

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Dyspepsia with or without *Helicobacter pylori* infection - Clinical Approach in Adults

Effective Date: December 1, 2009

Scope

This guideline applies to non-pregnant adult patients with Dyspepsia. Dyspepsia is defined in this guideline as persistent or recurring symptoms consisting of upper abdominal pain, discomfort, nausea or bloating. Alarm features that require prompt investigation include: gastrointestinal blood loss, weight loss, early satiety, dysphagia, persistent vomiting, or symptom onset after the age of 55 years.¹ The search for and eradication of *Helicobacter pylori* (*H. pylori*) is also discussed.

For patients presenting predominantly with reflux symptoms, please refer to the Gastroesophageal Reflux Disease guideline (GERD).

Diagnostic Codes: 536-Dyspepsia; 535 or 537-Gastritis and Duodenitis

Prevention and Risk Factors

Many medications have been associated with dyspepsia, particularly acetylsalicylic acid (ASA) and non-steroidal anti-inflammatory drugs (NSAIDs).² If such medications are identified, then dose reduction or discontinuation should be considered as a first step. Emotional stress is not considered a risk factor for peptic ulcer disease, but may frequently be associated with functional (non-ulcer) dyspepsia.³ Lifestyle factors such as the use of alcohol and tobacco are potential triggers. Risk factors for being infected with *H. pylori* include immigration from a developing country, poor socioeconomic conditions, and family overcrowding.⁴

Management

Management of Dyspepsia *with* alarm features:

Alarm features consist of: gastrointestinal blood loss, weight loss, early satiety, dysphagia, persistent vomiting, or symptom onset after the age of 55 years.¹ Referral for upper gastrointestinal endoscopy is recommended.^{1,5}

Management of Dyspepsia *without* alarm features:

Patients with mild or infrequent symptoms can be managed without further investigation using non-prescription acid reducing agents.¹ Many medications can cause dyspeptic symptoms. A drug history including non-prescription medications is recommended.

For patients with more persistent symptoms, one of two approaches may be used:

1. Test and treat for *H. pylori* infection – see below: Management of *H. pylori* infection.

This approach is most appropriate for patients who have not been previously screened and is especially applicable in individuals who have an increased risk for *H. pylori* infection.

Individuals with dyspepsia who currently have an endoscopically or radiographically confirmed duodenal or gastric ulcer,⁶ or have had one within the past five years, should be tested for *H. pylori* infection (refer to Table 1). This does not apply to patients in whom successful eradication has been previously confirmed.

2. Empiric Therapy

This approach is most appropriate for patients who are unlikely to have *H. pylori* infection or who have previously tested negative for *H. pylori*. A 4-8 week course of treatment with a proton pump inhibitor (PPI) or H₂-receptor antagonist (H₂RA) may be prescribed. Refer to Appendix A.

Management of Chronic Dyspepsia:

Patients with chronic non-progressive symptoms previously investigated with negative results and no alarm symptoms, almost certainly have functional dyspepsia. This is a benign but chronic relapsing condition and does not require further investigation. It has not been established that long term pharmacotherapy improves outcomes for dyspepsia and its use should be reassessed periodically. Education, reassurance and support are the foundations of care.⁷

Management of *H. pylori* Infection:

- a) Test as per Table 1. **Serology is recommended as an initial test to detect *H. pylori*.** If the patient has had previously positive serology or other testing, then a urea breath test (UBT) is the recommended test. It is not necessary to order both serology and UBT for initial testing.
- b) Offer eradication treatment if the test is positive (see Table 2). Emphasize the importance of adherence to therapy.
- c) Confirmation of eradication is recommended in patients who have had a complicated duodenal ulcer (perforation or hemorrhage), gastric ulcer or mucosa associated lymphoid tissue (MALT) lymphoma. Persisting symptoms after eradication treatment should be followed by retesting or endoscopy. Retesting is otherwise not routinely required.
- d) An initial attempt to eradicate *H. pylori* may fail in as many as 20% of patients.⁸ Refractory *H. pylori* infection is seldom treated successfully by repeating the same regimen.⁶ A “rescue” or second line treatment is recommended (see Table 3).

Tests for <i>H. pylori</i>	Test identifies	Sensitivity	Specificity
Serology*	Antibody*	High	Moderate
C13 urea breath test** (UBT) (non-radioactive)	Active infection	High	High
Endoscopic gastric biopsy**	Active infection	High	High
Fecal antigen testing** (available in selected centres)	Active infection	High	High

* Unable to differentiate active from past infection. Antibody tests will remain positive for several years following successful eradication; repeat serology testing is not recommended.

** Test results may be affected by medications such as antibiotics and acid lowering agents; therefore, it is essential that bismuth and antibiotics be withheld for at least 28 days and a PPI for 7-14 days prior to testing.^{6,11,15}

Table 2: First line <i>H. pylori</i> Treatment Regimens ^{8,9,10}			
Agents used	Dose	Approximate cost/day† generic \$	Duration
PPI* amoxicillin clarithromycin	bid 1000 mg bid 500 mg bid	\$8.50 – 10.50	for 1 week **
PPI* metronidazole clarithromycin	bid 500 mg bid 250 mg bid	\$5.00 – 7.00	for 1 week **
PPI* Bismuth subsalicylate metronidazole tetracycline	bid 2 tabs qid 250 mg qid 500 mg qid	\$4.75 – 6.75	for 1 week **

Note: In patients not allergic to penicillin, the PPI, amoxicillin, clarithromycin regimen is the preferred first line treatment because of high rates of metronidazole resistance.

Table 3: Second line <i>H.pylori</i> Treatment Regimen ⁶			
Agents used	Dose	Approximate cost/day† generic \$	Duration
PPI* Bismuth subsalicylate metronidazole tetracycline	bid 2 tabs qid 250 mg qid 500 mg qid	\$4.75 – 6.75	for 2 weeks**

Table 4: Rescue <i>H.pylori</i> Treatment Regimen ⁶			
Agents used	Dose	Approximate cost/day† generic \$	Duration
PPI* levofloxacin*** amoxicillin	bid 250 mg bid 1000 mg bid	\$10.50 – 12.50	for 10 days**

* PPI: rabeprazole 20 mg, lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg, esomeprazole 20 mg; for coverage details please see Appendix A.

** See rationale for discussion of treatment duration.

*** Levofloxacin has not been approved by Health Canada for this indication and has no coverage through PharmaCare.

† Pricing as of March 2009 PharmaNet and does not include professional fees

N.B. Antibiotic PharmaCare coverage: amoxicillin, clarithromycin, metronidazole, and tetracycline are full and/or partial benefits.

Rationale

Dyspepsia is a common clinical problem that seldom represents life-threatening disease. A description of the symptoms does not reliably differentiate ulcers from non ulcer disease. Functional dyspepsia is ultimately the most common diagnosis, but other possible diagnoses to consider include ulcer disease, gastroesophageal reflux disease and gastric cancer. Malignancy is an unlikely diagnosis in the absence of any alarm features, especially in patients under the age of 55 years.⁷

Alarm features suggest a higher risk of significant disease and require prompt investigation. Endoscopy is recommended to identify gastric and duodenal ulcers as well as esophageal and gastric cancers.^{7,11} Gastric ulcers are potentially malignant and require endoscopic biopsy.

Patients whose symptoms persist after an initial negative investigation are considered to have functional dyspepsia. The association between *H. pylori* and functional dyspepsia is unclear, although a minority of patients (from 1% to 15%) may improve after eradication treatment.^{6,12} Dyspepsia continuing after treatment of *H. pylori* is more likely the result of GERD or functional dyspepsia.

Infection with *H. pylori* is a chronic indolent process that in the majority of patients causes asymptomatic gastritis. New infection or re-infection with *H. pylori* is an uncommon event (less than 2% per year); therefore, repeated screening is generally unnecessary.¹³ General population or family screening is not strongly supported by the literature.

Although *H. pylori* is the major cause of duodenal ulcer, gastric ulcer, gastric carcinoma and MALT lymphoma, these complications arise in a minority of infected patients.⁶ For patients with peptic ulcer disease, eradication of *H. pylori* reduces the rate of ulcer recurrence from 67 to 6% in duodenal ulcers and from 59 to 4% in gastric ulcers.¹¹ *H. pylori* testing (other than serology) will reliably confirm eradication.

The duration of treatment for *H. pylori* is somewhat controversial. While a seven day treatment is most often recommended, a fourteen day treatment is thought to yield a 5% increase in eradication success rates.¹⁶ This increase must be weighed against added cost and risk of adverse events which include *Clostridium difficile* colitis, allergic reactions, and increased antibiotic resistance.⁶

NSAIDs are the second leading cause of gastric and duodenal ulcer and may be co-pathogenic with *H. pylori*.¹⁴

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List of Abbreviations

ASA	Acetylsalicylic acid
GERD	Gastroesophageal reflux disease
H2RA	Histamine2-receptor antagonist
MALT	Mucosa associated lymphoid tissue
NSAID	Non steroidal anti-inflammatory drugs
PPI	Proton pump inhibitor
UBT	Urea breath test

Appendices

Appendix A – Prescription Medication Table for Oral Acid Suppression

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association and adopted by the Medical Services Commission.

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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DISCLAIMER

The Clinical Practice Guidelines (the “Guidelines”) have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems.

Appendix A – Prescription Medication Table for Oral Acid Suppression†

Drug	Standard dosing range	Approximate cost/day‡: generic \$ (brand \$)	Pharmacare coverage
H₂-receptor antagonists (H₂RA)			
ranitidine*‡(G) (Zantac®)	150 – 300 mg per day in 1 to 2 divided doses	\$0.20 – 0.40 (\$0.45 – 0.90)	regular benefit, LCA (n.b. Zantac® is LCA)
cimetidine‡(G) (Tagamet®)	200 –1200 mg per day in 1 to 2 divided doses	\$0.08 – 0.40 (\$0.50 – 1.50)	regular benefit, LCA
nizatidine‡ (G) (Axid®)	150 – 300 mg per day in 1 to 2 divided doses	\$0.50 – 1 (\$0.90 – 1.70)	limited coverage, LCA, RDP
famotidine*‡(G) (Pepcid®)	20 – 80 mg per day in 1 to 2 divided doses	\$0.60 – 2 (\$1.15 – 4)	limited coverage, LCA, RDP
Proton pump inhibitors (PPI's)			
rabeprazole‡(G) (Pariet®)	20 mg per day	\$0.98 (\$1.40)	limited coverage
omeprazole (G) (Losec®)	Dyspepsia: 20 mg once daily for 4 weeks	\$1.15 (\$2.40)	limited coverage
pantoprazole‡(G) (Pantoloc®)	40 mg per day	\$1.40 (\$2.15)	limited coverage
lansoprazole ‡ (Prevacid®)	15 – 30 mg per day x 4-8 weeks	\$1.08 – 2.15	limited coverage
esomeprazole‡ (Nexium®)	20 – 40 mg per day	\$2.25 – 4.50	limited coverage

† Please see Tables 2 and 3 for H. pylori treatment regimens.

‡ Pricing as of March 2009 PharmaNet and does not include professional fees.

* Available with or without a prescription, but non-prescription medications are not reimbursed by PharmaCare or most private drug plans

‡ Dyspepsia: these medications have not been approved by Health Canada for this indication. However standard dosing of PPI's (which have been shown to have equivalent efficacy in initial dyspepsia treatment) have been shown to be effective for the treatment of dyspepsia. (Note-studies were small and the patients symptoms in many of these studies significantly overlapped with GERD symptoms thus management often mirrors that of GERD)^{1,2,3}

Nb: Please review product monographs and regularly review current listings of Health Canada advisories, warnings and recalls at:

http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html

G: indicates that generics are available. See <http://www.health.gov.bc.ca/pharmacare/> for further information.

Regular benefit drugs: do not require Special Authority. Patients may receive full (F) or partial coverage (P), since some of these drugs are included in the Low Cost Alternative (LCA) program or Reference Drug Program (RDP).

LCA: When multiple medications contain the same active ingredient (usually generic products), patients receive full coverage for the drug with the lowest average PharmaCare claimed price. The remaining products are partial benefits.

RDP: When a number of products contain different active ingredients but are in the same therapeutic class, patients receive full coverage for the drug that is medically effective and the most cost-effective. This drug is designated as the Reference Drug. The remaining products are partial benefits.

Limited coverage drugs: require Special Authority. These drugs are not normally regarded as first-line therapies or there are drugs for which a more cost-effective alternative exists.

In all cases: coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles.

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