thermore, in many institutions, ventilation scans cannot be performed on ventilator-dependent patients. To implicate PEEP-induced shunting then as a cause of respiratory deterioration, a large region of atelectasis or consolidation on chest radiograph must be found that is relatively hyperperfused on scintigraphy. To increase awareness of possible deleterious PEEP effects when regional lung disease is present and to confirm the generality of these limited previous reports, we offer a recent adult case from our institution.

A previously healthy 18-yr-old female became lethargic after a motor vehicle accident and was intubated before arriving at the hospital. Following surgical evacuation of a left temporoparietal subdural hematoma, she remained comatose on ventilatory support. After several days, chest radiographs showed evidence of increasing left lower-lobe atelectasis and consolidation. Her blood gases progressively deteriorated with her fraction of inspired oxygen (FiO_2) continuously increased to maintain adequate blood oxygenation. On the third day of hospitalization, PEEP was raised to 10 cm H_2O, and the FiO_2 was raised to 70% with arterial blood gas results pH 7.41, pCO_2 33 Torr, PO_2 56 torr, and an A-a gradient of ~400 Torr. A portable chest radiograph (Fig. 1) at that time shows the degree of left lower-lobe involvement.

Since the patient was at high risk, a perfusion scan was ordered to rule out PE as the cause of hypoxemia and increased A-a gradient. No evidence of PE was found, but the entire left lower lobe appeared markedly hyperperfused and there was some redistribution of perfusion away from the upper portions of both lungs (Fig. 2). After discussions with the pulmonary consultation, PEEP was lowered to 2.5 cm H_2O with a subsequent improvement in respiratory status. A left lower-lobe pneumonia was confirmed by identification of *E. Coli* in sputum cultures, and serial chest radiographs showed improvement after several days on appropriate i.v. antibiotic coverage.

Apparently, the pneumonia effectively prevented regional alveolar expansion under PEEP. The vascular resistance of the left lower lobe then remained inappropriately low and the patient's respiratory status deteriorated as blood was shunted through this large underventilated area. This condition subsequently corrected as PEEP was lowered and the pneumonia was treated.

Although ordered to rule out PE, perfusion scintigraphy played an important role in diagnosing an alternative correctible underlying cause of respiratory deterioration. This case confirms the generality of findings previously reported by Kim and Heyman (*1*) and others (*7,8*) when PEEP-induced regional shunting occurs; namely, the appearance of a marked reverse V/Q defect at the site of the compromised lower lung and some broad V/Q mismatch involving both upper lungs. Besides PE, then, the possibility of PEEP-induced abnormalities should also be considered when ventilatory-dependent patients undergo pulmonary scintigraphy.

REFERENCES

1. Kim CK, Heyman S. Ventilation/Perfusion mismatch caused by positive pressure ventilatory support. *J Nucl Med* 1989; 30:1268–1270.
2. Meignan M, Palmer E, Waltman A, Strauss HW. Zones of increased perfusion on perfusion lung scans (Hot Spots) (Abstract). *J Nucl Med* 1989; 30:734.
3. Miron SD, Feiglin DH, Gentili A, Bellon EM. Reversed mismatch on ventilation-perfusion ratio (VPR) images—Evidence of non-thromboembolic lung disease [Abstract]. *J Nucl Med* 1989; 30:734.
4. Seo IS, Quevedo A, Sy WM, Tai K, Desai J. Reversed V/Q mismatch (rV/Q): its incidence and clinical significance (Abstract). *J Nucl Med* 1989; 30:734.
5. Palmaz JC, Barnett CA, Reich SB, Krumpe PE, Farrer PA. Reverse ventilation mismatch. *Clin Nucl Med* 1984; 9:6–9.
6. Sostman HD, Neumann RD, Gottschalk A, Greenspan RH. Perfusion of nonventilated lung: failure of hypoxic vasoconstriction. *AJR* 1983; 141:151–156.
7. Goodwin CA, Epstein DH. Lung perfusion scanning. The case of "reverse mismatch." *Clin Nucl Med* 1984; 9:519–522.
8. Slavin JD, Mathews J, Spencer RP. Pulmonary ventilation/perfusion and reverse mismatches in an infant. *Clin Nucl Med* 1985; 10:708–709.

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REPLY: We are pleased to see the case of relative hyperperfusion caused by PEEP to the area of lobar pneumonia reported by Wegener, and that his findings are essentially in agreement with findings described by us and others (*1–3*).

Some points need further clarification:

1. In the first paragraph of the above letter, it appears that Wegener mistook a part of our discussion. The statement "Alveolar pressure exceeds pulmonary arterial and venous pressure in the uppermost part of the upright lung, resulting in the collapse of the capillaries, and therefore blood flow occurring only at the peaks of the pulsatile pressure wave in this zone (*4–6*)" was made by us in order to explain physiologic uneven regional distribution of pulmonary perfusion in normal persons (upper lung < lower lung) (*7–9*), so that the understanding of the mechanism of diminished perfusion in normally ventilated (therefore more inflated iatrogenically by PEEP), nonatelectatic upper and middle lobes in our case, could be facilitated. We did not intend to say that PEEP effect was more pronounced normally in the upper lungs.
2. If we are not mistaken, Wegener implies in the last sentence of the first paragraph of his letter that inappropriate hyperperfusion in the atelectatic or consolidated lobe due to low vascular resistance is the primary event, and hypoperfusion in the remainder of the lung is the result of a steal phenomenon.

   Alveolar pressure in areas of poorly ventilated lung that cannot expand would be lower than usual, which may result in lower vascular resistance and increased blood flow. On the other hand, vascular resistance in this area is increased secondary to a local hypoxic reflex (*10,11*). The fact that perfusion is generally diminished on scintigram to a variable degree in areas of poorly ventilated lung (atelectasis or pneumonia), indicates that the degree of increased vascular resistance due to a hypoxic reflex generally exceeds that of decreased vascular resistance offered by decreased alveolar pressure.

   The effect of PEEP is not that of directly lowering the vascular resistance in nonventilated areas, but of increasing alveolar pressure and vascular resistance in areas of normally ventilated lung. The consequence is "relatively" lower vascular resistance in nonventilated areas, and increased shunt fraction through this zone.

Therefore it would be appropriate to state that decreased perfusion in inflated areas is the primary event, resulting in redistribution of blood flow (hyperperfusion) through nonventilated areas.

Overall, we agree that, besides PE, the possibility of PEEP-induced abnormalities also should be considered when ventilatory-dependent patients undergo lung scintigraphy, and we appreciate the confirmation of the generality of findings described by us and others (*1–3,12*).

REFERENCES

1. Kim CK, Heyman S. Ventilation/perfusion mismatch caused by positive pressure ventilatory support. *J Nucl Med* 1989; 30:1268–1270.
2. Goodwin CA, Epstein DH. Lung perfusion scanning. The case of "reverse mismatch." *Clin Nucl Med* 1984; 9:519–522.
3. Slavin JD, Mathews J, Spencer RP. Pulmonary ventilation/perfusion and reverse mismatches in an infant. *Clin Nucl Med* 1985; 10:708–709.
4. Maloney JE, Bergel DH, Glazier JB, et al. Effect of pulsatile pulmonary artery pressure on distribution of blood flow in isolated lung. *Respir Physiol* 1968; 4:154–167.
5. Maloney JE, Bergel DH, Glazier JB, et al. Transmission of pulsatile blood pressure and flow through the isolated lung. *Circ Res* 1968; 23:11–24.
6. Secker-Walker RH. The respiratory system. In: Harbert J, da Rocha AFG, eds. *Textbook of nuclear medicine*, Volume II: *clinical applications*. Philadelphia: Lea & Febiger; 1984:311.
7. West JB. Pulmonary function studies with radioactive gases. *Ann Rev Med* 1967; 18:459.
8. Anthonisen NR, Milic-Emili J. Distribution of pulmonary perfusion in erect man. *J Appl Physiol* 1966; 21:760.
9. Kaneko K, Milic-Emili J, Dolovich MB, et al. Regional distribution of ventilation and perfusion as a function of body position. *J Appl Physiol* 1966; 21:767–777.
10. Fishman AP. Respiratory gases in the regulation of the pulmonary circulation. *Physiol Rev* 1961; 41:214–280.
11. Fishman AP. Hypoxia on the pulmonary circulation. How and where it acts. *Circ Res* 1976; 38:221–231.
12. Rosen JM, Romney BM. Pulmonary atelectasis associated with relative hyperperfusion. *Eur J Nucl Med* 1988; 14:629–631.

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Preparation of [^{99m}Tc]HM-PAO

TO THE EDITOR: Technetium-99m d,l-hexamethyl propyleneamine oxime ([^{99}Tc]HM-PAO) is a new radiopharmaceutical that is being used extensively in regional cerebral perfusion studies (*1*) and in labeling of blood cell elements (*2*).

The efficient use of this radiopharmaceutical is often limited because the technetium labeling of a freeze-dried HM-PAO kit produces an assortment of impurities (pertechnetate, reduced-hydrolyzed technetium, and secondary complex), which change with time.

Kit instructions recommend a maximum of 1.11 GBq (30 mCi) of pertechnetate; eluate eluted <2 hr previously from a generator eluted no more than 24 hr before, and utilization of the [^{99m}Tc]HM-PAO within 30 min of reconstitution (*3*).

We have noted that, along with the economical and practical problems associated with these instructions, 30 min after preparation the radiochemical purity is not >85%.

To avoid these problems, we offer an alternative preparation which begins by dissolving the freeze-dried vial with physiological saline solution, and then separating the resulting liquid into fractions for labeling just before to use.

On four different occasions, four vials of exametazime (Amersham UK) were diluted with 5 ml of saline solution and separated into five fractions of 1 ml. At the same time, the generator eluate was separated into five doses of 0.92–1.30 GBq (25–35 mCi). Pertechnetate was added for labeling as the fractions were prepared: at 0 min (Fraction 1), at 30 min (Fraction 2), at 60 min (Fraction 3), at 120 min (Fraction 4), and at 180 min (Fraction 5).

Five minutes after each of the fractions was labeled, the lipophilic [^{99m}Tc]HM-PAO was calculated by means of the chloroform extraction method (*4*). While this process was performed on each of the fractions, the lipophilic [^{99m}Tc]HM-PAO of Fraction 1 also was calculated in order to obtain a reference of its radiopharmaceutical instability.

Table 1 compares radiochemical purity to the time elapsed between the separation of the fractions and the labeling. Better results were obtained when the fractions were refrigerated (4–8°C) for up to 240 min (Table 2).

The labeling of HM-PAO with freshly eluted technetium within 180 min and 240 min of their separation into refrigerated fractions gave 95.8% ± 1.6% and 94.0% ± 2.0% (n = 5) of [^{99m}Tc]HM-PAO lipophilic, respectively.

We conclude that the dissolving of the freeze-dried vial with saline and its separation into refrigerated fractions, which are not labeled until just prior to use, is an alternative method of preparation of [^{99m}Tc]HM-PAO with the benefit of high radiochemical purity and reduced cost.

TABLE 1
Radiochemical Purity Results

	Times				
	0 min	30 min	60 min	120 min	180 min
% [^{99m}Tc]HM-PAO Lipophilic	(Fraction 1) 95.0 ± 2.7	(Fraction 2) 94.1 ± 4.2	(Fraction 3) 92.0 ± 5.1	(Fraction 4) 84.1 ± 7.0	(Fraction 5) 74.0 ± 20.9
% [^{99m}Tc]HM-PAO Lipophilic	(Fraction 1) 95.0 ± 2.7	(Fraction 1) 78.5 ± 5.0	(Fraction 1) 73.5 ± 7.4	(Fraction 1) 54.2 ± 6.9	(Fraction 1) 40.5 ± 10.1