Procedure Guideline for Carbon-14-Urea Breath Test

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PART I: PURPOSE

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting and reporting the results of the ^{14}C-urea breath test (UBT). The test was approved by the U.S. Food and Drug Administration in May 1997.

PART II: BACKGROUND INFORMATION AND DEFINITIONS

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

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

The presence of active HP infection can be diagnosed noninvasively with the ^{14}C-UBT. This test is based on the detection of the enzyme urease, which is produced by HP. 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 HP infection.

In the presence of urease, orally administered ^{14}C-urea will be hydrolyzed into ammonia and $^{14}CO_2$. This $^{14}CO_2$ is absorbed into the circulation and exhaled by the lungs. The presence of a significant amount of $^{14}CO_2$ in the exhaled breath indicates active HP infection.

The ^{14}C-UBT consists of oral administration of ^{14}C-urea followed by sampling exhaled breath at timed intervals. The breath samples are then analyzed in a liquid scintillation counter.

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Note: All 26 SNM-approved procedure guidelines are available on the Society's home page. We encourage you to download these documents via the Internet at www.snm.org. If you would like information on the development of this guideline or to order a compendium of all 26 procedure guidelines for $20.00, contact Marie Davis, Society of Nuclear Medicine, at (703) 708-9000, ext. 250, or by e-mail at mdavis@snm.org.

PART III: COMMON INDICATIONS

The test is used to detect the presence of HP in the stomach.

A. Given the very high probability of DU patients being infected with HP, the ^{14}C-UBT has not been routinely recommended for initial diagnosis but has been recommended to document HP eradication following anti-HP therapy. Eradication should be confirmed no sooner than 1 mo, and preferably longer, after completion of therapy.
B. Since the prevalence of HP in GU patients (non–NSAID-induced GUs) is about 80%, the ^{14}C-UBT may be used for initial diagnosis as well as follow-up in this patient subset.

PART IV: PROCEDURE

A. Patient Preparation
   1. Patients should be off the following medications:
      a. Antibiotics and bismuth compounds (e.g., Pepto Bismol) for 30 days before the test.
      b. Sucralfate (Carafate), proton-pump inhibitors [e.g., omeprazole (Prilosec), lansoprazole (Prevacid)] for 2 wk before the test.
   2. Patients should receive nothing by mouth 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, including the time of their most recent administration.
C. Precautions
   None
D. Radiopharmaceutical (Table 1)
   Carbon-14-urea in capsule form containing 1 mg urea labeled with 37 kBq (1 μCi) ^{14}C. This preparation is currently available as PYtest from Ballard Medical Products (Draper, UT).
   Carbon-14 is a pure beta emitter with a physical half-life of 5730 yr and maximum energy of 160 keV. To measure beta emissions, ^{14}C is counted in a liquid scintillation counter.
E. Procedure
   1. Breath sample collection
      Testing begins with the patient swallowing the capsule containing 37 kBq (1 μCi) ^{14}C-urea with 20 ml lukewarm water. At 3 min postdose the patient drinks another 20 ml lukewarm water. At 10 min postdose 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 postdose.
   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) contains 1 mmol hyamine, methanol and thymolphthalein. The air from the balloons is transferred into the scintillation vials using an air pump

TABLE 1
Radiation Dosimetry for Carbon-14 Urea*

Patient	Administered activity KBq (μCi)	Organ receiving the largest radiation dose+ mGy (rad)	Effective dose equivalent+ mSv (rem)
HP-positive woman	37 p.o. (1)	0.14 Urinary bladder wall (0.5)	0.08 (0.3)
HP-negative woman	37 p.o. (1)	0.19 Urinary bladder wall (0.69)	0.049 (0.18)
HP-positive man	37 p.o. (1)	0.10 Urinary bladder wall (0.38)	0.062 (0.23)
HP-negative man	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 carbon-14-labeled urea breath test. *J Nucl Med* 1993;34:821–825.
+Per MBq (per mCi).
HP = *Helicobacter pylori*; p.o. = by mouth.

and plastic tubing. The color change of the collection fluid (from blue to colorless) indicates the endpoint of transfer. At this point, 1 mmol CO_2 has been trapped. Immediately after breath collection, 10 ml suitable scintillation fluid [e.g., Econo-Safe (Research Products International Corp., Mount Prospect, IL)] is added to each vial and mixed thoroughly.

b. All timed breath samples, a blank (background) sample (i.e., an identically treated breath sample from a person not receiving ^{14}C-urea) and a standard (a calibrated ^{14}C standard added to another blank) are counted for 5–20 min in a liquid scintillation counter using a ^{14}C window.

c. Calculations
Raw sample counts per minute (cpm) should be background corrected and can be converted into disintegrations per minute (dpm) using the following formula:

$$DPM = \frac{(\text{Sample cpm} - \text{Blank cpm})}{\text{Efficiency}}. \quad \text{Eq. 1}$$

Liquid Scintillation Counter Efficiency
A ^{14}C standard should be prepared by adding a known volume (e.g., 50 μl) of a calibrated ^{14}C reference standard [known activity (dpm) stated on vial] to a blank (no ^{14}C) breath sample. The same volume of scintillation fluid as used for patient samples is added. This sample should be counted with every set of patient samples. The efficiency of the counter for this particular test and scintillation cocktail can then be determined as follows:

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

3. Off-site analysis
Balloons with breath samples may also be shipped to another institution or 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 (Ballard Medical Products) are as follows:
<50 dpm at 10 min = negative for HP
50–199 dpm at 10 min = indeterminate for HP
≥200 dpm at 10 min = positive for HP

I. Reporting
Aside from patient demographics, the report should include the following information:
1. Indication for the study (e.g., suspected HP infection, follow-up after anti-HP therapy, etc.)
2. Procedure (i.e., radiopharmaceutical and dosage, number and timing of breath samples collected)
3. Result (i.e., net dpm in 10-min sample)
4. Reference ranges (normal values)
5. Study limitations and confounding factors
6. Interpretation (i.e., positive, negative, indeterminate for the presence of active HP infection)

J. Quality Control
Liquid scintillation counter
Proper calibration and quality control of the liquid scintillation counter 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 [e.g., omeprazole (Prilosec), lansoprazole (Prevacid)] if administered within 14 days of the test
   e. Nonfasting
   f. Resective gastric surgery
   g. Difficulty with swallowing test capsule (additional breath samples collected at 15 or even 20 min postdose may be helpful)
2. Causes of potential false-positive results:
   a. Resective gastric surgery with potential resultant bacterial overgrowth (non-HP urease)
   b. Achlorhydria
3. Chemiluminescence
If a value of 50–300 dpm is obtained immediately after 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 chemiluminiscence.

PART V: 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.

PART VI: ISSUES REQUIRING FURTHER CLARIFICATION

None

PART VII: CONCISE BIBLIOGRAPHY

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PART VIII: LAST HOUSE OF DELEGATES APPROVAL DATE

June 7, 1998

PART IX: NEXT ANTICIPATED APPROVAL DATE

2000

PART X: ACKNOWLEDGMENTS

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FIRST IMPRESSIONS
Thoracic Uptake of Technetium-99m-HDP

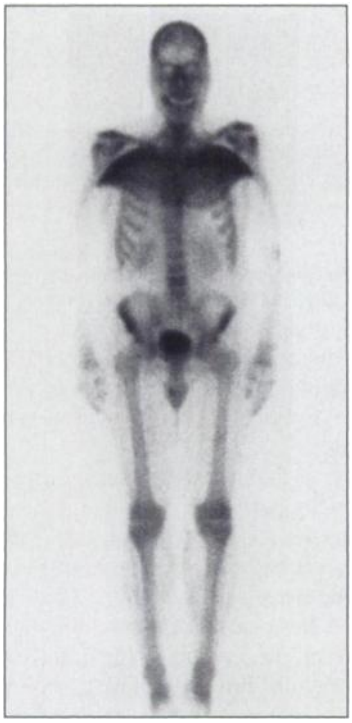

Figure 1.

PURPOSE
A 46-yr-old man with history of B-cell lymphoma who has been weight lifting for the past several months was referred for a bone scan to follow-up osseous metastasis. A ^{99m}Tc-oxidronate (HDP) whole-body scan (Fig. 1) showed markedly intense and symmetric increased soft-tissue uptake in the region of both pectoralis major muscles, which had a bat wings appearance. This striking extraosseous localization reflects sequelae of a muscle injury related to weight lifting. Prominent deltoid tuberosities are likely due to stress reaction related to this exercise as well. Otherwise, stable bone scan appearance compared with 6 mo earlier.

TRACER
Technetium-99m-HDP (960 MBq)

ROUTE OF ADMINISTRATION
Intravenous injection

TIME AFTER INJECTION
2 hr

INSTRUMENTATION
GE Maxxus (Milwaukee, WI) gamma camera equipped with low-energy, all-purpose, parallel-hole collimator

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