Canadian Helicobacter pylori Consensus Conference Update: Infections in adults

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HELICOBACTER PYLORI
Mise à jour de la conférence canadienne de consensus sur Helicobacter pylori : Infections chez les adultes

RÉSUMÉ : La première conférence canadienne de consensus sur Helicobacter pylori s’est tenue en avril 1997. Les recommandations initiales de la conférence ont été publiées au début de 1998. Une réunion de mise à jour de ces recommandations s’est tenue en juin 1998. Le présent article actualise et complète les premières recommandations. Parmi les changements clés, on note que les recommandations concernant le dépistage et le traitement de l’infection à H. pylori chez les patients connus pour être atteints d’un ulcère gastro-duodénal ont été

voir page suivant

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SPECIAL SECTION
Canadian Helicobacter pylori Consensus Conference Update
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Guest Editors:
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The management of *Helicobacter pylori* infection is evolving. Substantial progress to characterize the nature and implications of this major gastroduodenal pathogen has been made in Canada and elsewhere. This progress is helping to define the clinical implications of infection and indications for treatment. To keep pace with new scientific evidence, the Canadian *Helicobacter pylori* Study Group (CHSG) (previously named Canadian *Helicobacter pylori* Study Group) held its second conference in Ottawa, Ontario, from June 5 to 7, 1998. The goals of the conference were to review and to update the first set of guidelines on the basis of recent advances. Such advances have helped to facilitate accurate diagnosis and effective treatment of *H pylori* infection, thereby providing opportunities to improve patient care.

The evidence that eradication of *H pylori* infection can cure peptic ulcer disease was a driving force behind the first Canadian Consensus Conference held in April 1997 (1). This evidence is unequivocal, establishing new treatment standards in Canada for one of the most common gastrointestinal diseases. However, the relationship between *H pylori* and the human host is complex. Most individuals have lifelong *H pylori* colonization of the stomach with few significant clinical consequences. A subset of infected individuals develop peptic ulcer disease, gastric cancer or gastric lymphomas.

Guidelines unique to Canada are essential. The expected benefits from *H pylori* eradication may be influenced by a variety of country-specific factors, including the prevalence of infection, and the costs of diagnosis and treatment. Differences among the published guidelines for Canada, Europe, the United States and the Asia Pacific region (Table 1) reflect the influence of these factors and demonstrate how some of the more controversial issues have been variably interpreted in the absence of definitive evidence.

The Canadian update conference convened a broad representation of interest groups. Participants included adult and pediatric gastroenterologists, infectious disease specialists, primary care clinicians, pathologists, basic science researchers, pharmacists, and representatives from government and the pharmaceutical industry. The conference was organized by CHSG and was sponsored by the Canadian Association of Gastroenterology, the Canadian Digestive Disease Foundation, the Canadian Society for Clinical Investigation, the Canadian Infectious Diseases Society and the Canadian Paediatric Society. Major financial support for the Consensus Conference was provided through equal, unrestricted educational grants from Abbott Laboratories Ltd, Astra Pharma Inc, Axcan Pharma Inc, Byk Canada/Solvay Pharma Inc and Glaxo Wellcome Inc.

**CONSENSUS RECOMMENDATIONS:**

**AN UPDATE**

In the short time since publication of the Canadian *Helicobacter pylori* infection in different countries

<table>
<thead>
<tr>
<th>Indications</th>
<th>European (2)</th>
<th>United States (3)</th>
<th>Asia Pacific (4)</th>
<th>Canada (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past or present duodenal or gastric ulcer disease* without prior treatment in patient not taking NSAIDs</td>
<td>Test and treat</td>
<td>Test and treat</td>
<td>Test and treat</td>
<td>Test and treat</td>
</tr>
<tr>
<td>Uninvestigated dyspepsia</td>
<td>Test and treat if patient is less than 45 years of age or has no alarm symptoms</td>
<td>Test and treat if patient is less than 45 years of age</td>
<td>Test and treat if patient has no alarm symptoms</td>
<td>Test and treat if patient shows symptoms for three or more months, is less than 45 years of age and has no alarm signals or features</td>
</tr>
<tr>
<td>Patients on NSAID therapy</td>
<td>Test and treat</td>
<td>Not addressed</td>
<td>Test and treat if patient has a history of dyspepsia</td>
<td>Testing not indicated</td>
</tr>
</tbody>
</table>

Other possible indications for *Helicobacter pylori* testing include mucosa-associated lymphoid tissue lymphoma, family history of gastric cancer and patient request for testing. *No indication of malignancy. NSAID Nonsteroidal anti-inflammatory drug.
cobacter pylori Consensus Conference recommendations in The Canadian Journal of Gastroenterology in January 1998 (1), several important advances have clarified the practical management of H pylori infection. These include better understanding of the relative utility of available diagnostic tests or investigations, and therapeutic options. The key recommendations of the Consensus Conference have been extended from testing and treating H pylori infection in patients with known peptic ulcer disease to testing and treating patients with ulcer-like dyspepsia.

**DIAGNOSTIC RECOMMENDATIONS**

1) Testing for H pylori infection should be performed only in patients suspected of having an H pylori-related condition such as peptic ulcer disease, and only when treatment is planned if the result is positive.

   **Comment:** Routine testing of asymptomatic individuals for H pylori is not endorsed because many patients harbour this infection with no significant clinical consequences. However, when infection with H pylori has been confirmed, failure to act on a positive result is inappropriate. Patients should either be investigated further or offered eradication treatment.

2) Nonendoscopic testing for the presence of H pylori infection is recommended in any patient with a current or past peptic ulcer. Testing can be considered in carefully selected dyspepsia patients with chronic symptoms consistent with peptic ulcer disease (‘ulcer-like’ dyspepsia) if the adult patient is younger than 50 years and has no alarm features.

   **Comment:** If a dyspepsia patient is tested, the patient must understand that H pylori treatment may not improve his or her symptoms, and should understand that H pylori is associated with gastric cancer and can cause mucosa-associated lymphoid tissue lymphoma (MALToma). However, there is no evidence that eradicating H pylori in dyspepsia patients will reduce the potential risks of future disease and outweigh the current risks of antimicrobial therapy (eg, allergic reaction, antibody resistance or Clostridium difficile-associated complications), or the possible adverse outcome of eradicating H pylori (some controversial data suggest that H pylori may even protect against gastrointestinal esophageal reflux disease and esophageal cancer).

3) The noninvasive urea breath test should be used for routine diagnosis of H pylori infection unless endoscopy is indicated for another reason.

   **Comment:** The $^{13}$C or $^{14}$C urea breath test is the preferred first-line diagnostic investigation because of its excellent sensitivity, specificity and ease of use. Relative to breath tests, the accuracy of serology is associated with more variability among laboratories, and serology has a higher rate of false positive results in young patients, in whom the prevalence of infection is lower. This is an especially important consideration when the prevalence of H pylori infection is relatively low, such as in dyspeptic patients from developed countries seen in Canada. In this setting, the rate of false positive serology tests is markedly higher. This reduces the positive predictive value of serology testing for H pylori in Canadian communities with a low prevalence of H pylori, such as in adults younger than 45 years of age, in whom the prevalence is about 20% to 30%.

Several alternative diagnostic methods are under evaluation; these include assays for stool antigen and serum labelled bicarbonate, which may provide alternative nonendoscopic tests and be less costly than urea breath tests, while retaining validity for confirming eradication of infection after eradication treatment.

One emerging and important finding that will alter future management recommendations is the evidence that the proportion of patients with duodenal ulcer due to causes other than H pylori or nonsteroidal anti-inflammatory drugs (NSAIDs) is increasing. This observation has been made primarily in the United States, and Canadian data are urgently needed.

A related, unresolved issue concerning diagnosis is the need for antibiotic sensitivity testing. Current antibiotic combination therapies used to eradicate H pylori infection appear to overcome some degree of resistance to metronidazole or clarithromycin, but resistance is associated with lower rates of response. Therefore, it is important to have more than one regimen (as listed in the ‘Recommended therapies’ section) to address local resistance patterns. Prospective information about resistance in Canada is considered important, and necessary to verify that treatments are effective and, thus, appropriate. Monitoring of antibiotic resistance patterns is strongly recommended. A Canadian resistance network is now being established and is funded by CHSG through contributions from sponsors.

**TREATMENT RECOMMENDATIONS**

- All H pylori-positive patients with duodenal or gastric ulcer, whether symptomatic or asymptomatic, should receive eradication treatment.
- Eradication is recommended whenever there is known H pylori infection.
- All H pylori-positive patients with gastric MALToma should receive eradication treatment.

**COMMENTARY ON TREATMENT RECOMMENDATIONS**

Although the World Health Organization has designated H pylori as a group 1 carcinogen, there is no unequivocal evidence that eradication can reduce the risk of a subsequent gastric cancer, even in high risk populations. Potential benefits remain theoretical. A number of long term intervention studies are underway, and the first results are anticipated in three to five years. The relationships between H pylori infection and gastroesophageal reflux disease, NSAID-associated ulcer and nonulcer dyspepsia remain unresolved.

**TREATMENT REGIMENS**

Treatments have been classified as ‘recommended’ when
controlled trials have demonstrated at least an 80% eradication rate by an intention to treat analysis. Alternative treatments of potential benefit are considered 'endorsed', even when associated with lower cure rates; such treatments may, for example, be useful in special circumstances, such as when a patient is allergic to a certain antibiotic or does not have an appropriate reimbursement plan to cover first-line therapies. Although the most common reasons for treatment failure include poor compliance and antibiotic resistance, it should be noted that the regimens listed for consideration in treatment failures have not been shown, in controlled trials, to have specific efficacy for this indication.

RECOMMENDED THERAPIES

- Twice daily, seven-day regimen of a proton pump inhibitor (PPI) (omeprazole 20 mg, lansoprazole 30 mg or pantoprazole 40 mg) or ranitidine bismuth citrate (RBC) 400 mg, clarithromycin 500 mg and amoxicillin 1000 mg; or
- A twice daily, seven-day regimen of a PPI or RBC, clarithromycin 500 or 250 mg, and metronidazole 500 mg.

ENDORSED THERAPIES

- A twice daily, seven-day regimen of PPI, metronidazole 500 mg and amoxicillin 1000 mg; or
- A twice daily, 14-day regimen of bismuth subsalicylate two tablets qid, metronidazole 250 mg qid and tetracycline 500 mg qid (bismuth plus metronidazole plus tetracycline [BMT])

Treatment failure in patients who received metronidazole in the first course:
- A twice daily, seven- to 14-day regimen of PPI or RBC, amoxicillin 1000 mg and clarithromycin 500 mg; or
- A 14-day course of PPI plus BMT.

Treatment failure in patients who received amoxicillin in the first course:
- PPI or RBC, metronidazole 500 mg and clarithromycin 500 mg; or
- A 14-day course of PPI plus BMT.

OTHER CONSIDERATIONS IN THE MANAGEMENT OF H PYLORI INFECTION

Much work remains to define the relationship between H pylori infection and diseases other than peptic ulcer. A periodic review of the guidelines is appropriate. Reassessments to accommodate new information are essential. The risk posed by H pylori infection for life-threatening conditions, such as cancer, may prove to be great enough to justify more aggressive strategies of testing and treatment recommendations. Conversely, H pylori colonization of the human stomach may modify pH level or other factors to ameliorate (offer some protection from) some diseases in certain specific disease states (ie, gastrointestinal esophageal reflux disease and NSAID-induced ulcers).

A key focus is pediatric H pylori infection. In part due to lack of information, there has been relatively little clinical guidance provided for clinicians confronted with H pylori infection in children. The Canadian Consensus Conference on H pylori infection in childhood took place in November 1998 to address specifically guidelines for the management of H pylori in the pediatric population. The conclusions and guidelines will be reported later in 1999.

SUMMARY

Eradication of H pylori infection in patients with peptic ulcer disease has profound implications for reducing adverse health outcomes in Canada. Moreover, eradication treatments are cost effective relative to symptomatic treatment with antisecretory therapies. Despite the increasing availability of effective and readily tolerated treatment regimens, much still needs to be done to ensure widespread availability, acceptance and use of urea breath testing, and appropriate reimbursement by provincial and third-party payers. Primary care physicians must join with specialists in the effort to identify and treat H pylori infection in appropriate patients. Recognizing when diagnosis and treatment of H pylori infection can improve patient care is important. The present guidelines are designed for simplicity and ease of implementation as an update to the recommendations from the previous Canadian Consensus Conference (1997) (1).

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REFERENCES

APPENDIX: PARTICIPANTS IN THE UPDATE CONFERENCE OF THE CANADIAN HELICOBACTER PYLORI CONSENSUS CONFERENCE

The following people were participants in the update conference of the Canadian *Helicobacter pylori* Consensus Conference and are co-authors of the present paper:
- David Armstrong, Andrew Badley, Alan Barkun (official representative of the Canadian Association of Gastroenterology), William Bartle (official representative of the Canadian Pharmaceutical Association), Linda Best, Ted Bosworth, Trudy Burnside (official representative of Astra Pharma Inc), Hugh Chaun, Naoki Chiba, Pierre Cloutier...


representative of Abbott Laboratories), Alan Cockeram, Ken Croitoru, Larry DaCosta, Mario deSales-Monteiro, Collette Deslandres, Reggie Downey (official representative of Axcan Pharma Inc), Eric Drouin, Brian Feagan, Nigel Flook (official representative of the College of Family Physicians of Canada), Gilles Fortin (official representative of Abbott Laboratories), Avery Goodwin, Maha Guindi, Eric Hassall, Paul Hoffman, Nicola Jones, Raymond Lahaie, Bryan Laskey (official representative of Glaxo Wellcome Inc), Rob Logan (official representative of Byk Canada Inc/Solvay Pharma Inc), Nicholas Makris, Francois Martin (official representative of Axcan Pharma Inc), Philippa McDonald (official representative of the Health Protection Branch), Myron Pyzyk (official representative of Byk Canada Inc/Solvay Pharma Inc), Robert Riddell, Raphael Saginur (official representative of the Canadian Infectious Diseases Society), Micheline Ste Marie, Vinod Sharma (official representative of the Province of New Brunswick), Phil Sherman, Joe Sidorov, Paul Sinclair (official representative of Astra Pharma Inc), Fiona Smaill, Lesley Smith, Connie Switzer, Diane Taylor, Gervais Tougas, Trevor Trust (official representative of Boston Research Center), Scott Whittaker, Russell Williamson (official representative of Glaxo Wellcome Inc) and Gloria Zaror-Behrens (official representative of the Health Protection Branch).