Helicobacter pylori: corrections and comments

In the article "*Helicobacter pylori*: new developments and treatments" (*Can Med Assoc J* 1997;156[11]:1565-74), by Dr. Sander J.O. Veldhuyzen van Zanten and associates, the 4th drug regimen (for omeprazole in combination with 3 other drugs), presented in Table 1 and discussed in the text on page 1591, does not match the regimen presented in reference 97, the article cited for this information. The original *Lancet* article[1] recommended omeprazole 20 mg twice daily, not once daily. Patients in the omeprazole group received that drug for 3 days before initiation of treatment with the other drugs (bismuth subsalicylate, metronidazole and tetracycline [BMT]). In addition, the dosage for metronidazole was 250 mg 3 times daily, not 4 times. Finally, the volume number for the reference was given incorrectly; it is 345, not 335.

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Received via email

Reference

1. De Boer W, Driessen W, Jansz A, Tytgat GNJ. Effect of acid suppression on efficacy of treatment for *Helicobacter pylori* infection. *Lancet* 1995;345:817-20.

The authors of this article cite a long list of references, 112 in all, which I assume represents a fairly comprehensive review of the available scientific data on the subject of *Helicobacter pylori* infection and ulcers. However, the words "double blind" appear in the title of only one paper of those listed (reference 63),[1] and the title of that paper suggests that the outcome was judged by biochemical rather than patient findings.

Despite an interest in *H. pylori* and the effect of its eradication, I have yet to see a double-blind trial comparing documented ulcer recurrence over a substantial period in patients receiving conventional therapy plus placebo and those receiving conventional therapy plus *H. pylori* eradication therapy.

If such a trial exists, I would be grateful to have it brought to my attention. Without such evidence, *H. pylori* eradication is a pack of cards supported only by the massive investments in marketing by the makers of proton-pump inhibitors.

Paul Cary, MB, BS
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Reference

1. Veldhuyzen van Zanten SJO, Hunt RH, Cockeram A, Schep G, Malatjalian D, Matisko A, et al. Adding omeprazole 20 mg once a day to metronidazole/amoxicillin treatment of Hp-gastritis: a randomized double blind trial. The importance of metronidazole resistance [abstract A417]. *Am J Gastroenterol* 1994;89:1389.

[The authors respond:]

We would like to thank Janet Cooper for pointing out the errors in our article. Although the dosing schedule from reference 97 was indeed quoted incorrectly, the dosages for omeprazole-BMT quadruple therapy given in Table 1 were correct: omeprazole 20 mg, bismuth subsalicylate 2 tablets qid, metronidazole 250 mg qid and tetracycline 500 mg qid. This was based on our "best estimate" from the published literature, including references 98 and 99 in our paper as well as other recently published studies.[1–3]

Unfortunately, there are no definitive, head-to-head comparative studies resolving all of the questions about doses and treatment duration. The following issues are still unclear: Is a twice-daily dose of omeprazole better than a once-daily dose? Does treatment with omeprazole before the initiation of BMT improve success? What is the best dose and frequency for metronidazole, and what is the optimal duration of treatment? Future studies should help resolve these uncertainties.

Paul Cary is correct in noting that randomized controlled trials (RCT) are the gold standard for the evaluation of new therapies. He is mistaken in stating that few such trials are available for *H. pylori*. Indeed, several of the studies evaluating treatment that we cited in our paper are high-quality RCTs meeting the criteria of grade I evidence. In fact, for duodenal ulcer trials the evidence is so overwhelming that the US Food and Drug Administration now accepts successful cure of *H. pylori* infection as a surrogate endpoint, and proof of a decrease in the frequency of recurrence of the ulcer is no longer required.

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References

1. Hosking SW, Ling TKW, Chung SCS, Yung MY, Cheng AFB, Sung JJY, et al. Duodenal ulcer healing by eradication of *Helicobacter pylori* without anti-acid treatment: randomized controlled trial. *Lancet* 1994;343:508-10.
2. De Boer WA, van Etten RJXM, Schade RWB, Ouwehand ME, Schneeberger PM, Tytgat GNJ. 4-day lansoprazole quadruple therapy: a highly effective cure for *Helicobacter pylori* infection. *Am J Gastroenterol* 1996;91(9):1778-82.
3. Kung NNS, Sung JJY, Yuen NWF, Ng PW, Wong KC, Chung ECH, et al. Anti-*Helicobacter pylori* treatment in bleeding ulcers: Randomized controlled trial comparing 2-day versus 7-day bismuth quadruple therapy. *Am J Gastroenterol* 1997;92(3):438-41.

Needle exchange programs

The thing that bothers me about articles on needle exchange programs, such as the one by Michelle Gold and associates ("Needle ex-