The urea breath test for *Helicobacter pylori* infection: taking the wind out of the sails of endoscopy

Carlo A. Fallone, Sander J.O. Veldhuyzen van Zanten, Naoki Chiba

Technology: Urea breath test (UBT)
Use: Detection of *Helicobacter pylori* infection
History: *H. pylori* is found in the stomach of an estimated 20%–40% of Canadians.[1] It was discovered almost by accident in 1982 by Warren and Marshall on culture plates left incubating over a long weekend. To prove that *H. pylori* was a pathogen, Marshall swallowed these bacteria to cause histologic gastritis. There is now irrefutable evidence that this bacterium plays a decisive role in the development of duodenal and gastric ulcers and low-grade gastric lymphoma and that it is associated with gastric adenocarcinoma.

The diagnosis of *H. pylori* infection has traditionally involved endoscopy with biopsies of the gastric mucosa for histology and culture. In search for less intrusive methods, serological tests measuring IgG antibody levels have been developed. However, these tests have suboptimal sensitivity and specificity (85% and 79%).[2] Also, because the prevalence of *H. pylori* infection is about 30% among 40-year-old Canadians, the positive predictive value of a typical serological test would be 63%, which translates to a large false-positive rate of 37%.[3]

Breath tests have been used in gastroenterology since the 1970s to detect malabsorption. For the most part, they measure exhaled hydrogen as an indication of bacterial breakdown of sugars. The concept of a breath test for *H. pylori* detection was simultaneously developed by Graham and colleagues[4] and Marshall and Surveyor.[5] It is based on the finding that *H. pylori* possesses a very active and specific urease enzyme. The patient ingests an isotope-labelled urea solution, which is broken down by the urease enzyme into carbon dioxide (CO_2) and ammonia (Fig. 1). A high level of labelled CO_2 in the patient's breath suggests *H. pylori* infection.
Promise: Numerous variations of the UBT have been successfully tested and validated, with a sensitivity and specificity of about 95%.[3] It is the noninvasive test of choice for diagnosing active *H. pylori* infection and for confirming eradication after treatment.[3] Serologic tests generally cannot be used to confirm eradication. Indeed, the UBT may be considered the gold standard for *H. pylori* detection because it avoids the potential sampling error present with endoscopic biopsy of this sometimes patchy gastric infection.

With the advantage of potentially avoiding endoscopy, UBT is very attractive. The carbon-14 (radioactive) UBT is available at some university health centres but must be performed in a nuclear medicine facility. With the carbon-13 (nonradioactive, stable) UBT, breath samples can be collected anywhere (e.g., physician's office) and then mailed to a centre for analysis. Several ^{13}C UBTs are being developed and marketed in Canada.

Recently a number of consensus conferences have recommended an "*H. pylori* test and treat" approach to patients presenting with dyspepsia.[6] Those under 50 years of age without alarm symptoms are tested for *H. pylori* with a noninvasive test and treated if the result is positive. This approach reduces the number of endoscopies needed to manage such patients and has been found to be cost-effective in both the United States and Canada.[7] Based on these economic models using Canadian data, the UBT could thus reduce health care costs. Although more expensive than serologic testing in this approach, it is more effective.[7]
Problems: The biggest problem with the UBT is that it is not yet widely available. Another problem is that most third-party payers have yet to provide reimbursement. Also, this new technology facilitates *H. pylori* testing in patients who may not have a valid indication for testing. Indiscriminant testing is discouraged because physicians increasingly feel obligated to treat any patient whose test result is positive. Widespread use of antibiotics may then lead to antibiotic resistance in the

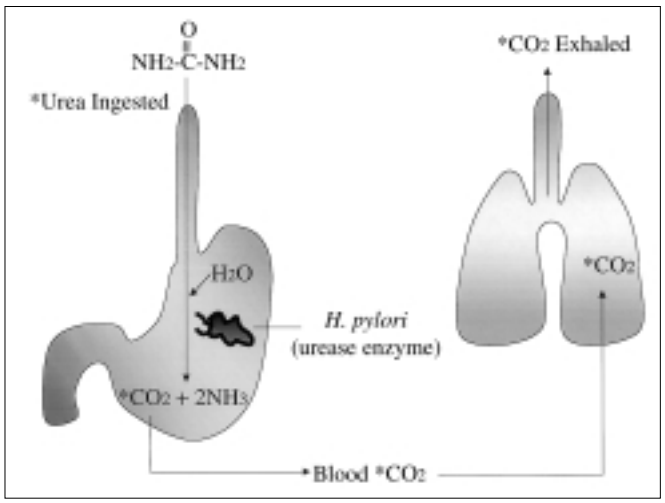

Fig. 1: Urea breath test. Urea, labelled with either carbon-13 or carbon-14 (*), is ingested by the patient. If *Helicobacter pylori* infection is present, the bacterium's urease enzyme breaks down the urea in the stomach. The labelled carbon dioxide ($*CO_2$) is subsequently absorbed in the blood and exhaled.

community. Testing should be performed 4 weeks after antibiotics have been stopped and 7–14 days after proton pump inhibitors or H_2 antagonists have been stopped, to avoid false-negative results. Another problem is that important structural abnormalities, such as esophagitis, ulcer disease and cancer, are missed if endoscopy is not performed in people who require this procedure, notably patients with alarm symptoms (weight loss, signs of bleeding, advanced age).

Prospects: The UBT is a simple test that, when used properly, can help cure peptic ulcer disease and rid a certain proportion of people with non-ulcer dyspepsia of their symptoms without the need for a gastroscopic or barium examination. This technology has great potential, and its use will likely increase. Provided that clear indications for testing are developed and communicated to physicians, the UBT has the potential to save cost and improve patient care.

Competing interests: Drs. Fallone and Chiba have received research funding and consultation fees for work related to upper gastrointestinal disorders from several pharmaceutical companies (including Abbott Laboratories, AstraZeneca, Axcan Pharma, Solvay Pharma and Glaxo Wellcome). Dr. van Zanten received research funding from Alimenterics Inc., New Jersey, for clinical trials of a UBT; he has also received funding for research involving the upper gastrointestinal area from several pharmaceutical companies (including Abbott Laboratories, AstraZeneca, Axcan Pharma, Pfizer and Glaxo-Wellcome) and speaker fees and travel assistance to attend meetings from several of the companies listed.

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Dr. Fallone is with the Division of Gastroenterology, Royal Victoria Hospital, and the McGill University Health Centre, McGill University, Montreal, Que.; Dr. van Zanten is with the Queen Elizabeth II Health Sciences Centre, Dalhousie University, Halifax, NS; and Dr. Chiba is with the Surrey GI Clinic/Research, Guelph, Ont., and the Division of Gastroenterology, McMaster University, Hamilton, Ont.