

## A 20-Minute Breath Test for *Helicobacter pylori*

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In this study, we evaluated a simplified rapid  $^{14}\text{C}$ -urea breath test for the diagnosis of *Helicobacter pylori*. Fasting patients undergoing initial assessment for *H. pylori* drank 5  $\mu\text{Ci}$  of  $^{14}\text{C}$ -urea in 20 ml of water. Breath was collected at intervals for 30 min. Samples were counted in a  $\beta$ -counter, and the results were expressed as counts per minute (cpm). In the same week, patients underwent endoscopy, and a blinded investigator examined biopsy samples of gastric mucosa by culture and histology for *H. pylori*. There were 49 *H. pylori*-negative (HP-) and 104 *H. pylori*-positive (HP+) patients in the study. HP+ patients expired a mean of 4398 cpm (SD 2468) per mmol  $\text{CO}_2$  in a sample taken 20 min after ingestion of the isotope. In contrast, HP- patients expired only 340 cpm (SD 196). If the mean +3 SD of HP- patients was used as a cutoff value, the 20-minute sample gave a sensitivity of 97% and a specificity of 100% for detecting *H. pylori*. The radiation exposure from this test is less than 1% of that received from an upper gastrointestinal series, and the short collection time makes it both convenient and cost effective.

### INTRODUCTION

*Helicobacter pylori* infection of the gastroduodenal mucosa causes active chronic gastritis and may predispose to peptic ulceration (1, 2). Until recently, the diagnosis of *H. pylori* has relied upon endoscopic biopsy of the gastric mucosa. Fortunately, *H. pylori* produces large amounts of urease, an enzyme that may buffer surrounding hydrogen ions by the production of ammonia and bicarbonate (3). Urease is not present in mammalian tissues unless there is bacterial colonization (4), so the presence of abundant gastric urease is diagnostic of *H. pylori* infection (5).

Graham *et al.* (6) were the first to report the use of a breath test for the detection of gastric urease activity. Because of inherent limitations in the  $^{13}\text{C}$ -urea method

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(see Discussion), a liquid meal was used to delay gastric emptying, and  $^{13}\text{C}$  was measured in breath collected for 60–90 min. Bell *et al.* (7) and Rauws *et al.* (8) used  $^{14}\text{C}$ -urea in an almost identical fashion and measured cumulative  $^{14}\text{CO}_2$  excretion.

Marshall and Surveyor (9) described an alternative method in which  $^{14}\text{C}$ -urea was administered in water to fasting patients.  $^{14}\text{CO}_2$  excretion peaked before 20 min, leading the authors to suggest that a single breath sample taken between 10 and 20 min might be sufficiently accurate for routine use in diagnosis. Most investigators have allowed for endogenous  $\text{CO}_2$  production by correcting for body weight (7, 8, 10, 11), thus mandating the continued use of awkward calculations.

In the present paper, we describe further evaluation of the rapid  $^{14}\text{C}$ -urea breath test with the aim of defining criteria for diagnosis of *H. pylori* from a single breath sample.

### SUBJECTS AND METHODS

The study was approved by the Human Investigation Committee of the University of Virginia Health Sciences Center, and all participants signed informed consent. Patients were consecutive new cases on whom endoscopy was performed at the Gastritis Clinic. Patients with a history of gastric surgery or who had recently taken antibiotics or bismuth medication were excluded from the study. Females who could have been pregnant were tested within 10 days after the start of their last menstrual period.

#### *Preparation of isotope and reading of samples*

Lyophilized  $^{14}\text{C}$ -urea was obtained in a 9250-kBq (250- $\mu\text{Ci}$ ) ampule, and was reconstituted with 25 ml of sterile water. One hundred eighty-five kBq (0.5 ml) of the solution was pipetted into a 20-ml vial with an additional 2.0 ml of sterile water. A 0.01-ml sample of this solution was used as a batch standard. Each 2.5-ml dose was frozen at  $-20^\circ\text{C}$  until it was used. Immediately before use, the solution was thawed to room temperature, and 17.5 ml of tap water were added.













