic.

Increasing age is a positive risk factor associated with *H. pylori* infection. In a multicenter epidemiological study investigating *H. pylori* and links to gastric cancer, the EUROGAST Study Group found that the prevalence of *H. pylori* infection was higher in older age groups, defined as 55 to 64 years old. Younger patients, defined as ages 25 to 34 years, did not have as many reported positive *H. pylori* infections (EUROGAST Study Group, 1993). According to the Helicobacter Foundation (2006), in Western countries such as the United States, *H. pylori* is more common in adults older than 50 years.

Older adult populations may present with other comorbidities, which can mask dyspeptic signs and symptoms or may be asymptomatic. Although older adult populations have a higher prevalence of *H. pylori* infection, unfortunately many are not followed by more frequent testing and eradication therapy (Gugler, 2004).

Screening and Diagnosis of *H. pylori* Infection

Not all gastric ulcers are caused by *H. pylori*, but certain factors may make an individual who has *H. pylori* infection susceptible to developing an ulcer. There are risk factors particularly in older adult populations, which include current treatment with NSAIDs and aspirin, cigarette smoking, excessive alcohol intake, and current comorbid conditions (Howden & Hunt, 1998). Certain modifiable risk factors can be controlled by patients to prevent ulcer proliferation and development of peptic ulcers. Risk factors contributory to increasing the likelihood of gastric metaplasia include *H. pylori* infection, physical stress, excess secretion of gastric acid, and a positive family history of ulcers. Once thought to be contributory to peptic ulcer disease, caffeine intake and spicy foods are not risk factors (Marshall & Warren, 1984).

Dyspeptic signs and symptoms need to be taken seriously when deciding to screen for *H. pylori*. Diagnosis of infection is usually made by first investigating dyspeptic signs and symptoms, then deciding on testing methods (which depend on the signs and symptoms exhibited or reported by the patient). Common and typical, nonthreatening dyspeptic symptoms include epigastric pain or discomfort, abdominal fullness, bloating, belching, nausea, and heartburn; however, there are specific alarm symptoms in dyspepsia that should raise a red flag. These alarm symptoms include anemia; anorexia; weight loss; progressive, worsening symptoms; melena or hematemesis; older than 45 years; family history of gastric cancer; previous peptic ulcers; and swallowing difficulties (American Gastroenterological Association [AGA], 1998).

According to the AGA's (1998) medical position statement for evaluation of dyspepsia, it is recommended that patients younger than 55 years without

H. pylori be treated for dyspepsia without further diagnostic investigation for *H. pylori*. Patients with recent onset of dyspepsia or other risk factors and who are older than 55 years need urgent upper-GI work-up including endoscopy. Investigation for *H. pylori* should be performed when there is moderate to high prevalence in the individual's community or region of inhabitance, when risk factors are present, or when the individual comes from an ethnic background with enhanced risk (National Institute for Clinical Excellence [NICE], 2004).

Specific Tests to Detect *H. pylori*

According to guidelines set forth by the data from the Maastricht 2-2000 Consensus Report, a "test and treat" approach is recommended in adult patients 45 years of age and younger presenting in primary care with dyspeptic signs and symptoms, NSAID users, and those with alarm symptoms (Malfertheiner et al., 2002). Diagnosis of infection should be by urea breath test or stool antigen test. In the primary care setting, initial serology testing has proven to be effective, accessible, and affordable, while endoscopy should be reserved for patients with alarm signs, unresponsive to treatment, or ulcer complications (Meurer & Bower, 2002). Any patient who presents with dyspeptic alarm symptoms or complicated ulcer, regardless of age, should be referred for GI endoscopy. Cultures of the biopsied gastric contents may also be performed to test for antimicrobial resistance, which will help guide decision making when treating *H. pylori* infection.

When considering a patient's age and other comorbidities, noninvasive testing for *H. pylori* may be more sufficient in the older adult populations. The most common noninvasive and reliable test to detect *H. pylori* is the serology antibody test. It detects IgG antibodies to *H. pylori* and indicates current or past infection. The urea breath test is also noninvasive and has greater sensitivity and specificity for detecting *H. pylori*, especially in elderly patients (Pilotto, 2001). In a primary care setting, serology is preferred. The urea breath test is usually performed in the hospital setting and has significantly higher diagnostic accuracy than the serology antibody test, though cognitive function, disability, and comorbidities are not taken into account. Stool testing is also noninvasive, highly sensitive and specific, and easy for older adult populations. The *H. pylori* diagnosis needs to be at the primary care level, making noninvasive diagnostic testing an important clinical entity.

H. pylori Treatment

When considering screening and testing for *H. pylori*, it is essential to have a treatment plan available. The best evidence for the effectiveness of *H. pylori* eradication exists for the treatment of *H. pylori*-associated ulcers (Forbes et al., 1994). In this case, treatment of *H. pylori* infection in patients with ulcers almost always cures the disease and reduces the risk of serious complications. Treatment and eradication of *H. pylori* has shown to dramatically reduce reoccurrence of ulcers and has helped decrease gastric metaplasia (Malfertheiner, 2007).

In a typical primary care setting, a patient most commonly will be asymptomatic, and endoscopy will not be referred. In this case, a test-and-treat modality is advocated for *H. pylori*. If dyspepsia is present, diagnostic screening is recommended and eradication therapy is indicated. Any patient with active gastric or duodenal ulcers or documented history of ulcers, regardless of age, should be tested for *H. pylori* and, if positive, treated. In a recent randomized control study, *H. pylori* "test and treat" versus use of proton pump inhibitors (PPIs) in the initial management of dyspepsia were compared. It was found that "test and treat" and acid suppression were equally cost-effective. Interestingly though, a randomized 343 patients were tested for *H. pylori* with 100 reported positive. Given PPI treatment and standard first-line therapy for 28 days, eradication rate was 78% (Delaney et al., 2008).

According to recommended guidelines, eradication regimens should be well tolerated, simple, and achieve an 80% eradication rate on intention-to-treat analysis (Malfertheiner & Miehlke, 1997). One controlled study in elderly patients showed triple therapy for 1 week and was highly effective (with an 84% eradication rate) and well tolerated (Pilotto et al., 1996).

Previous to earlier evidence that antacids, H_2 antagonists, or PPIs alone could eradicate *H. pylori*, current literature presented by the AGA conference from 1997 to present conveys that the gold standard for *H. pylori* eradication is triple therapy. Triple therapy requires twice daily treatment for 1-2 weeks with amoxicillin, clarithromycin, and a PPI. More importantly, the AGA suggests that an upper limit of 90% cure rate may be linked to longer 2-week treatment with the drug therapies recommended. Recommendations from the recent Maastricht III Consensus Report suggest *H. pylori* therapy initiation in patients with gastric and peptic ulcer disease, patients with atrophic gastritis, and first-degree relatives of patients with history of gastric cancer. In a study investigating whether risk of gastric cancer is modified in patients with gastritis, however, it was found that male gender and increasing age appeared to be associated with a reduction in the effectiveness of *H. pylori* treatment (Gulten et al., 2002).

In the primary care setting, a "test and treat" recommendation using noninvasive testing methods is advised in adult patients with persistent dyspepsia

younger than 45 years (Malfertheiner et al., 2006). Recent therapy recommendations have made peptic ulcer disease curable and controllable, where previous therapy regimens were used only for symptom control. Because of recent antibiotic resistance in many older adults, treatment failure for *H. pylori* may be a concern. The SHARP study concludes that pretreatment antimicrobial resistance has a major impact on the efficacy of suggested treatment regimens. Using meta-analysis, clarithromycin was found to be significantly more resistant in older populations; therefore, clinicians need to be extra sensitive and aware of which patients should have susceptibility testing when choosing appropriate treatment regimens, especially in the older adult population who may be resistant (Meyer et al., 2002). In such situations, quadruple therapy may be indicated.

Treatment for *H. Pylori* includes furazolidon, bismuth subsalicylate/metronidazole/tetracycline, amoxicillin, and omeprazole or lansoprazole for 14 days. Because of lengthy treatment period, tolerability and convenience may become an important clinical decision. In clinical trials, success with shorter duration of treatment is reported; however, in the United States, continued therapy for 14 days is the most reliable and effective regimen (Howden & Hunt, 1998). In terms of compliance, tolerability of 1- to 2-week antibiotic use, and cost, it was found that in patients older than 55 years with no previous history of peptic ulcer disease, new short-term quadruple therapy is efficacious, safe, well tolerated, cost-effective, and showed the best treatment outcome (Treiber, Wittig, Ammon, Walker, Dooran, & Klotz, 2002).

Also important is investigation of current medication regimens in older patients due to crossover of antibiotic use and concurrent treatment with PPIs. On the basis of clinical guidelines, successful eradication should always be confirmed by the urea breath test, endoscopy if clinically indicated, or stool antigen testing (Malfertheiner et al., 2002). In addition, time of eradication is important, and strict follow-up after eradication should be implemented in older patients with atrophic gastritis (Takata et al., 2006).

Clinical Implications for the Nurse Practitioner and Nurse Clinician

H. pylori is a bacteria that is cause for great concern in all patient populations, especially older adult populations secondary to concurrent comorbidities and underlying pathology. Importantly, clinicians should recognize the importance of this organism and potential risks that link *H. pylori* to gastric pathology. Screening, alarm signs and symptoms, and diligent maintenance should be conducted and taken just as seriously as other annual screenings. In being more cognizant and aware of this potential carcinogen, proper screening and treatment should be initiated when admissible. Clinicians should also be aware of the nonspecific presentation of dyspeptic signs and symptoms in caring for older adult populations. In a cost–benefit analysis of *H. pylori* screening, screening was found to be more favorable in older adult cohort groups. The total cost to screen for *H. pylori* was significantly favorable when compared with what it would cost once diagnosed with gastric cancer. In patients 45 years and older, *H. pylori* screening and cost–benefit ratio was the greatest, favoring most cost savings per case (Leivo et al., 2004). Similarly, early *H. pylori* screening, testing, and eradication therapy once in a lifetime seem more cost-effective than does surveillance; however, the choice is still confounded by variables such as infection risk, detection of early carcinoma, and intervention timing (Lee et al., 2007). In addition, patients should be informed that even though eradication therapy is paramount, avoidance of other factors such as NSAIDs and tobacco are equally important in decreasing their risk of developing dyspeptic symptoms and peptic ulcer disease (Kurata & Nogawa, 1997).

Eradicating *H. pylori* in vulnerable populations such as older adults means that clinicians may reduce morbidity and mortality and consequently save patient and healthcare system costs. More stringent guidelines for screening recommendations may be needed in clinical practice to ascertain that all clinicians are following standards. Any GI complaint, sign, or symptom must be taken seriously, and *H. pylori* should be ruled out as a causative factor. The current "test and treat" approach is vital to clinically specific screening recommendations based on patient age. Mere increased surveillance of dyspeptic signs and symptoms that could be linked to peptic and duodenal ulcers may also shed light on *H. pylori* infection. With increased utility of testing and eradication, the older adult populations may be spared morbidity and mortality, specifically gastric pathology, in the future. It is every clinician's duty to recognize and understand *H. pylori*; current screening, testing, and diagnostics for detection; and treatment recommendations.

In a study of hospitalized patients, it was found that 58%-78% of patients aged 65 years and older have peptic ulcer disease (Pilotto, 2001). Similarly, in the patients hospitalized for ulcer disease, the rate of diagnostic screening for *H. pylori* infection was less than 60%. More alarming was that only 50%-73% who tested positive for *H. pylori* were pharmacologically treated (Pilotto, 2001). If a powerful infection such as *H. pylori* can be easily tested for and treated so that hospitalizations, healthcare costs, and GI metaplasia are significantly decreased, perhaps clinicians should

be bound to tighter and more efficient guidelines. More research should be conducted in older adult populations to confirm specific age-related priorities. At present, current literature suggests a "test and treat" modality, hopefully with better clinician compliance and *H. pylori* eradication success in the future (Howden et al., 2007).

Summary

Nurses need to take the time with patients listening to any reported GI complaint, sign, or symptom. The precious role of patient advocate and educator should be paramount to educate patients about the implications of *H. pylori* and the possible outcomes, if not detected and treated. *H. pylori* is a bacterial inhabitant of the human gut that many patients are unaware of, making education regarding this topic even more important so that it does not become the next healthcare epidemic. The CDC, the WHO, and the National Cancer Institute have excellent patient and provider information that is precise and current regarding *H. pylori* (CDC, 1998; NCI, 2006).

Medically appropriate Web sites are important tools for patients in their endeavors to understanding *H. pylori* and its complexities. Nurse practitioners and clinicians, along with the entire medical community, can make *H. pylori* education a priority in practice, be more aggressive with screening and detection, and continue to appropriately treat these patients, therefore providing the possibility of significantly eradicating *H. pylori* in older adult populations. With more cognizant providers and patients regarding this matter, *H. pylori* morbidity and mortality rates may be decreased along with healthcare and patient costs.✪

REFERENCES

American Gastroenterological Association. (1998). American Gastroenterological Association medical position statement: Evaluation of dyspepsia. *Gastroenterology, 114*, 579-581.

Bode, G., Brenner, H., Adler, G., & Rothenbacher, D. (2002). Dyspeptic symptoms in middle-age to old adults: The role of *Helicobacter pylori* infection, and various demographic and lifestyle factors. *Journal of Internal Medicine, 252*, 41-47.

Centers for Disease Control and Prevention. (1998). *Helicobacter pylori: Fact sheet for health care providers*. Retrieved July 19, 2009, from http://www.cdc.gov/ulcer/files/hpfacts.PDF

Delaney, B. C., Qume, M., Moayyedi, P., Logan, R., Ford, A., Elliott, C., et al. (2008). *Helicobacter pylori* test and treat versus proton pump inhibitor in initial management of dyspepsia in primary care: Multicentre randomised controlled trial (MRC-CUBE trial). *BMJ, 336*, 651-654.

EUROGAST Study Group. (1993). Epidemiology of, and risk factors for, *Helicobacter pylori* infection among 3194 asymptomatic subjects in 17 populations. *Gut, 34*, 1672-1676.

Fennerty, M. B. (1994). *Helicobacter pylori*. *Archives of Internal Medicine, 154*, 721-727.

Forbes, G., Glaser, M., Cullen, D., Warren, J., Christiansen, K., Marshall, B., et al. (1994). Duodenal ulcer treated with *Helicobacter pylori* eradication: Seven-year follow-up. *Lancet, 343*, 258-260.

Gugler, R. (2004). The elderly patient with esophageal and gastric disease. *Praxis, 93*(51/52), 2151-2154.

Gulten, T., Tokyay, N., Demiray, M., Gulten, M., Ercan, I., Evke, E., et al. (2002). The role of triple therapy, age, gender, and smoking on the genotoxic effects of *Helicobacter pylori* infection. *Journal of International Medical Research, 3*, 380-385.

Helicobacter and Cancer Collaborative Group. (2001). Gastric cancer and *Helicobacter pylori*: A combined analysis of 12 case control studies nested within prospective cohorts. *Gut, 49*, 347-353.

Howden, C., Blume, S., & Lissovoy, G. (2007). Practice patterns for managing *Helicobacter pylori* infection and upper gastrointestinal symptoms. *American Journal of Managed Care, 13*, 37-44.

Howden, C., & Hunt, R. (1998). Guidelines for the management of helicobacter infection. *American Journal of Gastroenterology, 93*(12), 2330-2338.

Kuipers, E., Thijs, J., & Festen, H. (1995). The prevalence of *Helicobacter pylori* in peptic ulcer disease. *Ailments of Pharmacology & Therapeutics, 9*, 59-69.

Kurata, J., & Nogawa, A. (1997). Meta-analysis of risk factors for peptic ulcer. Nonsteroidal anti-inflammatory drugs, *Helicobacter pylori*, and smoking. *Journal of Clinical Gastroenterology, 24*, 2-17.

Lee, Y., Lin, J., Wu, H., Liu, T., Yen, M., Chiu, H., et al. (2007). Cost-effectiveness analysis between primary and secondary preventive strategies for gastric cancer. *Cancer Epidemiology, Biomarkers, & Prevention, 16*(5), 873-874.

Leivo, T., Salomaa, A., Kosunen, T., Tuominen, R., Farkkila, M., Linna, M., et al. (2004). Cost–benefit analysis of *Helicobacter pylori* screening. *Health Policy, 70*(1), 85-96.

Malfertheiner, P. (2007). *Helicobacter pylori*: A timeless source of lessons and research initiatives. *Helicobacter, 12*(2) 85-89.

Malfertheiner, P., Megraud, F., O'Morain, C., Bazzoli, F., El-Omar, E., Graham, D., et al. (2006). Current concepts in the management of *Helicobacter pylori* infection: The Maastricht III Consensus Report. *Gut, 56*, 772-781.

Malfertheiner, P., Megraud, F., O'Morain, C., Hungin, A. P., Jones, R., Axon, A., et al. (2002). Current concepts in the management of *Helicobacter pylori* infection: The Maastricht 2-2000 Consensus Report. *Alimentary Pharmacology & Therapeutics, 16*, 167-180.

Malfertheiner, P., & Miehlke, S. (1997). *Helicobacter pylori* infection in ulcer pathogenesis. *Digestion, 58*(1), 17-20.

Marshall, B., & Warren, J. (1984). Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet, 1*(8390), 1311-1315.

Meurer, L., & Bower, D. (2002). Management of *Helicobacter pylori* infection. *American Family Physician, 65*(7), 1327-1336.

Meyer, J., Silliman, N., Siepman, N., Sugg, J., Morris, D., Zhang, J., et al. (2002). Risk factors for *Helicobacter pylori* resistance in the United States: The surveillance of *H. pylori* antimicrobial resistance partnership (SHARP) study, 1993-1999. *Annals of Internal Medicine, 136*(1), 13-24.

Naja, F., Kreiger, N., & Sullivan, T. (2007). *Helicobacter pylori* infection in Ontario: Prevalence and risk factors. *Journal of Gastroenterology, 21*(8), 501-506.

National Cancer Institute. (2006). H. pylori *and cancer: Fact sheet*. Retrieved July 19, 2009, from http://www.cancer.gov/cancertopics/factsheet/hpylori

National Institute for Clinical Excellence (NICE). (2004). *Dyspepsia: Management of dyspepsia in adults in primary care*. Retrieved from http://www.nice.org.uk/nicemedia/pdf/CG017fullguideline.pdf

Ohkuma, K., Okada, M., Murayam, H., Seo, M., Maeda, K., Kanda, M., et al. (2000). Association of *Helicobacter pylori* infection with atrophic gastritis and intestinal metaplasia. *Journal of Gastroenterology and Hepatology, 15*, 1105-1112.

Pilotto, A. (2001). *Helicobacter pylori*-associated peptic ulcer disease in older patients: Current management strategies. *Drugs & Aging, 18*(7), 487-494.

Pilotto, A., Di Mario, F., Franceschi, M., Leandro, G., Soffiati, G., Scagnelli, M., et al. (1996). Cure of *Helicobacter pylori* infection in the elderly: Effects of eradication on gastritis and serological markers. *Ailments of Pharmacology & Therapeutics, 10*, 1021-1027.

Pilotto, A., Franceschi, M., Leandro, G., Rassu, M., Zagari, R., Bozzola, L., et al. (2000). Noninvasive diagnosis of *Helicobacter pylori* infection in older subjects. *Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 55*, M163-M167.

Shirotani, T., Okada, M., & Murayama, H. (1996). Effect of the eradication of *Helicobacter pylori* on duodenal ulcer healing and ulcer relapse: Randomized controlled study in Japan. *Journal of Gastroenterology, 31*, 175-181.

Snyder, D. (2005). Evidence-based recommendations for older adults with *Helicobacter pylori* of those using nonsteroidal anti-inflammatory drugs. *Gastroenterology Nursing, 28*(4), 309-314.

Takata, S., Ito, M., Yoshihara, M., Tanaka, S., Imagawa, S., Haruma, K., et al. (2006). Host factors contributing to the discovery of gastric cancer after successful eradication of *Helicobacter pylori*: Preliminary report. *Journal of Gastroenterology and Hepatology, 22*, 571-576.

The Helicobacter Foundation. (2006). *Information regarding* Helicobacter pylori: Helicobacter pylori. Retrieved July 19, 2009, from http://www.helico.com/disease_stomach.html

Treiber, G., Wittig, J., Ammon, S., Walker, S., Dooran, L., & Klotz, U. (2002). Clinical outcome and influencing factors of a new short-term quadruple therapy for *Helicobacter pylori* eradication (MACLOR study). *Archives of Internal Medicine, 162*, 153-160.