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# *Metered Dose Inhaler Aerosol Characteristics Are Affected by the Endotracheal Tube Actuator/Adapter Used*

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**The authors studied the particle size of aerosols of metaproterenol produced by three different actuators designed for use in patients with endotracheal tubes in place. These were compared with the metaproterenol aerosol produced by the actuator (provided by Boehringer-Ingelheim [BI]) that was supplied by the manufacturer for use in patients whose tracheas are not intubated. The volume of particles in the respiratory size range (1.0–5.1 μm) delivered to the end of the endotracheal tube were measured using adapters designed by Intec (IT), Instrumentation Industries (II), and Monaghan (MAIS). Particle numbers were measured using a CSAS 100 scattering-aerosol laser spectrometer, and volumes were calculated by assuming the particles were spheres. The authors found that the volume of particles in the respiratory range with the IT, II, and MAIS adapters plus endotracheal tube were 11, 31, and 66%, respectively, of the volume produced in the respiratory range by the BI. When particles likely to impact before reaching the lower airways (>5 μm) were measured, almost none was produced by the adapters plus endotracheal tube, whereas the majority of drug volume in the BI aerosol was in the >5 μm range. It was concluded that the aerosol produced by different actuators differ from each other, that all three produced less drug in the respiratory range than was produced by the manufacturer-supplied actuator, and that large particles are effectively removed by the adapter plus endotracheal tube. (Key words: Anesthetic techniques: tracheal intubation. Lung, asthma: aerosols.)**

DELIVERY OF AEROSOLIZED bronchodilators to patients with endotracheal tubes (ETT) in place has traditionally been accomplished using small volume nebulizers (SVN). Disadvantages of SVN include cost of unit doses, set-up time, and interference with ventilator triggering.[1,2] Because of these problems, clinicians have adapted metered dose inhalers (MDI) to the ventilator circuit to deliver medications.[3] The MDI, however, are designed to be used with actuators provided by the manufacturer to deliver a defined volume of aerosol of a given particle size distribution to patients in whom the trachea is not intubated. Manufacturers independent of the MDI distributors have now designed actuators for use with ventilator circuits. We hypothesized that such actuators would provide a distribution of particle size and total dose that would differ from that of the actuator supplied for use by the awake patient. Because these actuators are used to deliver medication *via* an endotracheal tube, we studied the particle volume and size distribution of the aerosol created by three such devices as the aerosol exited from an endotracheal tube.

## Materials and Methods

The actuators studied were the Intec 172275 (IT; Intec Medical, Inc, Blue Springs, MO), the Instrumentation Industries RTC-22 (II; Instrumentation Industries, Bethel Park, PA), and the Monaghan Aerochamber In-line Spacer (MAIS; Monaghan, Littleton, CO). The aerosol produced by these using a metaproterenol (Alupent, Boehringer-Ingelheim Ltd, Ridgefield, CT) canister with an ETT in the circuit was compared with that produced by the canister plus actuator combination as supplied by Boehringer-Ingelheim (BI).

### MEASURING SYSTEM

A classical scattering aerosol spectrometer system (model number CSAS 100, Particle Measuring Systems, Boulder, CO) was used.[4,5] This device operates on the principle that the light scattered by a particle within a laser cavity is directly a function of its size. It is designed with four overlapping size ranges, with each size range divided into 15 linear size intervals providing a total of 60 size channels. Size range 0 is from 2–20 μm in 1.6-μm intervals, size range 1 is from 1–12.25 μm in 0.75-μm intervals, size range 2 is from 0.5–2.75 μm in 0.15-μm intervals, and size range 3 is from 0.32–0.75 μm in 0.029-μg intervals. Since each range is sampled sequentially in time and data, all four size ranges must be integrated together to obtain the full range of the CSAS. This was accomplished with the CSAS operating in automatic mode, such that the spectrometer analyzed size ranges 0 through 3 sequentially and then repeated the procedure. A computer (Toshiba T3100) was used to collect the analog data from the CSAS 100. The interfacing of the

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computer with the CSAS was achieved with an integrated software package that automatically collected the data and submitted it to a spreadsheet for analysis. We collapsed the channels into three ranges of particle size: small (<1.0 μm in diameter), respiratory range (1.0–5.1 μm), and large (5.1–20 μm). These ranges were chosen because of the different outcomes of particles in these sizes: small particles tend to be exhaled in high numbers, respiratory range particles have a high rate of deposition in the lung, and large particles tend to deposit before entering the lung.

### Conversion of Particle Data to Volumes

We assumed that the particles generated by the nebulizers are essentially spheres and that the average size of the particles in one bin or channel is represented by the midpoint value of that interval. The total volume of the particles in one channel can then be calculated by multiplying the number of particles in that channel by the volume of the average size of a particle in that bin, *i.e.*:

$$V_i = (N_i 4\pi r_i^3)/3$$

where $V_i$ represents the total volume of particles in the $_i$th channel, $N_i$ is the number of particles in that channel, and $r_i$ is the average radius of the particles in that channel.

After calculation of the numbers of particles in each channel, the computer was programmed to add all of the channels from 0.3–1.0 μm in diameter (small particles), 1.0–5.1 μm (respirable range), and 5.1–20 μm (large particles). The CSAS 100 measures only a fraction (<0.01%) of the particles flowing through the instrument[5]; thus, measurements of volumes represent the particles flowing past the laser beam. Volumes are reported in cubic microns but absolute volumes are not meaningful: the volumes are useful only relative to the volumes produced by the other devices studied.

We first studied the hand-held actuator provided by BI. Five separate canisters and actuators were activated sequentially 16 times each for a total of 80 actuations per run. Multiple canisters were used to prevent skewing of the data by any individual canister. Actuations were 4 s apart so no canister was fired until 20 s after its previous firing. Four series of 80 firings each were performed.

The in-line devices were studied using a Hamilton Veolar ventilator (Hamilton Medical, Inc, Reno, NV) set to deliver an 800-ml tidal volume at 60-l/min flow rate as a square wave *via* a 7.5-mm ETT. Each breath was 4 s after the previous breath, and the canister was activated manually as the ventilator initiated the breath. We again used five separate canisters 16 times each, and fresh canisters were used for each run. The actuators were placed as close to the ETT as possible (*i.e.*, the II at the elbow and the other two at the Y-piece). Again, four series of 80 actuations each were performed.

Data are mean ± SEM. Differences among the actuators were tested using analysis of variance, and specific differences between devices were tested using Student's *t* test.

Both numbers of particles and volumes are relative numbers since only a fraction of the aerosol was sampled by the spectrometer. Thus, volumes and numbers can be compared among devices but do not provide absolute information on the total volume or numbers of particles produced.

TABLE 1. Number of Particles in Each Range

| Device | Small (<1.0) | Respiratory (1.0–5.1) | Large (5.1–20) |
|---|---|---|---|
| IT | 110.0 ± 7.5†‡ | 57.5 ± 5.1†‡ | 0.3 ± 0.3‡ |
| II | 316.0 ± 12.6*† | 160.8 ± 8.5*† | 0.0 ± 0.0 |
| MAIS | 694.3 ± 20.7*‡ | 358.3 ± 23.5*‡ | 0.0 ± 0.0 |
| BI | 271.5 ± 13.5*† | 159.3 ± 8.7*† | 16.5 ± 0.7* |

Data are numbers of particles counted in 80 puffs. The spectrometer samples the flow but does not measure the total flow. Thus, numbers should be evaluated relative to each other rather than as absolute totals
Sizes are diameters.
Data are mean ± SEM.
* $P < 0.01$ *versus* IT.
† $P < 0.01$ *versus* MAIS.
‡ $P < 0.01$ *versus* BI.

TABLE 2. Volumes of Particles in Each Range

| Device | Small (<1.0) | Respiratory (1.0–5.1) | Large (5.1–20) |
|---|---|---|---|
| IT | 10.3 ± 0.9†‡ | 294.3 ± 31.4†‡ | 3.3 ± 2.0‡ |
| II | 28.5 ± 1.2*† | 807.0 ± 44.7*†‡ | 2.8 ± 1.6 |
| MAIS | 64.8 ± 2.2*‡ | 1733.8 ± 137.0*‡ | 6.8 ± 2.7‡ |
| BI | 28.3 ± 1.9*† | 2611.5 ± 121.6*† | 8114.5 ± 1152.6*† |

Volumes are in cubic microns. The particles sampled represent only a fraction of the total particles produced and thus numbers are best evaluated relative to each other rather than as absolutes.
Sizes are diameters.
Data are mean ± SEM.
* $P < 0.01$ *versus* IT.
† $P < 0.01$ *versus* MAIS.
‡ $P < 0.01$ *versus* BI.

## Results

Under all four conditions tested, the majority of the particles produced are in the small range (table 1). However, because of the small diameter of these particles, the total volume of these particles was negligible compared to the volumes in the larger two ranges (table 2).

No large particles were detected using any of the three devices with the ETT, but a few were present using the hand-held actuator. The volume of drug contained in these particles, however, was the major portion of the volume of the aerosol.

The volume of particles in the respiratory range was largest for the hand-held adapter (table 2). The volume in the respiratory range for the in-line adapters (expressed

as a percentage of that provided by the hand-held adapter) was 11, 31, and 66% for the IT, II, and MAIS, respectively.

## Discussion

Particle size of an aerosol is critical in determining the outcome of the particles.[6,7] The inertia of particles larger than 5 μm in diameter causes them to impact against structures such as the pharynx or the ventilator circuit and tube. Particles less than 1 μm are inhaled deeply into the lung but are influenced little by gravity and hence have a low rate of deposition in the lung.[6] Drug is most likely to be deposited in the lung by particles of 1–5 μm, *i.e.*, those in the respiratory range.[6] Although the particle size determines its location of deposition in the respiratory tract, it is the collective volume of particles that determines the dose of drug delivered to the lung. Therefore, the volume of the particles from 1–5 μm gives the clinically important data.

Studies of patients in whom the trachea is not intubated and who use MDIs suggest that even when used under ideal circumstances, no more than 10–20% of the drug is deposited in the lung.[8] This is not surprising given that we found that 81% of the drug is contained in large particles that tend to impact in the pharynx.

We previously found, using the IT, that efficiency of delivery to the end of the ETT depended on several factors, including tube size and flow pattern[9]; however, we studied only one adapter and did not examine particle size. In this study we found that the adapter used has a major effect on the aerosol exiting the ETT. Thus, there was a nearly five-fold variation between the volume in the respiratory range using the IT compared to the volume produced with the MAIS.

In the patient whose trachea is not intubated, systemic effects of bronchodilator drugs result primarily from absorption of drug from the mouth and pharynx where large particles impact. To minimize oropharyngeal deposition, "spacer" devices are sometimes used. Spacers are placed between the patient and the actuator to slow the flow of aerosol and increase impaction and sedimentation of large particles.[10] The lack of particles in the large range using the adapters we studied is undoubtedly due to impaction in the elbow and ETT. We previously found that more than 90% of the weight of the aerosol could be found in the elbow and the ETT, with most of that in the elbow.[9] Visual inspection of the ETT suggested that almost all of the impaction in the tube was in the few centimeters closest to the elbow. Thus, the elbow and ETT act as a "spacer" device. This has the potential benefit of decreasing systemic effects of the drug if the elbow and proximal ETT were cleaned or swabbed following drug administration.

The variability of drug delivered among the three in-line adapters has important implications for dosing. Our data are *in vitro* and dosing must be based on clinical response. However, based on our data, to achieve a dose in the respiratory range equivalent to that provided by the hand-held adapter for the patient whose trachea is not intubated, the number of actuations provided would need to be increased from 50 to 800%, depending on the adapter used. Increased dosage must be accompanied by monitoring for evidence of systemic effects of the medications.

We based our clinical use of inhaled bronchodilators on the findings presented in this article without significant systemic side-effects. Indeed, even with a larger number of puffs, the systemic dose may be substantially smaller because of the "spacer" effect.

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