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A 20-Minute Breath Test for *Helicobacter pylori*

Barry J. Marshall, M.B.B.S., F.R.A.C.P., Michael W. Plankey, C.N.M.T., Susie R. Hoffman, R.N., B.S.N., Cheryl L. Boyd, M.S., Kevin R. Dye, M.D., Henry F. Frierson, Jr., M.D., Richard L. Guerrant, M.D., and Richard W. McCallum, M.D.

Department of Internal Medicine, Division of Gastroenterology, University of Virginia Health Sciences Center, Charlottesville, Virginia

In this study, we evaluated a simplified rapid ^{14}C-urea breath test for the diagnosis of *Helicobacter pylori*. Fasting patients undergoing initial assessment for *H. pylori* drank 5 μCi of ^{14}C-urea in 20 ml of water. Breath was collected at intervals for 30 min. Samples were counted in a β-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 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}C-urea method (see Discussion), a liquid meal was used to delay gastric emptying, and ^{13}C was measured in breath collected for 60–90 min. Bell *et al.* (7) and Rauws *et al.* (8) used ^{14}C-urea in an almost identical fashion and measured cumulative $^{14}CO_2$ excretion.

Marshall and Surveyor (9) described an alternative method in which ^{14}C-urea was administered in water to fasting patients. $^{14}CO_2$ 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 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}C-urea breath test with the aim of defining criteria for diagnosis of *H. pylori* from a single breath sample.

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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}C-urea was obtained in a 9250-kBq (250-μCi) 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°C until it was used. Immediately before use, the solution was thawed to room temperature, and 17.5 ml of tap water were added.

Breath samples were collected in the following manner (Fig. 1). Patients blew through a disposable drinking straw attached to a liquid trap, into a 20-ml glass scintillation vial containing 2.5 ml of methanol in which 1 mmol of hyamine (methylbenzethonium hydroxide) was dissolved and to which thymolphthalein pH indicator had been added. The blue (alkaline) solution became colorless, upon CO_2 saturation, at which time a constant amount (≈1.0 mmol) of CO_2 had been collected.

Ten milliliters of liquid scintillant (Ready-Safe; Beckman catalog #158735) were added to each vial, and each sample was counted in a liquid scintillation counter ("Rackbeta"; Pharmacia LKB), using a quenching correction with the output expressed as counts per minute (cpm). A standard provided by the manufacturer indicated the counting efficiency of the machine to be 93.6%. Throughout the remainder of the paper, disintegrations per minute (dpm) may thus be derived by multiplying cpm by 1.068 (100/93.6).

Preliminary studies

To define the $^{14}CO_2$ excretion pattern immediately after ingestion of ^{14}C-urea, we studied 10 volunteers whose *H. pylori* status was known from previous biopsy studies (six HP−, four HP+).

We studied six subjects (six HP−) to determine whether urease from the oral bacterial flora was an important factor. For each subject, 37 kBq (1 μCi) of ^{14}C-urea were dissolved in 10 ml of water given as a mouthwash. The solution was not swallowed. After 15 s, the liquid was expectorated, and subjects subsequently washed their mouth for 15 s with tap water. Breath samples were collected before the subjects used the ^{14}C-urea mouthwash, and at 2, 4, 8, 12, and 20 min.

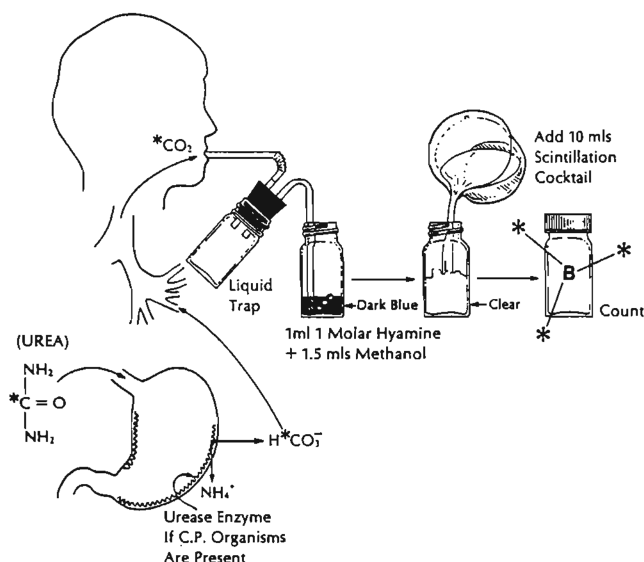

FIG. 1. If urease (*H. pylori*) is present in the gastric mucosa, isotope-labeled urea is hydrolyzed, forming $^{14}CO_2$ which is expired in the breath. Patients blow through a disposable drinking straw attached to a liquid trap, into a 20-ml vial containing methanol, hyamine, and a pH indicator. The blue (alkaline) solution becomes colorless upon CO_2 saturation. Ten milliliters of scintillation fluid are added to the sample, which is then counted for 5 min in a scintillation counter. (Note: caution is required handling hyamine solution, a strong base.)

To define the ^{14}C excretion curve due to bacterial urease in the esophagus and stomach, we studied six subjects (two HP−, four HP+). A 12-inch pediatric nasogastric tube was passed through the mouth into the upper esophagus, and 37 kBq of ^{14}C-urea in 20 ml of water were injected. Breath samples were collected from the subjects before they received the ^{14}C-urea, and at 2, 4, 8, 12, and 20 min.

To define the general shape of the ^{14}C excretion curve in HP− subjects, 185 kBq of ^{14}C-urea were dissolved in 20 ml of water, given by mouth. Breath samples were collected as described above.

Main study

Patients took the breath test during their week of endoscopy. After they had fasted for at least 6 h, a baseline breath sample was collected. Patients then removed false teeth (if present), cleansed their mouths with toothpaste, and were then given 185 kBq (5 μCi) of ^{14}C-labeled urea dissolved in 20 ml of water. Patients swallowed the radioisotope in a single swallow, attempting to prevent the solution from coating the inside of the mouth. They cleansed their mouth a second time by rinsing with water and remained seated during the remainder of the test. A breath sample was taken at 2 min in order to quantify urea hydrolysis in the oropharynx, and further samples were taken at 15, 20, 25, and 30 min.

At endoscopy, four antral and two body mucosa biopsies were taken. The antral biopsies were taken in the dependent portion of the greater curve, 5 cm proximal to the pylorus (2). The first antral biopsy was used for a CLOtest rapid urease test (Tri-Med, Kansas). The second antral specimen was placed in 150 μl of sterile saline and transported within 2 h to the microbiology laboratory for culture.

Two biopsy specimens for histologic examination were taken from the same area of the antrum and two others from the body mucosa. These specimens were fixed in formalin, embedded in paraffin, and stained with hematoxylin-and-eosin and Geimsa stains.

Data were collected prospectively and independently by the microbiologist, histopathologist, and nuclear medicine technologist.

H. pylori-positive (HP+) patients had cultures that grew the organism, or biopsies in which short, curved rods were seen adjacent to the mucosal cells in the Giemsa-stained sections. *H. pylori*-negative (HP−) persons were those in whom all tests for *H. pylori* (histology, CLOtest, and culture) failed to detect the organism.

Discordant results were rechecked and reconciled, sometimes by repeat endoscopy and biopsy.

To analyze the results, we used the descriptive statistics of the SAS statistical package (The SAS Institute, Cary, NC) (12). Initial breath tests from the 49 HP− patients were used to define normal ranges. Body surface area was calculated by the formula derived by Haycock *et al.* (13). Correlation and linear regression analyses were used to explore relationships between cpm values and body surface area.

RESULTS

Preliminary studies

When given as a mouthwash, ^{14}C-urea solution caused an immediate peak of $^{14}CO_2$ excretion in a 2-min breath sample. After this peak, breath activity declined, with a half-time of 2–3 min, to reach near-baseline levels after 12 min. Although the magnitude of the peak varied in different subjects, the shape of the curve was similar (Fig. 2).

When ^{14}C-urea solution was given directly into the esophagus, bypassing the oropharynx, two patterns were seen. In HP− subjects, isotope excretion did not increase more than 50 cpm above the baseline value (Fig. 3). In HP+ subjects, $^{14}CO_2$ excretion rose within 4 min and peaked between 8 and 20 min (Fig. 3).

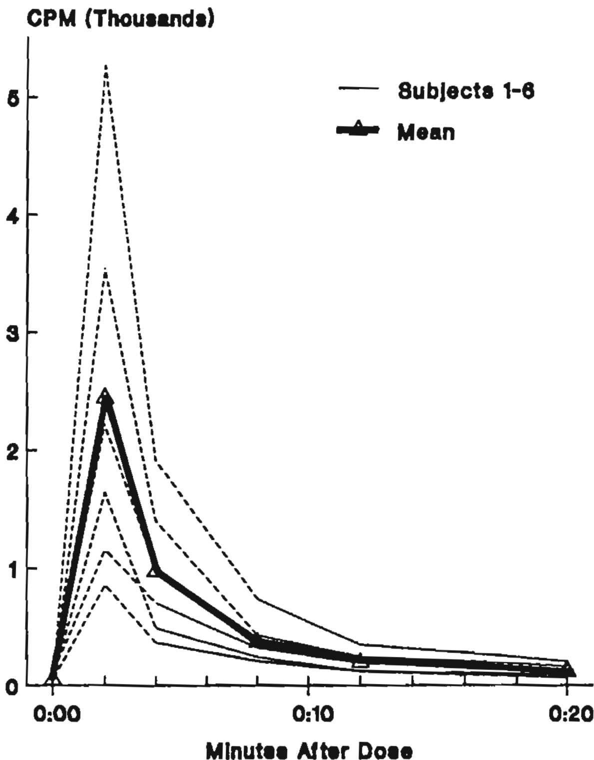

FIG. 2. When ^{14}C-urea is given as a mouthwash, there is an immediate rise in $^{14}CO_2$ excretion that peaks before 2 min and then falls rapidly to approach baseline levels by 12 min.

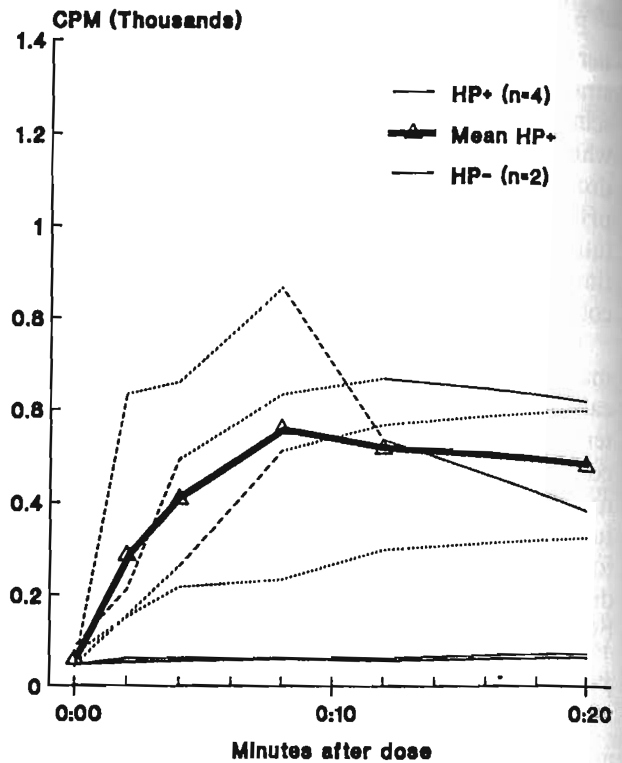

FIG. 3. When ^{14}C-urea is given directly into the esophagus, a gradual rise in $^{14}CO_2$ excretion is seen in HP+ subjects (*upper curves*). In HP-subjects, only a very small rise in $^{14}CO_2$ excretion is seen (*flat lines near bottom of graph*).

When six HP− subjects were given 185 kBq orally, ^{14}C excretion curves were identical in shape to those of the ^{14}C-urea mouthwash experiment. This indicated that, in the HP− persons, oropharyngeal urease activity was the only source of breath $^{14}CO_2$.

Main study

One hundred fifty-three patients (77 female, 76 male) took part in the main study. Of these, 104 were HP+ as determined by combined analysis of the culture, CLOtest, and histology specimens.

Breath tests from the 49 HP− patients were used to define the negative (normal) range. For any time point, "normal" was a cpm value below the mean + 3 SD obtained for this group. The specificity of the test was the percent of HP− patients who were included in the normal range by these criteria. This was then applied to the HP+ group to determine the percentage that was "abnormal" (had ^{14}C excretion above the normal range), *i.e.*, the sensitivity of the test. The sensitivity and specificity of the test at times 15, 20, 25, and 30 min are shown in Table 1. A scattergram of 20-min samples from the 153 patients is shown in Figure 4.

TABLE 1
Accuracy of Samples Taken between 15 and 30 Minutes after Ingestion of ^{14}*C-Urea*

Time (min)	15		20		25		30	
Mean HP neg (SD)	472 (316)		340 (196)		290 (164)		254 (144)	
Cut-off value (Mean + 3 SD)	1422		928		784		687	
Breath test result	−	+	−	+	−	+	−	+
HP−	35	0	49	0	25	1	25	2
HP+	5	73	3	101	2	66	1	67
Positive predictive value	100%		100%		98.5%		98.5%	
Negative predictive value	87%		94%		93%		96%	
Efficiency	87%		94%		92%		96%	

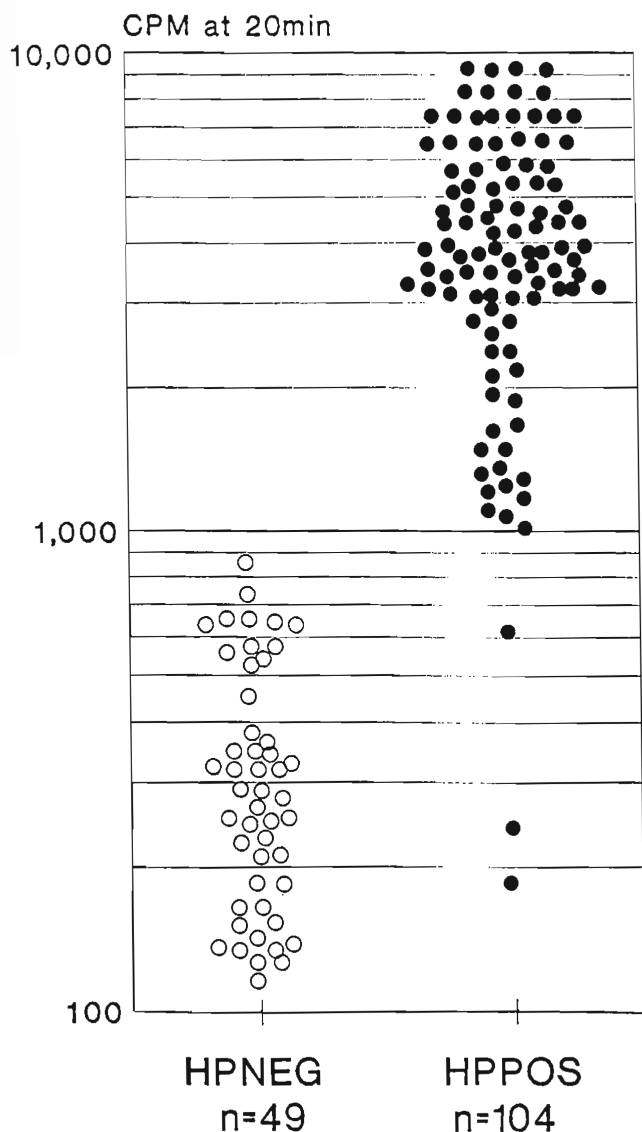

FIG. 4 ^{14}C-Urea breath tests from 153 patients. (With the logarithmic Y axis, large differences between HP- and HP+ are less apparent).

Effect of sex and body surface area

Other investigators have corrected $^{14}CO_2$ excretion for body weight in order to allow for the effect of endogenous CO_2 production on measured gastric urease activity. For example, a large person generates more unlabeled CO_2 causing $^{14}CO_2$ to be more dilute, resulting in lower cpm values in a collected 1 mmol sample. In practice, we found this effect relatively unimportant. Correlation between isotope excretion and body surface area was poor ($r^2 = 0.0137$), and the relationship was not significant in HP+ patients ($p < 0.3$). In general, HP+ males gave slightly lower cpm than HP+ females (Fig. 5). This difference was significant by Wilcoxon test ($p < 0.01$), but did not affect the ability of the breath test to discriminate between HP+ and HP− patients. This was because sex did not affect $^{14}CO_2$ excretion in HP− subjects, so the upper limit of the normal range was the same for males and females.

Accuracy was not improved either if the total $^{14}CO_2$ excretion was estimated as the area under the excretion curve. From Figure 5, it can be seen that the excretion rate fell in an almost linear fashion after 15 min; therefore, the absolute height of the curve at 20 min was an excellent indicator of the area beneath it ($r^2 = 0.93$, $p < 0.0001$).

DISCUSSION

Our preliminary studies served to characterize sources of urease in the oropharynx. Urease from com-

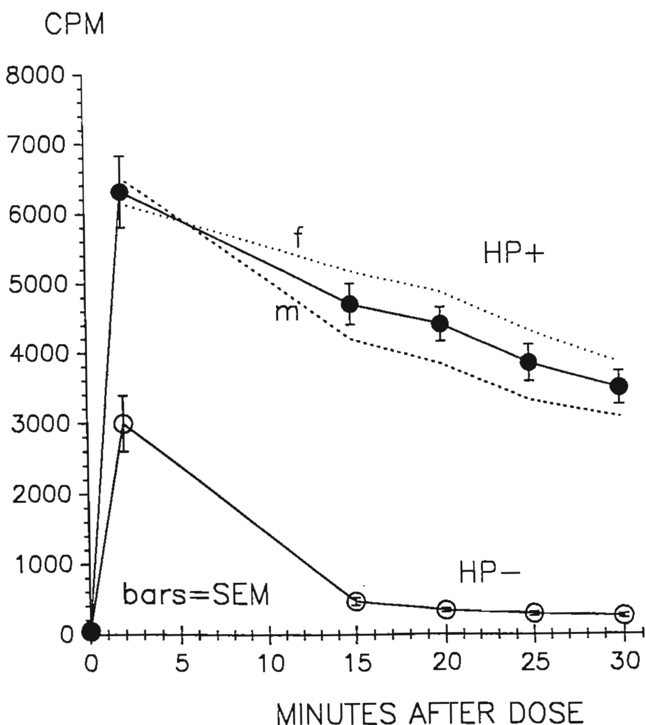

FIG. 5. Graph displaying the ^{14}C excretion between 2 and 30 min. Females with *H. pylori* give slightly higher cpm due to lower endogenous $^{12}CO_2$ production. Fine details of HP-negative curve are given in Table 1.

mensal mouth organisms resulted in $^{14}CO_2$ generation in the oral mucosa which contaminated the exhaled breath. This occurred only in the first 10 min after the isotope was ingested (Fig. 2).

Subsequent experiments suggested that this contamination was direct rather than reflecting absorption of isotopic CO_2 and exhalation through the lungs. When ^{14}C-urea was instilled directly into the esophagus, there was no immediate rise in isotope excretion (Fig. 3). Apparently, if any CO_2 was generated in the esophagus, it did not enter the bloodstream, and neither could it directly contaminate the expired breath.

When ^{14}C-urea was instilled into the esophagus of HP+ subjects, $^{14}CO_2$ excretion rose smoothly and reached 75% of the maximal value within 10 min. In subjects with high gastric urease activity, excretion peaked by 8 min, whereas in persons with low gastric urease activity, $^{14}CO_2$ excretion was still rising 20 min after receiving ^{14}C-urea. We believe that when gastric urease activity was very high, the ^{14}C-urea substrate was rapidly decomposed in the stomach. This resulted in a very high peak $^{14}CO_2$ excretion, which was still relatively high at 20 min. In persons with low gastric urease activity, a continuous rise in $^{14}CO_2$ excretion was seen for up to 20 min. Thus, presence of gastric urease in HP+ subjects was reflected by the absolute height of the curve, and also by its positive slope in the first 10 min after ingestion of the isotope (Fig. 3).

In subjects who did not have *H. pylori,* ingestion of ^{14}C-urea resulted in an isotope excretion curve identical in shape to that seen with ^{14}C-urea mouthwash. This was further evidence that initial $^{14}CO_2$ excretion was due solely to mouth flora. In HP− subjects, urea hydrolysis occurred only in the mouth, so that, by 10 min, $^{14}CO_2$ excretion had returned to near-baseline values.

Since $^{14}CO_2$ excretion peaks between 8 and 20 min after ingestion of the isotope, it is likely that the substrate is exhausted by this time. Exhaustion of the substrate reflects three processes: urea hydrolysis, absorption of intact urea, and emptying from the stomach. Marshall and Surveyor (9) found that about half of the isotope was absorbed unchanged and excreted in the urine. To our knowledge, the amount of unchanged urea absorbed in other test methods has never been estimated.

Comparison with other ^{13}C and ^{14}C-urea breath tests

Unlike other published methods (6, 7, 11, 14, 15), our breath test does not require a test meal, thus allowing undiluted isotope to be fully exposed to gastric mucosal urease. The total amount of urea ingested is less than 1 μmol, but ^{14}C is very rare in nature (16), so the isotope is easily detected as a low-energy β emission in breath CO^2. Our initial studies show that in HP+ patients, hydrolysis peaks 10 min after ingestion, so there is no need to give patients a calorie-rich meal to delay gastric emptying of the solution. As a result, a short breath collection time is possible. Since we have shown that mouth urease interferes with breath samples taken before 15 min, it is sensible to take the critical sample after this time. Our ability to diagnose nearly all HP+ patients with a single sample taken at 20 min may provide a cost advantage for this type of breath test.

Whereas ^{14}C is rare, ^{13}C (a nonradioactive isotope) makes up about 1.1% of all carbon in nature. In addition, the ratio of ^{13}C to ^{12}C expired in the breath varies with diet and the level of physical activity (16). Thus, a relatively large dose of ^{13}C-urea substrate is necessary to measurably increase $^{13}CO_2$ excretion. In practice, 2.5–5 mg/kg of urea (150–250 mg/patient) is used to obtain the necessary >0.6% increase in ^{13}C seen in infected patients (6, 17). Aware of these limitations, Graham and Klein (6, 17) collected a baseline sample to control for intersubject variation, then used a high calorie liquid test meal to hold the isotopic urea in the stomach. *H. pylori* urease enzyme has a K_m of around 1 mmol of urea (18), a concentration far exceeded in the ^{13}C-urea test. This made it necessary to hold the reagents in the stomach while the reaction proceeded. For these reasons, the ^{13}C-urea breath test had a longer collection time. Besides using a nonradioactive isotope, the advantage of the ^{13}C-urea test was its ability to accurately quantify gastric mucosal urease, since the enzyme was always saturated, allowing urea hydrolysis to proceed at a constant rate independent of substrate concentration. The disadvantage was the relatively large investment in patient and technician time, the cost of the isotope, the number of samples required, and as a result, the expense.

Subsequent studies in which ^{14}C-urea was used appear to have copied Graham's methodology, in that the isotope is given with a liquid meal (7, 8, 11, 15). Our data suggest that retention in the stomach with a meal is not necessary, because the actual amount of isotopic urea ingested is very small, and $^{14}CO_2$ excretion is detectable within minutes of ingesting the isotope. Our mean ^{14}C excretion gave a cpm of 4398 at 20 min, much higher than counts described in meal-based ^{14}C-urea breath tests cited above (7, 11, 14, 15). The higher recovery enables speedy scintillation counting, with most of our 20-min samples differentiating as either positive or negative after 5 min.

We believe that giving the ^{14}C-urea with a meal dilutes it and decreases contact between isotope and gastric mucosa. Rauws *et al.* (14) reported that the test meal caused higher counts to be obtained, but their data involved only seven positive patients, the time intervals used may have missed a peak, and they diluted the ^{14}C isotope with 350 mg cold urea. Extrapolating

from their published data, cpm in the range of 1500 were obtained. Their error is demonstrated by Van Zanten's data in which a mean cpm of only 1400 was obtained in the HP+ group (15).

Most investigators have given the ^{14}C-urea with non-labeled urea so that the enzyme will be saturated, as in the ^{13}C urea breath test (14, 15). Provided that the isotope and test meal are evenly distributed within the stomach, this allows the amount of ^{14}C appearing in the breath to reflect the total amount of gastric urease. Whereas exact quantification of gastric urease may be of value in a research setting, we believe its clinical usefulness has not been substantiated. We also maintain that the addition of complicated equations to allow for endogenous CO_2 production serves only to bewilder physicians, and increases the chance of error. In support of data expressed in cpm, Van-Zanten (15) found no advantage in such calculations, even with a meal-based test.

Safety of ^{14}C-urea

The safety of ^{14}C-urea is poorly described in the available gastroenterology literature. The units for radiation dosimetry have changed several times, and some authors have made errors in published papers which have then been perpetuated by others (19, 20, 14). Most of the concern relates to the long half-life of ^{14}C, which is really of little relevance for compounds such as urea and CO_2, which are so rapidly excreted.

To allow radiation sources to be compared, emissions of various origins are expressed in "dose equivalence units" (DE). The DE for ^{14}C takes into account the fraction of isotope sequestered in each organ, the biological half-life of the isotope in that tissue, the effective energy of β particles compared with standard ionizing radiation (a 200 kV x-ray source), and the administered dose. Since ^{14}C has a long half-life, the activity of the administered isotope can be regarded as constant for the time it is present in the body. DE is expressed in Sieverts (1 Sievert = 100 rem). Since Sieverts are not widely used in the U.S. literature, the following discussion will use the older unit of DE, rem and millirems (mrem).

The average DE exposure to naturally occurring radiation is a minimum of 88 mrem/yr (21). In addition, the population of the United States is exposed to approximately 50 mrem/yr of radiation due to diagnostic x-rays (22). Put another way, the gonadal or bone marrow DE for the average American is 2–3 mrem/wk. Natural radiation is doubled for persons living in Colorado, and may also be increased by airplane travel at the rate of 0.3 mrem/h. Because most people in the United States do not concern themselves with the risk of radiation from air travel or living in Colorado, radiation doses of less than 10 mrem/yr are generally regarded as trivial.

The radiation dose from the ^{14}C-urea breath test was calculated by Marshall and Surveyor (9), who measured unchanged ^{14}C-urea in urine and obtained breath CO_2 excretion from the data of Yap *et al.* (23). In the first 5 h, 75% of the ^{14}C is expired in the breath. Twenty-two percent of the ^{14}C is taken up by metabolic processes with an excretion half-life of 10–12 days, and 3% enters bone with an excretion half-life of 40 days. To allow for genetic damage due to the incorporation of ^{14}C into DNA, Totter *et al.* (24) suggest that the effective DE for ^{14}C should be doubled, but other sources state that incorporation of the ^{14}C into DNA does not significantly increase the effective DE of ^{14}C above that of an equivalent gamma ray source (25).

Table 2 details organ exposures from the ^{14}C-urea breath test and compares the values with other common radiation sources. It can be seen that gonadal and marrow exposures from the urea breath test are many times less than the variation in yearly environmental exposure present throughout the United States (21). Natural radiation in 2 days gives more exposure to marrow and gonads than our test (26), and 100 breath tests give less marrow exposure than a single upper GI series (27).

Possible improvements and theoretical limitations of the test

Using a 5-μCi dose of ^{14}C-urea, we obtain cpm of less than 930 in *H. pylori*-negative patients. To define a sample as 930 cpm ± 2.5% requires a counting time of only 8 min. If the patient dose was decreased from 5 μCi to 1 μCi, the upper limit of normal would be around 236 cpm, which would require a counting time of 33 min for a borderline sample (28). Collection of more than 1 mmol of breath CO_2 would allow further reduction of the dose, but we believe this is impractical, insofar as it requires quite a prolonged breath collection. The test could be shortened to 10 min if mouth urease was erased with a urease inhibitor mouthwash such as acetohydroxamic acid. Alternatively, by supplying the isotope in a tablet form, the ^{14}C-urea would not be exposed to mouth urease. However, a tablet formulation could not be expected to contact the gastric mucosa as well as an aqueous vehicle—therefore, a larger dose of ^{14}C-urea might be required. We are currently evaluating each of these various proposals.

Practical application of the ^{14}C-urea breath test

In a our preliminary studies, we noted that samples taken before 15 min reflected urea hydrolysis in the oropharynx and did not specifically represent gastric *H. pylori* infestation. In practice, however, the 2-min sample has been useful for quality control. For example, on one occasion, a patient was given water without

TABLE 2

The ^{14}C-Urea Breath Test Compared with Other Common Sources of Radiation Exposure (data from references 9, 23, 26, 27)

	185 kBq (5 μCi) ^{14}C-Urea (mrem)†	Chest X-ray (mrem)	Upper GI Series (mrem)	Natural Sources,* 2 Wk (mrem)	Round Trip by Air: L.A.–N.Y. (mrem)
Bone	14.2			5.0	3.0
Breasts	3.5	14.0	53.0	5.0	3.0
Lungs	0.5	4.0	476.0	5.0–40.0‡	3.0
Thyroid	0.3	6.5	7.0	5.0	3.0
Marrow	0.3	3.0	114.0	5.0	3.0
Testes	0.3	<0.01	0.4	5.0	3.0
Ovaries	0.3	0.06	45.0	5.0	3.0

* Highest in Colorado (9 mrem); lowest in Louisiana (3 mrem).
† 1 mrem = 10^{-5} Seivert (Sv).
‡ Lung doses much higher in high radon areas.

radioisotope. Very low cpm in the 2-min sample (< 100 cpm) signaled this technical error. In another patient, the cpm at 2 min was 37,000; this was far above the mean for both HP− and HP+ patients, and may have been due to heavy oropharyngeal contamination with radioisotope. In HP− subjects, the 20-min reading is affected by the height of the 2-min peak. To allow for this effect, we now repeat the test if the 20-min sample gives a low positive result (900–1500 cpm) and the 2-min sample is higher than the mean + 2 SD of the normal negative range (8,500 cpm).

For the above reasons, we routinely collect two breath samples. After cleaning the mouth, swallowing the radioisotope, and cleaning the mouth again, the 2-min sample is taken. Subsequently, patients have a final sample taken at 20 min. It is possible for a technician to perform three tests simultaneously in one 30-min period.

Many hospitals and universities already have a liquid scintillation counter. If it is located nearby, as in our hospital, breath samples can be counted immediately, and results are available 10 min later. When the 20-min sample is clearly positive (> 2000), the 2-min sample does not need to be counted. However, if a value below 2000 is obtained, then the 2-min sample serves to insure that the radioisotope was given, and that mouth contamination (urease from the oral flora) was not excessive.

Although use of raw cpm makes conversion to disintegrations per minute (dpm) unnecessary, we check each batch for dose accuracy. Correctly dispensed, 0.01 ml of a 2.5 ml ^{14}C-urea patient sample (74 kBq/ml, 2 μCi/ml) should result in cpm of 41,558 in our machine (*i.e.*, 93% of 44,400 dpm).

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Reprint requests: Barry J. Marshall, M.D., Box 145, Internal Medicine, University of Virginia Health Sciences Center, Charlottesville, VA 22908.

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