

Society of Nuclear Medicine Procedure Guideline for C-14 Urea Breath Test

version 3.0, approved June 23, 2001

Authors: Helena R. Balon, MD (William Beaumont Hospital, Royal Oak, MI); Eileen Roff, RN, MSA, (William Beaumont Hospital, Royal Oak, MI); John E. Freitas, MD (St. Joseph Mercy Hospital, Ann Arbor, MI); Vanessa Gates, MS (William Beaumont Hospital, Royal Oak, MI); and Howard J. Dworkin, MD (William Beaumont Hospital, Royal Oak, MI).

I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting and reporting the results of the C-14 urea breath test.

II. Background Information and Definitions

The discovery of the Gram-negative spiral rod, *Helicobacter pylori*, in the 1980s radically changed the approach to treatment of peptic ulcer disease (PUD). The causal relationship between *H. pylori* infection and chronic gastritis is well established. Although only a small fraction of *H. pylori*-positive patients develop PUD, essentially all patients with duodenal ulcers and about 80% of patients with other than non-steroidal anti-inflammatory drug (NSAID)-induced gastric ulcers are infected with *H. pylori*. Eradication of *H. pylori* markedly reduces ulcer recurrence to <10% in 1 yr vs. 60-100% recurrence rate in 1 yr with conventional anti-ulcer therapy.

There is also evidence that *H. pylori* infection is associated with adenocarcinoma and lymphoma of the stomach, although in the United States fewer than 1% of *H. pylori*-infected people will develop gastric cancer. Further research is needed to determine the role of *H. pylori* eradication in gastric cancer prevention.

The presence of active *H. pylori* infection can be diagnosed non-invasively with the C-14 urea breath test. This test is based on the detection of the enzyme urease produced by *H. pylori*. Since urease is not present in normal human tissues, and since other urease-producing bacteria do not colonize the stomach, the presence of urease in the stomach can be equated with *H. pylori* infection.

In the presence of urease, orally administered C-14 urea will be hydrolyzed into ammonia and $^{14}\text{CO}_2$. $^{14}\text{CO}_2$ is absorbed into the circulation and exhaled by the lungs. The presence of a significant amount of $^{14}\text{CO}_2$ in the exhaled breath indicates active *H. pylori* infection.

The C-14 urea breath test consists of the oral admin-

istration of C-14 urea, followed by sampling of the exhaled breath at timed intervals. The breath samples are then analyzed in a liquid scintillation counter.

III. Common Indications

Detection of the presence of *H. pylori* in the stomach.

- A. Given the very high probability of patients with duodenal ulcers being infected with *H. pylori*, the C-14 urea breath test has not been routinely recommended for initial diagnosis, but has been recommended to document *H. pylori* eradication following anti-*H. pylori* therapy. Eradication should be confirmed no sooner than 1 month, and preferably longer, after completion of therapy.
- B. Since the prevalence of *H. pylori* in gastric ulcer patients (non-NSAID-induced gastric ulcers) is about 80%, the C-14 urea breath test may be used for initial diagnosis as well as follow-up in this patient subset.

IV. Procedure

- A. Patient Preparation
 1. Patients should be off the following medications:
 - a. Antibiotics and bismuth compounds for 30 days before the test.
 - b. Sucralfate and proton pump inhibitors (e.g., omeprazole, esomeprazole, lansoprazole, rabeprazole, pantoprazole) for 2 wk before the test.
 2. Patients should be NPO for at least 6 hr before the test.
- B. Information Pertinent to Performing the Procedure
A relevant history should be obtained; particularly, a list of relevant medications and the time of their most recent administration should be available.
- C. Precautions
None

Radiation Dosimetry for C-14 Urea*

Patient	Administered Activity KBq (μ Ci)	Organ Receiving the Largest Radiation Dose mGy/MBq (rad/mCi)	Effective Dose Equivalent ⁺ mSv/MBq (rem/mCi)
HP-positive female	37 p.o. (1)	0.14 urinary bladder wall (0.52)	0.08 (0.30)
HP-negative female	37 p.o. (1)	0.19 urinary bladder wall (0.70)	0.049 (0.18)
HP-positive male	37 p.o. (1)	0.10 urinary bladder wall (0.37)	0.062 (0.23)
HP-negative male	37 p.o. (1)	0.14 urinary bladder wall (0.52)	(0.038) (0.14)

*from Stubbs JB, Marshall BJ. Radiation dose estimates for the C-14 labeled urea breath test. *J Nucl Med* 1993; 34:821-825

D. Radiopharmaceutical

C-14 urea in a capsule form containing 1 mg urea labeled with 37 kBq (1 μ Ci) C-14. This preparation is currently available as PYTestTM from Kimberly-Clark/Ballard Medical Products.

C-14 is a pure beta-emitter with a physical half life of 5730 yr and maximum energy of 160 keV. To measure beta emissions, C-14 is counted in a liquid scintillation counter.

E. Procedure

1. Breath sample collection

At time zero, the patient swallows the capsule containing 37 kBq (1 μ Ci) C-14 urea with 20 ml lukewarm water. At 3 min post-dose, the patient drinks another 20 ml lukewarm water. At 10 min post-dose, the patient is asked to take a deep breath, hold it for approximately 5–10 sec and then exhale through a straw into a mylar balloon. Another optional breath sample (into another balloon) can be obtained at 15 min post-dose.

2. On site breath sample analysis

a. For each balloon, 2.5 ml trapping solution is pipetted into a scintillation vial. The trapping solution (collection fluid) is available from the manufacturer and contains 1 mmol hyamine, methanol and thymolphthalein. The air from the balloons is transferred into the scintillation vials using an air pump and plastic tubing. The color change of the collection fluid (from blue to colorless) indicates the end point of transfer. At this point 1 mmol CO₂ has been trapped. Ten milliliters of suitable scintilla-

tion fluid (e.g., BCSTM, Econo-SafeTM) is added to each vial immediately after breath collection and mixed thoroughly.

- b. A C-14 standard should be prepared by adding a known volume (e.g., 50 ml) of a calibrated C-14 reference standard (the known activity is stated on the vial) to a blank breath sample (a breath sample containing no C-14). The same volume of scintillation fluid that is used for patient samples is added to this standard.
- c. A blank (background) sample should be prepared using an identically treated breath sample from a person not receiving C-14 urea.
- d. All timed breath samples, the blank sample and the C-14 standard are counted for 5–20 min in a liquid scintillation counter (LSC), using a C-14 window.
- e. Calculations
Raw sample counts per minute (cpm) should be background-corrected and converted into disintegrations per minute (dpm) using the following formula:

$$\text{DPM} = \frac{(\text{sample cpm} - \text{blank cpm})}{\text{Efficiency}} \quad (\text{eq. 1})$$

LSC Efficiency

The C-14 standard (see section E.2.b.) should be counted with every set of patient samples. The efficiency of the counter for the specific procedure and the specific scintillation cocktail can then be determined as:

$$\text{Efficiency} = \frac{\text{standard cpm} - \text{blank cpm}}{\text{standard dpm}} \quad (\text{eq. 2})$$

3. Off site analysis

Balloons with breath samples can also be shipped to another institution/laboratory, if a liquid scintillation counter is not available on site.

F. Interventions

None

G. Processing

None

H. Interpretation Criteria

Reference values recommended by the manufacturer are as follows:

< 50 dpm at 10 min	Negative for <i>H. pylori</i>
50-199 dpm at 10 min	Indeterminate for <i>H. pylori</i>
200 dpm at 10 min	Positive for <i>H. pylori</i>

I. Reporting

Aside from patient demographics, the report should include the following information:

1. Indication for the study (e.g., suspected *H. pylori* infection, follow-up after anti-*H. pylori* therapy, etc.)
2. Procedure (i.e., radiopharmaceutical and dosage, number and timing of breath samples collected)
3. Result (i.e., net dpm in the 10 min sample)
4. Reference ranges (normal values)
5. Study limitations, confounding factors
6. Interpretation (i.e., positive, negative, indeterminate for the presence of active *H. pylori* infection)

J. Quality Control (QC)

Liquid scintillation counter (LSC)

Proper calibration and QC of the LSC should be performed as per facility procedure.

K. Sources of Error

1. Causes of potential false-negative results:
 - a. Antibiotics (if administered within 30 days of the test)
 - b. Bismuth (if administered within 30 days of the test)
 - c. Sucralfate (if administered within 14 days of the test)
 - d. Proton pump inhibitors (see examples in section IV.A.b.) if administered within 14 days of the test
 - e. Non-fasting
 - f. Resective gastric surgery
 - g. Difficulty with swallowing test capsule (additional breath samples collected at 15

or even 20 min post-dose may be helpful)

2. Causes of potential false-positive results:
 - a. Resective gastric surgery with potential resultant bacterial overgrowth (non- *H. pylori* urease).
 - b. Achlorhydria
3. Chemiluminescence
If a value of 50–300 dpm is obtained immediately after the addition of the scintillation fluid, the sample should be recounted in 1–2 hr or the next day, to exclude falsely elevated counts due to chemiluminescence.

V. Issues Requiring Further Clarification

None

VI. Concise Bibliography

Friedman LS. *Helicobacter pylori* and nonulcer dyspepsia (editorial). *New Engl J Med*. 1998;339: 1928–1930.
 NIH Consensus Statement. *Helicobacter pylori* in peptic ulcer disease. *JAMA*. 1994;272:65–69.
 PYTest™ package insert. Ballard Medical Products, Draper, Utah; August 1997.
 Soll AH. Consensus Statement. Medical treatment of peptic ulcer disease - practice guidelines. *JAMA*. 1996;275:622–629.
 Stubbs JB, Marshall BJ. Radiation dose estimates for the C-14 labeled urea breath test. *J Nucl Med*. 1993;34:821–825.

VIII. Disclaimer

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high quality nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different than the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.