Alternatives to Technetium 99m Pentetate for Radioaerosol Inhalation Lung Imaging

James A. Ponto, Michael M. Graham, and John A. Bricker

Radioaerosol inhalation lung imaging is a standard diagnostic procedure commonly performed in conjunction with perfusion lung imaging in the evaluation of pulmonary embolism. Although a variety of radiopharmaceuticals have been investigated,[1] technetium 99m pentetate (^{99m}Tc DTPA) has become the preferred radiopharmaceutical for these procedures.[2,3] One limitation of ^{99m}Tc DTPA radioaerosol, however, is its relatively rapid absorption across the pulmonary capillaries into the blood, which is accelerated in the presence of inflammation, including that caused by smoking.[1,4] In certain situations, such as a delay between administration and imaging or single photon emission computed tomography imaging, this clearance may present problems for diagnostic interpretation. Interpretation may be further complicated by nonuniform clearance.[4] A clinical concern, then, is the potential for misinterpretation of pulmonary embolism (i.e., mismatched perfusion defects) as other nonembolic lung disease (i.e., matched perfusion defects) due to significantly faster clearance of ^{99m}Tc DTPA from regions affected by pulmonary emboli.[5] Hence, a radiopharmaceutical with longer retention in pulmonary airways would be desirable.

Particulate radiopharmaceuticals are not readily absorbed across the capillary membranes. Rather, they are very slowly eliminated by mucociliary transport up the airways.[1] Past problems of excessive deposition of ^{99m}Tc sulfur colloid in large airways with poor or patchy peripheral penetration[1,6] have been resolved with improvements in aerosol delivery systems[1] and use of the commercial product with the smallest particle size.[7] Other factors to be considered in the selection of a radiopharmaceutical include radiochemical stability, expense, simplicity of preparation, and adverse effects. Relevant characteristics of radiopharmaceuticals currently used for inhalation lung imaging are summarized in Table 1.

After due consideration, we selected ^{99m}Tc sulfur colloid as the best available radiopharmaceutical for routine radioaerosol inhalation lung imaging. Experience in more than 500 patients to date has affirmed our decision. Images have typically been judged to be of excellent quality (see Figure 1a and Figure 2a); images of suboptimal quality have been rare and were the result of technical problems and/or patient-related characteristics rather than the radiopharmaceutical. None of our patients have experienced any adverse effects.

Our procedure (abridged) for performing radioaerosol inhala-

Table 1. Relevant Characteristics of Radiopharmaceuticals for Inhalation Lung Imaging

Radiopharmaceutical	$t_{1/2}$[a] (Normal)	$t_{1/2}$ (Smoker)	Advantages	Disadvantages
^{99m}Tc pentetate (DTPA)	~ 86 minutes[4]	~ 30 minutes[4]	Use for this procedure is approved by the U.S. Nuclear Regulatory Commission[8] and is clinically accepted[2,3]; inexpensive	Relatively fast, nonuniform lung clearance if patient is a smoker or has inflammatory lung disease[1,4]; mediocre radiochemical stability[1]
^{99m}Tc pyrophosphate (PYP) or medronate (MDP)	~ 9 hours[9]	~ 2 hours[1]	Inexpensive; somewhat longer retention in lungs (incorporated into surfactant or binding to alveolar phosphate receptors)[9]	Not approved use; theoretical concern of allergic reactions, especially with MDP
^{99m}Tc human serum albumin	~ 20 hours[10]	ND[b]	Somewhat longer retention in lungs (mucociliary clearance)[1]	Not approved use; moderately expensive; not consistently commercially available
^{99m}Tc sulfur colloid	~ 2 days[4]	ND[b]	Inexpensive; prolonged retention in lungs; superior radiochemical stability (useful for up to 18 hours)	Not approved use; less uniform airway deposition with older models of aerosol delivery systems; theoretical concern of adverse reactions to gelatin (stabilizing agent); slightly longer preparation time
^{99m}Tc Technegas	~ 77 hours[11]	ND[b]	Superior uniform airway deposition[1,11]; prolonged retention in lungs	Preparation requires a special heating chamber[1,11]; not commercially available in U.S.

[a]Biological half-life in lungs.
[b]ND = not determined; difference, if any, assumed to be clinically insignificant.

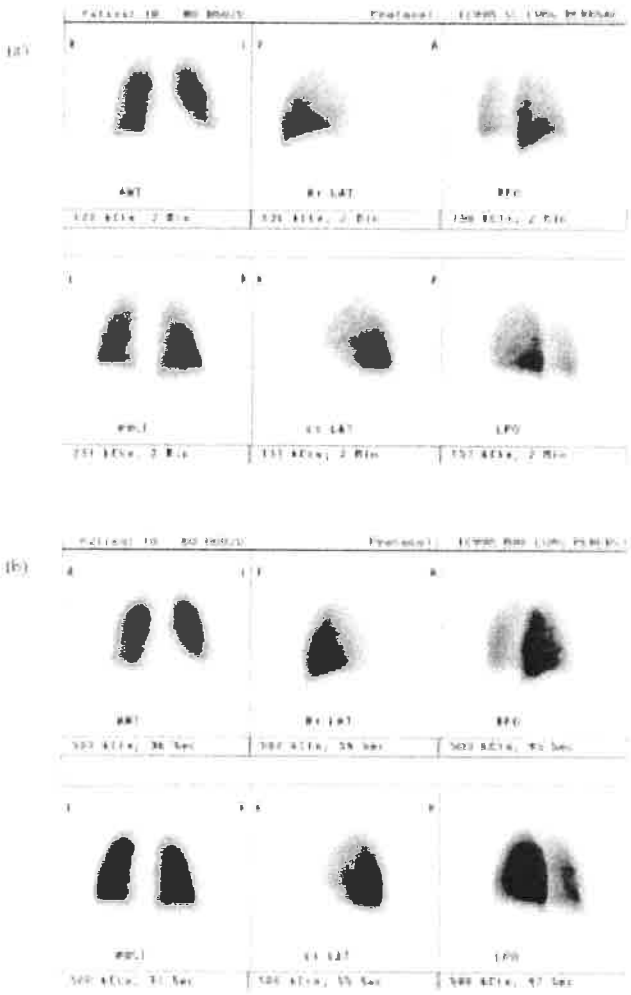

Figure 1. Inhalation/perfusion imaging procedure in a 42-year-old woman with pleuritic left-sided chest discomfort. (a) The inhalation images (^{99m}Tc sulfur colloid aerosol) show normal ventilation in both lungs. (b) The perfusion images (^{99m}Tc MAA) show good, uniform perfusion in both lungs. Physician's interpretation: study within normal limits. Note also the slight gravity-related gradient in the inhalation images, common with all radioaerosols when administered to patients in a sitting position.

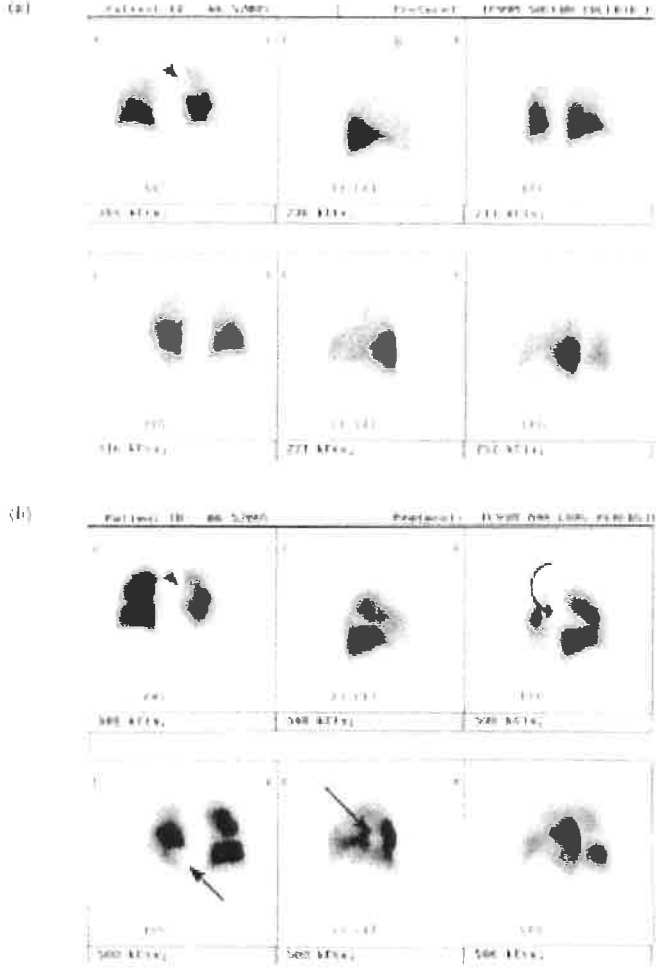

Figure 2. Inhalation/perfusion imaging procedure in a 70-year-old woman with shortness of breath and deep-vein thrombosis. (a) The inhalation images (^{99m}Tc sulfur colloid aerosol) show uptake in the defects seen in the perfusion images. (b) The perfusion images (^{99m}Tc MAA) show a large defect in the superior segment of the right lower lobe (curved arrow) and subsegmental defects in the posterior-basal and lateral-basal segments of the left lung (arrows). Physician's interpretation: high probability for pulmonary emboli. Note also a matched defect in the left hilar region (arrowheads), the site of a known colorectal carcinoma metastatic lesion, and partial collapse of the upper lobes.

tion lung imaging is as follows:

1. Inject 30 to 60 mCi ^{99m}Tc sulfur colloid diluted with normal saline, if necessary, to a total volume of 3 mL, into a shielded aerosol delivery system (Aero/Vent Plus—Medi Nuclear).
2. Attach oxygen line as directed and gradually increase the flow rate to 10–14 L/minute.
3. Administer the radioaerosol as directed for 3–5 minutes or until a count rate of 1K counts/sec is achieved in order to deliver 0.5 to 1.0 mCi into the lungs.
4. Image as directed.
5. Perform standard perfusion imaging procedure using a nominal dosage of 6 mCi ^{99m}Tc macroaggregated albumin (^{99m}Tc MAA).

Figures 1 and 2 illustrate lung inhalation/perfusion imaging procedures in patients with and without pulmonary embolism, respectively.

In summary, based on its biological, chemical, and physical characteristics, ^{99m}Tc sulfur colloid radioaerosol is a superior radiopharmaceutical for inhalation lung imaging. Outside of the United States, other ^{99m}Tc colloid products (e.g., albumin colloid [nanosized], antimony sulfide colloid, rhenium sulfide colloid, tin colloid) would be expected to provide similar superiority, especially compared with ^{99m}Tc DTPA.

J Am Pharm Assoc. 2002;42:112–4.

James A. Ponto, MS, BCNP, is chief nuclear pharmacist, Division of Nuclear Medicine, University of Iowa Hospitals and Clinics, and clinical professor, College of Pharmacy, University of Iowa, Iowa City. Michael M. Graham, PhD, MD, is professor, Department of Radiology, and head, Division of Nuclear Medicine; John A. Bricker, BS, CNMT, is technical director, Division of Nuclear Medicine, University of Iowa Hospitals and Clinics, Iowa City.

The authors declare no conflicts of interest or financial interests in any product or service mentioned in this article, including grants, employment, stock holdings, gifts, or honoraria.

An earlier version of this article was presented at the American Pharmaceutical Association Annual Meeting and Exposition, March 16–20, 2001.

Correspondence: James A. Ponto, MS, RPh, BCNP, Nuclear Medicine, Room 3832 JPP, University of Iowa Hospitals & Clinics, 200 Hawkins Drive, Iowa City IA 52242-1077. Fax: 319-384-6389. E-mail: james-ponto@uiowa.edu.

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Amlodipine Therapy in Pediatric Patients With Hypertension

Marcie L. Parker, Renee F. Robinson, and Milap C. Nahata

While awareness of hypertension in children has increased with the development of standard blood pressure (BP) guidelines for the pediatric population, the lack of research studies on the long-term efficacy and safety of antihypertensive drugs in pediatric patients has hindered treatment of the disease in children and adolescents.

Traditionally, BP measurements have not been a part of routine pediatric physical examinations. Normal BP, as defined by the second National Heart, Lung, and Blood Institute Task Force,[1] is systolic and diastolic BP below the 90th percentile for age, sex, and height. The diagnosis of hypertension is made when at least three separate BP readings are greater than or equal to the 95th percentile.[1] Approximately 1% of children and adolescents have primary or secondary hypertension.[2] Primary hypertension is defined as sustained high BP when secondary causes such as renovascular disease, pheochromocytoma, aldosteronism, or other known etiologies are absent.[3]

Elevated BP during childhood has been correlated with hypertension in adults. If left untreated, sustained elevated BP in adults can lead to cardiovascular, renal, hepatic, and ocular damage.[4] Nonpharmacologic methods that promote weight reduction, such as a balanced diet and exercise, have been shown to offer benefits in lowering BP in children and adults. However, because compliance with such regimens is only about 50%,[5] pharmacotherapy plays a critical role in reducing elevated BP, maintaining ideal BP, and lowering the risks associated with hypertension in the pediatric population. Current literature and guidelines support the use of drug treatment to lower and maintain BP in children below the 95th percentile (based on age, height, and sex).[1]

Although routinely used in adults, antihypertensive medications have not been adequately studied in the pediatric population, nor have they been labeled for pediatric use by the Food and Drug Administration (FDA). In addition, the lack of liquid or chewable formulations limits the options for treating children who are unable to swallow tablets or capsules. In 1998 FDA extended certain patents so that the pharmaceutical industry could complete clinical trials for new drugs of potential utility in the pediatric population.[6]

The only calcium channel blocker (CCB) approved by FDA with a pediatric indication is nifedipine, but its use is problematic.