Clinical Assessment of a Commercial Delivery System for Aerosol Ventilation Scanning by Comparison with Krypton-81m

Per Wollmer, Leif Eriksson, and Ann-Christin Andersson

University of Lund, Lund, Sweden

A commercial aerosol delivery system* for ventilation scanning was evaluated in 23 patients with lung disease involving regional disturbances of ventilation. Ventilation scans obtained after inhalation of an aerosol labeled with In-113m were compared with Kr-81m ventilation scans. An indirect comparison was also made with a settling bag technique.

There was close agreement between the aerosol and the Kr-81m ventilation scans in all of the patients. The aerosol outlined the ventilated parts of the lung adequately, and central deposition of particles was minimal. The penetration of the aerosol into the lung was higher with the delivery system than with a settling bag system. The aerosol delivery system appears suitable for clinical pulmonary ventilation scintigraphy.

Ventilation scintigraphy after inhalation of radioactive aerosol was introduced in 1965 (*1-3*). The rationale for the technique is that small (less than about 2 μm) inhaled particles will be deposited by sedimentation or diffusion in the periphery of the lung in proportion to regional ventilation (*4*). If the aerosol contains a poorly soluble compound, clearance of the deposited tracer is slow, and qualitative images of ventilation of high statistical quality can be obtained in multiple views after the inhalation. Deposition of inhaled particles larger than about 2 μm occurs mainly by impaction in major airways (*4*). In this case, deposition does not reflect regional ventilation, but is more dependent on turbulence and other changes in the direction of air flow. Deposition of particles by impaction is seen in the scan as central hot spots, which may impede interpretation of the image. For a given aerosol, deposition by impaction increases with increasing bronchial obstruction (*5, 6*). Aerosol ventilation scans of high quality are therefore especially difficult to obtain in patients with obstructive airway disease.

For reprints contact: Per Wollmer, Dept. of Clinical Physiology, Lasarettet, S-221 85 Lund, Sweden.

The clinical use of aerosol ventilation scanning has been hampered by the lack of simple techniques for generating aerosols with sufficiently small particles. An air jet nebulizer, which produces an aerosol with very small particles (0.45 μm mass median diameter, according to the manufacturer) has recently become commercially available. The aim of this study was to evaluate this aerosol delivery system by a comparison between aerosol ventilation scans and Kr-81m ventilation scans in patients with abnormal regional ventilation.

The protocol was the same as that used in a previous study of a settling bag technique (*6*), and an indirect comparison could thus be made between the UltraVent system and the settling bag technique. The settling bag (50 l) can collect the aerosol and allow gravity settling to remove large droplets before inhalation by the patient.

MATERIALS AND METHODS

Patients

Twenty-three patients were studied, 15 men and eight women, with a mean age of 60.8 $\pm$ 12.5 (SD) years. All of these patients had a well established diagnosis of a lung disease affecting regional ventilation. Most of the patients suffered from chronic bronchitis, emphysema, or bronchial asthma, but there were also a few who had intersitial lung disease or carcinoma of the bronchus. The study was approved by the local research ethics committee, and informed consent was obtained from each patient.

Pulmonary Function Tests

Spirometry, including vital capacity (VC) and forced expiratory volume in 1 sec (FEV_1), was performed in all patients immediately prior to the scintigraphic examination.

Ventilation Scanning

Ventilation scans in four projections (anterior, posterior, and

right and left posterior obliques) were obtained during continuous inhalation of Kr-81m (*7*). A large field scintillation camera, equipped with a low energy, all-purpose collimator was used. In each projection, 300,000 counts were accumulated. Analog images were acquired on photographic film, and the digital images were stored in a computer.

A radioactive aerosol was generated by nebulizing In-113m colloid with the air jet nebulizer. The In-113m colloid was prepared by adding 1 ml of phosphate buffer (pH 8.0) to 4 ml of eluate from the Sn-113—In-113m generator. The aerosol delivery system is shown in Fig. 1. The patient inhales the aerosol directly from the nebulizer via a unidirectional flow circuit. The exhaled air and excess aerosol is passed through a collection filter. The patients inhaled the aerosol by tidal breathing for approximately 10 min, and ventilation scans in four projections were subsequently obtained using a high-energy collimator.

In ten patients, the efficiency of the aerosol delivery system was assessed by relating the activity nebulized to that deposited in the lungs of the patients. The activity contained in the nebulizer was measured before and after the inhalation. The activity deposited in the lungs was estimated from the count rate over the lungs using a previously determined calibration factor (*6*).

Data Analysis

Data were analyzed qualitatively by image-inspection and quantitatively by measuring the penetration of the aerosol to the periphery of the lung. A penetration index (PI) was calculated in the same way as described earlier (*5, 6*). Two regions of interest, one peripheral and one central, were selected over each lung in the posterior and the anterior projection (Fig. 2, inset). The quotient between the count density in the peripheral region and that in the central region defined the PI. The PI was calculated for both the Kr-81m and the In-113m scans, and the PI for In-113m was normalized to the PI for Kr-81m in each patient. A quotient of < 1 thus signifies a reduced penetration of the aerosol. Student's t-test was used for statistical analysis.

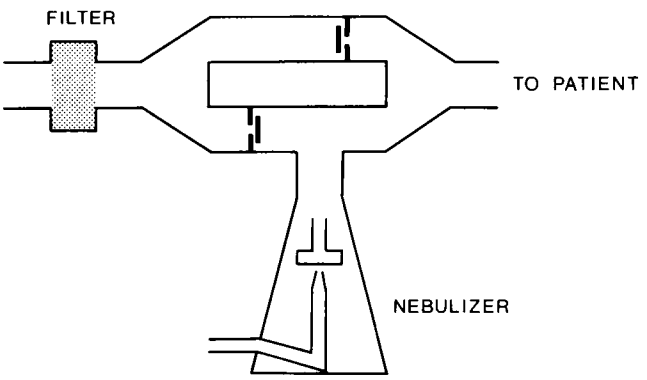

FIG. 1. Schematic drawing of the aerosol delivery system. The patient inhales the aerosol from the nebulizer via a unidirectional flow circuit. Excess and exhaled aerosol is passed through a filter.

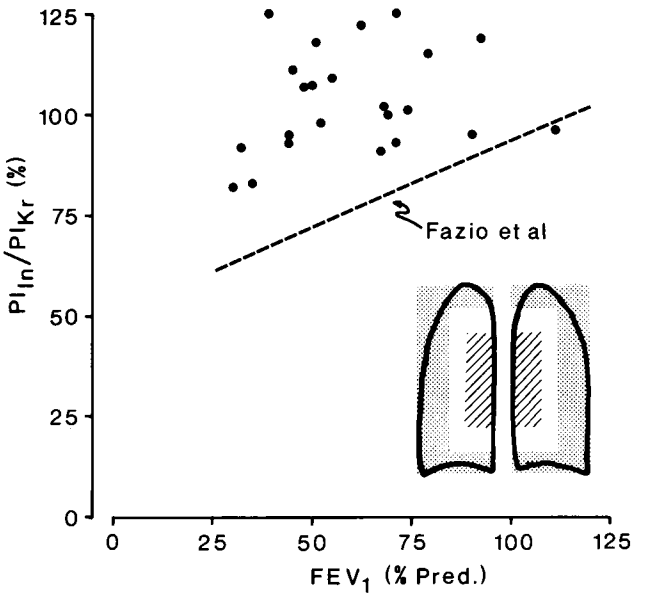

FIG. 2. Relationship between the penetration of the In-113m aerosol and the degree of bronchial obstruction, measured as FEV_1. A PI was calculated as the quotient between the count density in a peripheral region and a central region in each lung (inset). The mean PI for the two lungs was calculated and the PI for In-113m was normalized to the PI for Kr-81m in each patient. The penetration of the aerosol was higher than that in a previous study of a settling bag system (*6*).

RESULTS

An obstructive pattern was seen in nearly all of the patients at spirometry (Table 1). Ventilatory impairment ranged from slight to very severe. All of the patients were, however, able to inhale the aerosol without discomfort.

Between 3 and 5 ml of In-113m colloid with a specific activity of 15mCi/ml were put in the nebulizer. After a 10-min inhalation, an initial count rate of approximately 1,500 counts per sec was obtained on the gamma camera. Approximately 20% of the activity nebulized was retained in the lungs of the patient.

There was close agreement between the Kr-81m and the In-113m ventilation scans. In eight patients, three of whom are described below, there was noticeable central deposition of the aerosol. Even in these cases, however, there was sufficient penetration of particles to the periphery of the lung to adequately outline the ventilated regions.

The mean ratio between the PI for In-113m and for Kr-81m was 1.03 ± 0.13 (SD). There was no significant correlation be-

TABLE 1. Results of Spirometry

Item	VC (% Predicted)	FEV_1 (% Predicted)
Mean (n=23)	72.7	60.0
SD	15.9	20.7
Range	42–100	30–111

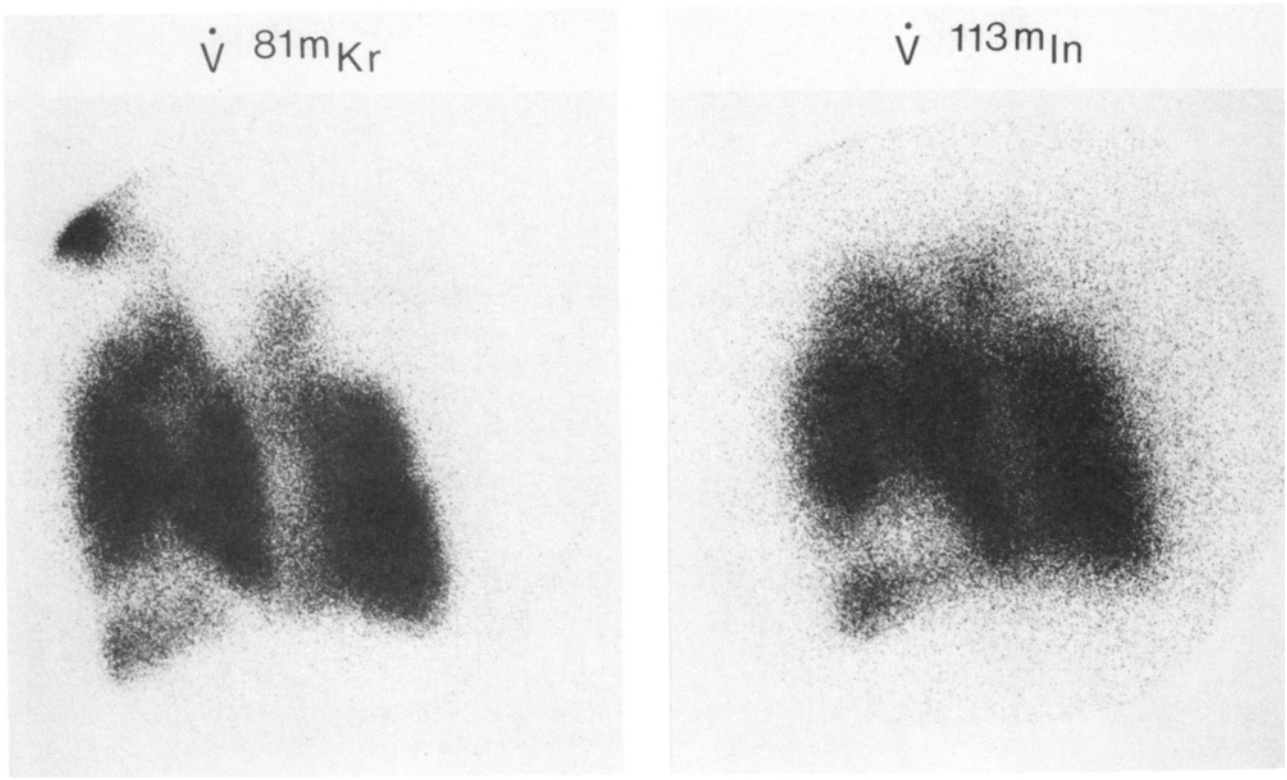

FIG. 3. Kr-81m (left) and In-113m aerosol (right) ventilation scans in the left posterior oblique view from a patient with bronchial asthma.

tween the ratio of the PIs and FEV_1 (Fig. 2). The penetration index obtained with the present method was higher than that reported by Fazio et al. (*6*) in a study of a settling bag system.

The following three cases are presented to illustrate the results.

Case 1:

A 30-yr-old female patient was admitted to the hospital with an exacerbation of bronchial asthma. At the time of study, she was being treated with bronchodilators, corticosteroids, and antibiotics. The VC was 76%, and FEV_1 62% of predicted values. The ventilation scans (Fig. 3) show large, well demarcated defects of ventilation in both lungs. There is no detectable central deposition of aerosol. The resolution is slightly lower and the contribution from the remote lung is higher in the In-113m image than in the Kr-81m image.

Case 2:

A 57-yr-old man who was a heavy smoker and had a long record of chronic bronchitis and emphysema. He had severe functional impairment with shortness of breath during minimal exercise. The patient's VC was 61%, and his FEV_1 32% of predicted values. The ventilation scans (Fig. 4) show multiple defects of ventilation in both lungs. There is close agreement between the two images, and even small defects are clearly seen in the In-113m aerosol scan. There is some central deposition of the aerosol, and this patient had one of the lowest PI_{In}/PI_{Kr} values measured.

Case 3:

An 81-yr-old male, an ex-smoker, had a long record of chronic bronchitis and emphysema. He was in chronic respiratory failure and dependent on continuous oxygen treatment. His VC was 79%, and his FEV_1 44% of predicted values. The ventilation scans (Fig. 5) show extensive reduction of ventilation in the left lung. All ventilated regions are outlined by the aerosol, even if some central deposition is seen.

DISCUSSION

When aerosol ventilation scanning was introduced in the mid-1960s (*1–3*), simple air jet or ultrasonic nebulizers were used. The particles generated by such nebulizers are larger than the optimal size for ventilation scanning and do not always penetrate to all ventilated regions of the lungs in patients with pulmonary disease (*8*). Efforts to solve this problem have included the development of techniques for removing larger particles from the poly-dispersed aerosol generated by an air jet nebulizer. A simple means of achieving this is by passing the aerosol through a settling bag (*9*). The settling bag technique reduces central deposition of particles (*9,10*), and the scans obtained provide clinically useful information about regional ventilation even in patients with obstructive airway disease (*6,10*).

The use of a nebulizer producing an aerosol with smaller particles potentially eliminates the need for a settling bag, and thus simplifies the scanning procedure. Patients with obstructive airway disease present the greatest difficulties in aerosol

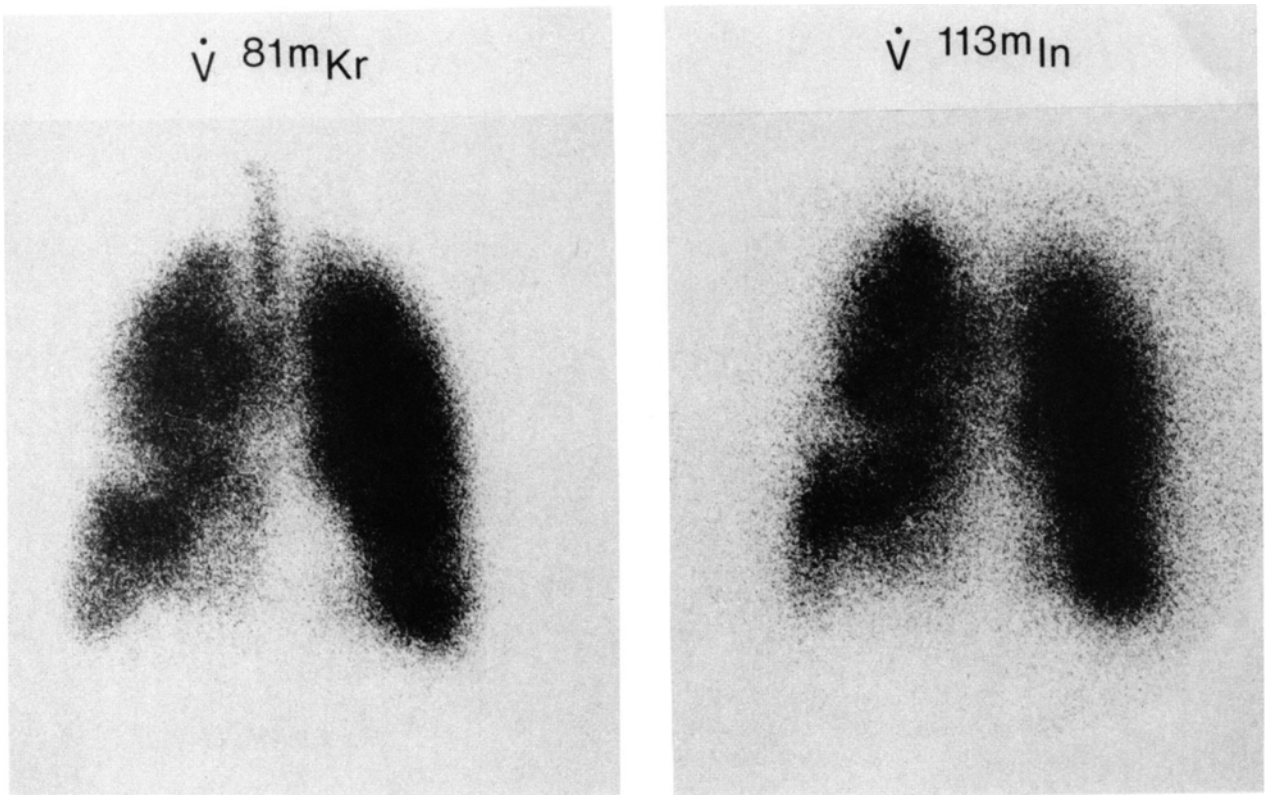

FIG. 4. Kr-81m (left) and In-113m aerosol (right) ventilation scans in the anterior view from a patient with chronic bronchitis and emphysema.

ventilation scanning, and previous studies of aerosol techniques have demonstrated a correlation between aerosol penetration and the degree of airflow obstruction (*5,6*). A large number of patients with obstructive airway disease were therefore included in the present study of the UltraVent aerosol delivery system.

The UltraVent aerosol delivery system proved to be easy to use. A limiting factor common to most aerosol techniques is the rather poor efficiency of the different systems. This is partly due to the low retention of inhaled particles in the desired size-range (*4*), but it is also influenced by the design of the aerosol delivery system. With the UltraVent system (Fig. 1), the aerosol is diluted with room air entering via the filter during most of the inspiration. A simple way of increasing the efficiency by reduction of the dilution of the aerosol would be to introduce a small (0.75 l) reservoir bag and an extra unidirectional flow valve between the port of the nebulizer and the patient's mouthpiece (Fig. 6). This reservoir bag accumulates the aerosol generated while the patient exhales, and empties itself during the ensuing inspiration. Such a modified system has been used in 10 patients undergoing routine V̇/Q̇-scanning, and it was found that approximately 25% of the activity nebulized was retained in the lungs, compared to 20% for the original system and the settling bag (*6*).

Indium-113m was chosen because it has an energy (393 keV) that can easily be separated from that of Tc-99m. Ventilation scanning with this isotope can be performed immediately following a perfusion scan with Tc-99m albumin microspheres. This is particularly useful for lung scanning for pulmonary embolism (*11*). The spatial resolution in the In-113m image is lower than that in the Kr-81m image due to the difference in photon energy. Small defects of ventilation will not be as readily detected with In-113m as with Kr-81m. This may in actual practice be of little importance for the diagnosis of pulmonary embolism, because the specificity for V̇/Q̇-mismatch at sub-segmental level is rather low (*12*).

The aerosol outlined the ventilated parts of the lung in all of the patients. When central deposition of the aerosol occurred, this did not impede the interpretation of the scan. The high penetration of the aerosol was confirmed by the quantitative analysis of the PI. The mean ratio of unity between the PI for In-113m and Kr-81m should, however, not be taken to indicate that the distribution of the two isotopes was identical. The PI is affected by a number of technical factors, such as differences in collimation and attenuation due to the differing photon energies of the two isotopes, and the presence of Kr-81m in central airways during continuous inhalation of the gas. From the calculations of the PI, it is, however, clear that the penetration of the aerosol generated by the UltraVent system is higher than the penetration of the aerosol obtained from the settling bag system (Fig. 2). This difference is probably due to the difference in particle size of the aerosols. In contrast to the previous study of a settling bag system, it was found that there was no significant correlation between the PI and the degree of airway obstruction.

In conclusion, this study has shown that the UltraVent aerosol delivery system is suitable for clinical ventilation scintigraphy. Scintigrams that adequately outline the ventilated

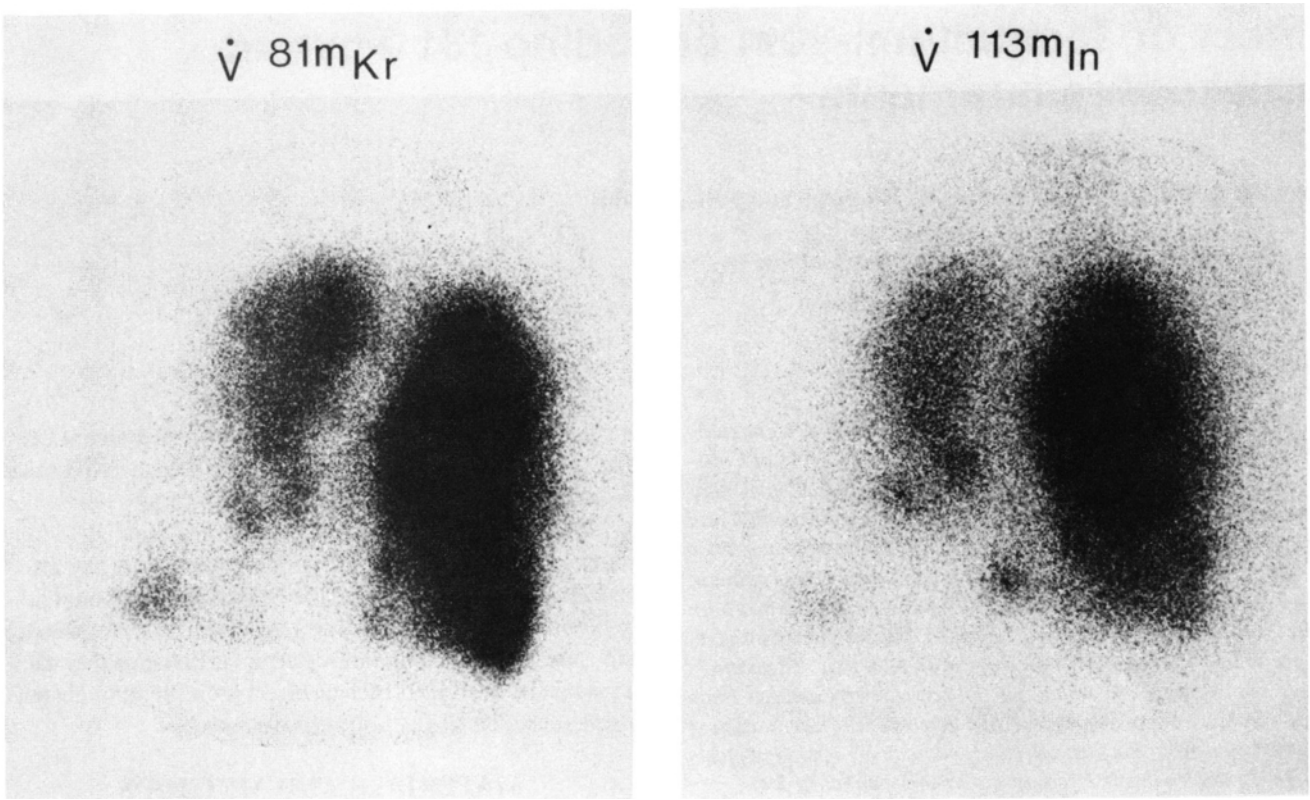

FIG. 5. Kr-81m (left) and In-113m aerosol (right) ventilation scans in the posterior view from a patient with chronic bronchitis and emphysema.

regions of the lungs can be obtained even in patients with obstructive airway disease.

ACKNOWLEDGMENTS

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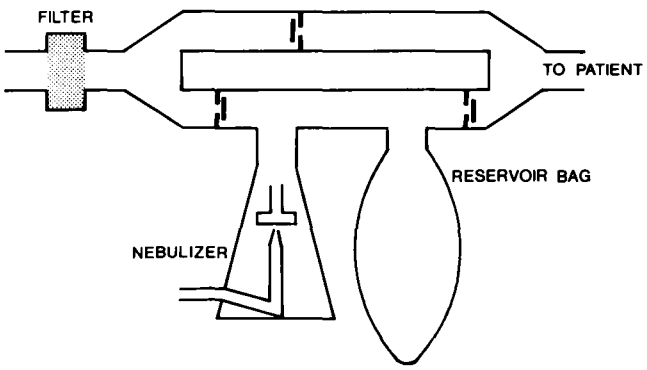

FIG. 6. Modified aerosol delivery system. A small reservoir bag (0.75 l) accumulates the aerosol generated during the patient's expiration. The bag empties during the ensuing inspiration, and dilution of the aerosol is reduced.

FOOTNOTE

*UltraVent™ (Formerly SynteVent®, Synaco, Inc., Palo Alto, CA), Diagnostic Products Div., Mallinckrodt Inc., St. Louis, MO.

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