A High-Frequency Ultrasonic Nebulizer System for Radioaerosol Delivery

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A prototype high-frequency ultrasonic nebulizer, coupled with a nebulization chamber, has been designed specifically to overcome the problem of inefficient and unpredictable radioaerosol delivery. The objective was to reduce mean particle size, increase aerosol concentration, and minimize dead space. Thirty-nine patients were studied, including 15 patients in significant respiratory distress. Delivery of the radioaerosol proved to be rapid, efficient, and reproducible, and excellent alveolar distribution patterns were obtained in all 39 patients. Minimal nonpathologic tracheal deposition occurred in five patients, but this did not interfere with the interpretability or diagnostic validity of the study. All other instances of airway aerosol deposition correlated with documented airway disease. The images obtained with this system are a reliable measure of ventilatory distribution and airway turbulence.

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Radioaerosols have certain inherent advantages over ^{133}Xe for measuring the distribution of ventilation. Radioaerosols are relatively inexpensive to produce. They can be delivered under tidal respiration, and even acutely ill patients can be adequately studied. When ^{99m}Tc-labeled aerosols are employed, images of high information density, comparable to perfusion images with ^{99m}Tc-macroaggregated albumin, can be obtained. Perhaps most importantly, aerosol inhalation images can be obtained in several projections, permitting close comparison with the distribution of perfusion. Despite these advantages, radioaerosol lung scintigraphy has not been widely adopted. One major objection to the technique has been the inefficient and unpredictable nature of aerosol delivery. Larger aerosol particles tend to deposit in the trachea and major bronchi and may not parallel ventilatory distribution as measured by ^{133}Xe.

The major factors that determine the pulmonary distribution of aerosols are particle size, aerosol concentration, air flow rate, and airway turbulence (*1,2*). With these factors in mind, a nebulization chamber has been designed specifically for radioaerosol delivery. This chamber has been coupled with a prototype high-frequency ultrasonic nebulizer.

MATERIALS AND METHODS

The prototype nebulizer (DeVilbiss Model 900) uses a frequency of approximately 4 MHz, which is higher than most standard ultrasonic nebulizers. The nebulization chamber (Fig. 1) is designed so that the larger aerosol particles are impacted and recovered for renebulization. This design generates a higher proportion of particles in the 0.5–3.0-μm size range. It is primarily particles of this size that are deposited in peripheral bronchioles and alveoli (*3–7*). In addition, the impaction sphere traps the generated aerosol in a small volume, which is then released during inspiration as a fairly compact bolus.

The nebulization chamber is attached to a standard model blower, which assists passage of the aero-

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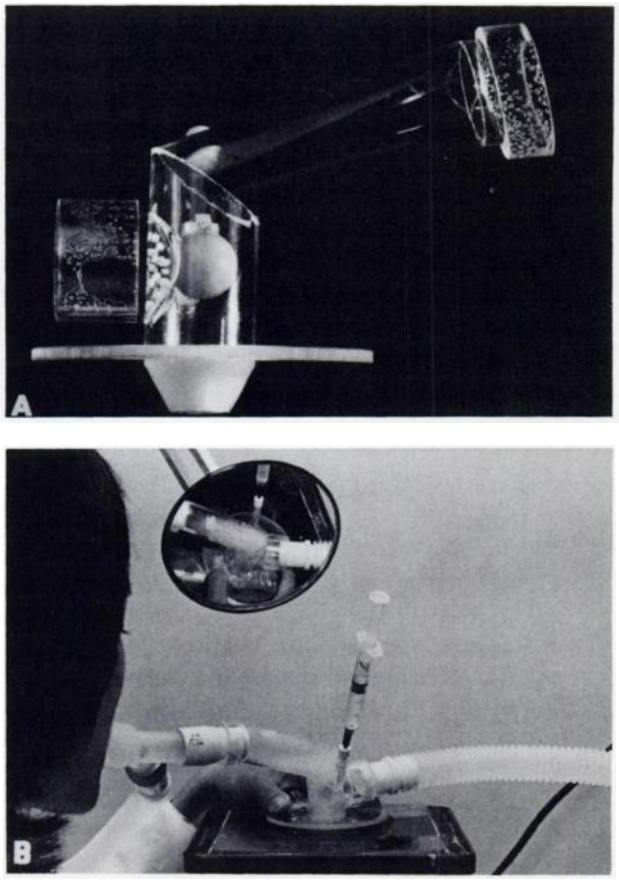

FIG. 1. (A) Side view of nebulization chamber, showing position of impaction sphere. Aerosol is trapped below sphere until patient inhales. (B) Nebulization chamber atop ultrasonic unit, with shielding removed. Injection inlet permits gradual addition of ^{99m}Tc-phytate during delivery. Concentrated aerosol bolus and impaction sphere can be seen in mirror view of chamber.

sol bolus from the reservoir through the mouthpiece after movement has been initiated by inspiration. One-way valves maintain a closed system except during inspiration. The entire system, except for the patient mouthpiece, is enclosed within a lead shield. The technologist exposure rate during delivery is less than 0.3 mR/hr. The nebulization rate must be individually adjusted for each patient, and proper instruction and encouragement of the patient are absolutely necessary.

All studies were performed using a scintillation camera after inhalation of ^{99m}Tc-phytate. The advantages of labeled phytate for radioaerosols have been reported previously by Isitman et al. (*8*). Most of the radioaerosol studies were performed 24 hr after ^{99m}Tc-MAA perfusion lung scans. The perfusion images were obtained in the anterior, posterior, both lateral, and both posterior oblique views. The radioaerosol images were obtained in at least four views, depending upon which views best showed the perfusion abnormalities. Generally, the posterior oblique views have been more valuable than the lateral views.

The lung retention of ^{99m}Tc-phytate was determined by comparing the posterior count rate with the count rate from ^{99m}Tc-MAA, where the activity injected was known. The amount of lung retention was then expressed as a percentage of the total dose originally added to the nebulizer.

RESULTS

A total of 39 aerosol inhalation studies were performed with this system. Each study was evaluated for efficiency of delivery, image quality, diagnostic validity, and nonpathologic airway deposition. Delivery efficiency is defined as the percentage of the total dose added to the nebulizer that is actually deposited and retained in the lungs. The delivery efficiencies ranged from 3.1% to 23.0%, with an average of 10.7%. It should be noted that 15 of the 39 patients were in significant respiratory distress at the time of the study, and eight of these 15 patients were in the supine position during aerosol delivery. The dose added to the nebulization chamber varied over 20–35 mCi, depending upon the patient's condition. The time required for aerosol delivery was 3–15 min. The retained dose usually ranged over 1–4 mCi, thus permitting images of high information density and proportionately rapid imaging times.

Image quality was evaluated as follows:

Excellent: no significant tracheal or gastric activity.

Good: minimal tracheal or gastric activity, which does not interfere with interpretability.

Fair: excess tracheal activity, requiring delayed images for interpretation.

Poor: image is not interpretable due to poor alveolar deposition or excess tracheal or gastric activity.

Of the 39 studies performed, 29 were rated excellent, nine as good, and one as fair.

Fourteen of the 39 studies showed aerosol deposition in the trachea or major bronchi. In nine of these 14 patients the sites of aerosol deposition correlated with those of documented airway disease. In the remaining five patients, the aerosol deposition occurred at the tracheal bifurcation. The amount of tracheal deposition was minimal in all of these patients, and it cleared rapidly by normal ciliary action. When nonpathologic tracheal deposition did occur, imaging after a 2-hr interval allowed for clearance of the tracheal activity and thus permitted adequate imaging of the alveolar aerosol distribution. When tracheal activity was eliminated, all 39 studies were considered to be interpretable and diagnostically valid.

Figure 2 shows three typical studies. The system's ability to estimate ventilatory distribution to segmental and subsegmental regions is a distinct advantage, as illustrated by Figs. 2B and 2C. It is not unusual to find perfusion defects that are best visualized, or even only visualized, on the posterior oblique view. In these instances, it is advantageous to be able to image ventilation in the identical oblique position.

DISCUSSION

Particle size, aerosol concentration, air flow rate, and airway turbulence are major determinants of aerosol distribution in the lungs (*1,2*). The high-frequency nebulizer used in these studies produces a higher proportion of particles in the desired 0.5–3.0-μm range. In addition, the impaction sphere in the nebulization chamber collects most larger particles, which are then renebulized. Aerosol concentration is also enhanced by the impaction sphere, which traps the aerosol in a small volume until the patient inhales. The air flow rate is more difficult to control, and proper instruction and encouragement of the patient are essential. For maximum delivery efficiency, the nebulization rate should be adjusted to match the patient's respiratory rate and volume.

Airway turbulence obviously cannot be controlled, although a lower air flow rate would be expected to reduce turbulence (*5*). However, except at the tracheal bifurcation, turbulence (and therefore aerosol deposition) appears to be a sensitive and reliable indicator of airway disease. In this regard, our experience is in agreement with the findings of Taplin et al. (*9–11*).

An objective method to evaluate and compare radioaerosol delivery techniques is needed. Delivery efficiency, as reported here, indicates the percentage of the total original dose that is deposited in the peripheral bronchioles and alveoli. It is not of much practical use to define delivery efficiency as the percentage of the *nebulized* dose, since retention of activity in the delivery equipment has been a major disadvantage of previous delivery systems. Nor is it practical to determine delivery efficiency for normal

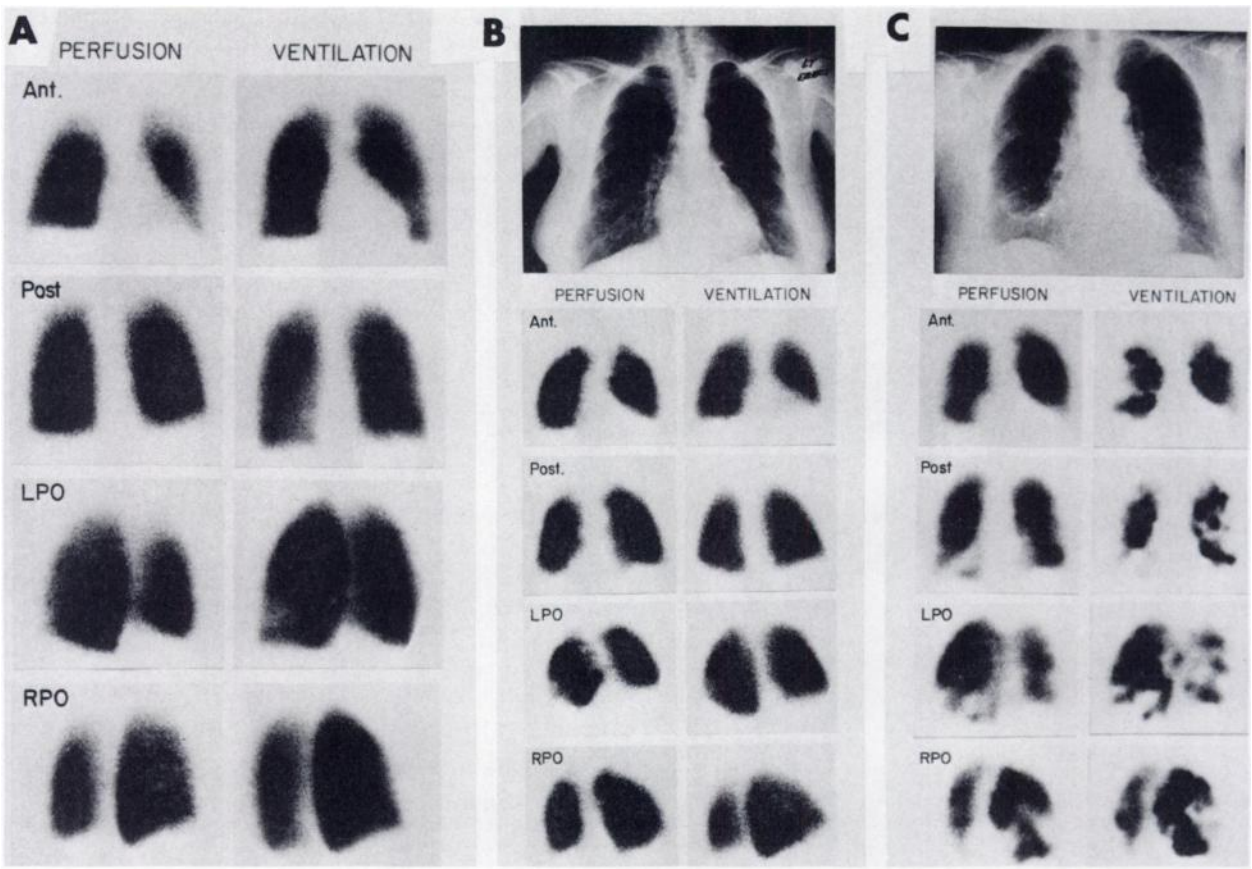

FIG. 2. (A) Normal ventilation–perfusion study. (B) Typical findings in patient with pulmonary embolism. Although perfusion is absent to posterior basilar segment of left lower lobe, this is not readily apparent on perfusion image alone. However, when LPO perfusion is compared to LPO ventilation, V/Q mismatch is apparent. (C) Typical findings in patient with chronic obstructive airway disease. Each perfusion defect can be precisely matched to corresponding loss of ventilation.

subjects, who differ considerably from the patients routinely referred for ventilation–perfusion lung imaging. More than one-third of our patients were in significant respiratory distress; thus, the reported overall delivery efficiency represents what can be expected in clinical practice. Lastly, excessive tracheal or gastric activity does not represent efficient delivery and should not be included in calculations of delivery efficiency. In this series of patients the tracheal and gastric activity has been minimized and therefore the efficiency figures are not falsely elevated by extrapulmonary activity.

Image quality and interpretability should also be evaluated. Thirty-eight of our 39 patients showed little or no extrapulmonary activity. All 39 studies were considered interpretable.

The use of ^{99m}Tc labels for both perfusion and ventilation is not ideal, since a 24-hr interval must separate the two studies. From a logistical standpoint, ^{113m}In radioaerosols would be preferable, since a ventilation study could then be performed immediately after an abnormal perfusion study. An efficient delivery system makes the use of ^{113m}In aerosols more practical and economical than they have been previously.

Radioaerosol inhalation studies reflect the *distribution* of ventilation, and not ventilatory rates or quantities. However, since most ventilation lung scans are performed to assist the interpretation of perfusion lung scans, ventilatory distribution is the information being sought. Xenon-133 would therefore appear to have no inherent advantages for this purpose. The additional advantages of radioaerosol delivery, as noted above, have made it the preferred procedure in our laboratory.

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