Extreme Variability in Aerosol Output of the DeVilbiss 646 Jet Nebulizer*

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Ten new jet nebulizers (DeVilbiss 646) were studied to determine their consistency of output. Each nebulizer, containing 2 ml of saline solution, was run for 1 min in triplicate at four different straw (capillary tube) positions, keeping all other variables constant. Total output in milliliters per minute and volume of aerosol in the respirable range (1.0 to 5.0 μm) were measured. There was significant variability in output and volume of output in the respirable range (VORR) for every nebulizer at each of the tested straw positions (p<0.0001). Irregularities in manufacture of the bowl and straw appear to be responsible for this significant variability. In summary, there is considerable intranebulizer and internebulizer variability that could influence both patient care and medical use for diagnostic purposes.

(Chest 1991; 100:1339-44)

ANOVA = analysis of variance; %RR = percentage of aerosol in the respirable range; VORR = volume of output in the respirable range

Jet nebulizers have become a primary method of delivery of medication to patients with asthma. Nebulizers are also frequently used to administer agents for bronchial challenges and occasionally for the delivery of antimicrobial agents. Each of these uses requires that the particular nebulizer be predictable in its delivery of aerosol. Inaccuracies or inconsistencies in aerosol output could have major consequences in the management of disease.

In a recent separate study,1 we observed large variations in aerosol output by some DeVilbiss 646 nebulizers. In that study, ten different DeVilbiss 646 nebulizers were studied in triplicate with a 3-ml volume fill for 1 min. The mean outputs for these nebulizers with the air vent closed ranged from 0.238 to 0.353 ml/min. The study employed two of these nebulizers that had similar outputs (0.290 ± 0.012 ml/min and 0.287 ± 0.013 ml/min). During the course of the study, there were more than 50 instances of 225 trials when one or the other of the nebulizers produced aerosol outputs that were markedly different from previous runs with the same conditions of nebulization. Many times it appeared that little or no aerosol was produced. On examining the nebulizers with covers removed, we found that manipulation of the straw (capillary tube) caused marked differences in visible output. These differences occurred when the straw was rotated with varying orientations in relation to the nebulizer bowl and when varied vertically with respect to the outflow jet orifice (Fig 1).

There are two other descriptions of similar difficulties with output from the DeVilbiss 646 nebulizer in the literature. Both of these studies noted marked variability in solution output for different nebulizers of the same model. One study, which was recently published as an abstract, showed marked variability in volume of output in the respirable range.2 This study examined four DeVilbiss 646 nebulizers but did not attempt to determine whether differences in straw position, age of nebulizer, or manufacturing defects led to this variability. A similar study by Massey et al3 was undertaken after they noted visible differences in aerosol output with the DeVilbiss 646 nebulizers they were using for bronchoprovocation testing. They reported that the output of the nebulizers varied with cleaning technique and variation of the jet position in regard to the aerosol output port. The study was flawed by altering more than one variable simultaneously, thus precluding the determination of the variables contributing to inconsistency.

We recently conducted a survey by mail of 1,100 physicians and respiratory therapists in the United States to determine usual nebulization practices. From the 178 respondents, we found that the DeVilbiss 646 was the nebulizer most widely employed by this group for administration of medication to asthmatics (30.0 percent). Because of the marked variability in aerosol output observed by us and others, we prospectively studied ten new DeVilbiss 646 nebulizers to verify the significance of these observations.

**Materials and Methods**

**Nebulizers**

Ten new (never used) DeVilbiss 646 nebulizers were studied. As suggested in the instruction pamphlet, the air vent cap was open and the T-piece cap closed (see Fig 1) to attain maximal aerosol output.
output. The instructions provided by the company do not specify straw (capillary tube or jet) position. We varied the direction so that each straw pointed analogous to the clock positions 12, 3, 6, and 9. The 12-o’clock position was with the straw pointed towards the aerosol outlet port (Fig 1).

Driving Flow

The nebulizers were attached via tubing to the same DeVilbiss model 5610D compressor which produces a flow of 6.2 L/min from the nebulizer output port. Multiple measurements of the flow failed to reveal any significant variability.

Weighing of Nebulizers

To calculate the output, the nebulizers were weighed before and after each run. A Mettler balance with an accuracy of 0.01 g was employed.

Aerosol Characterization

The output of the nebulizer was analyzed continuously with an "Active Scattering Aerosol Spectrometer Probe" (Particle Measuring Systems, Boulder, CO, model CSASP-100-HV). The aerosol was analyzed for particles 0.5 to 32 μm in diameter. Sampling was performed over three different size ranges (see below) sequentially at a set interval. The interval of analysis for each range was 5 s. This allowed a complete measurement of the entire range every 15 s.

![Diagram of nebulizer components](Image)

**Figure 1. Parts of the nebulizer.**

Each of the three ranges of analysis contain 15 channels of increasing incremental size.

<table>
<thead>
<tr>
<th>Range</th>
<th>Size, (μm)</th>
<th>Increment, (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>0.5-8.0</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>1.0-16.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1</td>
<td>2.0-32.0</td>
<td>2.0</td>
</tr>
</tbody>
</table>

There is some overlap among ranges with range "3" being the most precise due to its smaller increments. A computer program automatically discarded the values from the channels in each range that overlapped with a more precise channel. This program also scaled the values from each range to that of range "2" (1.0 = μm increments) so that comparisons between ranges could be easily plotted. The program summed the particles from each similar channel for each time period analyzed and then converted the particle numbers into volumes by the formula \( V = \pi r^2 \) (r = radius). Next, a volume distribution was determined by calculating the percentage of total volume in each size channel. From this profile, the percentage of total aerosol in the respirable range (1.0 to 5.0 μm)\(^3\) was calculated. The product of the percentage of aerosol volume in the respirable range and the total milliliter output results in the volume of output in the respirable range (VORR)\(^0\) in milliliters per minute.

**Study Design**

Ten new DeVilbiss 646 nebulizers were run with the straw placed and seated firmly in each of the four positions described. Each nebulizer was run ten times, and the average of the ten runs was recorded as the output measurement. The variables measured included aerosol output, rate of re-expansion, and the rate of output at the end of the aerosol output (VORR). The output was determined using the Stop Watch Method. The samples were assessed for variability using a typical statistical analysis.

| Table 1 — Mean and Standard Deviations for the Ten DeVilbiss 646 Nebulizers |
|-----------------|---|---|---|---|---|---|---|---|---|---|
| Nebulizer | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 |
| Output | Mean | 0.438 | 0.5 | 0.503 | 0.516 | 0.463 | 0.3876 | 0.296 | 0.388 | 0.29 | 0.519 |
|          | SD  | 0.045 | 0.038 | 0.049 | 0.037 | 0.134 | 0.136 | 0.207 | 0.138 | 0.229 | 0.38 |
| RR      | Mean | 71.84 | 71.09 | 72.83 | 73.69 | 75.81 | 74.81 | 73.72 | 74.41 | 79.09 | 71.14 |
| VORR    | Mean | 0.315 | 0.355 | 0.366 | 0.361 | 0.344 | 0.289 | 0.214 | 0.283 | 0.217 | 0.369 |
|          | SD  | 0.036 | 0.025 | 0.044 | 0.045 | 0.098 | 0.102 | 0.141 | 0.097 | 0.162 | 0.028 |

1340

Extreme Variability of Aerosol Output of Jet Nebulizer (Hollie et al)
Tukey's multiple comparisons procedure. Analysis did reveal that the assumption of equal variances needed for the one-way ANOVA was violated; however, this effect is minimal in the case of equal sample sizes, so the result of our one-way ANOVA is minimally affected. The effect of the variability of the VORR and output was illustrated by calculating the 95 percent prediction intervals for each nebulizer. Finally, a two-way ANOVA model was constructed that allowed us to determine if an optimal straw position for this particular model of nebulizer could be recommended. Significant difference was defined as a p value $\leq 0.05$.

**Results**

Table 1 shows the mean and standard deviations for output, %RR, and VORR for each of the ten nebulizers. The results of Tukey's multiple comparison's procedure reveal that the means of nebulizers 7 and 9 are significantly different when compared with the means of nebulizers 2, 3, 4, 5, and 10 ($p<0.05$).

The total volume delivered from the nebulizers at all straw positions ranged from 0.04 to 0.62 ml/min while the VORR varied from 0.020 to 0.456 ml/min. Bartlett's test revealed that the amount of variability

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**Statistics**

Statistical analysis was performed using several different methods. Bartlett's test for equality of variances was performed on the variance estimates for the VORR, percentage of aerosol in the respirable range (%RR) and milliliter output to determine if the amount of variability across nebulizers was significantly different. For this analysis, specific straw positions were not accounted for since routine patient use of this nebulizer would not consider this factor. The data were also analyzed to determine if there were significant differences in the means of the VORR, %RR, and outputs across nebulizers. This was determined with a one-way analysis of variance (ANOVA) model and by testing differences in means with

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**Mean Solution Output by Straw Position**

**10 DeVilbiss 646 Nebulizers**

**Figure 2.** Mean solution output by straw position of ten DeVilbiss 646 nebulizers.
Volume of Output in the Respirable Range by Straw position  
10 DeVilbiss 646 Nebulizers

![Graph showing output vs straw position](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21636/)

Figure 3. Volume of output in the respirable range by straw position in ten DeVilbiss 646 nebulizers.

across nebulizers was significant for both of these measures (p<0.0001). The standard deviations ranged from 0.053 to 0.215 for output and from 0.004 to 0.175 for the VORR.

The 95 percent confidence intervals for each of the nebulizer outputs is illustrated in Table 2. These intervals contain the upper and lower limits for output and VORR that a nebulizer will deliver 95 percent of the time. The wider the prediction interval, the more variable the nebulizer. Nebulizers 5 through 9 exhibit larger prediction intervals than the other nebulizers. In fact, nebulizers 7 and 9 have lower limits of zero, which does not preclude the possibility that these nebulizers could occasionally deliver no aerosol.

Figures 2 and 3 illustrate the milliliter output and VORR of the nebulizers by straw position. It is clear that each nebulizer has a different output and VORR depending on straw position. A two-way ANOVA with the straw position as a fixed effect and both nebulizer and the interaction between nebulizer and straw position as random effects were fit to the output, %RR, and VORR data separately. In both the models for VORR and output, the interaction term was significant (p<0.0001). This indicates that the effect of straw positions across nebulizers is not consistent and thus no optimal straw position of the ones tested can be recommended. The interaction term for the %RR model was only of borderline significance (p = 0.0532), which indicates that the various straw positions actually have little effect on the percentage of total aerosol in the respirable range.

Once the data were analyzed and significant variability among the different 646 nebulizers was ascertained, we completed further testing to help discern if the inconsistency resided more from manufacture of the straw, the bowl, or a combination of the two.

Nebulization time was measured after interchanging the straws and bowls from two of the more consistent nebulizers (1 and 2) with the two least consistent nebulizers as determined by the size of the 95 percent confidence interval (nebulizers 7 and 9). For example, when measuring the effect of the straw on inconsistency, the straws from nebulizers 7 and 9 were used with the bowls from nebulizers 1 and 2. This led to measurements of the following pairings: 7s-1b, 7s-2b, 9s-1b, and 9s-2b (s = straw and b = bowl). The straws were seated firmly at the 6-o’clock position since it manifested the most variability (see Fig 2 and 3). The time in seconds required to nebulize 2 ml of normal saline solution was measured for each combination. Time was measured from the start of nebulization until air was first observed being siphoned into the straw. Aerosolization time was analyzed with the nebulizer tops removed since differences in tops could confound delineating the contribution to observed variability from the straw, bowl, or both.
Effect of Interchanging Straws & Bowls from consistent & Inconsistent Nebulizers

FIGURE 4. Effect of interchanging straws and bowls from consistent and inconsistent nebulizers.

Figure 4 illustrates the results of this study to determine what contributions the straw and bowl have on the DeVilbiss 646 variability. The output time and variability (standard deviation) is clearly lowest when both the straw and bowl come from the consistent nebulizers. When inconsistent straws are paired with consistent bowls, the nebulization rate decreases 54 percent, while the consistent straw and inconsistent bowl combination leads to a 174 percent reduction in aerosol output. The combination of both inconsistent straws and bowls is associated with a 13-fold fall in nebulization rate compared with the consistent straw and bowl pairs. The standard deviations of the means parallel the increase in nebulization times.

DISCUSSION

Jet nebulizers are commonly used in medicine, primarily for the aerosol delivery of bronchodilators, antimicrobial agents, and for bronchial challenge studies. Inconsistency in delivery of medication could significantly influence patients’ therapy. In the asthmatic, inadequate delivery of bronchodilator could lead to increasing severity of symptoms. The use of an inconsistent jet nebulizer for the delivery of methacholine and histamine for measure of bronchial hyperresponsiveness could lead to improper diagnoses and management.

The DeVilbiss 646 jet nebulizer consists of three pieces: a top, a bottom (bowl), and a straw (capillary tube). The straw is placed in the bottom of the nebulizer bowl and siphons the solution into the jet stream of air. There are no specific instructions provided regarding placement of the straw into the nebulizer bowl and therefore its placement is random. We studied four different orientations of the straw in each nebulizer, analogous to the 12-, 3-, 6-, and 9-o’clock positions on a clock (Fig 1).

Our study shows inconsistent aerosol delivery both in total output and volume in the respirable range that varies with straw position for all the nebulizers studied (Fig 2 and 3). The inconsistency of output and VORR is evident in Table 2 where the 95 percent confidence intervals for aerosol delivery are listed. Nebulizers 5, 6, 7, 8 and 9 show especially large ranges of outputs. These differences can result in nearly ten times less aerosol delivery simply by a change in straw position (eg, nebulizer 9 output, position 12 vs position 9). The other five nebulizers (1, 2, 3, 4, and 10) behaved somewhat more consistently both in output and VORR at all four positions (Fig 2 and 3).

It is important to note that in every instance when poor output was measured, rotation of the straw resulted in normal aerosol output, thus ruling out any clogging of the straws or other problem in the system on that particular run. In addition, in nearly every case of poor output, there was adequate mist produced.
to moisten the sides of the nebulizer and output port; therefore, the user would not be easily alerted to a problem of inadequate aerosol generation.

The inconsistency of the DeVilbiss 646 nebulizer appears to arise from several possible sources. The two-way ANOVA model (straw: fixed effect, nebulizer and interaction of straw/nebulizer: random effect) revealed that the effect on output of the straw or nebulizer alone was only marginally significant; however, the interaction of the two was very significant (p<0.0001). Our secondary study, which interchanged more consistent straws and bowls with those from the two least consistent nebulizers, indicated that the nebulizer bowl contributes more to the variability of the system than the straw, while the interaction of the two causes an even greater decrease in output. It is our supposition that irregularities of the bowl contour (and possibly unevenness in the base of the straw) lead to misalignment of the straw over the jet air port. Since the jet air port itself is stable, little change in flow rate or pressure drop would be expected from changes in straw position. Therefore, changes in alignment of the straw over the jet would lead to changes in the amount of fluid suctioned through the tube; however, the suctioned fluid would still impact the same jet of air leading to a similar aerosol size profile. The fact that the percentage of aerosol in the respirable range was not significantly altered by changes in straw position (Table 1) supports this view. One would also expect that outputs would tend to vary as the straw and bowl are rotated with respect to each other (Fig 2 and 3), and similar straw and bowl positions for each individual nebulizer should have reproducible outputs. This is generally true for our data (Fig 2 and 3) since most of the outputs at specific straw positions were very reproducible. These flaws in bowl or straw contour could easily occur during the manufacturing process from buckling of the plastic as it undergoes rapid cooling in the nebulizer mold.

It should be noted that for each of the nebulizers tested, there was always at least one position where the output was similar to the more consistent nebulizers (>0.3 ml/min). Thus, if the user happened to randomly place the straw in this position, no problem would occur. On the other hand, if the straws from nebulizers 5 through 9 were placed in one of the poorer output positions (6 or 9 o'clock), inadequate aerosol delivery might occur.

Arossa et al. reported marked variability in the DeVilbiss 646 nebulizer and concluded that it was not accurate enough to be chosen as a standard nebulizer for bronchial provocation. It has also been noted by us in other studies with the DeVilbiss 646 that over time with multiple uses, the straws fit more loosely in the nebulizers, which also resulted in inconsistent output. This suggests that the manufacturer's statement in the instruction pamphlet that the "nebulizer should give years of dependable service" should be accepted with caution.

Several modifications could be helpful in overcoming this problem of inconsistency. First, the manufacturer could apply stricter quality control to the manufacturing process. Second, units could be tested in the factory and specific instructions be given regarding positioning of the straw. Furthermore, physicians and respiratory therapists should be aware of this problem and instruct patients using this nebulizer that if they are not receiving the usual therapeutic benefit, they should consider a defect in the nebulizer as one of the possibilities.

In summary, there is significant intranebulizer and internebulizer variability in total output and VORR observed in the DeVilbiss 646 jet nebulizer. This variability appears to be related to defects in manufacture of the nebulizer and the straw (jet). Medical personnel using or prescribing these nebulizers should be aware of this possible inconsistency since it may lead to problems in patient treatment.

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REFERENCES