OBJECTIVE
Alberta clinicians will understand the indications to test for *Helicobacter pylori* (*H. pylori*), different testing methods available (urea breath test [UBT], histology on gastroscopy, stool tests), and the different treatment regimens available.

TARGET POPULATION
Adults meeting specific clinical criteria (see Indications)

EXCLUSIONS
Pregnant or breastfeeding women
Children (under 18 years of age)

RECOMMENDATIONS

INDICATIONS

✓ Testing for *H. pylori* can be performed with (non-invasive) Urea Breath Test (UBT) or (invasive) endoscopically guided biopsy. The UBT is the preferred approach for dyspeptic patients without alarm features.

See Algorithm (summarizing diagnosis and treatment process described below).

✓ Patients who would benefit from *H. pylori* testing using UBT include:
  o Dyspepsia and younger (< 50 years of age) with no alarm features
  o Gastric or duodenal ulcers confirmed by upper gastrointestinal (GI) radiography (if endoscopy not being considered)
  o Family history of gastric cancer
  o Long-term use of non-steroid anti-inflammatory agents (NSAIDS)

PRACTICE POINT

*Patients with GERD predominant symptoms do not require UBT.*

✓ Assess by endoscopy to exclude complicated disease and/or upper GI malignancy those patients with:
  o New onset persistent dyspepsia in patients > 50 years of age
  o No or limited response to acid-suppression treatment
  o Dyspepsia and any alarm features

PRACTICE POINT

*When further assessment is required for dyspeptic patients, upper GI endoscopy is the preferred investigation. Barium swallow or CT scan can be ordered as a substitute if limited access to gastroscopy exists.*
• Alarm Features can be recalled by the mnemonic VBAD.

<table>
<thead>
<tr>
<th>VBAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>“V”omiting</td>
</tr>
<tr>
<td>“B”leeding or anemia</td>
</tr>
<tr>
<td>“A”bdominal mass or unexpected weight loss</td>
</tr>
<tr>
<td>“D”ysphagia</td>
</tr>
</tbody>
</table>

✓ Treat patients who test positive for H pylori infection.

**DIAGNOSIS**

X DO NOT use IgG serology test and stool antigen tests (SATs) for diagnosis of H. pylori infection.

✓ Refer to TOP’s clinical practice guideline (CPG) for Diagnosis and Management of Gastroesophageal Reflux Disease (GERD) when symptoms are predominantly heartburn and/or acid regurgitation.

✓ Refer to TOP’s CPG for Diagnosis and Treatment of Chronic Undiagnosed Dyspepsia in Adults for approach to patients with dyspepsia.

**TREATMENT**

See Table 1: Options for Treatment.

✓ Consider the efficacy, simplicity, expense and patient preferences when selecting treatment regimens.

**PRACTICE POINT**

If one eradication therapy fails, use a different regimen.

**PRACTICE POINT**

All treatment regimens should ideally be prescribed for 14 days but no less than seven days. There is an additional improvement of H. pylori eradication of 1% per day if treatment continued beyond seven days.

✓ Inform patient that no eradication protocol is 100% effective.

**TREATMENT REGIMENS AVAILABLE**

✓ Discuss treatment options with patient. Efficacy, complexity, cost, previous eradication therapies used and patient preferences should help guide choice of regimen.

○ To compare medication costs for various treatment options see: https://www.acfp.ca/2016-price-comparison-of-commonly-prescribed-drugs-available/.
### POSSIBLE H. pylori ERADICATION REGIMENS (PATIENTS NOT ALLERGIC TO PENICILLIN)

<table>
<thead>
<tr>
<th>Options for first line treatment</th>
<th>Notes: Efficacy</th>
<th>Notes: Ease of use/cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CLAMET Quadruple Regimen x 14 days</strong></td>
<td>1. PPI* (1 tablet) two times a day 2. Amoxicillin (1 g) two times a day 3. Clarithromycin (500 mg) two times a day 4. Metronidazole (500 mg) two times a day</td>
<td>Recommended first line therapy by Canadian expert consensus.(^1) Potentially greater adverse events compared to other therapies.(^2)</td>
</tr>
<tr>
<td><strong>Bismuth Quadruple Regimen x 14 days</strong></td>
<td>1. PPI (1 tablet) two times a day 2. Bismuth subsalicylate (Pepto Bismol®) (2 tablets) four times a day 3. Metronidazole (500 mg) four times a day 4. Tetracycline (500 mg) four times a day</td>
<td>Recommended as alternate first line by Canadian expert consensus.(^1)</td>
</tr>
<tr>
<td><strong>Sequential Therapy x 14 days</strong></td>
<td>PPI bid 1-14 days Amoxicillin (1 g) two times a day for 1-7 days then Clarithromycin (500 mg) and Metronidazole (500 mg) two times a day 7-14 days</td>
<td>No longer recommended by Canadian expert consensus.(^1)</td>
</tr>
<tr>
<td><strong>Standard Triple Therapy (PAC) x 14 days</strong></td>
<td>1. PPI two times a day 2. Amoxicillin (1 g) two times a day 3. Clarithromycin (250 mg) two times a day or Metronidazole (500 mg) two times a day</td>
<td>No longer recommend by Canadian expert consensus.(^1)</td>
</tr>
</tbody>
</table>

**Second line treatment – rescue therapy for failed first line**

- Use an alternate first line therapy
  - See above.
  - See above.

**Option for third line treatment – if second line treatment failure (no amoxicillin allergy) and consider referral to Gastroenterology x 14 days**

1. PPI (1 tablet) two times a day
2. Amoxicillin (1 g) two times a day
3. Levofoxacin (250 mg) two times a day

**TREATMENT OPTIONS (PENICILLIN ALLERGIC OPTIONS)**

### First line treatment (Amoxicillin allergy)

<table>
<thead>
<tr>
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<td>Recommended expert consensus for first line (amoxicillin allergy). As above.</td>
</tr>
<tr>
<td><strong>Modified Triple Therapy (PCM) x 14 days</strong></td>
<td>1. Pantoprazole 40 mg two times a day 2. Clarithromycin (500 mg) two times a day 3. Metronidazole (500 mg) two times a day</td>
<td>Less effective than first line treatment</td>
</tr>
</tbody>
</table>

Table 1: Options for Treatment

*proton pump inhibitor (PPI)
CONFIRMING ERADICATION

✓ Order UBT to confirm H. pylori eradication for:

1. Patients whose symptoms remain or recur after treatment:
   - Do not treat H. pylori empirically without confirming that H. pylori is still present.
2. Patients with H. pylori positive gastric or duodenal ulcer or gastric cancer (if endoscopy not being performed)

POST-THERAPY RE-TESTING WITH UBT

✓ Wait to re-test with UBT at least 28 days following any antibiotic use (including H. pylori eradication therapy).

- Testing before 28 days may result in false negative results.

✓ Discontinue proton pump inhibitor (PPI) therapy for at least three days.

- Recommend OTC antacids if needed to control symptoms.

Please see Dynalife/Calgary Lab Services (CLS) for instructions.

THE REPEAT UBT IS NEGATIVE (AND PATIENT IS STILL SYMPTOMATIC)

✓ Reconsider other potential causes of the symptoms.

- For (non-ulcer) dyspepsia see TOP’s Diagnosis and Treatment of Chronic Undiagnosed Dyspepsia in Adults CPG.

THE REPEAT UBT IS POSITIVE, H. pylori IS PRESENT AND ERADICATION THERAPY HAS FAILED

✓ Always use a different eradication regimen.

✓ Consider initial reason for H. pylori testing and a gastroenterologist referral to further assess (i.e., test H. pylori culture and sensitivity) after two or three unsuccessful treatment attempts.

BACKGROUND

EPIDEMIOLOGY

H. pylori infection is common in Canada, although decreasing because the incidence is low in children born in Canada. The prevalence increases with age, varies by region and ethnic sub-groups ranging from about 20% to 40% in some adult populations. The prevalence is high, often greater than 50%, in First Nations populations living in northern Canada.

Although the source of H. pylori infection has not yet been found, it is likely transmitted from human to human in childhood.
**RELATIONSHIP BETWEEN H. pylori AND GASTRITIS, GASTRIC/DUODENAL ULCERS**

It is estimated that 10% to 20% of *H. pylori*-positive patients will have a lifetime risk of developing ulcer disease and a 1% to 2% risk of developing distal gastric cancer.\(^6\)

*H. pylori* infection may be associated with dyspepsia symptoms but treating *H. pylori* doesn’t always improve dyspepsia symptoms.\(^3\) If symptoms persist despite successful cure of infection these patients may benefit from ongoing acid suppressive therapy. (See the section on empiric therapy in Diagnosis and Treatment of Chronic Undiagnosed Dyspepsia in Adults CPG.)

Aspirin® and NSAIDS are common causes of peptic ulcer disease. There is an increased risk of peptic ulcers if both *H. pylori* infection is present and NSAIDS or aspirin are used.\(^7\) Therefore, patients contemplating or currently on long term NSAIDs should be considered for UBT and eradicating *H. pylori* if positive.\(^8\)

**RELATIONSHIP BETWEEN H. pylori AND GASTRIC MALIGNANCY**

*H. pylori* is associated with the development of gastric cancer. The lifetime risk of gastric cancer is about 2% for male and 1% for female Canadians.\(^9\) A recent systematic review of randomized controlled studies found that in patients in which *H. pylori* was eradicated, the incidence of gastric cancer is reduced relatively by about 33%.\(^10\) The absolute benefit depends on the population studied who would have differing baseline rates.

Other risk factors for gastric cancer include family history of gastric cancer and lifestyle factors such as smoking, drinking alcohol, and a diet low in fruits and vegetables or high in salted, smoked, or nitrate-preserved foods.\(^11\)

**TESTING FOR H. pylori – UREA BREATH TEST**

The urea breath test (UBT) is a simple non-invasive diagnostic test used to identify *H. pylori*.

Overall, performance characteristics of the UBT are superior to any other diagnostic test with sensitivity and specificity generally exceeding 95% in most reports\(^12\)-\(^14\) and test reproducibility is high.\(^15\)

The UBT can also be used for post-treatment testing.\(^16\)-\(^19\) However, test sensitivity is decreased by medications (such as bismuth containing compounds, antibiotics, and PPIs) that reduce the organism’s urease activity or density,\(^20\) therefore a washout period is required. See respective lab services for washout instructions:

TESTS NOT RECOMMENDED FOR H. pylori DETECTION

*H. pylori* antibody testing (IgG serology) detects antibodies to the bacteria but will not distinguish a previous infection from the current one (i.e., test would be positive if the patient ever had *H. pylori*) so additional testing would always be required. However, if the test result is negative, it is unlikely that a person ever had an *H. pylori* infection.

The *H. pylori* stool antigen test (SAT) was found to have a lower diagnostic value than UBT when evaluating the outcome of anti-*H. pylori* therapy. Temperature, consistency of stool, interval between stool sample collection and measurement of stool can also affect the results of SATs. The use of SATs should only be considered if the UBT is not available.

**H. pylori** TREATMENT

The standard triple therapy-proton pump inhibitor-clarithromycin/amoxicillin (PCA) has been the recommended approach to treat *H. pylori* with a high level of treatment success (>80% eradication) in Canada. However, studies from other countries suggest there has been a steady worldwide decline in the success rate of triple therapy primarily due to clarithromycin resistance. Unfortunately local resistance rates are not readily available in Alberta or Canada.

A meta-analysis of 17 Canadian trials reviewed the eradication success with differing treatments regimens:

- Standard Triple therapy (PCA) 84% (79 to 90% range)
- Modified Triple therapy (PCM) 82% (76 to 88% range)
- Bismuth Quadruple Therapy 87% (80-95% range)

When patient adherence with prescribed regimen was >75%:

- Quadruple therapy about the same as triple therapy (91-94% range)

More recent unpublished tertiary care Alberta data found that triple therapy was only successful in 55% of patients.

A randomized control trial (RCT) conducted in the North West Territories found 10 days of triple therapy or sequential therapy successfully eradicated *H. pylori* in only 55 and 57% of patients respectively. Of 77 participants with complete medication adherence, effectiveness improved to 63% (95% CI 43% to 82%) for triple therapy and 81% (95% CI 63% to 99%) for sequential therapy. This study was however limited by about 20% of patients lost to follow up (were considered to still be *H. pylori* positive). This would result in lower than anticipated eradication rates.

See Table 2 for a more recent network meta-analysis of *H. pylori* eradication regimens data.
Table 2: H. pylori Eradication Regimens and Effects

From the meta-analysis described in Table 2, the CLAMET quadruple therapy was based on one low quality study of 119 Japanese patients where clarithromycin resistance is >20%, no studies could be located directly comparing 10 or 14 days to 7 days of Triple Therapy.

Recent Canadian guidelines no longer recommending triple or sequential therapy but recommend Clarithromycin, Amoxicillin, Metronidazole (CLAMET) quadruple regimen as first line therapy.¹

TREATMENT DURATION

Canadian guidelines recommend that all treatment durations for H. pylori be 14 days.¹

Generally, for every day of therapy beyond seven days, an additional 1% of patients will be successfully eradicated.²⁹ This benefit must be balanced with potentially greater risk of adverse events, costs and risk of non-adherence.²⁹

Patient non-adherence with treatment regimens increases chance of treatment failure. Patients must be informed that adherence with treatment regimen is critical to successful eradication to prevent antibiotic resistance. Patients must also understand that no eradication protocol is 100% effective and failure of treatment is possible.

TREATMENT FAILURE

First Failure: use an alternate therapy (do not repeat initial regimen). See Table 1.

Second failure: consider another alternative and referral to gastroenterologist.

CONFIRMING ERADICATION WITH UBT

UBT is the best non-invasive test for the presence or absence of H. pylori.²⁰

UBT testing for eradication of H.pylori should be considered for:

- Dyspeptic patients (without alarm features) who continue to be symptomatic after a full course of treatment to confirm either eradication of H.pylori or failure of treatment
- Dyspeptic patients who initially improve post eradication, but develop recurrent symptoms
- Patients treated for gastric or duodenal ulcer or gastric cancer to document cure of H. pylori (only if not considering gastroscopy). This will establish success of the anti-Helicobacter therapy regimen and in the case of gastric ulcer rule out any gastric cancer.²⁰
UBT INSTRUCTIONS

It is necessary to have at least a 28-day wash-out period before re-testing with UBT following completion of any antibiotics (including H. pylori eradication therapy). Testing before 28 days may result in false negative results.

PPI therapy can also result in false negative UBT results (as high as 40%) and therefore should be discontinued three days prior to UBT testing.

Antacids can be prescribed if needed to control symptoms should PPI be temporarily stopped.

See: Dynalife and Calgary Lab Services instructions.

If UBT is negative, but symptoms persist or recur, other causes must be considered.

If UBT is positive, H. pylori is present and first line eradication therapy has failed – use an alternative therapy for H. pylori. If subsequent treatment fails, consider the initial indication for H. pylori testing and consider a referral to a gastroenterology specialist.

CPG IMPLEMENTATION IN PRACTICE CONSIDERATIONS

- Primary care physicians can bookmark the link to the CPG or copy the tools within the CPG for easy access including the H.pylori treatment option tables, the algorithm for summary of the care process, and other tools such as the listing of drug costs for H. pylori treatment.

- Gastroenterologists and endoscopists can promote the use of the TOP H. pylori CPG among primary care physicians who may be unfamiliar with the approach for H. pylori assessment, diagnosis and treatment.
REFERENCES


SUGGESTED CITATION

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For more information see www.topalbertadoctors.org

GUIDELINE COMMITTEE
The committee consisted of representatives of, gastroenterology and primary care.

July 2000
Reviewed November 2001
Revised 2009
Major Revision June 2016
Minor Revision (medication) March 2017
**Algorithm**

**Diagnosis and Treatment of Helicobacter pylori in Adults**

*Excluding pregnant or breastfeeding women

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**See TOP’s Chronic Undiagnosed Dyspepsia CPG**

Consider other (non-ulcer) causes of dyspepsia symptoms

- **Symptoms Persist**
  - **H. pylori Negative**
  - **H. pylori Positive**
    - Order urea breath test (UBT) to test for H. pylori
    - Select an eradication (See Table 1)
    - Consider re-test UBT for eradication in certain patients
    - **H. pylori Positive**
      - Select second line rescue therapy (see Table 1)
      - Re-test UBT
      - **H. pylori Positive**
        - Failure to respond to therapy >2 times

**Patient <50 years old presents with dyspepsia symptoms and any active peptic ulcer disease on diagnostic imaging**

**Patient >50 years old presents with new onset dyspepsia symptoms and/or any age with:**
- **Alarm features VBAD** (Vomiting, Bleeding/anemia, Abdominal mass/unexplained weight loss, Dysphagia) or
- No response to acid suppression therapy

**Refer for Gastroscopy/Consult**

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These recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.