

# A GUIDE TO *Aerosol Delivery Devices*

## FOR *Respiratory Therapists*

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*With a Foreword by*

*Sam Giordano, Executive Director*

**American Association for Respiratory Care**



Produced in collaboration with the  
American Association for Respiratory Care

Supported by an educational grant  
from Respironics, Inc.

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Aerosol therapy is both an art and a science. And for respiratory therapists, who are the experts in aerosol therapy, the terms “art” and “science” take on a practical meaning. Respiratory therapists are the only health care providers who receive extensive formal education in aerosol therapy and who are tested for competency in aerosol therapy. In fact, administration of prescription drugs via the lungs is a major component of the scope of practice for all respiratory therapists. Respiratory therapists are *the* experts when it comes to the art and science of aerosol therapy.

How does art combine with science in the context of aerosol therapy? “Science” includes pharmacology, cardiopulmonary anatomy and physiology, physics, and mathematics. In order to claim expertise in aerosol therapy and optimize its many uses, one must have a thorough understanding of the drug formulation, know its mode of action, and understand the conditions where it is effective. One must also know the contraindications to avoid harm and to influence decisions related to effective use of aerosols. The same 5 rights that apply to all medication delivery apply also to aerosol therapy: the right patient, the right medication, the right time, the right route, and the right dose.

For aerosol therapy, the right dose is technique-dependent. One can select the right drug and fail to administer the right dose because the medication was not delivered using correct technique. Here is where “art” comes into play. There is ample scientific evidence of ineffective use of aerosols when they are self-administered because the patient lacks knowledge about proper technique. Aerosol therapy is not a “fire and forget” clinical intervention. Many patients benefit from aerosol therapy, especially in hospitals, because it is administered by respiratory therapists. Many millions of other patients, however, do not receive optimum (or sometimes any) benefit from their prescribed metered-dose inhalers, dry powder inhalers, and nebulizers simply because they are not adequately trained to use them.

There is a critical juncture where science intersects with art. For aerosol therapy to be effective, the appropriate delivery system for the medication must be matched to the patient’s ability to use it correctly. The art of aerosol therapy does indeed arise from the science. First, we must identify the appropriate medication, based on physician diagnosis. Next, we must assess the patient’s ability to correctly use the aerosol delivery device. That assessment should be done by a respiratory therapist, as well as physicians and nurses who interact with the patient. This assessment should not be limited to respiratory function since other factors also contribute to effective use of aerosol delivery systems. For example, all too often patients are prescribed the appropriate inhaled medication but do not receive the prescribed dose because the patient cannot use the delivery system appropriately.

While respiratory therapists are best able to demonstrate complete and correct knowledge of aerosol delivery devices, there remains room for improvement. Because aerosol therapy is integral to our scope of practice, and because we are considered the experts in this area, we have a professional obligation to continue our learning in this area. Respiratory therapists have an opportunity to reinforce their value by updating their knowledge of aerosol delivery systems and combining that knowledge with effective assessment of patients requiring this therapy. Recommending an appropriate delivery system tailored specifically to the patient’s abilities is part of that assessment.

This booklet provides detailed and comprehensive information that, when combined with your dedication and commitment to be the professional experts in this important area, will empower you to provide guidance to your physician, nurse, and pharmacist colleagues, but, most importantly, to your patients.

With a widening array of effective inhaled medications and with billions of dollars spent on aerosol medications, you can have a profound impact on bringing about the appropriate match of medications and device delivery to your patients. You’ll not only improve the patient’s condition, but also contribute to more cost-effective use of health care system resources.

Here’s your opportunity to improve your expertise in this area. Accept the challenge and realize your potential as a respiratory therapist.

**Sam Giordano MBA RRT FAARC**  
**Executive Director**  
**American Association for Respiratory Care**

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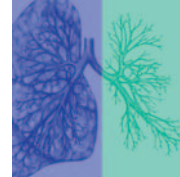
## Learning Objectives

You should expect to learn the following as you read this book.

1. State approximate amount of aerosol deposited in the lower respiratory tract for nebulizers, metered-dose inhalers, and dry powder inhalers.
2. List advantages and disadvantages of inhalation compared to other routes of drug administration.
3. Compare the principle of operation of a jet nebulizer, mesh nebulizer, and ultrasonic nebulizer.
4. Describe methods that are used to decrease aerosol loss from a nebulizer during exhalation.
5. List advantages and disadvantages of nebulizers for aerosol delivery.
6. Describe the basic components of a metered-dose inhaler.
7. List advantages and disadvantages of metered-dose inhalers.
8. Compare HFA and CFC propellants in metered-dose inhalers.
9. Explain the importance of priming and tracking the number of doses for a metered-dose inhaler.
10. Compare the design of holding chambers and spacers.
11. Describe factors that affect dose delivery from a holding chamber/spacer.
12. List advantages and disadvantages of dry powder inhalers.
13. Describe the principle of operation of various commercially available dry powder inhalers.
14. List the correct steps for use of a nebulizer, metered-dose inhaler, metered-dose inhaler with holding chamber/spacer, and dry powder inhaler.
15. Describe the proper technique of cleaning aerosol delivery devices.
16. Discuss criteria to assist clinicians in selecting an aerosol delivery device.
17. List common problems and errors with each type of inhaler.

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## Types of Aerosol Inhalers

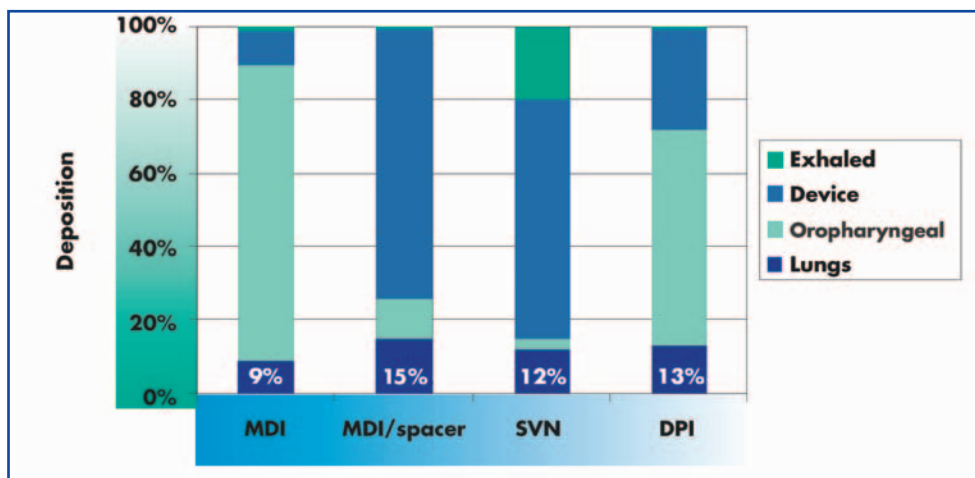
There are 3 common types of aerosol generators for inhaled drug delivery: the small volume nebulizer (SVN), the metered-dose inhaler (MDI), and the dry powder inhaler (DPI). Because of high medication loss in the oropharynx and hand-breath coordination difficulty with MDIs, holding chambers and spacers are often used as ancillary devices with an MDI.

## Terminology

In everyday clinical usage the term ‘aerosol’ often denotes use of a nebulizer, whereas the term ‘inhaler’ is often taken to mean an MDI, with or without a holding chamber/spacer. In correct context, all 3 device types are aerosol inhalers. An ‘aerosol’ is a suspension of liquid (nebulizer or MDI) or solid particles (MDI or DPI) in a carrier gas, and not necessarily a liquid spray only. We suggest that specific, correct terminology be used, such as ‘nebulizer’ or ‘metered-dose inhaler’ or ‘dry powder inhaler’ when referring to an aerosol drug delivery system or device. The term ‘aerosol’ should be used to refer to the plume of particles produced by the aerosol generator.

## Where Does an Inhaled Aerosol Drug Go?

Lung deposition is 10-20% for most aerosol systems.<sup>1-4</sup> For example, of 200 micrograms ( $\mu\text{g}$ ) of albuterol in two actuations or puffs from an MDI, only about 20-40  $\mu\text{g}$  reach the lungs with correct technique. The remaining drug is lost in the oropharynx, the device, the exhaled breath, and the environment. Figure 1 shows drug disposition for different aerosol systems, showing that oropharyngeal loss, device loss, and exhalation/ambient loss differ among aerosol device types, while lung deposition is similar.



*Figure 1. Drug disposition with 3 common aerosol inhaler devices, including an MDI with a spacer attached, showing similar lung deposition with varying amounts of loss in the oropharynx, device, and exhaled breath. MDI – metered-dose inhaler; SVN – small volume nebulizer; DPI – dry powder inhaler. (Modified, with permission, from Respir Care 2005; 50(3):367-382).*

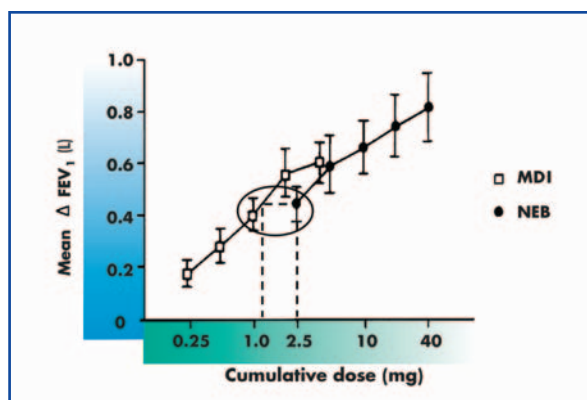
It is important to realize that different types of aerosol devices deposit the same approximate fraction of the total dose (also termed ‘nominal’ dose) in the lungs. However different types of aerosol device, eg, a nebulizer and an MDI, do not have the same nominal dose. Using albuterol as an example, the typical MDI nominal dose is 2 actuations, or about 200 µg, while the typical nebulizer nominal dose is 2.5 mg, or 12 times more drug. If the same percentage reaches the lungs, and the MDI has a smaller nominal dose than a nebulizer for the drug, more drug will be deposited in the lungs with the nebulizer. Table 1 lists both the MDI and nebulizer nominal doses for several drugs, showing this difference.

**Table 1.** Difference in nominal (total) dose between a metered-dose inhaler (MDI) and a nebulizer (SVN) for several drug formulations.

| <u>DRUG</u> | <u>MDI NOMINAL DOSE</u> | <u>SVN NOMINAL DOSE</u> |
|-------------|-------------------------|-------------------------|
| Albuterol   | 0.2 mg (200 µg)         | 2.5 mg                  |
| Ipratropium | 0.04 mg (40 µg)         | 0.5 mg                  |
| Cromolyn    | 2 mg                    | 20 mg                   |

### Equivalence of Aerosol Device Types

Clinically it is often thought that nebulizers may be more effective than MDIs, especially for short-acting bronchodilators in acute exacerbations of airflow obstruction. A number of studies have established that *either device can be equally effective*, if the lower nominal dose with an MDI is offset by increasing the number of actuations (“puffs”) to lung dose equivalence. Data in Figure 2 show that the lower-dose MDI can achieve the same clinical effect as the higher-dose nebulizer by increasing the number of MDI puffs.<sup>5</sup> Other studies have shown equivalent clinical results whether an MDI, a nebulizer, or a DPI is used, *provided that the patient can use the device correctly*.<sup>6</sup> For bronchodilators, the same clinical response is often achieved with the labeled dose from the MDI or nebulizer, despite the higher nominal dose for the nebulizer.



**Figure 2.** Mean change in FEV<sub>1</sub> versus cumulative dose from a metered-dose inhaler (MDI) and small volume nebulizer. Five puffs from the MDI (1.25 mg) of terbutaline gave an effect equivalent to the usual 2.5 mg dose from the nebulizer. (From Reference 5, with permission.)



Newer aerosol devices and drug formulations are increasing the efficiency of lung deposition compared to the traditional devices commonly used. For example, lung deposition for HFA-beclomethasone dipropionate (QVAR) is in the range of 40 - 50% of the nominal dose using an MDI formulation with hydrofluoroalkane (HFA) propellant to replace the older chlorofluorocarbon (CFC) propellants. Investigational devices such as the Respimat nebulizer and the Spiros DPI also have shown lung depositions of 40% or better.

### Advantages & Disadvantages with Inhaled Aerosol Drugs

There are a number of advantages with inhalation of drugs to treat pulmonary disease (Table 2). There are also disadvantages to the use of inhaled aerosol delivery, and clinicians should be realistic about these, including the relatively low lung deposition fraction of all aerosol delivery devices. The primary advantage of inhaled aerosol therapy is treating the

*Table 2. Advantages and disadvantages of the inhalation route of administration with aerosolized drugs in treating pulmonary diseases. MDI – metered-dose inhaler; SVN – small volume nebulizer; HPA – hypothalamic-pituitary-adrenal.*

#### **Advantages**

Aerosol doses are generally smaller than systemic doses; eg, oral albuterol is 2 to 4 mg; inhaled albuterol is 0.2 mg (MDI) to 2.5 mg (SVN).

Onset of effect with inhaled drugs is faster than with oral dosing; eg, oral albuterol is  $\leq 30$  min; inhaled albuterol is  $\sim 5$  min.

Drug is delivered directly to the target organ (lung), with minimal systemic exposure.

Systemic side effects are less frequent and severe with inhalation compared to systemic delivery (injection, oral); eg, less muscle tremor, tachycardia with  $\beta_2$ -agonists; lower HPA suppression with corticosteroids.

Inhaled drug therapy is less painful and relatively comfortable.

#### **Disadvantages**

Lung deposition is a relatively low fraction of the total aerosol dose.

A number of variables (correct breathing pattern, use of device) can affect lung deposition and dose reproducibility.

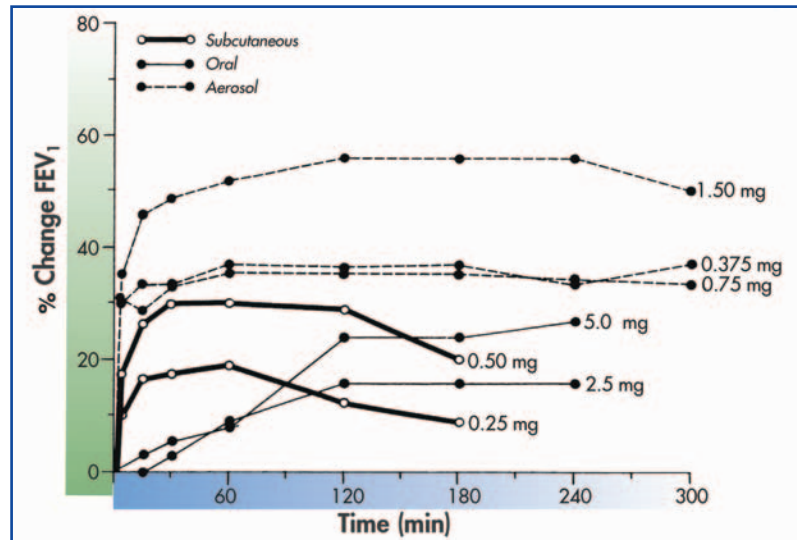
Difficulty coordinating hand action and inhalation with MDIs.

Lack of knowledge of correct or optimal use of aerosol devices by patients and clinicians.

The number and variability of device types confuses patients and clinicians.

Lack of standardized technical information on inhalers for clinicians.

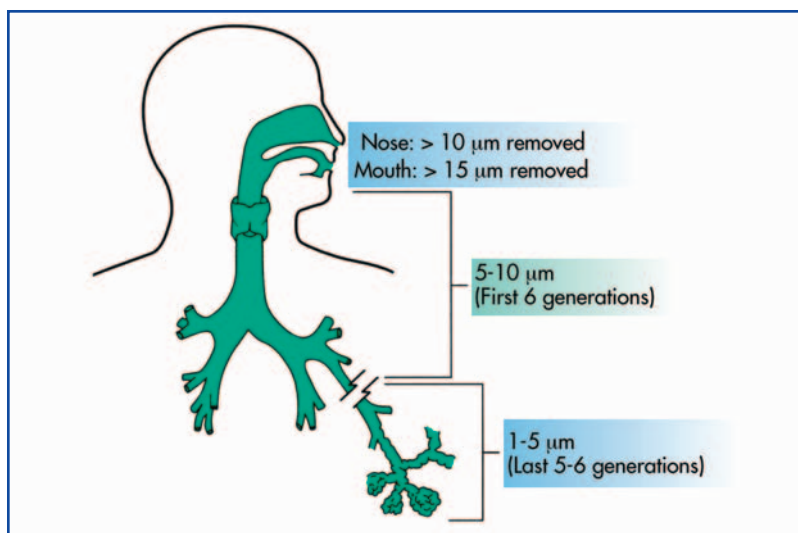
lung directly with smaller doses, resulting in fewer side effects than with oral delivery.<sup>7</sup> As seen in Figure 3, inhalation of terbutaline, a short-acting  $\beta_2$ -agonist, from an MDI resulted in better airflow than with a much larger oral dose, or even with a subcutaneous injection of drug.



*Figure 3. Changes in FEV<sub>1</sub> for three different routes of administration with terbutaline. Greater clinical effect was seen with drug delivered as inhaled aerosol from a metered-dose inhaler, compared to similar or larger doses delivered orally or by subcutaneous injection. (From Reference 7, with permission.)*

### Mechanisms of Aerosol Deposition and Particle Sizes

There are 3 mechanisms usually cited by which an aerosol particle can deposit: inertial impaction, gravitational settling (sedimentation) and diffusion. *Inertial impaction* occurs with larger, fast-moving particles. *Gravitational settling* is a function of particle size and time, with the rate of settling proportional to particle size. *Diffusion* occurs with particles smaller than 1  $\mu\text{m}$ . These mechanisms come into play as aerosol particles are inhaled orally or through the nose. Larger particles  $> 10 \mu\text{m}$  are filtered in the nose and/or oropharynx, most likely by inertial impaction; particles of 5-10  $\mu\text{m}$  generally reach the proximal generations of the lower respiratory tract, and particles of 1-5  $\mu\text{m}$  reach the lung periphery (Fig. 4).<sup>8</sup>



**Figure 4.** A simplified view of the effect of aerosol particle size on the site of preferential deposition in the airways (From Reference 8, with permission.)

Particle size plays an important role in lung deposition, along with particle velocity and settling time.<sup>9</sup> As particle size increases above 3  $\mu\text{m}$ , there is a shift in aerosol deposition from the periphery to the conducting airways. Oropharyngeal deposition also increases as particle sizes increase above 6  $\mu\text{m}$ . Exhaled loss is high with very small particles of 1  $\mu\text{m}$  or less. These data support the view that particle sizes of 1-5  $\mu\text{m}$  are best for reaching the lung periphery, while 5-10  $\mu\text{m}$  particles deposit preferentially in the conducting airways.

Aerosol devices in clinical use produce *heterodisperse* (also termed *polydisperse*) particle sizes, meaning that there is a mix of sizes in the aerosol. This is contrasted with *monodisperse* aerosols, which consist of a single particle size. A measure that can be useful in describing a polydisperse aerosol is the *mass median diameter* (MMD), which is defined as the particle size (in  $\mu\text{m}$ ) above and below which 50% of the mass of the particles is contained. This is the particle size that evenly divides the *mass*, or amount of the drug in the particle size distribution. This is usually given as the mass median aerodynamic diameter, or MMAD, due to the way sizes are measured. The higher the MMAD, the more particle sizes are of larger diameters.

### Currently Available Aerosol Drug Formulations

Some aerosol drugs are available in more than one formulation, and others (often newer drugs) are only available in a single formulation. Table 3 lists current aerosol drugs and their FDA-approved aerosol delivery devices. As the CFC propellants used in MDIs are phased out, some older aerosol drugs are being transitioned to the newer HFA propelled MDI formulations. New aerosol drugs are either formulated as an HFA-MDI (eg, MDI-levalbuterol) or, more commonly, as DPIs (eg, formoterol, tiotropium, mometasone).

**Table 3.** Common aerosol drug formulations with corresponding inhaler devices available for use in the United States in 2005. CFC – chlorofluorocarbon; HFA – hydrofluoroalkane; MDI – metered-dose inhaler; SVN – small volume nebulizer; DPI – dry powder inhaler. Cost information from [www.drugstore.com](http://www.drugstore.com).

| Drug                                 | Device                     | Cost  |
|--------------------------------------|----------------------------|---|
| <u>Short-acting Bronchodilators</u>  |                            |   |
| Albuterol                            | CFC-MDI                    | \$10.99/inhaler (generic) (200 actuations); \$0.05/puff<br>\$30.19 – \$35.99 (brand name) (200 actuations);<br>\$0.15 – \$0.18/puff                             |
|                                      | HFA-MDI                    | \$30.18 (generic)<br>\$37.63 – \$39.61 (brand name)   |
|                                      | SVN                        | \$15.00 for 20 mL bottle of 0.5%; \$0.38 per 0.5 mL (usual dose)<br>\$18.99 for 25 3-mL vials of 0.083%; \$0.76/vial  |
| Pirbuterol                           | Breath-actuated<br>CFC-MDI | \$94.76 MDI (400 actuations); \$0.24/puff   |
| Levalbuterol                         | HFA-MDI                    | \$48.99 (200 actuations); \$0.24/puff   |
|                                      | SVN                        | \$79.50 for 24 vials (0.31mg/3mL); \$3.31/vial<br>\$70.84 for 24 vials (0.63mg/3mL); \$2.95/vial<br>\$71.25 for 24 vials (1.25mg/3mL); \$2.97/vial              |
|                                      | HFA-MDI                    | \$81.75 (200 actuations); \$0.41/puff   |
| Ipratropium                          | SVN                        | \$77.32 for 25 vials (0.02% in 2.5mL); \$3.09/vial  |
| Ipratropium & albuterol              | CFC-MDI                    | \$91.99 (200 actuations); \$0.46/puff   |
|                                      | SVN                        | \$123.73 for 60 3-mL vials; \$2.06/vial   |
| <u>Long-acting Bronchodilators</u>   |                            |   |
| Salmeterol                           | DPI (Diskus)               | \$111.94 for 60 doses; \$1.87/dose  |
| Formoterol                           | DPI (Aerolizer)            | \$108.17 for 60 capsules; \$1.80/capsule  |
| Arformoterol                         | SVN                        | (Available in 2007)   |
| Tiotropium                           | DPI (HandiHaler)           | \$129.55 for 30 capsules; \$4.32/capsule  |
| <u>Corticosteroids</u>               |                            |   |
| Beclomethasone                       | HFA-MDI                    | \$60.84 40 mcg/puff (100 actuations); \$0.61/puff<br>\$73.57 80 mcg/puff (100 actuations); \$0.74/puff  |
|                                      |                            |   |
| Triamcinolone                        | CFC-MDI                    | \$105.99 100 mcg/puff (240 actuations); \$0.44/puff   |
| Flunisolide                          | CFC-MDI                    | \$77.55 250 mcg/puff (100 actuations); \$0.78/puff  |
|                                      | HFA-MDI                    | (Available in 2007)   |
| Fluticasone                          | HFA-MDI                    | \$78.24 44 mcg/puff (120 actuations); \$0.65/puff<br>\$104.74 110 mcg/puff (120 actuations); \$0.87/puff<br>\$170.82 220 mcg/puff (120 actuations); \$1.42/puff |
|                                      |                            |   |
|                                      |                            |   |
| Budesonide                           | SVN                        | \$149.35 for 30 vials of 0.25 mg/2 mL; \$4.98/vial<br>\$165.80 for 30 vials of 0.5 mg/2 mL; \$5.53/vial   |
|                                      | DPI (Turbuhaler)           | \$152.56 (200 inhalations); \$0.76/dose   |
| Mometasone<br>fluticasone/salmeterol | DPI (Twisthaler)           | \$143.62 (120 doses); \$1.20/dose   |
|                                      | DPI (Diskus)               | \$146.47 for 100/50 mcg/dose (60 inhalations); \$2.44/inhalation<br>\$166.99 for 250/50 mcg/dose (60 inhalations); \$2.82/inhalation                            |
|                                      |                            | \$229.87 for 500/50 mcg/dose (60 inhalations); \$3.83/inhalation  |
| Budesonide/formoterol                | DPI (Turbuhaler)           | (Available in 2007)   |
| <u>Others</u>                        |                            |   |
| Cromolyn                             | CFC-MDI                    | \$107.89 (200 actuations); \$0.54/puff<br>\$71.28 (112 actuations); \$0.64/puff   |
|                                      |                            | SVN   |
|                                      | Nedocromil                 | CFC-MDI   |
| Acetylcysteine                       | SVN                        | \$7.99 for 10 ml vial of 10% Solution<br>\$14.99 for 10 ml vial of 20% Solution<br>\$7.99 for 10 ml vial of 20% Solution  |
|                                      |                            |   |
|                                      |                            |   |
| Dornase alfa                         | SVN                        | \$1,589.32 for 30 2.5-mL vials; \$52.98/vial  |
| Tobramycin                           | SVN                        | \$3,391.92 for 56 5-mL vials; \$60.57/vial  |

## Age Guidelines for Use of Aerosol Devices

The 1997 National Asthma Education and Prevention Program (NAEPP) guidelines have recommended age limits for effective use of the different types of aerosol inhaler devices.<sup>10</sup> These are given in Table 4. Such guidelines are general suggestions only, representing expected maturity and physical coordination at a given age. Patient use of an aerosol delivery device at any age needs to be properly evaluated for optimal technique, and tailored to the patient's ability to use the device correctly.

*Table 4. Age guidelines for use of aerosol delivery device types. Based on NAEPP guidelines.<sup>10</sup>*

| <u>Aerosol System</u>                    | <u>Age</u> |
|--|------------|
| Small volume nebulizer                   | ≤ 2 years  |
| Metered-dose inhaler                     | > 5 years  |
| MDI with holding chamber/spacer          | > 4 years  |
| MDI with holding chamber/spacer and mask | ≤ 4 years  |
| Breath-actuated MDI<br>(eg, Autohaler)   | > 5 years  |
| DPI                                      | ≥ 5 years  |

# Small Volume Nebulizers

Nebulizers convert solutions or suspensions into aerosols of a size that can be inhaled into the lower respiratory tract. Pneumatic jet nebulizers are the oldest form of aerosol generator, and their basic design and performance have changed little in the past 30 years. Ultrasonic nebulizers, which have been available for many years but are not commonly used for inhaled drug delivery, use electricity to convert a liquid into respirable droplets. The newest generation of nebulizers uses mesh technology. General advantages and disadvantages with use of small volume nebulizers are listed in Table 5.

*Table 5. Advantages and Disadvantages of Small Volume Nebulizers.*

## ADVANTAGES

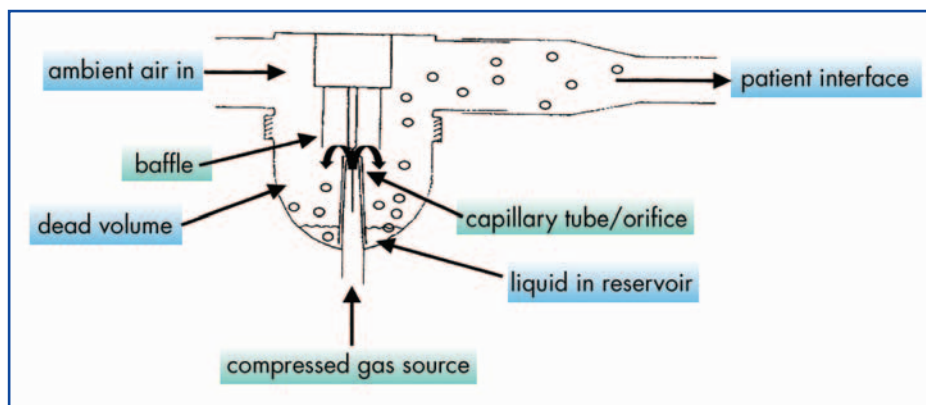
- Ability to aerosolize many drug solutions
- Ability to aerosolize drug mixtures (>1 drug), if drugs are compatible
- Normal breathing patterns can be used
- Useful in very young, very old, debilitated, or distressed patients
- An inspiratory pause (breath-hold) is not required for efficacy
- Drug concentrations can be modified

## DISADVANTAGES

- Treatment times are lengthy for pneumatically-powered nebulizers
- Equipment required may be large and cumbersome
- Need for power source (electricity, battery, compressed gas)
- Variability in performance characteristics among different brands
- Possible contamination with inadequate cleaning
- Wet, cold spray with facemask delivery
- Potential for drug delivery into the eyes with facemask delivery

## Pneumatic Jet Nebulizers

A pneumatic nebulizer delivers compressed gas through a jet, causing a region of negative pressure (Fig. 5). The solution to be aerosolized is entrained into the gas stream and is sheared into a liquid film. This film is unstable and breaks into droplets due to surface tension forces. A baffle in the aerosol stream produces smaller particles. The aerosol is further



*Figure 5. Cartoon illustration of the function of a pneumatic jet nebulizer.*

conditioned by environmental factors such as the relative humidity of the carrier gas. Nebulizer performance is affected by both technical and patient-related factors (Table 6).

**Table 6.** Factors affecting penetration and deposition of therapeutic aerosols delivered by jet nebulizers.

| <u>Technical Factors</u>            | <u>Patient Factors</u>                       |
|-------------------------------------|--|
| Manufacturer of nebulizer           | Breathing pattern                            |
| Flow used to power nebulizer        | Nose versus mouth breathing                  |
| Fill volume of nebulizer            | Composition of inspired gas                  |
| Solution characteristics            | Airway obstruction                           |
| Composition of driving gas          | Positive pressure delivery                   |
| Designs to enhance nebulizer output | Artificial airway and mechanical ventilation |
| Continuous versus breath-actuated   |  |

Dead volume refers to the solution that is trapped inside the nebulizer and is thus not made available for inhalation. Dead volume is typically in the range of 0.5-1 mL. In an attempt to reduce medication loss due to dead volume, clinicians and patients tap the nebulizer periodically during therapy in an effort to increase nebulizer output. Therapy may also be continued past the point of sputtering in an attempt to deliver medication from the dead volume, but this is unproductive and not recommended. Due to evaporative losses within the nebulizer, the solution becomes increasingly concentrated and cools during nebulization. Solution temperature affects nebulizer output, with output and droplet size varying directly with temperature.

The most important characteristic of nebulizer performance is the respirable dose provided for the patient. The respirable dose is sometimes reported as respirable mass, which is the output of droplets from a nebulizer in the respirable range (1-5 µm). Other important characteristics of nebulizer performance include nebulization time, ease of use, ease of cleaning and sterilization, and cost. Duration of nebulization is important for patient compliance in the outpatient setting and clinician supervision for hospitalized patients. A short nebulization time that delivers an effective dose is desirable. Many nebulizers are low cost, mass produced, single-patient-use devices. Newer more efficient nebulizers, however, are more expensive (Table 7).

**Table 7.** Approximate costs of nebulizers.

| <u>Device</u>                          | <u>Approximate Cost</u> |
|--|-------------------------|
| Single patient use pneumatic nebulizer | \$1 - \$3               |
| Reusable nebulizer with compressor     | \$50 - \$150            |
| Nebulizer with filter for pentamidine  | \$10 - \$12             |
| Nebulizer with reservoir bag           | \$5 - \$6               |
| Reusable breath-enhanced nebulizer     | \$15 - \$20             |
| Breath-actuated nebulizer              | \$4 - \$5               |
| Mesh nebulizer                         | \$250 - \$350           |
| Ultrasonic nebulizer                   | \$100 - \$150           |

A fill volume of 4-5 mL is recommended<sup>11</sup> unless the nebulizer is specifically designed for a smaller fill volume. The volume of some unit dose medications is suboptimal. Ideally, saline should be added to the nebulizer to bring the fill volume to 4-5 mL, but this might not be practical. The increased nebulization time with a greater fill volume can be reduced by increasing the flow used to power the nebulizer. Increased flow also decreases the droplet size produced by nebulizers; 6-8 L/min is recommended.<sup>11</sup> The flow from many compressors is unfortunately too low for optimal nebulizer performance. Several studies have reported performance differences between nebulizers of different manufacturers and among nebulizers of the same manufacturer. Due to cost considerations, disposable single-patient-use nebulizers are typically used for many treatments. Pneumatic nebulizers have been reported to function correctly for repeated uses provided that they are washed, rinsed, and air dried after each use. **TECHNIQUE BOX 1** lists generic steps in correct use of pneumatic nebulizers. Since newer nebulizer designs are entering the clinical market, respiratory therapists should modify these instructions by following manufacturers' recommendations.

### **TECHNIQUE BOX 1.** Steps for correct use of nebulizers.

#### **Jet nebulizer technique**

1. Assemble tubing, nebulizer cup, and mouthpiece (or mask).
2. Place medicine into the nebulizer cup; use fill volume of 4-5 mL.
3. The patient should be seated in an upright position.
4. Connect to power source; flow of 6-8 L/min or compressor.
5. Breathe normally with occasional deep breaths until sputter or no more aerosol is produced.
6. Keep nebulizer vertical during treatment.
7. Rinse nebulizer with sterile or distilled water and allow to air dry.

With technology that differs from that of a traditional jet nebulizer, clinicians should thoroughly review operating instructions prior to patient use and instruction.

#### Cleaning the jet nebulizer (home use)

##### After each use:

1. Remove the tubing from the compressor and set it aside – this tubing should not be washed or rinsed.
2. Shake remaining solution from the nebulizer cup.
3. Disassemble the equipment and rinse nebulizer cup and mouthpiece with either sterile water or distilled water.
4. Shake off excess water and air dry on an absorbent towel.
5. Store the nebulizer cup in a ziplock bag.

##### Once or twice a week:

1. Disassemble the nebulizer and wash it in a mixture of warm soapy tap water.
2. Soak the nebulizer cup and mouthpiece for 1 hour in a solution that is one part distilled white vinegar (5%) and three parts hot water (1.25% acetic acid). An alternative is to use quaternary ammonium compound (QAC) at a dilution of one ounce to one gallon of sterile or distilled water for at least 10 minutes.
3. Discard the vinegar solution after use. QAC can be reused for up to one week.
4. Rinse the nebulizer parts with sterile or distilled water.
5. Shake off excess water.
6. Air dry on an absorbent towel.
7. Store the nebulizer in a ziplock bag.
8. Clean the surface of the compressor with a damp cloth or sponge. An alcohol or disinfectant wipe can also be used. Never put the compressor into water.



## TECHNIQUE BOX 1. CONTINUED

### Mesh nebulizer technique

1. Correctly assemble the equipment.
2. Follow manufacturer's instructions to perform a functionality test prior to the first use of a new device and after each disinfection to verify proper operation.
3. Pour the solution into the medication reservoir. Do not exceed the volume recommended by the manufacturer.
4. Turn on the power.
5. Hold the nebulizer in the position recommended by the manufacturer.
6. Breathe normally with occasional deep breaths.
7. If the treatment must be interrupted, turn off the unit to avoid waste.
8. At the completion of the treatment, disassemble and clean as recommended by the manufacturer.
9. Be careful not to touch the mesh during cleaning, as this will damage the unit.
10. Once or twice a week, disinfect the nebulizer following manufacturer's instructions.

Drug formulation can affect nebulizer performance, and in some cases, specific nebulizers are approved for use with specific formulations (Table 8). The density of the gas powering the nebulizer also affects nebulizer performance, such as powering the nebulizer with heliox, and the flow to the nebulizer should be increased by 1.5-2 times when heliox is used to power the nebulizer.

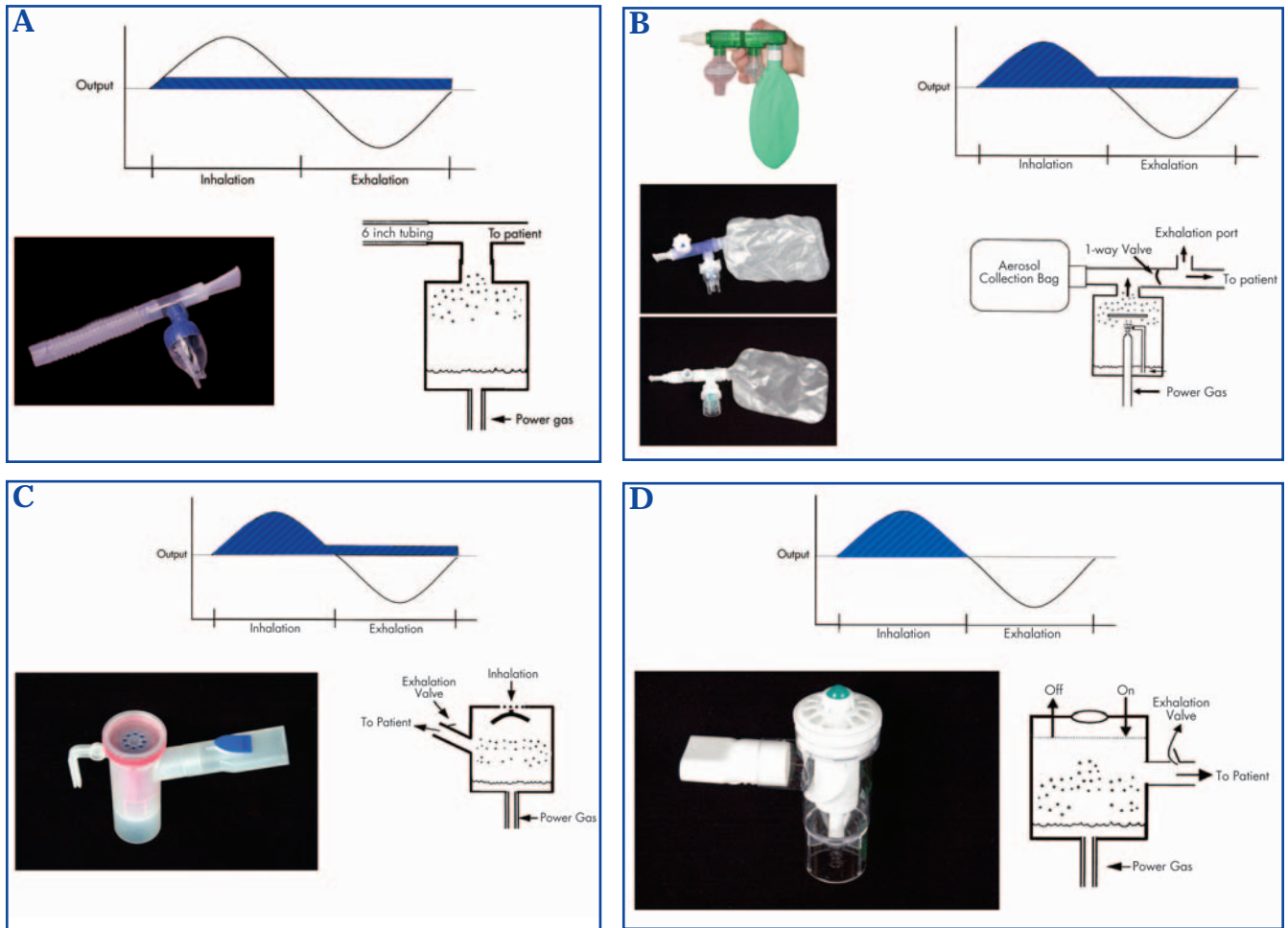
Breathing pattern affects the amount of aerosol deposited in the lower respiratory tract. Patients usually use the nebulizer with tidal breathing. To improve aerosol penetration and deposition in the lungs, the patient should be encouraged to take periodic deeper breaths during the treatment. Nebulizer aerosols can be administered using either a mouthpiece or a face mask. Ideally, a mouthpiece should be used. Use of a mask increases the amount of aerosol deposited on the face, in the eyes, and in the nasal passages. Whether a mouthpiece or a face mask is used, it is important to instruct the patient to inhale through the mouth during nebulizer therapy. Blow-by therapy is sometimes used for patients such as infants who do not tolerate a mouthpiece or face mask. However, this is very inefficient and thus is discouraged. It is also important to note that the delivered dose is significantly reduced in a child who is crying during the treatment.

**Table 8.** Formulations and approved nebulizers for that formulation.

| <b>Formulation</b>              | <b>Approved Nebulizer</b>   |
|---------------------------------|---|
| Bronchodilators                 | No bronchodilator formulation has been approved for a specific nebulizer        |
| Budesonide (Pulmicort Respules) | Should not be used with ultrasonic nebulizer                                    |
| Tobramycin (TOBI)               | Pari LC   |
| Dornase alfa (Pulmozyme)        | Hudson T Up-draft II, Marquest Acorn II, Pari LC, Durable Sidestream, Pari Baby |
| Pentamidine (NebuPent)          | Marquest Respigard II   |
| Ribavirin (Virazole)            | Small Particle Aerosol Generator (SPAG)   |
| Iloprost (Ventavis)             | ProDose or I-neb  |
| Hypertonic saline               | Randomized controlled trials were performed using the Pari LC                   |

## Designs to Decrease Aerosol Waste During Exhalation

Several designs can be used to reduce the amount of aerosol loss during exhalation with a pneumatic nebulizer (Figure 6). It is common practice to use a T-piece and corrugated tubing as a reservoir for small volume nebulizers. This concept can be extended by use of a bag to collect aerosol during exhalation. With the breath-enhanced nebulizer, a mainstream design is used with valves so that the patient breathes through the nebulizer during inspiration, which enhances the nebulizer output. Aerosol waste during the expiratory phase can be eliminated if the nebulizer is only active during the inspiratory phase, which is used in the breath-actuated, dosimetric nebulizer design.



**Figure 6.** Nebulizer designs. *A. Jet nebulizer with reservoir tube. B. Nebulizer with aerosol collection bag. C. Breath-enhanced nebulizer. D. Breath-actuated nebulizer. In each case, the aerosol output of the device is indicated by the shaded area.*

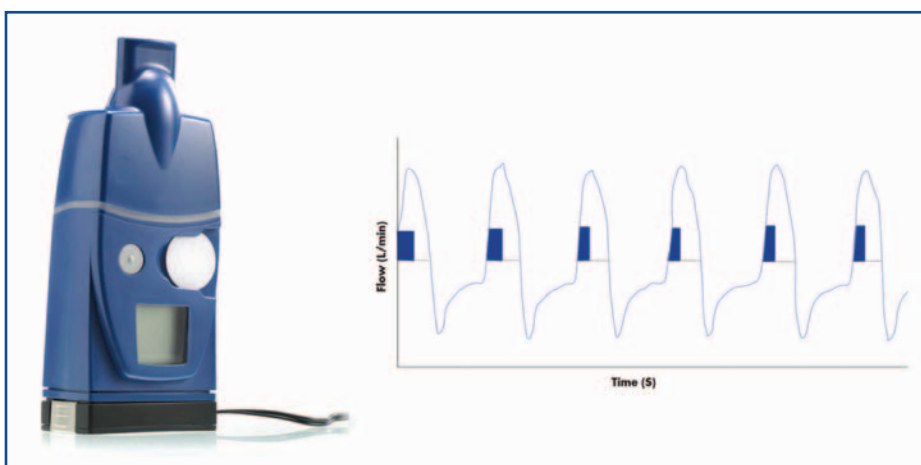
## Mesh Nebulizers

Several manufacturers have developed aerosol devices that use a mesh or plate with multiple apertures to produce a liquid aerosol (Figure 7). This operating principle uses an aperture plate attached to a piezoelectric material that vibrates at high frequency. The



*Figure 7. Mesh nebulizer. Top. Principle of operation of the device. Bottom. Representative commercially available devices.*

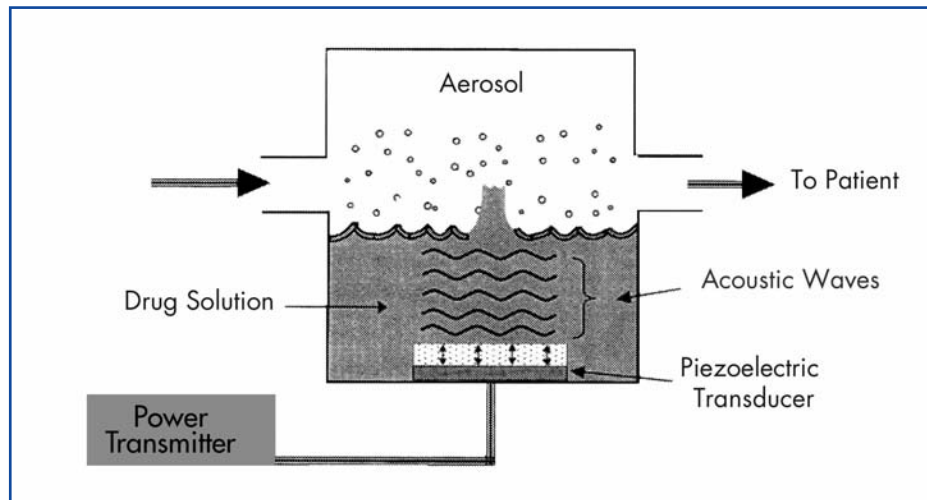
rapid vibration of the aperture plate creates a pumping action to produce the aerosol from a liquid solution. Alternatively, the solution can be forced through the mesh to create the aerosol. These devices are able to generate aerosols with a high fine-particle fraction, which results in more efficient drug delivery compared to conventional nebulizers. The aerosol is generated as a fine mist, and no internal baffling system is required. They have a high rate of aerosol production and they are portable and battery-operated. They have minimal residual dead volume and some are breath-actuated. This design can be coupled with *adaptive aerosol delivery*, as used by the I-neb (Respironics, Inc.) in which the nebulizer senses the patient's breathing pattern over several breaths and then releases aerosol pulses during a predetermined portion of the inspiratory phase (Figure 8).



*Figure 8. Adaptive aerosol delivery as provided by the Respironics I-neb. As illustrated, aerosol is injected into the breath at the beginning of inhalation.*

## Ultrasonic Nebulizers

The ultrasonic nebulizer converts electrical energy to high frequency ultrasonic waves. The transducer vibrates at the frequency of the ultrasonic waves applied to it (piezoelectric effect). Ultrasonic waves are transmitted to the surface of the solution to create an aerosol (Figure 9). Small volume ultrasonic nebulizers are commercially available for delivery of inhaled bronchodilators. A potential issue with the use of ultrasonic nebulizers is the possibility for drug inactivation by the ultrasonic waves, although this has not been shown to occur with common aerosol medications. Use of these devices has been hampered by their tendency for mechanical malfunction.



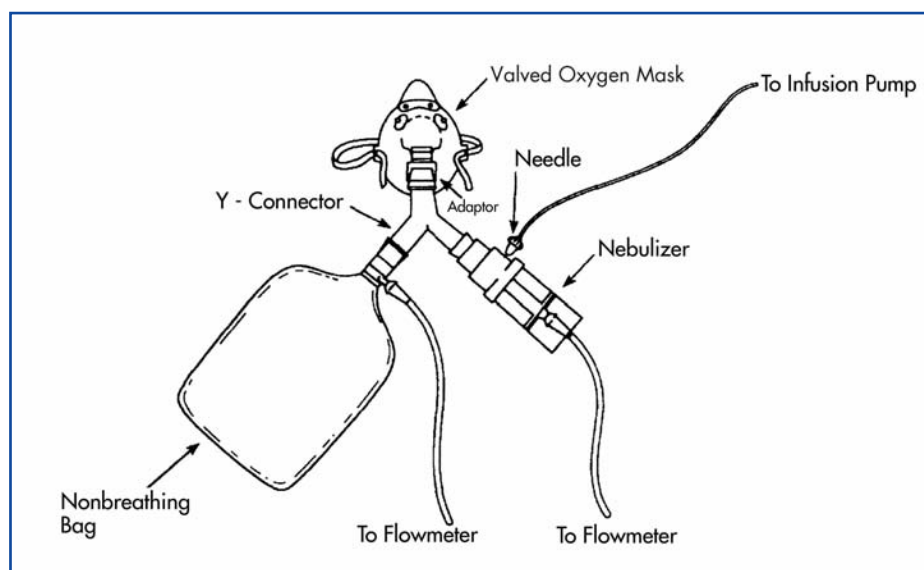
*Figure 9. Components of an ultrasonic nebulizer.*

## Nebulizers for Specific Applications

Specially constructed small volume nebulizers, such as those for aerosolized pentamidine, are used when contamination of the ambient environment with the aerosolized drug needs to be avoided. This nebulizer is fitted with one way valves and filters to prevent gross contamination of the environment. The Small Particle Aerosol Generator (SPAG) is used specifically to aerosolize ribavirin. It consists of a nebulizer and a drying chamber that reduces the MMAD to about 1.3  $\mu\text{m}$ . Because ribavirin is potentially teratogenic, a scavenging system is used when ribavirin is administered.

## Continuous Aerosol Delivery

Continuous aerosolized bronchodilators are occasionally used in the treatment of acute asthma. The available evidence suggests that this therapy is safe, at least equally effective as intermittent nebulization, and may be superior to intermittent nebulization in patients with the most severe pulmonary function. Several configurations have been described for continuous nebulization, including frequent refilling of the nebulizer, use of a nebulizer and infusion pump (Figure 10), and use of a large volume nebulizer.



*Figure 10. Setup for continuous aerosol therapy.*

## Cleaning and Disinfection of Nebulizers

Patients who utilize a nebulizer at home need to be sure that it is periodically cleaned and disinfected. While there is no universally accepted standard, patients who routinely use a nebulizer in the home should adhere to the following steps in order to maintain a minimal level of disinfection.<sup>12</sup> After every nebulizer treatment the patient should shake the remaining solution from the cup. The cup should be rinsed with either sterile or distilled water and left to air dry on an absorbent towel.

Once or twice a week, the nebulizer should be disinfected. The nebulizer is disassembled and washed in a mixture of soapy tap water (aqueous detergent). The cup should then be disinfected by using either a 1.25% acetic acid (white vinegar) mixture or a quaternary ammonium compound at a dilution of 1 ounce to one gallon of sterile or distilled water. The acetic acid soak should be no less than an hour, but a quaternary ammonium compound soak need only be 10 minutes. It is also important to remember that the acetic acid should not be reused, but the quaternary solution can be reused for up to one week.<sup>13</sup>

Nebulizer disinfection is impractical in the hospital. However, there are some important hygienic considerations. Nebulizers are disposable single-patient-use and should not be used by more than one patient. Nebulizers should not be rinsed with tap water between treatments, but may be rinsed with sterile water and allowed to dry between treatments. Drying can be enhanced by attaching gas flow to the nebulizer for a short time after it is rinsed. The frequency at which disposable nebulizers are changed should be determined through collaboration between the respiratory care and infection control departments.

# Metered-Dose Inhalers



Figure 11. Common metered-dose inhalers and dry powder inhalers available in the United States.

The MDI is designed to provide a precise (metered) dose of medication in a fine mist to be inhaled directly into the airways for the treatment of respiratory diseases such as asthma and COPD. The original MDI in 1955 was conceived by Dr George Maison, the president of Riker Labs (now 3M Pharmaceuticals, St Paul, Minnesota) in response to his teenage asthmatic daughter's request for a better delivery system.<sup>14</sup> One year later, Medihaler-Iso (isoproterenol) and Medihaler-Epi (epinephrine) were approved as new drug applications by the FDA. Today, a number of aerosol formulations are available as MDIs (Figure 11). General advantages and disadvantages with the use of MDIs are listed in Table 9.

**Table 9.** *Advantages and Disadvantages of Metered-Dose Inhalers.*

**ADVANTAGES**

- Portable and compact
- Short treatment time
- Reproducible dose emitted

**DISADVANTAGES**

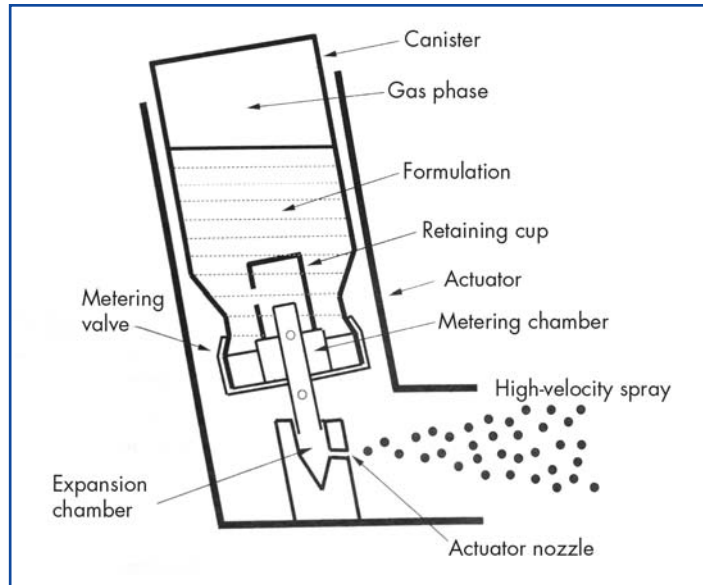
- Hand-breathing coordination is difficult for many patients
- Proper inhalation pattern (slow inspiration to total lung capacity) and breath-hold can be difficult
- Canister depletion is difficult to determine (no dose counter)
- High oropharyngeal impaction unless a holding chamber or spacer is used
- Failure to shake can alter drug dose
- Fixed drug concentrations
- Reaction to propellants or excipients have occurred in some patients
- Foreign body aspiration from debris-filled mouthpiece
- Limited range of drugs

The propellant-driven MDI is currently the most frequently used device for asthma and COPD. Since the MDI is pressurized, the components of the device are protected from contamination by pathogens and moisture. As with other respiratory drug delivery systems, even when used correctly the MDI only delivers approximately 10-20% of the nominal dose per actuation or puff.<sup>15-17</sup> Deposition may be lower in children due to differences in breathing pattern or when technique is less than optimal. The basic necessity of any MDI drug formulation is that the device accurately and reproducibly delivers an aerosol dose containing a significant fraction of drug particles in the fine particle fraction range (aerodynamic diameter <5 µm). Most MDIs are designed to deliver a drug dose in the range of 100-200 µg per actuation.

MDIs, regardless of manufacturer or active ingredient (drug), typically consist of some standard components (Table 10 and Figure 12) that have very specific functions in the drug delivery system. The components of the MDI include the container (usually aluminum), the

**Table 10.** *The basic components of the metered-dose inhaler (MDI).*

| <b>Component</b> | <b>Particulars</b>   |
|------------------|--|
| Container        | Inert, able to withstand high internal pressures and utilize a coating to prevent drug adherence   |
| Propellants      | Liquefied compressed gases in which the drug is dissolved or suspended   |
| Drug Formulary   | Particulate suspensions or solutions, in the presence of surfactants or alcohol that allocate the drug dose and the specific particle size   |
| Metering Valve   | Most critical component that is crimped onto the container and is responsible for metering a reproducible volume or dose.<br>Elastomeric valves are responsible for sealing and prevention of drug loss or leakage |
| Actuator         | Frequently referred to as the “boot,” partially responsible for particle size, based on the length and diameter of the nozzle for the various MDIs   |
| Dose Counter     | Newest component of the MDI delivery system. This component provides a visual tracking of the number of doses remaining in the MDI.  |



**Figure 12.** Standard components of a metered-dose inhaler (Modified, with permission, from Newman SP. Principles of metered-dose inhaler design. *Respir Care* 2005; 50(9):1177-1188).

propellant (CFC or HFA), the formulation (suspension or solution), the metering valve, and the actuator (press-and-breathe or breath-actuated). The actuator nozzle is MDI specific and is a key determinant of aerosol dose and particle size. The amount of medication delivered is related to nozzle size, cleanliness, and lack of moisture.

### Propellants

MDI canisters contain propellants, surfactants, and the medication. MDI drugs can either be dissolved in the propellant (or a co-solvent such as ethanol) or as a suspension in the propellant. It is occasionally necessary to utilize a surface-active agent to ensure that the active drug is well suspended, as well as serving as a lubricant for the metering valve. By weight, the propellants of an MDI represent 80% of the contents compared to about 1% of active medication. For many years, MDIs used CFC propellants and drug suspensions. CFCs have a detrimental effect on the Earth's ozone layer and the Montreal Protocol on Substances That Deplete the Ozone Layer (January 1989) set a timetable for elimination of CFC use that will take effect in January 2008. This led to a search for propellants that could be used as alternatives and have less of an effect on the environment. As a result, HFAs have become more common and their solution formulations are increasingly used. HFAs are pharmacologically inert and have similar properties to the CFC propellants they replaced. HFA-MDIs do not contain or use surfactants for dispersion, but instead use alcohol for this purpose. Interestingly, use of an HFA propellant is able to overcome some of the issues with CFC-MDIs, including priming, temperature effects, tail-off, and plume geometry. HFA-MDIs are effective and safe, but clinicians must be aware of differences in characteristics



**Table 11.** Differences in Characteristics between CFC and HFA MDIs.

| <b>Physical Component</b>         | <b>CFC</b>                                 | <b>HFA</b>                                    |
|-----------------------------------|--|---|
| <b>Delivery of Dose</b>           |  |   |
| From a near-empty canister        | Variable                                   | Consistent                                    |
| With variable ambient temperature | Variable                                   | Consistent (to -20°C)                         |
| <b>Spray</b>                      |  |   |
| Force                             | Higher Impaction                           | Lower (3 times)                               |
| Temperature                       | Colder                                     | Warmer (approx. 30°C)                         |
| Volume                            | Higher                                     | Lower   |
| <b>Taste</b>                      | Different from HFA                         | Different from CFC                            |
| <b>Breath-hold</b>                | Less important with CFC                    | More important with HFA                       |
| <b>Priming</b>                    | Important following short period of nonuse | Longer time of nonuse allowed without priming |

between CFC- and HFA-MDIs (Table 11). For patients switching from CFC-MDI to HFA-MDI, it is important that they understand that the taste and feel of the plume in the mouth will be different.

With the HFA-MDI, the actuator (ie, boot) design becomes much more critical in determining the correct particle size and plume geometry. The HFA steroid inhalers deliver smaller particle sizes that provide a greater distribution of medication into the lungs with less deposition in the oropharynx. Smaller particle sizes seen with the HFA-propelled steroids also reduce the reliance on actuation-breath timing and higher inspiratory flow rates.<sup>18,19</sup> These differences in the HFA delivery system make it extremely important not to mismatch the actuator boots of different HFA-MDIs or to utilize generic actuators for drug delivery.

### **MDI Preparation for Use**

The dose from a CFC-MDI has been shown to be significantly reduced when the canister is colder than standard ambient temperatures. This can be very problematic in colder climates during winter months for patients that need to carry a rescue inhaler like albuterol. The HFA-MDI delivers a consistent dose to temperatures as low as -20 °C. MDIs in which the drug is in suspension (eg, CFC and some HFA formulations) have a separation of drug and propellant when not used. This separation requires that the MDI be shaken to suspend the drug prior to use. Failure to shake the canister can result in up to a 33% reduction in the amount of drug delivered. Multiple actuations without shaking of a CFC-MDI results in a dose reduction due to the CFC propellant cooling the valve. The MDI requires initial and frequent priming to ensure that the device administers and delivers the appropriate dose. Priming releases one or more sprays into the air. When the MDI is new or has not been used for some time, the medication may separate from the other ingredients in the

canister and the metering chamber. Shaking the MDI will mix the ingredients in the drug reservoir but not in the metering chamber. The recommended guidelines for priming of the various MDIs are listed in Table 12.

### Proper Technique

The major limitation to optimal drug delivery with the MDI is related to poor technique. Poor technique can result in little or no drug delivery which can result in issues of adherence. Education to both patients and the healthcare team on the proper technique for MDI use is paramount to their clinical success. Failure to perform the optimal steps of proper inhaler technique can lead to a substantial reduction and ultimately the overall clinical effectiveness of the medication. Proper MDI technique centers on optimal actuation-inspiration coordination. Actuation of the MDI should occur at the beginning of the breath and continue to full inhalation at a relatively low flow. This technique is difficult and can be almost impossible for geriatric and pediatric patients, or patients in respiratory distress. There is considerable evidence that patients have a difficult time performing all the correct steps

**Table 12.** Priming Requirements for Commercially Available MDIs.

| Medication                    | Propellant | Time to Prime            | # of Sprays |
|-------------------------------|------------|--------------------------|-------------|
| <b>Albuterols</b>             |            |                          |             |
| albuterol (Warrick generic)   | CFC        | Prior to first use       | 4           |
|                               |            | With 4 days of nonuse    | 2           |
| albuterol sulfate (IVAX)      | HFA        | Prior to first use       | 3           |
|                               |            | With 3 days of nonuse    | 3           |
| Levalbuterol                  | HFA        | Prior to first use       | 4           |
|                               |            | With 3 days of nonuse    | 4           |
| Maxair <sup>®</sup> Autohaler | CFC        | Prior to first use       | 2           |
|                               |            | With 2 days of nonuse    | 2           |
| Proventil <sup>®</sup>        | CFC        | Prior to first use       | 4           |
|                               |            | With 4 days of nonuse    | 2           |
| Proventil <sup>®</sup>        | HFA        | Prior to first use       | 4           |
|                               |            | With 2 weeks of nonuse   | 4           |
| Ventolin <sup>®</sup>         | HFA        | Prior to first use       | 4           |
|                               |            | With 2 weeks of nonuse   | 4           |
| <b>Steroids</b>               |            |                          |             |
| Azmacort <sup>®</sup>         | CFC        | Prior to first use       | 2           |
|                               |            | With 3 days of nonuse    | 2           |
| Flovent <sup>®</sup>          | HFA        | Prior to first use       | 4           |
|                               |            | With < 3 weeks of nonuse | 1           |
|                               |            | With > 3 weeks of nonuse | 4           |
| QVAR <sup>®</sup>             | HFA        | Prior to first use       | 2           |
|                               |            | With 10 days of nonuse   | 2           |
| AeroSpan <sup>™</sup>         | HFA        | Prior to first use       | 2           |
|                               |            | With > 2 weeks of nonuse | 2           |
| <b>Others</b>                 |            |                          |             |
| Atrovent <sup>®</sup>         | CFC        | Prior to first use       | 3           |
|                               |            | With 1 day of nonuse     | 3           |
| Atrovent <sup>®</sup>         | HFA        | Prior to first use       | 2           |
|                               |            | With 3 days of nonuse    | 2           |
| Combivent <sup>®</sup>        | CFC        | Prior to first use       | 3           |
|                               |            | With 1 day of nonuse     | 3           |
| Intal <sup>®</sup>            | CFC        | Prior to first use       | 1           |

for proper MDI technique.<sup>20</sup> To make matters worse, clinicians often do a poor job providing correct MDI instruction and demonstration is poor.<sup>21,22</sup> The correct steps for proper MDI technique are listed in TECHNIQUE BOX 2.

**TECHNIQUE BOX 2.** *Steps for correct use of metered-dose inhaler (MDI) and breath-actuated MDI (Autohaler).*

### **MDI technique**

1. Hold the MDI to warm it to body temperature.
2. Remove the mouthpiece cover.
3. Inspect the mouthpiece for foreign objects.
4. Shake the MDI well (3 or 4 shakes).
5. If the MDI is new or has not been used recently, prime it by shaking and pressing the canister to deliver a dose into the room. Repeat several times.
6. Breathe out normally, away from the MDI.
7. Open the mouth and keep the tongue from obstructing the mouthpiece.
8. Hold the MDI upright, with the mouthpiece aimed at the mouth.
9. Place the mouthpiece between the lips or 4 cm (2 fingers) in front of the widely opened mouth.
10. Breathe in slowly and press the MDI canister down once at the beginning of inhalation.
11. Continue to inhale until the lungs are full.
12. Move the mouthpiece away from the mouth and hold breath for 5 to 10 seconds (or as long as comfortable).
13. Wait at least 15 - 30 seconds between doses.
14. Repeat for the prescribed number of doses.
15. Recap the mouthpiece.
16. If using a corticosteroid MDI, gargle and rinse the mouth with water or mouthwash after completing the dose.

### **Autohaler technique**

1. Hold the MDI to warm it.
2. Remove the mouthpiece cover.
3. Inspect the mouthpiece for foreign objects.
4. Hold the Autohaler upright; the arrow should point up; do not block the air vents.
5. If the MDI is new or has not been used recently, prime it using the following technique:
  - a. Remove mouthpiece cover.
  - b. Push the lever so that it stays up.
  - c. Push the white test fire slide on the bottom of the mouthpiece to release a priming spray.
  - d. To release the second priming spray, return the lever to its down position and repeat previous steps.
  - e. Return the lever to its down position.
6. Raise the lever so that it snaps into place.
7. Shake the Autohaler (3 or 4 shakes).
8. Breathe out normally, away from the MDI.
9. Open the mouth and keep the tongue from obstructing the mouthpiece.
10. Seal the lips tightly around the mouthpiece.

## **TECHNIQUE BOX 2. CONTINUED**

11. Inhale deeply through the mouthpiece with steady moderate force.
12. Listen for a click and the feel of a soft puff when the device triggers the release of medicine.
13. Continue to inhale until the lungs are full.
14. Remove the mouthpiece from the mouth and hold breath for 10 seconds (or as long as comfortable).
15. Hold the Autohaler upright and lower the lever after each inhalation.
16. Repeat for the prescribed number of doses.
17. Recap the mouthpiece.
18. Make sure the lever is down.

### **Cleaning the MDI** (once a week and as needed)

1. Look at the hole where the medicine sprays out from your inhaler. Clean the inhaler if you see powder in or around the hole.
2. Remove the metal canister from the mouthpiece.
3. Set the canister aside so it does not become wet.
4. Clean the plastic parts of the device using mild soap and water. (Never wash the metal canister or put it in water.)
5. Let the plastic parts dry in the air (eg, overnight).
6. Put the canister back inside the mouthpiece and replace the cap.
7. Test the MDI by releasing a puff into the air.

### **Cleaning the Autohaler** (once a week and as needed)

1. Remove the mouthpiece cover.
2. Turn the Autohaler upside-down.
3. Wipe the mouthpiece with a clean dry cloth.
4. Gently tap the back of Autohaler so the flap comes down and the spray hole can be seen.
5. Clean the surface of the flap with a dry cotton swab.
6. Recap the mouthpiece and make sure the lever is down.

### **Cleaning the MDI**

Appropriate dosing can be impacted by the cleanliness of the actuator or the number of doses remaining in a canister. Frequently the actuator orifice will be surrounded by a white, crusty residue caused by crystallization of the medication. Patients should inspect and clean the actuator as described in Technique Box 2. MDIs should be inspected daily and cleaned at least weekly, or more often if needed. Cleaning is particularly important for HFA-MDIs because medication residue may block the spray if the inhaler is not kept clean.

### **Dose Counting**

The lack of a dose-counting mechanism is a serious drawback to the MDI and potentially places patients at risk of continuing to use an empty inhaler. The instructions on package inserts from pharmaceutical manufacturers instruct patients to count their inhaled doses over the life of the canister. It is unfeasible, impractical, and undependable for patients to keep a running tally of the doses used, especially with their reliever medications. Recommendations to float the canister (without boot) in water are inaccurate to determine the remaining contents. Moreover, water entering the metering valve stem can reduce the

subsequent dose or occlude the inhaler completely. Ventolin HFA (GlaxoSmithKline) has a built-in dose counter, which is the ideal method to track MDI doses (Figure 13). Third-party dose-counting devices are commercially available, but the additional expense of these devices has limited their wide acceptance. Table 13 offers methods for dose tracking for controller and occasionally-used reliever medications, in addition to dose-counting devices.



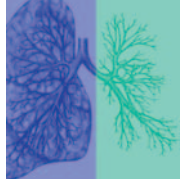
*Figure 13. Counter on Ventolin HFA MDI.*

**Table 13.** *Tracking Doses Remaining in MDI.*

- The number of puffs contained in the inhaler is printed on the side of the canister (Note: the number of puffs in inhalers varies). After the MDI has been used for that number of puffs, it must be discarded even if it continues to spray.
- Keep track of how many puffs have been used.
- Ventolin HFA has a built-in dose counter in the plastic actuator.
- A device can be used that counts down the number of puffs each time you press the inhaler. Examples include: the DOSER (MediTrack Products, Hudson, MA) and the MD Turbo™ (TEAMM Pharmaceuticals). The latter also provides breath actuation for the MDI.
- You can also calculate how long the MDI will last by dividing the total number of puffs in the MDI by the total puffs used every day. For example, the MDI has 200 puffs, and it is used for a total of 8 puffs per day. This canister will last 25 days (200 divided by 8 = 25 days). Determine when the medication will run out and mark this date on the calendar, and on the canister. If the inhaler is used more often than planned, the medication will run out sooner. Replace the inhaler by refilling the prescription before the calculated date.
- A “tally sheet” or Post-it® can be used to record the number of puffs in a given day for easier totaling. Keep the tally sheet in a convenient place such as the bathroom mirror.

### **Breath-Actuated MDI**

Breath-actuated MDIs detect the beginning of the patient’s inhalation and triggers the inhaler at that point to ensure synchrony. As these devices require a mechanical trigger to actuate the device upon inspiration, a flow rate of approximately 30 L/min is necessary and perhaps a limitation in some patients for this device. The correct steps for the breath-actuated Autohaler are found in TECHNIQUE BOX 2.



# Metered-Dose Inhaler Accessory Devices

These devices overcome some of the most common limitations of MDIs. By adding volume (space) between the metering valve and the patient's mouth, they reduce oropharyngeal deposition. They also reduce the need for coordination of actuation and inspiration, thus overcoming the problem of hand-breath coordination. Table 14 lists both advantages and some disadvantages seen with use of holding chambers and spacers. While the term *spacer* is used in clinical parlance to refer to all types of extension add-on devices, these devices are categorized into *spacers* or *holding chambers* (or *valved holding chambers*) based on their design. A spacer is a simple tube or extension device with no one-way valves to contain the aerosol plume after MDI actuation; its purpose is simply to allow space and distance between the mouth and the MDI mouthpiece. A holding chamber (valved holding chamber) is an extension device added onto the MDI mouthpiece or canister that contains one-way valve(s) to contain the aerosol until inhalation occurs. In addition to the major design difference that defines spacers versus (valved) holding chambers, there are other design differences among brands of holding chambers and spacers. *Volume* may vary, although in the United States, most holding chamber/spacer are less than 200 mL. *Direction of spray* may vary between forward (toward the mouth) and reverse (away from the mouth). The AeroChamber (Monaghan) and the OptiChamber (Respironics) are examples of forward sprays, and the Optihaler (Respironics), ACE (Aerosol Cloud Enhancer, DHD) and InspirEase are examples of reverse spray. Some holding chamber/spacers accept the manufacturer's mouthpiece-actuator (the boot), while others have a nozzle receptacle for accepting only the canister. As examples, the ACE and OptiHaler have canister nozzle receptacles, while the AeroChamber and OptiChamber have malleable openings to accept the MDI mouthpiece. Figure 14 shows examples of spacers and holding chambers.

*Table 14. Advantages and disadvantages of holding chambers or spacers (“add-on” devices) used in conjunction with metered-dose inhalers.*

## ADVANTAGES

- Reduced oropharyngeal drug impaction and loss
- Simplifies coordination of MDI actuation and inhalation
- Allows use of MDI during acute airflow obstruction with dyspnea

## DISADVANTAGES

- Large and cumbersome compared to the MDI alone
- Additional expense required
- Some assembly may be needed
- Patient errors include firing multiple puffs into chamber prior to inhaling, or delay between actuation and inhalation
- Possible contamination with inadequate cleaning



*Figure 14. Examples of valved holding chambers and spacers.*

## Spacers

The use of a spacer with CFC-MDIs produces at least an equivalent clinical effect to that of a correctly used MDI. A spacer provides additional volume that slows the aerosol velocity from a MDI, allowing a reduction in particle size. Aerosol retention and discharged dose depends on the size and shape of the spacer, and electrostatic charge on the inner walls of plastic spacers. Spacers decrease oral deposition, but they only provide limited protection against poor hand-breath coordination. When using a spacer, it is important for the patient to coordinate their inhalation to occur slightly before actuating the inhaler. Spacers may be an integral part of the MDI mouthpiece (eg, Azmacort), whereas others require removal of the inhaler canister from the manufacturer's actuator and incorporation into a special orifice on the spacer (eg, InspirEase or OptiHaler). It is important to understand that dose delivery can be affected in some spacer designs if the device does not fit the MDI properly or if the design uses a special orifice or actuator incorporated in the spacer itself. Occasionally, clinicians or patients construct homemade holding chambers from plastic containers (eg, soda bottle) or other devices (eg, toilet paper roll). These may function as a spacer, but their performance is variable and hence they should not be considered as a suitable replacement for a commercially available spacer.

## Valved Holding Chambers

A valved holding chamber has a low-resistance one-way valve that allows aerosol particles to be contained within the chamber for a short time until an inspiratory effort opens the valve. Although the presence of a one-way valve prevents aerosol particles from exiting the chamber until inhalation begins, *optimal* aerosol dosing still depends on inhaling as close to or simultaneously with MDI actuation into the chamber. Time delays can significantly reduce the available dose for inhalation from a valved holding chamber. The one-way valve has a low resistance so that it opens easily with minimal inspiratory effort. Ideally, there should be a signal to provide feedback if inspiratory flow is too high. Children with low tidal volumes (less than device dead space) may need to take several breaths from a valved holding chamber through a face mask for a single MDI actuation. In this case, the valved holding chamber should incorporate a one-way exhalation valve to decrease rebreathing. A valved holding chamber with mouthpiece costs as little as \$15-\$20, and a static free device with mask can cost as much as \$50-\$60.

## Drug Delivery and Technique

While spacers and valved holding chambers provide many benefits for optimal drug delivery with MDIs, there are also potential problems with use with these devices (Table 14). Improper technique may decrease drug delivery or, in some cases, cause the dose to be lost. Possible causes of decreased drug delivery include multiple actuations into the device, electrostatic charge, inhaling before actuating the MDI, or delay between actuation and inhaling the dose. In children, lack of a proper mask fit, a spacer volume that is greater than tidal volume (dead volume), and crying are problematic. Proper technique is provided in TECHNIQUE BOX 3.

## Care and Cleaning

Holding chambers should be replaced when damaged or worn. This implies that they should be inspected periodically by the patient and the clinician. Electrostatic charge may be present when a plastic spacer is new. Electrostatic forces on spacer walls cause particles to adhere and can decrease the dose delivered to the lungs, especially with delays in inhalation. The problem of electrostatic charge can be made worse by inappropriate cleaning. Electrostatic charge can be reduced by priming the chamber with several actuations of aerosol from the MDI. Another approach is to wash it in a dilute solution of household detergent (Technique Box 3). Allowing the chamber to air dry without rinsing or towel-drying creates a thin film of detergent adhering to the walls of the chamber reducing electrostatic build-up. Several commercially available valved holding chambers made from metal or non-static plastics are also available, such as the Vortex (PARI Respiratory Equipment) and the AeroChamber Max (Monaghan Medical).



**TECHNIQUE BOX 3.** Steps for correct use of MDI with holding chamber/spacer.

**Spacer Valved Holding Chamber Technique**

1. Hold the MDI to warm it.
2. Assemble the apparatus and check for foreign objects.
3. Take the cap off of the inhaler mouthpiece.
4. Attach the MDI to the holding chamber/spacer.
5. Shake the MDI (3 or 4 shakes).
6. Hold the canister in a vertical position.
7. Breathe out normally.
8. Open the mouth and keep the tongue from obstructing the mouthpiece.
9. Place the mouthpiece into the mouth (or place the mask completely over the nose and mouth).
10. Press the MDI canister once and simultaneously breathe in slowly through the mouth.
11. If the device produces a “whistle,” inspiration is too rapid.
12. Allow 15 - 30 seconds between puffs.
13. Move the mouthpiece away from the mouth and hold breath for 10 seconds (or as long as comfortable).
14. The technique is slightly different for a device with a collapsible bag: Open the bag to its full size. Press the MDI canister immediately before inhalation and inhale until the bag is completely collapsed (can breathe in and out of the bag several times to evacuate the medication).
15. The technique is slightly different if a mask is used with a child. Place the mask over the child’s mouth and nose, making sure the mask fits snugly against the face, keeping the child’s head level. Holding the mask in place, push down once on the top of the inhaler. Hold the mask in place while the child takes 6 normal breaths (inhales and exhales 6 times). Remove the mask from the child’s face.
16. Repeat for the prescribed number of doses.
17. Rinse the mouth if using inhaled steroids.

**Clean the Holding Chamber** (every 2 weeks and as needed)

Chamber device:

1. Disassemble the device for cleaning.
2. Wash in clean warm soapy water; rinsing is optional.
3. Drip-dry over night.
4. Do not towel dry the spacer as this will reduce dose delivery because of static charge.
5. Reassemble the spacer after it is dry.

Collapsible bag device:

1. Disassemble the device for cleaning.
2. Remove the plastic bag assembly from the mouthpiece.
3. The mouthpiece can be washed with warm water.
4. Drip dry over night.
5. Reassemble the device after it is dry.
6. The plastic bag should not be cleaned, but should be replaced every 4 weeks or as needed.

The first report of a dry powder inhaler (DPI) pre-dates the introduction of the MDI. In 1949, Krasno and Rhoads described the administration of penicillin dust using the Aerohalor for treatment of respiratory infections, particularly sinusitis. The introduction of the Spinhaler by Fisons for oral inhalation of cromolyn sodium (Intal), as described in 1971 by Bell, Hartley, and Cox, is usually cited as the first DPI in common clinical use, and was certainly the first in a line of DPIs introduced to date. DPI devices that are currently available in the United States are shown in Figure 11. There are several excellent reviews of the evolution of DPIs.<sup>23-25</sup>

The introduction of the Spinhaler was partly based on the problem of hand-breath coordination frequently observed with incorrect use of MDIs. DPIs are breath-actuated, thereby ensuring coordination between release of drug and inhalation. Further impetus to the development of aerosol formulations as powders came with the Montreal Protocol and the phase-out of ozone-destroying CFC propellants in MDIs. Advantages and disadvantages of DPIs are listed in Table 15. These pros and cons, with those of the particular DPI design, should be considered by clinicians when prescribing a DPI aerosol formulation for individual patients, and when performing follow-up evaluations of patient success with a DPI.

**TABLE 15.** *Advantages and disadvantages of dry powder inhalers.*

#### ADVANTAGES

- Small and portable
- Built-in dose counter
- Propellant-free
- Breath-actuated
- Short preparation and administration time

#### DISADVANTAGES

- Dependence on patient's inspiratory flow
- Patients less aware of delivered dose
- Relatively high oropharyngeal impaction can occur
- Vulnerable to ambient humidity or exhaled humidity into mouthpiece
- Limited range of drugs

#### Principle of Operation

DPIs do not contain propellants, and all current devices are breath-actuated. The patient's inspiratory effort, both inspiratory flow and volume, provide the energy to disperse and deliver the drug powder. All DPIs have an intrinsic resistance to airflow that differs among devices. For example, the HandiHaler has a higher resistance than the Turbuhaler, and both have higher resistances than the Diskus. The resistance determines how much inspiratory flow occurs through the device for a given inspiratory effort. As airflow occurs, a pressure drop between the intake and exiting mouthpiece occurs, thus lifting the powder from the drug reservoir, blister or capsule. The patient's inspiratory effort also deaggregates the powder into finer particles. Higher inspiratory flows generally improve drug deaggregation, fine particle production, and lung delivery. Excessive inspiratory flow, however, can increase impaction on the oral cavity and theoretically decrease lung deposition, although for current DPIs this is higher than the patient's capability.<sup>26</sup>

## Currently Available DPI Formulations and Designs

Table 16 lists the drug formulations available in a dry powder formulation. The device design largely describes whether the DPI is a unit dose (loading a single dose prior to each use) or multidose (containing an entire month's prescription). A primary disadvantage of unit dose DPIs is the time needed to load a dose for each use. All DPIs are potentially vulnerable to humidity and moisture, which can cause powder clumping and reduce deaggregation and fine particle development during inhalation. However, capsules and drug blisters generally offer more protection from ambient humidity than does a reservoir chamber containing multiple doses for dispensing when the device is primed for use. Fine particle mass from the Turbuhaler (multidose reservoir device) has been shown to be reduced in the presence of high ambient humidity, while dosing from the Diskus (a multidose blister strip) was relatively unchanged.<sup>27</sup>

**TABLE 16.** Currently available dry powder aerosol formulations in the US categorized by design features. See text for description of design features.

| Design    | Device     | Drug                      | Dosing System  |
|-----------|------------|---------------------------|----------------|
| Unit Dose | Aerolizer  | formoterol                | capsule        |
|           | HandiHaler | tiotropium                | capsule        |
| Multidose | Diskus     | salmeterol & fluticasone  | blister strip  |
|           |            | salmeterol<br>fluticasone |                |
|           | Turbuhaler | budesonide                | drug reservoir |
|           | Twisthaler | mometasone                | drug reservoir |

## Major Limitations with Dry Powder Inhalers

Two major limitations of DPIs are *exposure to humidity/moisture* and dependence on the patient's *inspiratory flow ability*. DPIs must be kept dry. Capsules offer better protection from ambient humidity as that encountered at the beach, coastal environments or steamy bathrooms. Designs such as the Turbuhaler (AstraZeneca) or Twisthaler should be either avoided in such environments or protected in some fashion. It is easy to keep a Turbuhaler out of the bathroom. It is more difficult to avoid ambient humidity if it is carried to the beach, kept in a house with no air conditioning, or left in a car. For such situations an alternative DPI design might be considered, but the limited availability of aerosol drug DPI formulations makes this difficult. Availability of the drug in a different aerosol system, such as an MDI, can also offer a solution. All DPIs are vulnerable to exhaled air introduced into the mouthpiece, especially after the device is cocked and loaded, when the powder is exposed. Patients must be cautioned to exhale away from the DPI prior to inhaling.

Since DPIs depend on the energy created by a forceful inspiration, there has been concern that some patients may not be able to generate an adequate inspiratory flow. This includes the very young child, and patients with acute airflow obstruction (asthma or COPD). DPIs are not generally recommended for children under 5 years of age. However, while patients with acute airflow obstruction, including those with COPD exacerbation, may not be able to generate the *optimal* flow, they generate an *adequate* flow. For example, it has been found that an inspiratory flow as low as 30 L/min from children using a

Turbuhaler gave an equivalent bronchodilator response to that of the recommended flow of 60 L/min.<sup>28</sup> However, very low inspiratory flows do result in reduced drug delivery, especially fine particle delivery. Patients should be evaluated for the ability to generate a minimal inspiratory flow if a DPI is to be used.

### **Correct Use of a Dry Powder Inhaler**

DPIs available in the United States differ in their mechanism of loading, cocking and priming to prepare for patient inhalation. Exceptions are the Turbuhaler and Twisthaler, which are similar in operation. Unfortunately this variation can confuse patients further in the correct use of DPIs. Correct technique for use of each model of DPIs is shown in TECHNIQUE BOX 4. Because of the similarity of DPI capsules and oral drug capsules, patients must be instructed not to ingest DPI capsules.

#### ***TECHNIQUE BOX 4. Steps for correct use of each model of dry powder inhaler (DPI).***

##### **Diskus**

1. Open the device.
2. Slide the lever from left to right.
3. Breathe out normally; do not exhale into the device.
4. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece.
5. Keep device horizontal while inhaling dose with a rapid and steady flow.
6. Remove the mouthpiece from the mouth and hold breath for 10 seconds (or as long as comfortable).
7. Be sure not to exhale into the device.
8. Store the device in a cool dry place.
9. Observe the counter for the number of doses remaining, and replace when appropriate.

##### **Turbuhaler**

1. Twist and remove cap.
2. Hold inhaler upright (mouthpiece up).
3. Turn grip right, then left, until it clicks.
4. Breathe out normally; do not exhale into the device.
5. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece.
6. Inhale dose with a rapid and steady flow; inhaler may be held upright or horizontal during inhalation.
7. Remove the mouthpiece from the mouth and hold breath for 10 seconds (or as long as comfortable).
8. Be sure not to exhale into the device.
9. Replace the cover and twist to close.
10. Store the device in a cool dry place.
11. When a red mark appears at the top of the dose indicator window, there are 20 doses remaining.
12. When the red mark reaches the bottom of the window, the Turbuhaler is empty and must be replaced.

## **TECHNIQUE BOX 4. CONTINUED**

### **Aerolizer**

1. Remove the mouthpiece cover.
2. Hold the base of inhaler and twist the mouthpiece counterclockwise.
3. Remove capsule from foil blister immediately before use; do not store the capsule in the Aerolizer.
4. Place the capsule in the chamber in the base of the inhaler.
5. Hold the base of the inhaler and turn it clockwise to close.
6. Simultaneously press both buttons; this pierces the capsule.
7. Keep the head in an upright position.
8. Do not exhale into the device.
9. Hold the device horizontal, with the buttons on the left and right.
10. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece.
11. Breathe in rapidly and as deeply as possible.
12. Remove the mouthpiece from the mouth and hold your breath for 10 seconds (or as long as comfortable).
13. Do not exhale into the device.
14. Open the chamber and examine the capsule; if there is powder remaining, repeat the inhalation process.
15. After use, remove and discard the capsule.
16. Close the mouthpiece and replace the cover.
17. Store the device in a cool dry place.

### **HandiHaler**

1. Immediately before using the HandiHaler, peel back the aluminum foil and remove a capsule; do not store capsules in the HandiHaler.
2. Open the dust cap by pulling it upward.
3. Open the mouthpiece.
4. Place the capsule in the center chamber; it does not matter which end is placed in the chamber.
5. Close the mouthpiece firmly until you hear a click; leave the dust cap open.
6. Hold the HandiHaler with the mouthpiece up.
7. Press the piercing button once and release; this makes holes in the capsule and allows the medication to be released when you breathe in.
8. Do not exhale into the device.
9. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece.
10. Keep head in an upright position.
11. Breathe in at a rate sufficient to hear the capsule vibrate, until the lungs are full.
12. Remove the mouthpiece from the mouth and hold breath for 10 seconds (or as long as comfortable).
13. Do not exhale into the device.
14. Repeat the inhalation from the HandiHaler.
15. Open the mouthpiece, tip out the used capsule, and dispose of it.
16. Close the mouthpiece and dust cap for storage of the HandiHaler.

## **TECHNIQUE BOX 4. CONTINUED**

### **Twisthaler**

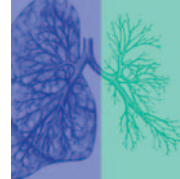
1. Hold the inhaler straight up with the pink portion (the base) on the bottom.
2. Remove the cap while it is in the upright position to make sure the right dose is dispensed.
3. Hold the pink base and twist the cap in a counter-clockwise direction to remove it.
4. As the cap is lifted off, the dose counter on the base will count down by 1. This action loads the dose.
5. Make sure the indented arrow located on the white portion (directly above the pink base) is pointing to the dose counter.
6. Breathe out normally – do not exhale into the device.
7. Place the mouthpiece into the mouth, with the mouthpiece facing toward the patient, and close the lips tightly around it.
8. Inhale the dose with a rapid and steady flow while holding the Twisthaler horizontal.
9. Remove the mouthpiece from the mouth and hold breath for 5 to 10 seconds (or as long as comfortable).
10. Be sure not to exhale into the device.
11. Immediately replace the cap, turn in a clockwise direction, and gently press down until you hear a click.
12. Firmly close the Twisthaler to assure that the next dose is properly loaded.
13. Be sure that the arrow is in line with the dose-counter window.
14. Store device in cool dry place.
15. The dose counter displays the number of doses remaining. When the unit reads 01, this indicates the last remaining dose. When the counter reads 00, the unit must then be discarded.

### **Do Not Clean the DPI**

The dry powder inhaler should not be cleaned.

It is important to keep the device dry, as moisture will decrease drug delivery.

If necessary, the mouthpiece can be wiped with a dry cloth.



The three types of aerosol devices have been shown to give equivalent clinical effects *if they are used correctly by the patient*. The following questions can be used to help in selecting an appropriate inhaler device for aerosol drug delivery.<sup>29</sup>

1. In what devices is the desired drug available? A list of common formulations currently available in various inhaler devices the United States is shown in Table 3. Unfortunately, in some cases the formulation is only available with one type of inhaler. For example, no long-acting bronchodilator is available as a nebulizer solution and no short-acting bronchodilator is available as a DPI. Where there is a choice of inhaler device, the clinician should attempt to match the drug/device with the patient's needs.
2. What device is the patient likely to be able to use properly, given the patient's age and the clinical setting? Device selection should be guided by the patient's age (Table 4) and ability.
3. For which device and drug combination is reimbursement available? This becomes an important issue, particularly for patients on a fixed income. With all other factors equal, a drug/device combination should be selected that requires the least out-of-pocket expense for the patient.
4. Which devices are the least costly? Costs of inhaled drugs vary widely (Table 3). With all other factors equal, a drug/device combination should be selected that is least costly.
5. Can all types of inhaled asthma/COPD drugs that are prescribed for the patient (eg, short-acting  $\beta$ -agonist, corticosteroid, anticholinergic, and long-acting  $\beta$ -agonist) be delivered with the same type of device (eg, nebulizer, manually actuated MDI, MDI with spacer/holding chamber, or breath-actuated device [ie, breath-actuated MDI or DPI])? Using the same type of device for all inhaled drugs may facilitate patient teaching and decrease the chance for confusion among devices that require different inhalation techniques.
6. Which devices are the most convenient for the patient, family (outpatient use), or medical staff (acute care setting) to use, given the time required for drug administration and device cleaning, and the portability of the device? With all other factors constant, the most convenient device should be selected. Portability of the device is important for outpatients, and time for drug administration is important for both outpatients and hospitalized patients.
7. How durable is the device? The device should be rugged enough to withstand the rigors of everyday treatment and cleaning.
8. Does the patient or clinician have any specific device preferences? All else equal, the preference of the patient and the clinician should guide the selection of device.



A number of problems occur with patient use of aerosol devices, and knowledge of these can help the respiratory therapist better instruct patients. Knowledge that there are problems with use of aerosol devices can also direct the therapist in evaluating a patient who has poor management of airways disease. Either poor *patient adherence* to prescribed aerosol therapy or *errors in the use of aerosol device* can reduce the effectiveness of inhaled drug therapy. Both of these problem areas should be evaluated and, if possible, ruled out in a patient who presents with poor control of their airway disease before other changes in disease management are initiated.

## Patient Adherence

A general problem with the use of inhaled medications is patient adherence with prescribed use, although this problem is not unique to inhaled drugs. “Adherence” refers to a patient’s choice to follow prescribed therapy, whereas “compliance” implies following of orders and passivity on the patient’s part. There are a number of ways to monitor patient adherence with prescribed aerosol therapy such as provider interview, patient self-report, dose counting, and electronic monitoring devices attached to the inhaler itself. Monitoring devices attached to inhaler devices are considered the most accurate and objective. In one study, diary reports from patients showed a median use of  $\beta$  agonists of 78%, while data from an electronic MDI monitor reported only 48%.<sup>30</sup> Therapists should be aware that patients tend to over-report use of inhaled drugs compared to data obtained from device monitors. Failure to adhere to prescribed therapy is categorized as “unintentional” or “intentional”. Table 17 lists both types of non-adherence with definitions and examples.<sup>31</sup>

*Table 17. General types of non-adherence to prescribed aerosol therapy and potential factors that can predispose to each type. (From Reference 31, with permission.)*

### **Unintentional** – not understanding therapy correctly

- Misunderstanding prescribed drug regimen (poor doctor-patient communication)
- Incorrect aerosol device technique
- Language barriers

### **Intentional** – understanding drug therapy but not adhering correctly

- Patient beliefs
  - do not really require regular medication
  - am not really sick
  - gain attention from parents, kept at home (children)
  - medication too expensive
  - concern about side effects
  - perceived lack of effect from medication
- Forgetfulness
- Stress and busy life style
- Complex, demanding aerosol regimens
- Psychological factors, eg, depression



Note that one example of unintentional non-adherence is incorrect aerosol device technique, which can be corrected through patient training. There is no perfect, fail-safe, error-proof inhaler on the market today. The MDI is recognized as a difficult inhaler for patients to use, and holding chambers and spacers were introduced to address this issue. DPIs were also introduced, in part, with the rationale that their use would be simpler than with a MDI. Nebulizers are probably the simplest inhaler type for a patient to use if we assume that assembly is not a problem. However there can be problems with all types of inhaler device. Table 18 lists the common errors and mistakes that can occur with each type of device.

**Table 18.** *Common problems, disadvantages and errors with each type of inhaler.*

### **Metered-dose inhalers<sup>32</sup>**

Errors in technique:

- Failure to coordinate MDI actuation on inhalation
- Too short a period of breath hold after inhalation
- Too rapid an inspiratory flowrate
- Inadequate shaking/mixing before use
- Abrupt discontinuation of inspiration as aerosol hits throat – cold Freon effect
- Actuating MDI at total lung capacity
- Firing MDI multiple times during single inhalation
- Firing MDI into mouth but inhaling through nose
- Exhaling during actuation
- Putting wrong end of inhaler in mouth
- Holding canister in the wrong position
- Failing to remove cap before use
- Excessive use of MDI beyond rated capacity (loss of dose count)
- Wasting of remaining doses
- Lack of adequate patient training in use of MDI
- Cognitive impairment of users
- Lack of adequate hand strength or flexibility to activate MDI
- Ideomotor dyspraxia

### **Holding Chambers/Spacers**

- Incorrect assembly of add-on device
- Failure to remove electrostatic charge in many holding chambers/spacers, which can decrease emitted dose in new holding chamber/spacer<sup>33</sup>
- Lengthy delay between MDI actuation and inhalation from holding chamber/spacer<sup>33</sup>
- Inhaling too rapidly
- Firing multiple puffs into holding chamber/spacer before inhaling<sup>33</sup>
- Lack of patient instruction in assembly or use

*Table 18. CONTINUED*

### **Dry Powder Inhalers**

Errors in technique:<sup>34</sup>

- Not holding device correctly while loading dose
- Exhaling through the mouthpiece
- Not exhaling to residual volume before inhaling
- Not inhaling forcefully
- Inadequate or no breath hold
- Exhaling into mouthpiece after inhaling
- Use of multi-dose reservoir designs (eg, Turbuhaler) in high ambient humidity which can reduce fine particle dose
- Lack of patient instruction in assembly or use

### **Nebulizers:**

- Failure to assemble equipment properly
- Spillage of dose by tilting some nebulizers
- Failure to keep mouthpiece in mouth during nebulization
- Failure to mouth breathe

### **Common Patient Errors with MDIs**

Although hand-breath coordination with an MDI has long been recognized as a problem, there are a number of other potential mistakes a patient can make when using an MDI (Table 18). Failure to shake an MDI before each use can interfere with correct drug release. Failure to prime an MDI can also affect correct drug release. A very practical problem, and a real inconvenience for users is the lack of a built-in dose counter to indicate when an MDI is empty. Dose counters are commercially available, but this involves purchasing an additional item. In one survey, 72% of patients said they continued to use their MDI until there was no sound when it was actuated.<sup>35</sup> An MDI can continue to produce a spray with propellant and little or no drug if it is actuated after its rated capacity, whether that is 120 or 200 puffs. Therapists should instruct patients in the importance of tracking the number of doses remaining in the MDI (Table 13).

### **Common Patient Errors with Holding Chambers/Spacers**

Common errors that can occur with holding chambers/spacers are also listed in Table 18. Incorrect assembly of the holding chamber/spacer is a potential problem. Many patients mistakenly believe that pausing before inhaling from a holding chamber/spacer after the MDI is actuated has no effect on the delivered dose. This technique can cause reduced drug availability. The ideal technique is to place the mouthpiece between the lips and take a slow, deep inhalation beginning when the MDI is actuated. Available dose can also be reduced if multiple puffs are fired into a holding chamber/spacer followed by a single inhalation. Electrostatic charge is present on the chamber walls of a new plastic holding chamber/spacer, which can be removed by pre-washing with an ionic detergent or by actuating 10-20 puffs from the MDI through the chamber.<sup>33</sup> An alternative is to purchase a non-electrostatic holding chamber/spacer.

## Common Patient Errors with Dry Powder Inhalers

Problems have also been identified with patient use of DPIs (Table 18). Error rates, defined as failure to correctly perform an essential step, have been shown to be similar for MDIs and DPIs (Aerolizer, Turbuhaler, and Diskus).<sup>34</sup> One of the unfortunate aspects of DPIs is that the models currently available in the United States all have a somewhat different design. They look different, and there are differences in the details of cocking and loading the DPIs. One of the highest error rates is failing to hold the device correctly, which is an aspect of loading and cocking the device for use.

## Common Patient Errors with Small Volume Nebulizers

The usual problems cited with SVN's are not problems of patient use, but rather general disadvantages with this type of aerosol device (Table 18). Disadvantages include bulk and size of equipment, need for external power source (compressed gas or electricity), and lengthy treatment times. Of all the inhaler devices however, nebulizers are the simplest for patients to use; normal tidal breathing and 60-90 inhalations (with most devices) to inhale the aerosol. Newer nebulizer technology is directed at reducing the overall size of devices, eliminating the need for an external power source, providing shorter treatment times, and eliminating drug loss during exhalation.

## Instructing and Evaluating Patients in the Use of Inhaler Devices

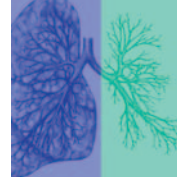
There is an increasing variety of aerosol devices and operation, even within the same category of device type (eg, DPIs). Confusion and errors of use can result. The following general steps are recommended to ensure correct patient use.

- Clinicians should review device instructions carefully, and practice with a placebo device themselves prior to teaching others.
- Demonstrate assembly and correct use of device to patients using a checklist.
- Provide the patient with written instructions on how to use the device, and include a written plan for use of the medication (frequency based on symptoms).
- Have the patient practice use of the device while being observed by the clinician.
- Review patient use of the device at each return visit.
- Review the patient's understanding of the inhaled medications at each return visit (when to use, purpose of drug, prescribed frequency).
- Have a high index of suspicion for incorrect use or non-adherence if poor management of airway disease occurs.



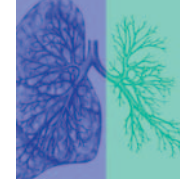
# Summary

Respiratory therapists are the only health care providers who receive extensive formal education in aerosol therapy and who are tested for competency in aerosol therapy. Thus it is incumbent upon respiratory therapists to have a sound knowledge of the use of the many aerosol delivery devices available today. Moreover, the respiratory therapist must be able to teach patients how to use these devices correctly. Correct instruction of the patient in the use of these devices adds value for the respiratory therapist and improves patient outcomes.



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