A Guide to Aerosol Delivery Devices for Respiratory Therapists, 3rd Edition

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DISCLOSURE
Douglas S. Gardenhire, EdD, RRT-NPS, FAARC has served as a consultant for the following companies: Westmed, Inc. and Boehringer Ingelheim.

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Aerosol therapy is considered to be one of the cornerstones of respiratory therapy that exemplifies the nuances of both the art and science of 21st century medicine. As respiratory therapists are the only health care providers who receive extensive formal education and who are tested for competency in aerosol therapy, the ability to serve patients with acute chronic respiratory disease as the experts in aerosol therapy allows the concept of “art” and “science” to take on a practical reality.

Respiratory therapists continue to be the experts when it comes to the art and science of aerosol therapy. With the rapidly changing field of aerosol medications and delivery systems, it is imperative that we not only share this expertise with patients but also other members of the health care delivery team across the continuum of care. With a renewed focus on wellness and prevention within the U.S. health care system and a determined focus to minimize cost and waste, the choice of appropriate respiratory medications and delivery devices makes selection of both the drug and optimum delivery device even more critical.

How does a therapeutic intervention around for centuries still combine the art with science in the context of aerosol therapy? The “science” component includes many different aspects such as pharmacology, cardiopulmonary anatomy and physiology, physics, and a thorough understanding of the different aerosol delivery technologies on the market today. In order to claim expertise in the science of aerosol therapy and optimize it for patients, the respiratory therapist must have concrete knowledge and understanding of the numerous drug formulations, their mode of action, and an understanding of the respiratory conditions where the drug and delivery is recommended and supported by the scientific evidence.

While the “art” of aerosol delivery is much more abstract than the science, it is as equally important to the appropriate delivery of respiratory medications for optimal outcomes. For aerosol therapy, the interaction between technology and human interaction is where “art” comes into play. There is ample scientific evidence of sub-optimal or ineffective use of aerosols when self-administered in large part due to lack of knowledge about proper technique by patients. All too often, patients 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 or evaluated on their proper use.

The combination of the right medication and the most optimal delivery device with the patient’s cognitive and physical abilities is the 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. When these two different, but synergistic components of medicine do not properly align, patient adherence decreases. Medication is wasted. Minimal patient benefit is derived.

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 our patients to continue our learning and competencies in the delivery of aerosolized medicines. Respiratory therapists must take advantage of this 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 guide will provide you the opportunity to advance your knowledge and expertise in aerosol delivery. Mastery of both the art and science of aerosol delivery can have a profound impact on appropriately matching medications and delivery devices to optimize your patients’ clinical outcomes. You will also contribute to more cost-effective use of health care system resources.

The third edition of this Aerosol Guide delivers 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.

Timothy R. Myers MBA, RRT-NPS, FAARC
Associate Executive Director
American Association for Respiratory Care
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- how to update your e-mail address so that registration confirmation can be sent to you.

Learning Objectives

As you read this book, you will be able to:

1. Identify the terminology used in aerosol medicine.
2. State approximate amount of aerosol deposited in the lower respiratory tract for nebulizers, pressurized metered-dose inhalers (pMDIs), and dry-powder inhalers (DPIs).
3. List advantages and disadvantages of inhalation compared to other routes of drug administration.
4. Identify hazards of aerosol therapy that can impact the patient receiving therapy as well as care providers and bystanders.
5. List advantages and disadvantages of nebulizers for aerosol delivery.
6. Compare the principle of operation of a jet nebulizer, mesh nebulizer, and ultrasonic nebulizer.
7. Describe types of pneumatic jet nebulizer designs and methods that are used to decrease aerosol loss from a jet nebulizer during exhalation.
8. Learn steps for correct use of jet, ultrasonic and mesh nebulizers.
9. Describe the basic components of a metered-dose inhaler.
10. List advantages and disadvantages of metered-dose inhalers.
11. Compare and contrast performance of pMDIs with HFA and CFC propellants.
12. Discuss factors affecting the pMDI performance and drug delivery.
13. Explain the importance of priming and tracking the number of doses for a metered-dose inhaler.
14. Compare and contrast the design of holding chambers and spacers.
15. Identify factors that affect dose delivery from a holding chamber/spacer.
16. List advantages and disadvantages of dry-powder inhalers.
17. Describe the principle of operation of various commercially available dry-powder inhalers.
18. Identify factors affecting the DPI performance and drug delivery.
19. Explain how you know that each DPI is empty.
20. List the correct steps for use of a nebulizer, metered-dose inhaler, metered-dose inhaler with holding chamber/spacer, and dry-powder inhaler.
21. Describe causes and solutions of problems seen with nebulizers, pMDIs and DPIs.
22. Discuss criteria to assist clinicians in selecting an aerosol delivery device.
23. Identify special considerations for neonatal and pediatric drug delivery.
24. Explain how to establish an infection control management system in aerosol drug delivery.
25. Describe the proper technique of cleaning aerosol delivery devices.
26. Discuss the importance of occupational health and safety for respiratory therapists.
27. List common problems and errors with each type of inhaler.
28. Describe how to instruct and evaluate patients in the use of inhaler devices.
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<table>
<thead>
<tr>
<th>Acronyms</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CDER</td>
<td>Center for Drug Evaluation and Research</td>
</tr>
<tr>
<td>CDRH</td>
<td>Center for Devices and Radiological Health</td>
</tr>
<tr>
<td>CF</td>
<td>cystic fibrosis</td>
</tr>
<tr>
<td>CFC</td>
<td>chlorofluorocarbon</td>
</tr>
<tr>
<td>DPI</td>
<td>dry-powder inhaler</td>
</tr>
<tr>
<td>FDA</td>
<td>U.S. Food and Drug Administration</td>
</tr>
<tr>
<td>FPF</td>
<td>fine-particle fraction</td>
</tr>
<tr>
<td>GSD</td>
<td>Geometric Standard Deviation</td>
</tr>
<tr>
<td>HFA</td>
<td>hydrofluoroalkane</td>
</tr>
<tr>
<td>IC</td>
<td>infection control</td>
</tr>
<tr>
<td>MMAD</td>
<td>mass median aerodynamic diameter</td>
</tr>
<tr>
<td>MMD</td>
<td>mass median diameter</td>
</tr>
<tr>
<td>pMDI</td>
<td>pressurized metered-dose inhaler</td>
</tr>
<tr>
<td>SPAG</td>
<td>small particle aerosol generator</td>
</tr>
<tr>
<td>SVN</td>
<td>small-volume nebulizer</td>
</tr>
<tr>
<td>VHC</td>
<td>valved holding chamber</td>
</tr>
</tbody>
</table>
Aerosols exist everywhere there is gas to breathe. From pollen and spores, to smoke and pollution, to man-made chemicals, the aerosol category includes any fine liquid or solid particles. A “medical aerosol” is any suspension of liquid (nebulizer or pMDI) or solid drug particles (pMDI or DPI) in a carrier gas. Our respiratory systems evolved to have filtration and elimination systems that must be overcome or bypassed in the process of providing local delivery of medications to the lung. Methods for generating aerosols, formulating drugs, and administering medications effectively to the desired site of action constitute the science of aerosol drug delivery. As is the case in any scientific discipline, one must first understand the terms and definitions used to describe the principles of aerosol medicine in order to subsequently master its methods.

**Terminology**

Definitions of key terms used in aerosol drug delivery are listed in alphabetical order below.

- **aerosol**: a suspension of liquid and solid particles produced by an aerosol generator such as the small-volume nebulizer (SVN), the pressurized metered-dose inhaler (pMDI), or the dry-powder inhaler (DPI)
- **aerosol deposition**: process of aerosol particles depositing on absorbing surfaces
- **aerosol generator**: a device used for producing aerosol particles
- **aerosol output**: mass of medication exiting an aerosol generator
- **aerosol therapy**: delivery of solid or liquid aerosol particles to the respiratory tract for therapeutic purposes
- **chlorofluorocarbon** (CFC): a liquefied gas propellant such as freon originally used in pMDIs (Its use was banned due to concerns of ozone destruction.)
- **dead volume** (or residual volume): the amount of medication that remains in the nebulizer after a treatment is complete
- **diffusion**: the mechanism of aerosol deposition for small particles less than 3 µm (Diffusion is also called Brownian motion.)
- **dry-powder inhaler**: an aerosol device that delivers the drug in a powdered form, typically with a breath-actuated dosing system
- **emitted dose**: the mass of medication leaving an aerosol generator as aerosol
- **fine-particle fraction** (FPF): percentage of the aerosol between 1–5 µm that deposits in the lung
- **heterodisperse**: aerosol particles of different sizes
- **hydrofluoroalkane** (HFA): A nontoxic liquefied gas propellant developed to be more environmentally friendly than CFCs and used to administer the drug from a pMDI
- **inhaled dose**: the proportion of nominal or emitted dose that is inhaled
- **inhaled mass**: the amount of medication inhaled
- **inhaler**: device used to generate an aerosolized drug for a single inhalation
- **inertial impaction**: the mechanism of aerosol deposition for particles larger than 5 µm
- **gravitational sedimentation** (gravitational settling): the settling rate of an aerosol particle due to gravity, particle size, and time
- **geometric standard deviation** (GSD): One standard deviation above and below the median particle sizes in an aerosol distribution that indicates the variability in aerosol particle size
mass median aerodynamic diameter (MMAD): average aerosol particle size as measured by a cascade impactor
monodisperse: aerosol particles of same or similar sizes
nebulizer: an aerosol generator producing aerosol particles from liquid-based formulations
nominal dose: the total drug dose placed in the nebulizer
plume: a bolus of aerosol leaving the pMDI or other aerosol devices
pressurized metered-dose inhaler (pMDI): a drug device combination that dispenses multiple doses by means of a metered valve; used interchangeably with pMDI
respirable mass: the product of the fine particle fraction multiplied by the inhaled mass
residual volume (or dead volume): the amount of medication that remains in the nebulizer at the end of a treatment
spacer: a valveless extension device that adds distance between the pMDI outlet and the patient’s mouth
valved holding chamber: a spacer with a one-way valve used to contain aerosol particles until inspiration occurs

Mechanisms of Aerosol Deposition and Particle Sizes
The major mechanisms of aerosol deposition include inertial impaction, gravitational sedimentation (settling), and diffusion. Inertial impaction occurs with larger (>3 µm), fast-moving particles. Gravitational settling is a function of particle mass and time, with the rate of settling proportional to particle size and mass. Diffusion occurs with particles smaller than 1 µm.
These mechanisms come into play as aerosol particles are inhaled orally or through the nose. Larger particles (> 10 µm) are filtered in the nose and/or the oropharynx, largely by inertial impaction; particles of 5–10 µm generally reach the proximal generations of the lower respiratory tract, and particles of 1–5 µm reach to the lung periphery.
Particle size plays an important role in lung deposition, along with particle velocity and settling time. As particle size increases above 3 µm, aerosol deposition shifts from the periphery of the lung to the conducting airways. Oropharyngeal deposition increases as particle size increases above 6 µm. Exhaled loss is high with very small particles of 1 µm or less. Consequently, particle sizes of 1–5 µm are best for reaching the lung periphery, whereas 5–10 µm particles deposit mostly in the conducting airways, and 10–100 µm particles deposit mostly in the nose.
Aerosol devices in clinical use produce heterodisperse (also termed polydisperse) particle sizes, meaning that there is a mix of sizes in the aerosol. Monodisperse aerosols, which consist of a single particle size, are rare in nature and medicine. A measure that quantifies a polydisperse aerosol is the mass median diameter (MMD). This measure determines the particle size (in µm) 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.
As seen in Figure 1, larger particles between 10–15 µm deposit mostly in the upper airways, particles within the 5–10 µm range reach the large bronchi, and particles of 1–5 µm penetrate to the lower airways and lung periphery.
Types of Aerosol Generators

Three common types of aerosol generators are used for inhaled drug delivery: the small-volume nebulizer (SVN), the pressurized metered-dose inhaler (pMDI), and the dry-powder inhaler (DPI). Each device type is described below.

- **Small-volume Nebulizer:** The SVN is an aerosol generator that converts liquid drug solutions or suspensions into aerosol and is powered by compressed air, oxygen, a compressor, or an electrically powered device.

- **Pressurized Metered-dose Inhaler:** The pMDI is a small, portable self-contained drug device combination that dispenses multiple doses by a metered valve. Because of high medication loss in the oropharynx and hand-held coordination difficulty with pMDIs, holding chambers and spacers are often used as ancillary devices with the pMDI.

- **Dry-powder Inhaler:** The DPI is an aerosol device that delivers drug in a powdered form, typically with a breath-actuated dosing system.

Where Does an Inhaled Aerosol Drug Go?

Lung deposition may range from 1–50% with clinical aerosol delivery systems.\(^3\)\(^–\)\(^7\) Deposition is dependent on a variety of factors such as the device, the patient, the drug, and the disease. For example, out of 200 micrograms (µg) of albuterol in two actuations or puffs from a pMDI, only about 20–40 µg reach the lungs with correct technique. The remaining drug is lost in the oropharynx, in the device, or in the exhaled breath. Figure 2 indicates the percentages of drug deposition for different aerosol systems, showing that oropharyngeal loss, device loss, and exhalation/ambient loss differ among aerosol device types, as do lung doses.
It is important to realize that different types of aerosol devices deposit a different fraction of the total dose of a given drug (also termed “nominal” dose) in the lungs. In addition, different types of aerosol devices such as nebulizers and pMDIs do not have the same nominal dose. Using albuterol as an example, the typical pMDI nominal dose is two actuations, or about 200 µg, while the typical nebulizer nominal dose is 2.5 mg, or 12 times more drug. Table 1 lists both the pMDI and nebulizer nominal doses for several drugs, showing this difference.

**Table 1. Differences in nominal (total) dose between a pMDI and an SVN for different drug formulations** *(Modified, with permission, from Reference 1)*

<table>
<thead>
<tr>
<th>Drug</th>
<th>pMDI Nominal Dose</th>
<th>SVN Nominal Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol</td>
<td>0.2 mg (200 µg)</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>Ipratropium</td>
<td>0.04 mg (40 µg)</td>
<td>0.5 mg</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>0.045 mg – 0.09 mg</td>
<td>0.31 mg – 1.25 mg</td>
</tr>
</tbody>
</table>

**Equivalence of Aerosol Device Types**

Historically, nebulizers were thought to be more effective than pMDIs, especially for short-acting bronchodilators in acute exacerbations of airflow obstruction. Contrarily, evidence has shown equivalent clinical results whether a pMDI, a nebulizer, or a DPI is used, provided that the patient can use the device correctly. For bronchodilators, the same clinical response is often achieved with the labeled dose from the pMDI or nebulizer, despite the higher nominal dose for the nebulizer. Because any of these aerosol generators, if used properly, can be effective with their label dose, dosage should be device specific and based on the label claim.

Newer aerosol devices and drug formulations are increasing the efficiency of lung deposition when compared to the traditional devices commonly used. For example, lung deposition for HFA-beclomethasone dipropionate (QVAR™, Teva Pharmaceuticals, North Wales, PA) is in the range of 40–50% of the nominal dose using a pMDI formulation with hydrofluorocarbon propellant, which replaces the older chlorofluorocarbon (CFC) propellants. New devices such as the Respimat® inhaler (Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT) have shown lung depositions of 40%. Although lung dose efficiency varies between...
Advantages and Disadvantages of Inhaled Aerosol Drugs

There are a number of advantages and disadvantages that go along with the inhalation of drugs to treat pulmonary disease (Table 2). The primary advantage of inhaled aerosol therapy is treating the lung directly with smaller doses, resulting in fewer side effects than with oral delivery. As seen in Figure 3, inhalation of terbutaline, a short-acting beta-2 agonist, from a pMDI resulted in better airflow than with a much larger oral dose or even with a subcutaneous injection of drug.

### Table 2. Advantages and disadvantages of the inhaled aerosolized drugs
(Modified, with permission, from Reference 1)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerosol doses are generally smaller than systemic doses.</td>
<td>Lung deposition is a relatively low fraction of the total dose.</td>
</tr>
<tr>
<td>Onset of effect with inhaled drugs is faster than with oral dosing.</td>
<td>A number of variables (correct breathing pattern, use of device) can affect lung deposition and dose reproducibility.</td>
</tr>
<tr>
<td>Drug is delivered directly to the lungs, with minimal systemic exposure.</td>
<td>The difficulty of coordinating hand action and inhalation with the pMDIs reduces effectiveness.</td>
</tr>
<tr>
<td>Systemic side effects are less frequent and severe with inhalation when compared to systemic delivery.</td>
<td>The lack of knowledge of correct or optimal use of aerosol devices by patients and clinicians decreases effectiveness.</td>
</tr>
<tr>
<td>Inhaled drug therapy is less painful than injection and is relatively comfortable.</td>
<td>The number and variability of device types confuses patients and clinicians.</td>
</tr>
<tr>
<td></td>
<td>The lack of standardized technical information on inhalers for clinicians reduces effectiveness.</td>
</tr>
</tbody>
</table>

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 pMDI, compared to similar or larger doses delivered orally or by subcutaneous injection
(From Reference 6, with permission)
Hazards of Aerosol Therapy

Hazards associated with aerosol drug therapy may occur as a result of inhaled medication, an aerosol generator being used, the aerosol administration technique, and the environment. Hazards of aerosol therapy can impact the patient receiving therapy, as well as care providers and bystanders.

Hazards for Patients

Adverse Reaction: Most hazards associated with aerosol therapy are attributed to adverse reactions to the drug being used. Therefore, inhaled medications should be administered with caution. Types of adverse reactions include headache, insomnia, and nervousness with adrenergic agents, local topical effects with anticholinergics, and systemic/local effects of corticosteroids. If any of these adverse reactions are seen during aerosol drug therapy, the treatment should be ended and the physician should be notified.

Bronchospasm: Administering a cold and high-density aerosol may induce bronchospasm in patients with asthma or other respiratory diseases. If bronchospasm occurs during aerosol therapy, the therapy should be immediately discontinued for 15-20 minutes. If it persists, the physician should be notified.

Drug Concentration: In both jet and ultrasonic nebulizers, drug concentration may increase significantly during aerosol therapy. An increase in drug concentration may be due to evaporation, heating, or the inability to efficiently nebulize suspensions. As a result of changes in drug concentration, the amount of the drug remaining in the nebulizer at the end of aerosol therapy is increased and the patient is exposed to higher concentrations of inhaled medications. This is a great problem with continuous-feed nebulization.

Infection: It has been well documented that aerosol generators can become contaminated with bacteria and increase the risk of infection in patients with respiratory diseases. The risk of transmission of an infection is dependent upon duration of exposure of drugs with pathogens and the procedures taken by respiratory therapists to avoid pathogen exposure. Proper practices of medication handling, device cleaning, and sterilization can greatly reduce this risk.

Eye Irritation: Inhaled medications delivered with a face mask may inadvertently deposit in the eyes and result in eye irritation. Improving the interface between the face mask and patient may eliminate this problem and increase the amount of drug delivered to the distal airways. Therefore, caution should be exercised when using a face mask during aerosol drug administration.

Hazards for Care Providers and Bystanders

Exposure to Secondhand Aerosol Drugs: Care providers and bystanders have the risk of exposure to inhaled medications during routine monitoring and care of patients. While workplace exposure to aerosol may be detectable in the plasma, it may also increase the risk of asthma-like symptoms and cause occupational asthma. The development and implementation of an occupational health and safety policy in respiratory therapy departments can minimize exposure to secondhand aerosol drugs.
**Infection:** Care providers, bystanders, and even other patients have the risk of inhaling pathogens during aerosol therapy. The risk of infection can be minimized with the development and implementation of an infection control management system including use of masks, filters, and ventilation systems.30-32

### Currently Available Aerosol Drug Formulations

Some aerosol drugs are available in more than one formulation. Others (often newer drugs) are available only in a single formulation. Table 3 provides currently available aerosol drug formulations, their brand names, their FDA-approved aerosol delivery devices, and their costs. As the CFC propellants used in pMDIs are phased out, older aerosol drugs are being transitioned to the newer HFA-propelled pMDI formulations. New aerosol drugs are either formulated as an HFA-pMDI (e.g., pMDI-levalbuterol) or, more commonly, as DPIs (e.g., formoterol, tiotropium, mometasone).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Device</th>
<th>Strength</th>
<th>Doses</th>
<th>Cost</th>
<th>Cost/Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-acting Bronchodilator</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol Sulfate</td>
<td>AccuNeb®</td>
<td>SVN</td>
<td>0.63</td>
<td>25</td>
<td>$51.93</td>
<td>$2.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.25</td>
<td>25</td>
<td>$51.93</td>
<td>$2.08</td>
</tr>
<tr>
<td>Albuterol Sulfate</td>
<td></td>
<td>SVN</td>
<td>2.5 bottle</td>
<td>25</td>
<td>$10.14</td>
<td>$0.41</td>
</tr>
<tr>
<td>ProAir® HFA</td>
<td></td>
<td>pMDI</td>
<td>200</td>
<td></td>
<td>$42.00</td>
<td>$0.21</td>
</tr>
<tr>
<td>Proventil® HFA</td>
<td></td>
<td>pMDI</td>
<td>200</td>
<td></td>
<td>$49.00</td>
<td>$0.25</td>
</tr>
<tr>
<td>Ventolin® HFA</td>
<td></td>
<td>pMDI</td>
<td>200</td>
<td></td>
<td>$46.37</td>
<td>$0.23</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>Xopenex®</td>
<td>SVN</td>
<td>0.31</td>
<td>24</td>
<td>$106.00</td>
<td>$4.42</td>
</tr>
<tr>
<td></td>
<td>Inhalation</td>
<td>SVN</td>
<td>0.63</td>
<td>24</td>
<td>$106.00</td>
<td>$4.42</td>
</tr>
<tr>
<td></td>
<td>Solution</td>
<td>SVN</td>
<td>1.25</td>
<td>24</td>
<td>$106.00</td>
<td>$4.42</td>
</tr>
<tr>
<td></td>
<td>Xopenex HFA™</td>
<td>pMDI</td>
<td>200</td>
<td></td>
<td>$55.00</td>
<td>$0.28</td>
</tr>
<tr>
<td>Metaproterenol</td>
<td></td>
<td>SVN</td>
<td>0.4</td>
<td>25</td>
<td>$72.75</td>
<td>$2.91</td>
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<td></td>
<td></td>
<td></td>
<td>0.6</td>
<td>25</td>
<td>$72.75</td>
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<td>Ipratropium and Albuterol Sulfate</td>
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<td>Cost/Dose</td>
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<td>Pulmicort Respules</td>
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<td>Pulmicort®</td>
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<td>Turbohaler®</td>
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<td>Ciclesonide</td>
<td>Alvesco®</td>
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<td></td>
<td></td>
<td>250/50</td>
<td>$216.00</td>
<td>$3.60</td>
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<td></td>
<td></td>
<td></td>
<td>500/50</td>
<td>$286.00</td>
<td>$4.77</td>
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<td></td>
<td>Flovent® HFA</td>
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<td>$1.00</td>
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</tr>
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<td></td>
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<td></td>
<td>220</td>
<td>$247.00</td>
<td>$2.06</td>
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<td>Mometasone</td>
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<td>220</td>
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<td></td>
<td></td>
<td>220</td>
<td>$168.00</td>
<td>$2.80</td>
<td></td>
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<tr>
<td>Combination Drugs</td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Fluticasone and Salmeterol</td>
<td>Advair HFA®</td>
<td>pMDI</td>
<td>45/21</td>
<td>$230.95</td>
<td>$1.92</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<td>$373.55</td>
<td>$3.11</td>
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</tr>
<tr>
<td></td>
<td>Advair Diskus®</td>
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<td>100/50</td>
<td>$186.00</td>
<td>$3.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>250/50</td>
<td>$216.00</td>
<td>$3.60</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>500/50</td>
<td>$286.00</td>
<td>$4.77</td>
<td></td>
</tr>
<tr>
<td>Budesonide and Formoterol</td>
<td>Symbicort®</td>
<td>pMDI</td>
<td>80</td>
<td>$172.00</td>
<td>$2.87</td>
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<td>160</td>
<td>$202.00</td>
<td>$3.37</td>
<td></td>
</tr>
<tr>
<td>Mometasone/ Formoterol</td>
<td>Dulera®</td>
<td>pMDI</td>
<td>100</td>
<td>$248.87</td>
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<td></td>
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<td>$248.87</td>
<td>$2.07</td>
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</table>
Table 3. (continued)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Device</th>
<th>Strength</th>
<th>Doses</th>
<th>Cost</th>
<th>Cost/Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mucoactive Drugs</strong></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Dornase Alpha</td>
<td>Pulmozyme®</td>
<td>SVN</td>
<td>30</td>
<td>$1,728.00</td>
<td>$57.60</td>
<td></td>
</tr>
<tr>
<td><strong>Other Drugs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zanamivir</td>
<td>Relenza®</td>
<td>DPI</td>
<td>20</td>
<td>$67.40</td>
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</tr>
<tr>
<td>Tobramycin</td>
<td>TOBI®</td>
<td>SVN</td>
<td>56</td>
<td>$7,266.28</td>
<td>$129.76</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DPI</td>
<td></td>
<td></td>
<td></td>
<td>Recently approved by FDA, no cost information at this time</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Cayston®</td>
<td>SVN</td>
<td>28</td>
<td>$6,181.09</td>
<td>$220.75</td>
<td></td>
</tr>
</tbody>
</table>
Small-volume nebulizers (SVNs) are popular aerosol generators with clinicians and patients as they convert drug solutions or suspensions into aerosols that deposit into the patient’s lower respiratory tract with minimal patient cooperation.

**Advantages and Disadvantages of SVNs**

Nebulizers have long been the cornerstone of medical aerosol therapy in the acute and critical care setting. Also, they are frequently the device selected for patients such as infants, small children, and the elderly who are unable to operate, coordinate, or cooperate with the use of various inhalers. This functionality offsets the issues of portability, weight, noise, cost, and time of administration associated with nebulizers. Table 4 lists the advantages and disadvantages of small-volume nebulizers.

Nebulizers are regulated as medical devices by the U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). They are tested in accordance with applicable standards for medical device electrical safety, electromagnetic compatibility, environmental temperature and humidity, shock and vibration as well as for their biocompatibility of materials.

Nebulizers are designed to be used with a broad range of liquid formulations. Drugs for use with nebulizers are approved by the FDA and the Center for Drug Evaluation and Research (CDER). Historically, drug solutions for inhalation were approved based on studies using standard jet nebulizers (the first type of SVN) ranging in efficiency from 6–12%. The use of more efficient nebulizers created the risk of delivering inhaled dose above the upper threshold of the therapeutic window, increasing the risk of side effects and toxicity. Consequently, the FDA requires that the drug label of new liquid formulations identify the nebulizers used in the clinical studies (Table 5). Because drug delivery varies with different nebulizer types, it is important to use the nebulizer cited on the drug “label” when possible. At the very least, clinicians should be aware of the relative performance of the “label” nebulizer.

---

**Table 4. Advantages and disadvantages of SVNs**

(Modified, with permission, from Reference 1)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to aerosolize many drug solutions</td>
<td>Treatment times may range from 5–25 minutes.</td>
</tr>
<tr>
<td>Ability to aerosolize drug mixtures (&gt;1 drug), if drugs are compatible</td>
<td>Equipment required may be large and cumbersome.</td>
</tr>
<tr>
<td>Minimal patient cooperation or coordination is needed.</td>
<td>Need for power source (electricity, battery, or compressed gas)</td>
</tr>
<tr>
<td>Useful in very young, very old, debilitated or distressed patients</td>
<td>Potential for drug delivery into the eyes with face mask delivery</td>
</tr>
<tr>
<td>Drug concentrations and dose can be modified.</td>
<td>Variability in performance characteristics among different types, brands, and models</td>
</tr>
<tr>
<td>Normal breathing pattern can be used, and an inspiratory pause (breath-hold) is not required for efficacy.</td>
<td>Assembly and cleaning are required. Contamination is possible with improper handling of drug and inadequate cleaning.</td>
</tr>
</tbody>
</table>
Table 5. Drug formulations and approved nebulizers for that formulation
(Modified, with permission, from Reference 1)

<table>
<thead>
<tr>
<th>Drug Formulation</th>
<th>Approved Nebulizer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchodilator</td>
<td>Nebulizer type not specified</td>
</tr>
<tr>
<td>Acetylcysteine</td>
<td>Nebulizer type not specified</td>
</tr>
<tr>
<td>Budesonide (Pulmicort Respules®)</td>
<td>Should not be used with ultrasonic nebulizer</td>
</tr>
<tr>
<td>Tobramycin (TOBI®)</td>
<td>Pari LC®, Sidestream Plus</td>
</tr>
<tr>
<td>Dornase alfa (Pulmozyme®)</td>
<td>Hudson T Up-draft II, Marquest Acorn® II, Pari LC®, Durable Sidestream®, Pari Baby™</td>
</tr>
<tr>
<td>Pentamadine (NebuPent)</td>
<td>Marquest Respirgard II</td>
</tr>
<tr>
<td>Ribavirin (Virazole®)</td>
<td>Small Particle Aerosol Generator</td>
</tr>
<tr>
<td>Iloprost (Ventavis®)</td>
<td>I-neb Adaptive Aerosol (AAD) System</td>
</tr>
<tr>
<td>Aztreonam (Cayston®)</td>
<td>Altera™ Nebulizer System</td>
</tr>
<tr>
<td>Treprostinil (Tyvaso®)</td>
<td>Tyvaso® Inhalation System</td>
</tr>
</tbody>
</table>

Pneumatic jet nebulizers most commonly used in the hospital or clinic are low-cost, mass-produced, single-patient-use disposable devices. Newer, more efficient nebulizers, however, are more expensive (Table 6). Nebulizer systems may include a nebulizer hand set, compressor or power pack, tubing, and accessories. In general, the compressor or electronics are durable and long-lasting, whereas handsets and accessories require more frequent replacement. Replacement costs are shown in Table 7.

Table 6. Relative costs of different nebulizer systems

<table>
<thead>
<tr>
<th>Nebulizer Type</th>
<th>Approximate Cost Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumatic compressor nebulizer</td>
<td>$50–$150</td>
</tr>
<tr>
<td>Ultrasonic nebulizer</td>
<td>$100–$250</td>
</tr>
<tr>
<td>Vibrating mesh/horn nebulizer</td>
<td>$200–$1,200</td>
</tr>
<tr>
<td>Microprocessor-controlled breath-actuated nebulizer</td>
<td>$750–$2,000</td>
</tr>
</tbody>
</table>

Table 7. Replacement costs of nebulizer components
(Modified, with permission, from Reference 1)

<table>
<thead>
<tr>
<th>Nebulizer Components (Interval)</th>
<th>Approximate Cost Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disposable jet nebulizer (1–7 days in acute care, longer use at home)</td>
<td>$1–3</td>
</tr>
<tr>
<td>Jet nebulizer with bag reservoir (1–3 days)</td>
<td>$4–15</td>
</tr>
<tr>
<td>Jet nebulizer with filter (1–3 days)</td>
<td>$10–12</td>
</tr>
<tr>
<td>Breath-enhanced nebulizer</td>
<td>$4–20</td>
</tr>
<tr>
<td>Breath-actuated jet nebulizer</td>
<td>$4–6</td>
</tr>
<tr>
<td>Ultrasonic nebulizer medication chamber (daily or weekly)</td>
<td>$1–5</td>
</tr>
<tr>
<td>USN handset replacement (3–12 months)</td>
<td>$100–250</td>
</tr>
<tr>
<td>Vibrating mesh replacement (3–12 months)</td>
<td>$40–150</td>
</tr>
</tbody>
</table>

Types of SVNs

Jet Nebulizers

Jet nebulizers are operated by compressed air or oxygen in order to aerosolize liquid medications. They are commonly used because they are the least expensive kind of nebulizer. A
jet nebulizer delivers compressed gas through a jet, causing a region of negative pressure. 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 performance of jet nebulizers is affected by both the technical and patient-related factors described in Table 8.

### Factors Affecting Jet Nebulizer Performance and Drug Delivery

There are many factors for respiratory therapists to keep in mind during aerosol therapy. Nebulizer design determines the size of particle and output performance produced, which results in the ultimate efficiency of medication according to the factors discussed below. Various types of nebulizers are available on the market, and several studies have indicated that performance varies between manufacturers and also between nebulizers from the same manufacturer.\(^1\)\(^,\)\(^,\)\(^3\)\(^3\),\(^3\)\(^4\)

- **Gas Flow and Pressure:** Jet nebulizers are designed to operate by means of varied levels of compressed gas flow and pressure. Each model of jet nebulizer is designed to work best at a specific flow, ranging from 2–8 L/min, which should be listed on the device label. Operating any jet nebulizer at a lower flow or pressure will increase particle size. For example, a jet nebulizer designed to operate at 6–8 L/min at 50 psi will produce larger particles if driven by a compressor producing 13 psi. Consequently, jet nebulizers should be matched with a compressor or gas source that matches their intended design. Gas flow is also inversely related to nebulization time. Using a higher gas flow rate in aerosol therapy will decrease the amount of treatment time needed to deliver the set amount of drug.

- **Fill and Dead Volumes:** Increasing the fill volume is another factor that increases the efficiency of jet nebulizers. These nebulizers do not function well with small fill volumes like 2 mL or less because this is close to dead volume (also termed residual volume). Jet nebulizers do not aerosolize below dead volume; therefore, it is recommended to use a fill volume of 4–5 mL unless the nebulizer is specifically designed for a smaller fill volume.\(^1\)\(^,\)\(^3\)\(^4\) This precaution dilutes the medication, allowing for a greater proportion to be nebulized, though it increases the treatment time. Dead volume, the amount of medication remaining in the jet nebulizer at the end of a treatment, can range from 0.5 to 2.0 mL. The greater the dead volume, the less drug is nebulized.

- **Gas Density:** By a similar offsetting, the density of gas used to run a jet nebulizer can impact aerosol deposition by affecting aerosol output and particle size. For example, delivering aerosol with heliox can increase lung deposition by as much as 50%. Using heliox at the same flow rate as with air or oxygen reduces particle size and aerosol output, ultimately increasing treatment times. Consequently, the flow with heliox should be increased by 1.5–2 times to bring particle size and output back to levels achieved with air or oxygen.

- **Humidity and Temperature:** Humidity and temperature can also affect particle size and residual volume. Specifically, water evaporation during aerosol therapy can reduce

### Table 8. Factors affecting penetration and deposition of therapeutic aerosols delivered by jet nebulizers (Modified, with permission, from Reference 1)

<table>
<thead>
<tr>
<th>Technical Factors</th>
<th>Patient Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design and model of nebulizer</td>
<td>Breathing pattern</td>
</tr>
<tr>
<td>Flow used to power nebulizer</td>
<td>Nose vs. mouth breathing</td>
</tr>
<tr>
<td>Fill volume of nebulizer</td>
<td>Composition of inspired gas</td>
</tr>
<tr>
<td>Solution characteristics</td>
<td>Airway obstruction</td>
</tr>
<tr>
<td>Composition of driving gas</td>
<td>Positive pressure delivery</td>
</tr>
<tr>
<td>Designs to enhance nebulizer output</td>
<td>Artificial airway and mechanical ventilation</td>
</tr>
<tr>
<td>Continuous vs. breath-actuated</td>
<td></td>
</tr>
</tbody>
</table>
the temperature of an aerosol, which results in an increase in solution viscosity and a decrease in the nebulizer output of drug.

- **Breathing Pattern:** Breathing pattern influences aerosol deposition in the lower respiratory tract. The patient should be instructed to do tidal breathing with periodic deep breaths during aerosol therapy.

- **Device Interface:** Medical aerosols can be administered using either a mouthpiece or a face mask. Ideally, a mouthpiece should be used. The nose tends to filter more aerosol than the mouth, so use of a mouthpiece should be encouraged, when appropriate. Mouthpieces cannot be used for infants and small children. In addition, the use of a mouthpiece may be uncomfortable for longer aerosol therapy. Use of a mask increases the amount of aerosol deposited on the face, in the eyes, and into the nose. Whether a mouthpiece or a face mask is used, it is important to instruct the patient to inhale through the mouth during aerosol therapy. Proper mask fit and design can optimize the inhaled dose and reduce deposition to the eyes. The respiratory therapist must keep all of these factors in mind when practicing or equipping patients.

**Types of Pneumatic Jet Nebulizer Designs**

Nebulizer design changes over the past decade have created different nebulizer categories.35,36 There are four different designs of the pneumatic jet nebulizer: jet nebulizer with reservoir tube, jet nebulizer with collection bag or elastomeric reservoir ball, breath-enhanced jet nebulizer, and breath-actuated jet nebulizer. All four of these are depicted in Figure 4 and described below.

**Figure 4.** Different types of pneumatic jet nebulizer designs and their aerosol output indicated by the shaded area: A. pneumatic jet nebulizer with reservoir tube; B. jet nebulizer with collection bag; C. breath-enhanced jet nebulizer; D. breath-actuated jet nebulizer. (From Reference 1, with permission)
A. Jet Nebulizer with a Reservoir Tube: This is the least expensive and most widely used nebulizer. It provides continuous aerosol during inhalation, exhalation, and breath-hold, causing the release of aerosol to ambient air during exhalation and anytime when the patient is not breathing (Figure 4-A). Consequently, only 10–20% of the emitted aerosol is inhaled. In order to decrease drug loss and increase inhaled mass, a t-piece and large bore tubing are attached to the expiratory side of the nebulizer. These types of nebulizers have been considered to be inefficient due to their providing a low percentage of the dose to the patient. Figure 5 illustrates the functioning of a jet nebulizer. Examples of a jet nebulizer with a reservoir tube model include the Sidestream Nebulizers™ (Philips Respironics, Murrysville, PA) and the Micro Mist® (Teleflex Medical, Research Triangle Park, NC).

B. Jet Nebulizer with Collection Bag or Elastomeric Reservoir Ball: These types of nebulizers generate aerosol by continuously filling a reservoir (Figure 4-B). The patient inhales aerosol from the reservoir through a one-way inspiratory valve and exhales to the atmosphere through an exhalation port between the one-way inspiratory valve and the mouthpiece. Figure 6 illustrates the principle of operation and patterns of gas flow during inhalation and exhalation with the Circulaire® (Westmed, Tucson, AZ) which is one model of the nebulizer with a collection bag or elastomeric reservoir ball.
C. Breath-enhanced Jet Nebulizer: Breath-enhanced nebulizers use two one-way valves to prevent the loss of aerosol to environment (Figure 4-C). When the patient inhales, the inspiratory valve opens and gas vents through the nebulizer. Exhaled gas passes through an expiratory valve in the mouthpiece. Figure 7 illustrates the operation principle of the breath-enhanced nebulizer. PARI LC® Plus (PARI, Midlothian, VA), NebuTech® (Salter Labs, Arvin, CA), and SideStream Plus® (Philips Respironics, Murrysville, PA) are the breath-enhanced nebulizers available on the market.

![Figure 7. Schematic illustration of the function of a breath-enhanced jet nebulizer (From Reference 37, with permission)](image)

D. Breath-actuated Jet Nebulizer: Breath-actuated nebulizers are designed to increase aerosol drug delivery to patients by generating aerosol only during inspiration. Consequently, loss of medication during expiration is greatly reduced, as shown in Figure 4-D.37 Whereas breath actuation can increase the inhaled dose by more than three-fold, this efficiency is achieved only by an increase in dosing time. Breath-actuation mechanisms can be classified as manual, mechanical, and electronic:

1. Manual Breath-actuated: The first generation of breath-actuated nebulizers uses a thumb control to regulate aerosol production during inspiration and expiration. Blocking the patient-controlled thumb port directs gas to the nebulizer only during inspiration; releasing the thumb at the port pauses the nebulization (Figure 8). The thumb control breath-actuated nebulizer wastes less of the medication being aerosolized, but it significantly increases the treatment time and requires good hand-breath coordination.

![Figure 8. Schematic illustration of the function of a manual breath-actuated jet nebulizer (From Reference 7, with permission)](image)
2. **Mechanical Breath-actuated:** The AeroEclipse II® (Monaghan Medical Corporation, Plattsburgh, NY) is an example of mechanical breath-actuated nebulizers. As shown in Figure 9, the mechanical breath-actuated nebulizer has a breath-actuated valve that triggers aerosol generation only during inspiration and eliminates the need for a storage bag or reservoir. Patients create an inspiratory force to trigger the nebulizer. Therefore, the sensitivity of this mechanism makes it suitable only for older children and adults.

![Figure 9. Schematic illustration of the function of a mechanical breath-actuated nebulizer (From Reference 37, with permission)](image)

3. **Microprocessor Breath-actuated:** The final type of breath-actuated jet nebulizer is more complex but more appropriate to a wider range of users. In this type, compressor-driven jet nebulizers are actuated by an electronic circuit, commonly triggered by a pressure transducer sensing inspiratory effort. For several decades these devices have been used in pulmonary function and research labs to administer precise boluses of aerosol for methacholine challenge. A newer generation of “smart” microprocessor-controlled breath-actuated nebulizers uses computer programs and sensing technology to control the pattern of aerosol generation and even to calculate and track the delivered dose. The I-neb AAD® system (Philips Respironics) is one model of the microprocessor, breath-actuated that uses vibrating mesh nebulization.

**Ultrasonic Nebulizers**

Ulasonic nebulizers convert electrical energy to high-frequency vibrations using a transducer. These vibrations are transferred to the surface of the solution, creating a standing wave that generates aerosol (Figure 10). Ultrasonic nebulizers were initially introduced as large-volume nebulizers most commonly used to deliver hypertonic saline for sputum inductions. Small-volume ultrasonic nebulizers are now commercially available for delivery of inhaled bronchodilators but should not be used with suspensions such as budesonide. Ultrasonic nebulizers tend to heat medication. This raises concerns about disrupting proteins, but that does not affect commonly inhaled medications. The MicroAir® Ultrasonic Model (Omron Healthcare, Bannockburn, IL) and MABISMist™ II (Mabis Healthcare, Waukegan, IL) are different models of the ultrasonic nebulizer.
Mesh Nebulizers

Mesh nebulizers use electricity to vibrate a piezo (at approximately ~128 KHz) element that moves liquid formulations through a fine mesh to generate aerosol. The diameter of the mesh or aperture determines the size of the particle generated. Mesh nebulizers are very efficient and result in minimal residual volume (0.1–0.5 mL). As seen in Figure 11, mesh nebulizers utilize two basic mechanisms of action: active vibrating mesh and passive mesh.

Active Vibrating Mesh: Active vibrating mesh nebulizers have an aperture plate with 1,000–4,000 funnel-shaped holes vibrated by a piezo-ceramic element that surrounds the aperture plate. The Aeroneb® Go and Solo (Aerogen, Galway, Ireland), Akita II (Inamed, Germany) and eFlow (PARI, Midlothian, VA) are models of the active vibrating mesh nebulizers (Figure 11, left).

Passive Mesh: These types of nebulizers utilize an ultrasonic horn to push fluid through a mesh (Figure 11, right). I-neb® AAD System® (Philips Respironics) and NE-U22 (Omron Healthcare) are models of the passive mesh nebulizer. A third-generation adaptive aerosol delivery (AAD) system such as the I-neb® has a small, battery-powered, lightweight, and silent drug delivery device designed to deliver a precise, reproducible dose of drug.
aerosol is created by a passive mesh, and aerosol is injected into the breath at the beginning of inhalation (Figure 12). The dosage of the drug is controlled through specific metering chambers. The metering chambers can deliver a pre-set volume ranging from 0.25 to 1.7 mL with a residual volume of about 0.1 mL. The I-neb® model incorporates an AAD algorithm that pulses medication delivery into 50–80% of each inspiration, based on a rolling average of the last three breaths. Throughout the treatment, the I-neb® provides continuous feedback to the patient through a liquid crystal display; and upon successful delivery of the treatment, the patient receives audible and tactile feedback.

Figure 12. Adaptive aerosol delivery as provided by the Philips Respironics I-neb®. As illustrated, aerosol is injected into the breath at the beginning of inhalation. (With permission of Respironics)

Nebulizers for Specific Applications

Nebulizer for Ribavirin Administration

The small-particle aerosol generator (SPAG) is a large-volume nebulizer designed solely to deliver aerosolized ribavirin (Virazole®, Valeant Pharmaceuticals, Aliso Viejo, CA) for prolonged periods of nebulization. It consists of a nebulizer and a drying chamber that reduces the MMAD to about 1.3 µm. Because of teratogenic characteristics of ribavirin, a scavenging system is strongly recommended for use during its administration.

Nebulizer for Aerosolized Pentamidine Administration

When administering aerosolized pentamidine, an SVN fitted with inspiratory and expiratory one-way valves and with expiratory filter is used. These valves prevent exposure of secondhand pentamidine aerosol and contamination of the ambient environment with exhaled aerosol.

Continuous Aerosol Therapy

Continuous aerosol drug administration is a safe treatment modality and is used to treat patients suffering acute asthma attack. Researchers reported that it may be as effective as intermittent aerosol therapy or may, in fact, be superior to intermittent nebulization in patients with severe pulmonary dysfunction. Figure 13 illustrates a basic setup for continuous aerosol therapy that includes an infusion pump, a one-way valved oxygen mask, and a reservoir bag. Commercial nebulizers used in continuous nebulization commonly have luer lock ports designed for use with infusion pumps. The nebulization is most commonly administered using standard aerosol masks.
Drug-delivery Technique

Because different types of nebulizers are available on the market, the respiratory therapist should carefully review operation instructions prior to giving aerosol therapy and certainly prior to instructing patients in at-home use. Proper technique is provided in Technique Box 1.

Technique Box 1. Steps for Correct Use of Nebulizers

**Technique for Jet Nebulizers:** When a jet nebulizer is used, the patient should:

1. Assemble tubing, nebulizer cup, and mouthpiece (or mask).
2. Put medicine into the nebulizer cup.
3. Sit in an upright position.
4. Connect the nebulizer to a power source.
5. Breathe normally with occasional deep breaths until sputter occurs or until the end of nebulization.
7. Rinse the nebulizer with sterile or distilled water and allow to air dry.

**Technique for Mesh and Ultrasonic Nebulizers:** When a mesh or ultrasonic nebulizer is used, the patient should:

1. Correctly assemble the nebulizer.
2. If applicable, follow manufacturer’s instructions in performing a functionality test prior to the first use of a new nebulizer as well as 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. Sit in an upright position.
5. Turn on the power.
6. Hold the nebulizer in the position recommended by the manufacturer.
7. Follow the instructions for breathing technique that is recommended by the manufacturer for these uniquely designed mesh and ultrasonic nebulizers.
8. If the treatment must be interrupted, turn off the unit to avoid waste.
9. At the completion of the treatment, disassemble and clean as recommended by the manufacturer.
10. When using a mesh nebulizer, do not touch the mesh during cleaning. This will damage the unit.
11. Once or twice a week, disinfect the nebulizer following the manufacturer’s instructions.
Technique Box 1. Steps for Correct Use of Nebulizers (continued)

General Steps To Avoid Reduced or No Dosing for All Nebulizers: When using nebulizers, the following steps should be used in order to avoid reduced or no dosing during aerosol treatment. The patient should:

1. Read and follow the instructions.
2. Make sure that the nebulizer is properly assembled.
3. Make sure that the nebulizer is cleaned and dried between uses.
4. Make sure that the nebulizer operated in its proper orientation.

Troubleshooting

Problem with Jet Nebulizers: Absent or Low Aerosol

<table>
<thead>
<tr>
<th>Causes</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loose or unattached connections</td>
<td>Check the connections and make sure that they are properly attached.</td>
</tr>
<tr>
<td>Inappropriate flowmeter setting</td>
<td>Check the flowmeter setting and adjust the flow if it is not appropriate.</td>
</tr>
<tr>
<td>Obstruction in the orifice of the jet nebulizer</td>
<td>Check the orifice of the jet nebulizer and clear obstructions when needed.</td>
</tr>
</tbody>
</table>

Problems with Mesh and Ultrasonic Nebulizers: The Unit Does Not Operate

<table>
<thead>
<tr>
<th>Causes</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect battery installation (seen in both mesh and ultrasonic nebulizers)</td>
<td>Check the battery installation and reinstall if needed.</td>
</tr>
<tr>
<td>External power source connection (seen in both mesh and ultrasonic nebulizers)</td>
<td>Check the connections with the AC adapter and the electrical output.</td>
</tr>
<tr>
<td>Overheated unit (seen in ultrasonic nebulizers)</td>
<td>Turn off the unit, wait until it cools down, and restart the unit.</td>
</tr>
<tr>
<td>Incorrect connection of the control module cable (seen in mesh nebulizers)</td>
<td>Check the connections with the control module cable and attach them properly, if needed.</td>
</tr>
<tr>
<td>Malfunctioning electronics (seen in both mesh nebulizers and ultrasonic nebulizers)</td>
<td>Replace the unit.</td>
</tr>
</tbody>
</table>

When Does the Treatment Need To Be Ended?

Nebulizers are commonly used for intermittent short-duration treatments and typically have a set volume of drug formulation placed in the medication reservoirs. The drug remaining in a nebulizer after therapy ranges from 0.1 to 2 mL. Whereas some respiratory therapists and patients tap the nebulizer in order to reduce dead volume and increase nebulizer output, others continue aerosol therapy past the point of sputtering in an effort to decrease dead volume. Some nebulizers will sputter for extended periods of time after the majority of the inhaled dose has been administered. Evidence suggests that after the onset of sputter, very little additional drug is inhaled. Because the time it takes to administer the drug is a critical factor for patient adherence to therapy, some clinicians have adopted recommendations to stop nebulizer therapy at, or one minute after, the onset of sputter. Newer nebulizers may use microprocessors to monitor how much dose has been administered and automatically turn off the nebulizer at the end of each dose.

Cleaning: Please refer to the Infection Control section on pages 48–50 for the cleaning instructions of small-volume nebulizers.
The pressurized metered-dose inhaler and dry-powder inhaler are medical aerosol delivery devices that combine a device with a specific formulation and dose of drug. Each actuation of the inhaler is associated with a single inspiration of the patient. These are typically single-patient-use devices dispensed from the pharmacy with a specific quantity of medication and disposed of when the medication has been depleted.

Inhalers are approved by the FDA Center for Drug Evaluation Research (CDER) as drug and device combinations. They typically are required to go through the complete drug development process from pre-clinical to pivotal trials in hundreds to thousands of patients. Inhaler-based drugs must have reproducible doses (+/- 20) from first to last dose and have a shelf life with drug of at least 12–24 months. Once an inhaler enters the Phase III trials, the design and materials are set and cannot be changed without additional expensive clinical trials.

There is a large variety of inhaler designs, and many drugs are available only in a single inhaler form (Figure 14). Patients are commonly prescribed several types of inhalers with different instructions for operation. Confusion between device operation can result in suboptimal therapy. For example, pMDIs typically require slow inspiratory flow (<30 L/min) with a breath-hold, while a DPI may require significantly high flows (30–90 L/min) based on their resistive properties to disperse a full dose. Patients may confuse which inspiratory flow to use with which device and may get much less drug from both devices. Therefore, education and repetitive return demonstration is the key to proper inhaler use.
**Anticholinergics**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiriva® Handihaler® (tiotropium bromide) Inhalation Powder</td>
<td>Boehringer Ingelheim Pharmaceuticals, Inc.</td>
</tr>
<tr>
<td>Atrovent® HFA (ipratropium bromide HFA) Inhalation Aerosol</td>
<td>Boehringer Ingelheim Pharmaceuticals, Inc.</td>
</tr>
<tr>
<td>Tudorza™ Pressair™ (aclidinium bromide) Inhalation Powder</td>
<td>Forest Pharmaceuticals, Inc.</td>
</tr>
<tr>
<td>Combivent® Respimat (ipratropium bromide and albuterol sulfate) Inhalation Aerosol</td>
<td>Boehringer Ingelheim Pharmaceuticals, Inc.</td>
</tr>
</tbody>
</table>

**β2-Agonists**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foradil® Aerolizer® (formoterol fumarate) Inhalation Powder</td>
<td>Novartis Pharmaceuticals</td>
</tr>
<tr>
<td>Maxair™ Autohaler™ (pirbuterol acetate) Inhalation Aerosol</td>
<td>Graceway Pharmaceuticals</td>
</tr>
<tr>
<td>ProAir® HFA (albuterol sulfate) Inhalation Aerosol</td>
<td>Teva Specialty Pharmaceuticals</td>
</tr>
<tr>
<td>Proventil® HFA (albuterol sulfate HFA) Inhalation Aerosol</td>
<td>3M Pharmaceuticals Inc.</td>
</tr>
<tr>
<td>Arcapta™ Neohaler™ (indacaterol) Inhalation Powder</td>
<td>Novartis Pharmaceuticals</td>
</tr>
<tr>
<td>Xopenex® HFA (levalbuterol tartare) Inhalation Aerosol</td>
<td>Sepracor Inc.</td>
</tr>
<tr>
<td>Ventolin® HFA (albuterol sulfate HFA) Inhalation Aerosol</td>
<td>GlaxoSmithKline</td>
</tr>
</tbody>
</table>

**Corticosteroids**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alvesco® (ciclesonide) Inhalation Aerosol</td>
<td>Nycomed</td>
</tr>
<tr>
<td>Asmanex Twisthaler® (mometasone) Inhalation Powder</td>
<td>Schering Corporation</td>
</tr>
<tr>
<td>Flovent® Diskus® (fluticasone propionate) Inhalation Powder</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>Pulmicort Flexhaler® (budesonide) Inhalation Powder</td>
<td>AstraZeneca LP</td>
</tr>
<tr>
<td>QVAR® (beclomethasone dipropionate) Inhalation Aerosol</td>
<td>Teva Specialty Pharmaceuticals</td>
</tr>
</tbody>
</table>

**β2-Agonist/Corticosteroid Combination**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advair Diskus® (fluticasone propionate and salmeterol) Inhalation Powder</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>Advair® HFA (fluticasone propionate and salmeterol xinafoate) Inhalation Aerosol</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>Dulera® (mometasone furoate/formoterol fumarate dihydrate) Inhalation Aerosol</td>
<td>Merck</td>
</tr>
<tr>
<td>Symbicort® (budesonide and formoterol fumarate dihydrate) Inhalation Aerosol</td>
<td>AstraZeneca</td>
</tr>
</tbody>
</table>

**Other**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relenza® (zanamivir) Inhalation Powder</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>TOBI Podhaler (tobramycin) Inhalation Powder</td>
<td>Novartis Pharmaceuticals</td>
</tr>
</tbody>
</table>
Since its development by Dr. George Maison in 1955, the pMDI has been the most common aerosol generator prescribed for patients with asthma and COPD. This is because it is compact, portable, easy to use, and provides multi-dose convenience in a single device.

**Advantages and Disadvantages of pMDIs**

The pMDI was designed and developed as a drug and device combination that delivers precise doses of specific drug formulations. Unlike nebulizers, drug preparation and handling is not required with pMDIs, and the internal components of pMDIs are difficult to contaminate. Table 9 gives the advantages and disadvantages associated with the use of pMDIs.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portable, light, and compact</td>
<td>Hand-breath coordination required</td>
</tr>
<tr>
<td>Multiple dose convenience</td>
<td>Patient activation, proper inhalation pattern, and breath-hold required</td>
</tr>
<tr>
<td>Short treatment time</td>
<td>Fixed drug concentrations and doses</td>
</tr>
<tr>
<td>Reproducible emitted doses</td>
<td>Reaction to propellants in some patients</td>
</tr>
<tr>
<td>No drug preparation required</td>
<td>Foreign body aspiration from debris-filled mouthpiece</td>
</tr>
<tr>
<td>Difficult to contaminate</td>
<td>High oropharyngeal deposition</td>
</tr>
<tr>
<td>Difficult to determine the dose remaining in the canister without dose counter</td>
<td></td>
</tr>
</tbody>
</table>

**Types of pMDIs**

There are three major types of pMDIs: conventional pMDIs, breath-actuated pMDIs, and soft-mist inhalers. Regardless of manufacturer or active ingredient, the basic components of the pMDI include the canister, propellants, drug formulary, metering valve, and actuator. The characteristics of each pMDI component are described in Table 10.

<table>
<thead>
<tr>
<th>Component</th>
<th>Particulars</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canister</td>
<td>Inert, able to withstand high internal pressures and utilize a coating to prevent drug adherence</td>
</tr>
<tr>
<td>Propellants</td>
<td>Liquefied compressed gases in which the drug is dissolved or suspended</td>
</tr>
<tr>
<td>Drug Formulary</td>
<td>Particulate suspensions or solutions in the presence of surfactants or alcohol that allocate the drug dose and the specific particle size</td>
</tr>
<tr>
<td>Metering Valve</td>
<td>Most critical component that is crimped onto the container and is responsible for metering a reproducible volume or dose</td>
</tr>
<tr>
<td>Elastomeric valves for sealing and preventing drug loss or leakage</td>
<td></td>
</tr>
<tr>
<td>Actuator</td>
<td>Frequently referred to as the “boot,” partially responsible for particle size based on the length and diameter of the nozzle for the various pMDIs (Each boot is unique to a specific pMDI/drug)</td>
</tr>
<tr>
<td>Dose Counter</td>
<td>This component provides a visual tracking of the number of doses remaining in the pMDI</td>
</tr>
</tbody>
</table>
Conventional pMDI

As seen in Figure 15, the pMDI consists of a canister, the medication, the propellant/excipient, a metering valve, the mouthpiece, and actuator. The medication represents only 1–2% of the mixture emitted from the pMDI and is either suspended or dissolved in the propellant/excipient mixture. The propellant of the pMDI makes up 80% of the mixture. A surface-active agent, such as surfactant, is occasionally used in order to maintain suitable particle sizes produced in the aerosol plume by chlorofluorocarbon (CFC) pMDIs. These agents prevent aggregation of the drug particles and lubricate the metering valve. They also ensure that the drug is well suspended in the canister. The metering valve acts to prepare a pre-measured dose of medication along with the propellant. The volume of the metering valve changes from 25–100 µL and provides 50 µg to 5 mg of drug per actuation, depending on the drug formulation.

![Figure 15. Standard components of pMDI (Modified with permission from Reference 42)](image)

The conventional pMDI has a press-and-breathe design. Depressing the canister into the actuator releases the drug-propellant mixture, which then expands and vaporizes to convert the liquid medication into an aerosol. The initial vaporization of the propellant cools the aerosol suspension. The canister aligns the hole in the metering valve with the metering chamber when it is pressed down. Then, the high propellant vapor pressure forces a pre-measured dose of medication out of this hole and through the actuator nozzle. Last, releasing the metering valve refills the chambers with another dose of the drug-propellant mixture.

The two types of propellants used with pMDIs are CFCs and HFAs. Because of CFCs' detrimental effect on the earth’s ozone layer and contributions to global warming, CFCs were banned worldwide. As a replacement, HFAs were developed and incorporated into pMDIs. HFAs are pharmacologically inert and have similar characteristics to CFCs. However, there are some important differences between CFC and HFA propellants. For example, CFCs use surfactant for dispersion; HFAs do not contain surfactant and use alcohol for this purpose. Figure 16 shows the spray differences between HFA pMDIs and CFC pMDIs. HFA pMDIs (Figure 16, left) have a softer spray than CFC pMDIs (Figure 16, right). Also, HFA pMDIs have a much warmer spray temperature than CFC pMDIs. Due to the cold mist from a pMDI, inhalation may be interrupted by patient sensitivity. Although the more widespread use of pMDI HFAs will overcome the issues associated with the use of pMDI CFCs, including priming, temperature effects, tail-off, and plume geometry, clini-
Clinicians must still understand the differences in characteristics between CFC and HFA pMDIs at the present time (Table 11). Clinicians should be sure to explain to their patients how the feel and taste of the HFA pMDI will be different from that of the CFC pMDI and justify their means of use accordingly.

![Figure 16. Spray differences between HFA pMDI (left) and CFC pMDI (right) (From New York Times, with permission)](image)

| Table 11. Differences in characteristics between CFC and HFA pMDIs (From Reference 1, with permission) |
|-------------------------------------------------|-------------------|-------------------|
| Physical Component                              | CFC               | HFA               |
| Dose Delivery                                   | Variable          | Consistent        |
| From a near-empty canister                      | Variable          | Consistent (to -20°C) |
| With variable ambient temperature               |                   |                   |
| Spray                                           |                   |                   |
| Force                                           | Higher impaction  | Lower (3 times)   |
| Temperature                                     | Colder            | Warmer            |
| Volume                                          | Higher            | Lower             |
| Taste                                           | Different from HFA| Different from CFC|
| Breath-hold                                     | Less important    | More important    |
| Priming                                         | Important following short period of nonuse | Longer time of nonuse allowed without priming |

**Breath-actuated pMDI**

The Autohaler™ (Graceway Pharmaceuticals, Bristol, TN) was the first flow-triggered breath-actuated pMDI. It was designed to eliminate the need for hand-held coordination during drug administration. Its mechanism is triggered by inhalation through a breath-actuated nozzle, which provides an automatic response to the patient’s inspiratory effort. In order to cause drug release with the Autohaler™, the lever on top of the device must be raised before use. Thereby, the vane of the device releases the spring, pushing the canister down and actuating the pMDI at the point when the patient’s inspiratory effort exceeds 30 L/min. Nozzle size, cleanliness, and lack of moisture are the three most important factors affecting the amount of drug delivered by breath-actuated pMDIs. If the patient has good coordination with the conventional pMDI, the use of a breath-actuated pMDI may not improve drug delivery. Nonetheless, studies have proven that breath-actuated pMDIs improve the delivery of inhaled medication in patients with poor coordination. It must be noted that the Autohaler™ uses CFC and will be removed from market December 31, 2013. Figure 17 shows the standard components of the Autohaler™.
**Soft-Mist pMDI**

The Respimat® (Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT) is a propellant-free soft-mist inhaler. The Respimat® utilizes mechanical energy in the form of a tensioned spring to generate the soft aerosol plume. The energy from turning the transparent base to the right one-half turn draws a predetermined metered volume of solution from the medication cartridge through a capillary tube into a micro-pump. When the dose release button is depressed, the energy from the spring forces solution to the mouthpiece, creating a soft aerosol plume that lasts approximately 1.5 seconds. Similar to pMDIs, the Respimat® will need to be primed before use and at times when the device has had no use. If not used for more than 3 days, actuate the inhaler once. After more than 21 days of no use, it is recommended to actuate the device until aerosol is seen, then actuate 3 more times. Since the device is propellant free, there is no need to shake it. The Respimat® has a dose indicator and will lock once all medication is used. Figure 18 shows the standard components of the Respimat®.

*Figure 18. Soft-mist inhaler*
Currently Available pMDI Formulations

A number of aerosol formulations are available for use in pMDIs today (Figure 14). Pressurized metered-dose inhalers are presently used to administer beta-2 agonists, anticholinergics, anticholinergic/beta-2 agonist combinations, corticosteroids, and anti-asthmatic drugs.

Factors Affecting pMDI Performance and Drug Delivery

Most pMDIs are designed to deliver a drug dose of 100 µm per actuation. Just like other aerosol generators, drug delivery with the pMDIs is approximately 10–20% of the nominal dose per actuation. The particle size of aerosols produced by the pMDIs is in the fine particle fraction range in which the aerodynamic diameter of aerosols is less than 5 µm. Several factors influence the pMDI performance and aerosol drug delivery. Understanding the effects of these factors will improve the efficacy of pMDIs when used for patients with pulmonary diseases. Therefore, both respiratory therapists and patients must actively control the following effects.

- **Shaking the Canister:** Not shaking a pMDI canister that has been standing overnight decreases total and respirable dose by 25% and 35%, respectively, because the drugs in pMDI formulations are usually separated from the propellants when standing. Therefore, pMDIs must be shaken before the first actuation after standing in order to refill the metering valve with adequately mixed suspension from the canister.

- **Storage Temperature:** Outdoor use of pMDIs in very cold weather may significantly decrease aerosol drug delivery. For example, although dose delivery from CFC pMDIs decreased by 70% at 10ºC, it was constant with HFA pMDIs over the range of -20º to 20ºC.

- **Nozzle Size and Cleanliness:** The amount of medication delivered to the patient is dependent upon nozzle size, cleanliness, and lack of moisture. Actuator nozzle is pMDI specific, and the coordination of the nozzle with the medication will influence both inhaled dose and particle size. In general, there is an inverse relationship between the inner diameter of the nozzle extension and the amount of drug delivered to the patient. White and crusty residue due to crystallization of medication may influence drug delivery. Therefore, the nozzle should be cleaned periodically based on the manufacturer’s recommendations.

- **Timing of Actuation Intervals:** The rapid actuation of more than two puffs with the pMDI may reduce drug delivery because of turbulence and the coalescence of particles. A pause between puffs may improve bronchodilation, especially during asthma exacerbations with episodes of wheezing and poor control of symptoms. In other cases, such as in the day-to-day management of preadolescents with a beta agonist (terbutaline) and a corticosteroid (budesonide), pauses between puffs have not been found to be beneficial. Although early research was mixed regarding the importance of a pause between the two actuations, recent literature suggests a pause of one minute between actuations for effective aerosol therapy.

- **Priming:** Priming is releasing one or more sprays into the air. Initial and frequent priming of pMDIs is required in order to provide an adequate dose. The drug may be separated from the propellant and other ingredients in the canister and metering valve when the pMDI is new or has not been used for awhile. Because shaking the pMDI will mix the suspension in the canister but not the metering chamber, priming of the pMDI is required. Table 12 provides the recommended guidelines for priming the various pMDIs available on the market.
Table 12. Priming requirements for commercially available pMDIs
(Modified, with permission, from Reference 1)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Time to Prime</th>
<th>No. of Sprays</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-acting Bronchodilators</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol Sulfate HFA</td>
<td>ProAir HFA®</td>
<td>New and when not used for 2 weeks</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Proventil® HFA</td>
<td>New and when not used for 2 weeks</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Ventolin® HFA</td>
<td>New and when not used for 14 days</td>
<td>4</td>
</tr>
<tr>
<td>Pirbuterol</td>
<td>Maxair Autohaler™</td>
<td>New and when not used for 2 days</td>
<td>2</td>
</tr>
<tr>
<td>Levalbuterol HCl</td>
<td>Xopenex HFA™</td>
<td>New and when not used for 3 days</td>
<td>4</td>
</tr>
<tr>
<td>Ipratropium Bromide HFA</td>
<td>Atrovent HFA®</td>
<td>New and when not used for 3 days</td>
<td>2</td>
</tr>
<tr>
<td>Ipratropium Bromide/Albuterol Sulfate Combination</td>
<td>Combivent® HFA</td>
<td>New and when not used for 24 hours</td>
<td>3</td>
</tr>
<tr>
<td><strong>Inhaled Corticosteroids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beclomethasone Propionate HFA</td>
<td>QVAR™</td>
<td>New and when not used for 10 days</td>
<td>2</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>Alvesco®</td>
<td>New and when not used for 10 days</td>
<td>3</td>
</tr>
<tr>
<td>Fluticasone Propionate</td>
<td>Flovent® HFA</td>
<td>New</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not used more than 7 days or if dropped</td>
<td>1</td>
</tr>
<tr>
<td><strong>Combination Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide combined with Formoterol</td>
<td>Symbicort® HFA</td>
<td>New and not used more than 7 days or if dropped</td>
<td>2</td>
</tr>
<tr>
<td>Fluticasone combined with Salmeterol</td>
<td>Advair HFA®</td>
<td>New</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not used more than 4 weeks or if dropped</td>
<td>2</td>
</tr>
</tbody>
</table>

- **Characteristics of the Patient**: Characteristics of the patient using the pMDI will result in a variability of aerosol deposition. For example, aerosol deposition will be lower in infants and children due to differences in their anatomy and their physical and cognitive abilities.

- **Breathing Techniques**: There are two primary techniques for using a pMDI without a spacer: the open-mouth technique and the closed-mouth technique. The manufacturers of pMDIs universally recommend the closed-mouth technique for using a pMDI. In this method, the mouthpiece of the boot is placed between the sealed lips of the patient dur-
ing drug administration. On the other hand, some researchers and clinicians have advocated an open-mouth technique in an attempt to reduce oropharyngeal deposition and increase lung dose. The open-mouth technique is recommended when the pMDI CFCs are administered. When using the open-mouth technique, the inhaler is placed two finger widths away from the lips of an open mouth and aimed at the center of the opening of the mouth. Studies suggest that the open-mouth technique reduces unwanted oropharyngeal deposition by allowing aerosol plume more distance to slow down before reaching the back of the mouth and up to two-fold more drug deposition to the lung than with use of the closed-mouth technique. In contrast, other researchers suggest that the open-mouth technique does not offer any advantage over the closed-mouth technique, but that it does create additional hazards such as the aerosol plume being misdirected from the mouth and into the eye or elsewhere. Therefore, the best technique should be determined based on the patient’s physical abilities, coordination, and preference. If the patient is well coordinated and can master the open-mouth technique better, it can be used by following the directions below. Also, the patient’s aerosol administration technique should be observed continuously and corrected when appropriate. Proper technique is provided in Technique Box 2.

**Drug-delivery Technique**

Because different types of pMDIs are available on the market, the respiratory therapist should carefully review operation instructions prior to giving aerosol therapy and certainly prior to instructing patients in at-home use. Proper technique is provided in Technique Box 2.

**Technique Box 2. Steps for Correct Use of pMDIs**

**Techniques for pMDIs**

**Open-mouth Technique:** The patient should be instructed to:

1. Warm the pMDI canister to hand or body temperature.
2. Remove the mouthpiece cover and shake the pMDI thoroughly.
3. Prime the pMDI into the air if it is new or has not been used for several days.
4. Sit up straight or stand up.
5. Breathe all the way out.
6. Place the pMDI two finger widths away from their lips.
7. With mouth open and tongue flat (tip of tongue touching inside of their lower front teeth), tilt outlet of the pMDI so that it is pointed toward the upper back of the mouth.
8. Actuate the pMDI as she/he begins to breathe in slowly.
9. Breathe slowly and deeply through the mouth and hold their breath for 10 seconds. If she/he cannot hold their breath for 10 seconds, then for as long as possible.
10. Wait one minute if another puff of medicine is needed.
11. Repeat Steps 2–10 until the dosage prescribed by the physician is reached.
12. If taking a corticosteroid, she/he should rinse their mouth after the last puff of medicine, spit out the water, and not swallow it.
13. Replace the mouthpiece cover on the pMDI after each use.

**Closed-mouth Technique:** The patient should be instructed to:

1. Warm the pMDI canister to hand or body temperature.
2. Remove the mouthpiece cover and shake the inhaler thoroughly.
3. Prime the pMDI into the air if it is new or has not been used for several days.
4. Sit up straight or stand up.
5. Breathe all the way out.
6. Place the pMDI between their teeth; make sure that their tongue is flat under the mouthpiece and does not block the pMDI.
7. Seal their lips.
8. Actuate the pMDI as they begin to breathe in slowly.
Technique Box 2. Steps for Correct Use of pMDIs (continued)

Closed-mouth Technique: (continued)
9. Hold their breath for 10 seconds. If they cannot hold their breath for 10 seconds, then for as long as possible.
10. Wait one minute if another puff of medicine is needed.
11. Repeat Steps 2–10 until the dosage prescribed by the patient’s physician is reached.
12. If taking a corticosteroid, she/he should rinse the mouth after the last puff of medicine, spit out the water and not swallow it.
13. Replace the mouthpiece cover on the pMDI after each use.

Breath-actuated pMDI (Autohaler™) Technique: When using the Autohaler™, the patient should be instructed to:
1. Warm the pMDI canister to hand or body temperature.
2. Remove the mouthpiece cover and check for foreign objects.
3. Keep the Autohaler™ in a vertical position while the arrow points up, and do not block the air vents.
4. Prime the Autohaler™ into the air if it is new or has not been used recently.
5. Push the lever up.
6. Push the white test fire slide on the bottom of the mouthpiece for priming the Autohaler™.
7. Push the lever down in order to release the second priming spray.
8. Return the lever to its down position and raise the lever so that it snaps into place.
9. Sit up straight or stand up.
10. Shake the Autohaler™ three or four times.
11. Breathe out normally, away from the Autohaler™.
12. Place the pMDI between their teeth. Make sure that their tongue is flat under the mouthpiece and does not block the pMDI.
13. Seal their lips around the mouthpiece.
15. Pay attention to the click sound and the feel of a soft puff when the Autohaler™ triggers the release of medicine.
16. Continue to inhale until the lungs are full.
17. Remove the mouthpiece from the mouth.
18. Hold breath for 10 seconds or as long as possible.
19. Repeat steps above until the dosage prescribed by the patient’s physician is reached.
20. Replace the mouthpiece cover and make sure the lever is down.

Soft Mist pMDI (Respimat™) Technique: When using the Respimat™, the patient should be instructed to:
Preparation:
1. With the orange cap closed, press the safety catch while pulling off the clear base. Be careful not to touch the piercing element located inside the bottom of the clear base.
2. Push the narrow end of the cartridge into the inhaler. The base of the cartridge will not sit flush with the inhaler. About 1/8 of an inch will remain visible when the cartridge is correctly inserted.
3. The cartridge can be pushed against a firm surface to ensure it is correctly inserted.
4. Do not remove the cartridge once it has been inserted into the inhaler.
5. Write the discard by date on the label of the inhaler. The discard by date is 3 months from the date the cartridge is inserted.
6. Put the clear base back into place. Do not remove the clear base again. The inhaler should not be taken apart after they have inserted the cartridge and put the clear base back.

Priming
7. Hold the inhaler upright with the orange cap closed to avoid accidental release of dose.
8. Turn the clear base in the direction of the white arrows on the label until it clicks (half a turn).
9. Flip the orange cap until it snaps fully open.
Technique Box 2. Steps for Correct Use of pMDIs (continued)

10. Point the inhaler toward the ground. Press the dose-release button. Close the orange cap.
11. Repeat steps 5, 6, and 7 until a spray is visible.
12. Once the spray is visible, repeat steps 5, 6, and 7 three more times to make sure the inhaler is ready for use.

Patient-use Instructions:
1. Hold the inhaler upright with the orange cap closed to avoid accidental release of dose.
2. Turn the clear base in the direction of the white arrows on the label until it clicks (half turn).
3. Flip the orange cap until it snaps fully open.
4. Breathe out slowly and fully, and then close lips around the end of the mouthpiece without covering the air vents.
5. Point inhaler toward the back of mouth.
6. While taking in a slow, deep breath through the mouth, press the dose-release button and continue to breathe in slowly for as long as possible.
7. Hold breath for 10 seconds or for as long as comfortable.
8. Close the orange cap until next prescribed dose.

General Steps To Avoid Reduced or No Dosing for pMDIs: When using pMDIs, the following steps should be used in order to avoid reduced or no dosing during aerosol treatment. The patient should:
1. Remove the cap of the pMDI from the boot.
2. Prime as directed (Table 12).
3. Clean and dry the boot of the pMDI based on the manufacturer’s guidelines.
4. Track remaining doses.

Troubleshooting: Problem with the pMDI: Absent or Low Aerosol

<table>
<thead>
<tr>
<th>Causes</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect pMDI assembly</td>
<td>Check the assembly and reassemble when needed.</td>
</tr>
<tr>
<td>Incorrect pMDI and spacer assembly</td>
<td>Check the assembly of the pMDI/spacer and reassemble if needed.</td>
</tr>
<tr>
<td>Empty the pMDI</td>
<td>Check the dose counter or daily log sheet to ensure there is enough medicine in the canister. Otherwise, replace the pMDI.</td>
</tr>
</tbody>
</table>

How To Know the pMDI Is Empty: Since their introduction in the 1950s, pMDIs have not been packaged with dose counters that allow patients to determine when a pMDI should be discarded.55-57 After the pMDI delivers the number of puffs stated on their label, it may look, taste, and feel like it is still working, but the dose delivered may be very low. This “tailing off effect” may last long after the pMDI is “empty of drug.”13,58 Also, the pMDI without a dose counter could lead to waste if the inhaler is discarded prematurely. Indirect methods such as floating the canister in water are misleading and can reduce the ability of the pMDI to work properly.57,59,60 Therefore, they should not be used to determine the amount of medication remaining in the canister.

The only reliable method to determine the number of doses remaining in a pMDI is counting the doses given either manually or with a dose counter. Manual methods include reading the label to determine the total number of doses available in the pMDI and using a log to indicate every individual actuation given (including both priming and therapy doses). This tally is subtracted from the number of actuations on the label until all have been used. At that time, the pMDI should be properly discarded. Unfortunately, manually counting
doses may be impractical and undependable, especially in patients who use reliever medications on the go.

Therefore, the U.S. Department of Health and Human Services FDA requires new pMDIs to have integrated dose counters and recommends that all pMDIs have dose counting devices that indicate when the pMDI is approaching its last dose.\textsuperscript{61} The dose counter is a counting device attached to the top of the pMDI canister or to the boot of the device. When the pMDI is actuated, it counts down the number of actuations from the total remaining in the canister. The Ventolin\textsuperscript{R} HFA (GlaxoSmithKline, Research Triangle Park, NC) and Flovent\textsuperscript{R} HFA (GlaxoSmithKline) have built-in dose counters (Figure 19).

Also, mechanical or electronic dose counters have been available from third parties for use by attachment to a range of pMDIs. Although research has confirmed acceptable performance and patient satisfaction by pMDIs with dose counters,\textsuperscript{62-64} care must be taken to assure that a third-party dose counter works with the specific pMDI being used.\textsuperscript{18,65} Some of the built-in counters may not fit the spacer, and improper fit to the canister may interfere with proper actuation, resulting in no or partial drug being emitted and in a miscount of remaining doses.\textsuperscript{65} Using a third-party dose-counting device increases the cost of aerosol therapy, which may limit their wide acceptance. Figure 20 shows currently available pMDI dose counters in the United States.

With any third-party counter, read the product label and accompanying package information for each pMDI before use and follow the manufacturer's recommended doses. When attempting to keep track of the number of puffs remaining in the pMDI, the following steps should be taken:
Without Dose Counter: The user should:
1. Determine the number of puffs that the pMDI has when it is full.
2. Calculate how long the pMDI will last by dividing the total number of puffs in the pMDI by the total puffs used (for a total of eight puffs per day). This canister will last 25 days (200 divided by 8 = 25 days). Also remember that the medication will run out sooner if the pMDI is used more often than planned.
3. Identify the date that the medication will run out and mark it on the canister or on the calendar.
4. Keep track of how many puffs of medicine administered on a daily log sheet and subtract them to determine the amount of medication left in the pMDI.
5. Keep the daily log sheet in a convenient place such as bathroom mirror.
6. Replace the pMDI when all of the puffs have been administered.

With Dose Counter: The user should:
1. Determine how many puffs of medicine that the pMDI has when it is full.
2. Track the pMDI actuations used and determine the amount of medication left in the pMDI by checking the counter display.
3. Learn to read the counter display. Each dose counter has a specific way of displaying doses remaining in the canister. For example, turning red indicates that the number of actuations is less than 20 puffs and it is time to refill the pMDI. Reading the manufacturer’s guidelines to interpret the counter display is recommended before its use.
4. When the last dose is dispensed, properly dispose of the pMDI.

Cleaning: Please refer to the Infection Control section on page 48 for the cleaning instructions for inhalers.
Metered-dose inhaler accessory devices were designed to overcome the difficulties experienced when using a pMDI and are available in different forms and sizes.

**Advantages and Disadvantages of pMDI Inhaler Accessory Devices**

The use of these devices improves the effectiveness of aerosol therapy and reduces oropharyngeal deposition by adding volume and space between the metering valve and the patient’s mouth. They overcome problems with hand-breath coordination. Table 13 lists both advantages and disadvantages seen with valved holding chambers (VHCs) and spacers used in conjunction with pMDIs.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced oropharyngeal drug impaction and loss</td>
<td>Large and cumbersome compared to the pMDI alone</td>
</tr>
<tr>
<td>Increased inhaled drug by two to four times</td>
<td>More expensive and bulky than a pMDI alone</td>
</tr>
<tr>
<td>Allows use of the pMDI during acute airflow</td>
<td>Some assembly may be needed</td>
</tr>
<tr>
<td>obstruction with dyspnea</td>
<td>Patient errors in firing multiple puffs into chamber prior to inhaling or there is a delay between actuation and inhalation</td>
</tr>
<tr>
<td>No drug preparation required</td>
<td>Possible contamination with inadequate cleaning</td>
</tr>
<tr>
<td>Simplifies coordination of pMDI actuation and inhalation</td>
<td></td>
</tr>
</tbody>
</table>

While the term *spacer* is used in clinical practice 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 which adds space and volume between the pMDI and mouth with no one-way valves to contain the aerosol plume after pMDI actuation. A holding chamber (valved holding chamber) is an extension spacer device with one-way valve(s) to contain the aerosol until inhaled and direct exhalation away from the aerosol in the chamber, reducing aerosol losses with poor hand-breath coordination. 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 chambers/spacers are less than 200 mL. Direction of spray may vary between forward (toward the mouth) and reverse (away from the mouth). The AeroChamber® (Monaghan Medical Corporation), OptiChamber Diamond® and the OptiChamber® Advantage (Philips Respironics) are examples of forward sprays. The ACE® Aerosol Cloud Enhancer (Smiths Medical, Dublin, OH) is an example of reverse spray. Some holding chambers/spacers accept the manufacturer’s mouthpiece-actuator (the boot), while others have a nozzle receptacle for accepting only the canister. As an example, the ACE® has a canister nozzle receptacle, while the AeroChamber®, OptiChamber Advantage® and OptiChamber Diamond® have malleable openings to accept the pMDI mouthpiece. While boots are designed specific to each pMDI, the canister nozzles vary and may not fit any one specific nozzle receptacle, reducing drug efficacy. Figure 21 shows examples of spacers and holding chambers.
Spacers

The use of a spacer with pMDIs should produce at least an equivalent inhaled dose and clinical effect to that of a correctly used pMDI alone. A spacer provides additional volume that slows the aerosol velocity from a pMDI, 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 require removal of the inhaler canister from the manufacturer’s actuator and incorporation into a special orifice on the spacer. It is important to understand that dose delivery can be affected in some spacer designs if the device does not fit the pMDI properly or if the design uses a special orifice or actuator incorporated into the spacer itself. Occasionally, clinicians or patients construct homemade holding chambers from plastic containers (e.g., soda bottle) or other devices (e.g., toilet paper roll). These may function as a spacer and provide protection against reduced dose with pMDI actuation before inhalation, but they do not protect against actuation during exhalation. Also, their performance is variable, so they should not be considered as suitable replacements for a commercially available spacer.

Valved Holding Chambers

A valved holding chamber (VHC) 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 pMDI actuation into the chamber. Time delays can significantly reduce the available dose for inhalation from a VHC. The one-way valve should have a low resistance so that it opens easily with minimal inspiratory effort. Valves placed between the chamber and the patient also act as an impaction point, further reducing oropharyngeal deposition. 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 VHC through a face mask for a single pMDI actuation. In this case, the VHC should incorporate one-way valves for both inhalation and exhalation to decrease rebreathing and avoid blowing aerosol from the chamber. A VHC with mouthpiece costs as little as $15–$20, and a static-free device with mask can cost as much as $50–$60.
Drug-delivery Technique

While spacers and VHCs provide many benefits for optimal drug delivery with pMDIs, there are also potential problems with their use (Table 13). 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 pMDI, 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 (mechanical dead space), and crying are problematic. Proper technique is provided in Technique Box 3.

Cleaning: Please refer to the Infection Control section on page 48 for cleaning instructions for the pMDI chamber and collapsible bag device.

Technique Box 3. Steps for Correct Use of pMDI with Spacer/VHC

Technique for pMDIs with Spacer/VHC: The patient should be instructed to:
1. Warm the pMDI canister to hand or body temperature.
2. Remove the mouthpiece cover and shake the inhaler thoroughly.
3. Prime the pMDI into the air if it is new or has not been used for several days.
4. Assemble the apparatus and check for foreign objects.
5. Keep the canister in a vertical position.
6. Sit up straight or stand up.
7. Breathe all the way out.
8. Follow the instructions below based on the type of device interface used:
   With the mouthpiece:
   a. Place the mouthpiece of the spacer between their teeth. Make sure that their tongue is flat under the mouthpiece and does not block the pMDI and seal their lips.
   b. Actuate the pMDI as they begin to breathe in slowly. Also make sure to inhale slowly if the device produces a “whistle” indicating that inspiration is too rapid.
   c. Move the mouthpiece away from the mouth and hold their breath for 10 seconds. If they cannot hold their breath for 10 seconds, then hold for as long as possible.
   With the mask:
   d. Place the mask completely over the nose and mouth and make sure it fits firmly against the face.
   e. Hold the mask in place and actuate the pMDI as they begin to breathe in slowly. Also make sure to inhale slowly if the device produces a “whistle” indicating that inspiration is too rapid.
   f. Hold the mask in place while the child takes six normal breaths (including inhalation and exhalation), then remove the mask from the child's face.
9. Wait 15–30 seconds if another puff of medicine is needed.
10. Repeat steps above until the dosage prescribed by the patient’s physician is reached.
11. If taking a corticosteroid, rinse the mouth after the last puff of medicine, spit out the water, and do not swallow it.
12. Replace the mouthpiece cover on the pMDI after each use.

General Steps To Avoid Reduced or No Dosing for pMDIs with Spacer/VHC: When using pMDIs with spacer or VHC, the following steps should be taken to avoid reduced or no dosing during aerosol treatment. The patient should:
1. Assure proper fit of the pMDI to the spacer or VHC.
2. Remove cap from the pMDI boot.
3. Clean and reassemble the pMDI spacers and VHCs based on the manufacturers’ instructions.
Dry-powder inhalers (DPIs) are portable, inspiratory flow-driven inhalers that administer dry-powder formulations to the lungs. DPIs do not contain propellant and are breath-actuated. The patient’s inspiratory effort, both their inspiratory flow rate and the volume inhaled, creates the energy to disaggregate the small drug particles from larger carrier particles and disperse the particles as aerosol emitted from the device. DPIs coordinate release of the drug with the act of inhalation. They have been developed to overcome the difficulties of using metered-dose inhalers and are often prescribed with the hope of providing the patient with an overall more user-friendly and predictable therapy.

**Advantages and Disadvantages of DPIs**

Dry-powder inhalers have both advantages and disadvantages as seen in Table 14. Because they do not require hand-held coordination, the patient’s inspiratory flow should be adequate enough to draw the drug from the device. It is important that the patient understands how the DPI works and how it should be used. For example, the patient should know that they should not exhale into the device. This will prevent the introduction of ambient humidity into the mouthpiece and the resulting negative effect to the medication. Such precautions and others explored in greater detail below, should be considered by clinicians when prescribing a DPI for individual patients and when performing follow-up evaluations of patient success with a DPI.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small and portable</td>
<td>Dependence on patient’s inspiratory flow</td>
</tr>
<tr>
<td>Built-in dose counter</td>
<td>Patient less aware of delivered dose</td>
</tr>
<tr>
<td>Propellant free</td>
<td>Relatively high oropharyngeal impaction</td>
</tr>
<tr>
<td>Breath-actuated</td>
<td>Vulnerable to ambient humidity or exhaled humidity into</td>
</tr>
<tr>
<td></td>
<td>mouthpiece</td>
</tr>
<tr>
<td>Short preparation and administration time</td>
<td>Limited range of drugs</td>
</tr>
<tr>
<td></td>
<td>Different DPIs with different drugs</td>
</tr>
<tr>
<td></td>
<td>Easy for patient to confuse directions for use with other devices</td>
</tr>
</tbody>
</table>

**Types of DPIs**

Currently, DPIs can be classified into three categories based on the design of their dose containers, i.e., single-dose DPIs, multiple unit-dose DPIs, and multiple-dose DPIs (Figure 22). While the single-dose DPIs have individually wrapped capsules that contain a single-dose of medication, multiple unit-dose DPIs disperse individual doses that are premetered into blisters of medication by the manufacturer. The third type, the multiple-dose DPI, either measures the dose from a powder reservoir or uses blister strips prepared by the manufacturers to deliver repeated doses. Regardless of the type of DPI, they all have the same essential components incorporated with the inhaler. They all have a drug holder, an air inlet, an agglomeration compartment, and a mouthpiece. The design of these components allows DPIs to induce sufficient turbulence and particle-to-particle collision that detaches particles from their carrier surface and deagglomerates larger particles into smaller particles.
**Single-dose DPIs**

Single-dose DPIs operate by evacuating powder medication from a punctured capsule. The Aerolizer® (Schering-Plough, Kenilworth, NJ) and the HandiHaler® (Boehringer Ingleheim) are examples of the single-dose DPIs (Figure 22). While the Aerolizer® is used for the delivery of formoterol, the HandiHaler® is utilized for the administration of tiotropium bromide. Although the Aerolizer® and HandiHaler® have different configurations, their principle of operation is similar. When using a single-dose DPI, the user places each capsule into the drug holder. Then, the user must prime the device by piercing the single-dose capsule and allowing entrainment of air into the device for dispersion with inhalation. The primary disadvantage of single-dose DPIs is the time needed to load a dose for each use. Also, patients should be instructed not to eat the capsules.

**Multiple Unit-dose DPIs**

The Diskhaler® (GlaxoSmithKline) is an example of the multiple unit-dose DPI. It is used for the administration of zanamivir through a rotating wheel that contains a case with four or eight blisters of medication. Each blister is mechanically punctured when the cover is lifted, allowing the medication to be inhaled through the mouth. When using the Diskhaler®, the inspiratory flow rate should be greater than 60 L/min to achieve an adequate drug deposition into the lungs.

**Multiple-dose DPIs**

Multiple-dose DPIs measure doses from a powder reservoir or disperse individual doses through pre-metered blister strips. The most common types of multi-dose DPIs include the Twiskhaler® (Schering-Plough), the Flexhaler® (AstraZeneca, Wilmington, DE) and the Diskus® (GlaxoSmithKline). The Twiskhaler® is a multi-dose DPI used to deliver mometasone furoate. The Flexhaler® delivers budesonide, and the Diskus® administers salmeterol, fluticasone, or a combination of salmeterol and fluticasone.

In the Twiskhaler® and the Flexhaler®, the DPI nozzle is comprised of two parts: a lower swirl chamber and an upper chimney in the mouthpiece. Their fluted chimney designs produce a stronger vortex with an increased number of particle collisions with the chimney for deagglomeration. When using a new Flexhaler®, it should be primed by holding it upright and then twisting and clicking the brown grip at the bottom twice. The Twiskhaler® does not require priming before use.

The Diskus® is a multi-dose DPI that contains 60 doses of dry-powder medication individually wrapped in blisters. The wrapping in blisters protects the drug from humidity and other environmental factors. Sliding the dose-release lever punctures the wrapped blister on a foil strip and prepares the dose for inhalation. When the Diskus® cover is closed, the dose release lever is automatically returned to its starting position. As with the Twiskhaler®, no priming is necessary with the Diskus®.

**Currently Available DPI Formulations**

As seen in Figure 22, the device design largely determines whether a DPI model is single dose (loading a single dose prior to each use), multiple unit-dose (loading four or eight blisters of medication), or multiple-dose (containing an entire month’s prescription).
Factors Affecting DPI Performance and Drug Delivery

Respiratory therapists and patients must actively control the following effects:

- **Intrinsic Resistance and Inspiratory Flow:** Each type of DPI has a different intrinsic resistance to airflow that determines how much inspiratory flow needs to be created in the device to release the correct amount of drug. For example, the HandiHaler® has a higher resistance than the Diskus® and therefore requires a greater inspiratory effort. When the patient inhales through the DPI, she/he creates an airflow with a pressure drop between the intake and exit of the mouthpiece. Thus, the patient can lift the powder from the drug reservoir, blister, or capsule depending on the model being used. The patient’s inspiratory effort is also important in its deaggregating of the powder into finer particles. Whereas higher inspiratory flows improve drug deaggregation, fine-particle production, and lung delivery, excessive inspiratory flow can increase impaction on the oral cavity and thus decrease total lung deposition.

- **The Patient’s Inspiratory Flow Ability:** DPIs depend on the patient’s ability to create adequate inspiratory flows. Very young children and patients with acute airflow obstruction due to asthma or COPD may not be able to generate an adequate inspiratory flow when using the DPI. Because very low inspiratory flows result in reduced drug delivery, especially fine-particle delivery, potential DPI patients should be evaluated for the ability to generate a minimal inspiratory flow.

- **Exposure to Humidity and Moisture:** Because all DPIs are affected by humidity and moisture, which can cause powder clumping and reduce deaggregation and fine-particle development during inhalation, they must be kept dry. Capsules and drug blisters generally offer more protection from ambient humidity than a reservoir chamber containing multiple doses for dispensing. Therefore, designs with a reservoir chamber such as the Twisthaler® should be protected from humidity and moisture as much as possible. Whereas it is easy to keep the Twisthaler® out of the bathroom, avoiding use in ambient humidity is difficult if it is carried to the beach, kept in a house with no air conditioning, or left in a car. An alternative DPI design or availability of the drug in a different aerosol system, such as a pMDI, might be considered for such situations. All DPIs are also affected by exhaled air introduced into the airway.
Drug-delivery Technique
Because different types of DPIs are available on the market, respiratory therapists should carefully review operation instructions prior to giving aerosol therapy and certainly prior to instructing patients in at-home use. Proper technique is provided in Technique Box 4.

Technique Box 4. Steps for Correct Use of Each Model of DPIs

**Technique for Single-dose DPIs**

**Aerolizer®:** The patient should be instructed to:
1. Remove the mouthpiece cover.
2. Hold the base of inhaler and twist the mouthpiece counter clockwise.
3. Remove capsule from foil blister immediately before use.
4. Place the capsule into 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 in order to pierce the capsule.
7. Keep their 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 their 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. Do not store the capsule in the Aerolizer®.
16. Close the mouthpiece and replace the cover.
17. Store the device in a cool dry place.

**HandiHaler®:** The patient should be instructed to:
1. Peel back the aluminum foil and remove a capsule immediately before using 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 they 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 they breathe in.
8. Exhale away from the HandiHaler®.
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. Exhale away from the HandiHaler®.
14. Repeat the inhalation from the HandiHaler®.
15. Open the mouthpiece, remove the used capsule, and dispose of it. Do not store capsules in the HandiHaler®.
16. Close the mouthpiece and dust cap for storage of the HandiHaler®.
17. Store the device in a cool, dry place.
Technique Box 4. Steps for Correct Use of Each Model of DPIs (continued)

**Technique for the Multiple Unit-dose DPI**

**Diskhaler®**: The patient should be instructed to:
1. Remove the cover and check that the device and mouthpiece are clean.
2. Extend tray and push ridges to remove tray.
3. Load medication disk on the rotating wheel.
4. Pull the cartridge all the way out and then push it all the way in until the medication disk is seen in the dose indicator. This will be the first dose that will be given to the patient.
5. Keep the device flat and lift the back of the lid until it is lifted all the way up to pierce the medication blister.
6. Click back into place.
7. Move the Diskhaler® away from mouth and breathe out as much as possible.
8. Place the mouthpiece between the teeth and lips and make sure the air hole on the mouthpiece is not covered.
9. Inhale as quickly and deeply as possible.
10. Move the Diskhaler® away from the mouth and hold breath for 10 seconds or as long as possible.
11. Breathe out slowly.
12. If another dose is needed, pull the cartridge out all the way and then push it back in all the way in order to move the next blister into place. Then repeat Steps 4 through 12.
13. Place the mouthpiece cover back on after the treatment. Make sure the blisters remain sealed until inspiration in order to protect them from humidity and loss.

**Technique for Multiple-dose DPIs**

**Diskus®**: The patient should be instructed to:
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.

**Twisthaler®**: The patient should be instructed to:
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 ensure 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 one. 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 you 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 five to 10 seconds or as long as possible.
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.
Technique Box 4. Steps for Correct Use of Each Model of DPIs (continued)

**Twisthaler®**: (continued)
13. Be sure that the arrow is in line with the dose-counter window.
14. Store device in cool, dry place.

**Flexhaler®**: The patient should be instructed to:
1. Twist the cover and lift it off.
2. Hold the Flexhaler® in the upright position (mouthpiece up) while loading a dose.
3. Do not hold the mouthpiece when the inhaler is loaded.
4. Twist the brown grip fully in one direction as far as it goes. It does not matter which way you turn it first.
5. Twist it full back in the other direction as far as it goes.
6. Make sure to hear a click during each of the twisting movements.
7. Be sure not to exhale into the device.
8. Place the mouthpiece into your mouth, seal the mouthpiece with your lips, and inhale deeply and forcefully through the inhaler.
9. Remove the inhaler from your mouth and exhale.
10. Make sure that you do not blow into the mouthpiece.
11. If more than one dose is required, repeat the steps above.
12. Put the cover back on the inhaler and twist it shut.
13. Rinse your mouth with water after each dose to reduce the risk of developing thrush. Do not swallow the rinsing water.

**Tudorza Pressair**: The patient should be instructed to:
1. Wash and dry your hands thoroughly.
2. Remove the protective cap by gently squeezing the marked arrows on each side of the cap and pulling outward.
3. Hold the inhaler with the mouthpiece facing toward you and the green button on top. DO NOT place in your mouth yet.
4. Press the green button all the way down and release it. DO NOT hold the button down.
5. Check the control window on the device (above the mouthpiece) to ensure the color has changed from red to green, indicating the dose and device are ready for use.
6. Exhale away from the device before placing the mouthpiece into your mouth.
7. Place the mouthpiece into your mouth and breathe in quickly and deeply.
8. You will hear a CLICK when the dose is delivered, but continue with your deep breath until your lungs are filled.
9. Remove the device from your mouth and breathe out.
10. Check the control window on the device (above the mouthpiece) to ensure the color has changed from green to red. IF NOT, repeat Step 7.
11. Replace the protective cap on the mouthpiece.

**General Steps To Avoid Reduced or No Dosing for DPIs**: When using DPIs, the following steps should be taken in order to avoid reduced or no dosing during aerosol treatment. The patient should:
1. Read and follow the instructions for proper assembly.
2. Make sure to keep the DPI clean and dry.
3. Keep the DPI in proper orientation during the treatment.
4. Be sure to puncture the capsule or blister pack.
5. Do not exhale into the DPI.
6. Make sure to generate adequate inspiratory flow.
7. Track the doses remaining in the DPI.

**Troubleshooting: Problem with DPIs: Malfunctioning DPIs**

<table>
<thead>
<tr>
<th>Causes</th>
<th>Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect DPI assembly</td>
<td>Check the assembly and reassemble, when needed.</td>
</tr>
<tr>
<td>Failure to discharge medicine</td>
<td>Replace the unit.</td>
</tr>
<tr>
<td>Empty DPI</td>
<td>Check the dose counter to ensure that it is not empty. Otherwise, replace the DPI.</td>
</tr>
</tbody>
</table>
How To Know the DPI Is Empty?

**Single-dose DPI:** Single-dose DPIs such as the Aerolizer® and the HandiHaler® use a single capsule for each dose, and only full capsules should be used when each dose is given. The capsule should be inspected to assure that the patient took the full dose. If there is powder remaining, the capsule should be returned to the inhaler and inhalation should be repeated. Then, the capsule should be disposed of after treatment. Prescription renewal should be based on the remaining capsules.

**Multiple Unit-dose DPI:** The Diskhaler® is a multiple unit-dose DPI with a refill disk that contains 4- or 8-unit-dose blisters. Because there is not a dose counter on the DPI, doses must be tracked manually. Therefore, visual inspection will confirm use of all packets. The disk is disposed of when all the doses have been used.

**Multiple-dose DPIs:** Multiple-dose DPIs historically come with integrated mechanical devices that indicate the number of doses remaining in the inhaler. The devices give a particular display when the doses are coming to an end so that a new DPI can be ordered from the pharmacist. The dose counter of each type of multiple-dose DPI is explained in the table below.

<table>
<thead>
<tr>
<th>Dose Container</th>
<th>Flexhaler® Reservoir</th>
<th>Twistrhaler® Reservoir</th>
<th>Diskus® Blister Strip</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Doses</td>
<td>60 or 120</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>Type of Dose Indicator</td>
<td>“0”</td>
<td>“01”</td>
<td>Red numbers</td>
</tr>
<tr>
<td>Meaning of Dose Indicator</td>
<td>Although the indicator counts down every time a dose is loaded, it will not move with each individual dose but intervals of five or so doses. The indicator is marked in intervals of 10 doses, alternating numbers and dashes. When it is down to “0,” it must be thrown away.</td>
<td>The dose display showing “01” indicates the last dose of medicine in the Twistrhaler®, and the medicine must be refilled.</td>
<td>The numbers turning red in the dose display indicates that there are five doses left. When the dose window shows “0,” there is no medicine left, and the discus should be disposed.</td>
</tr>
</tbody>
</table>

**Cleaning:** Please refer to the Infection Control section on page 48 for the cleaning instructions for DPIs.
The selection of the delivery device is very important for optimizing the results of aerosol drug therapy. Evidence indicates that all three types of aerosol generators can be equally effective if they are used correctly by the patient. The criteria to select an aerosol generator can be divided into four categories: patient-related, drug-related, device-related, and environmental and clinical factors.

Patient-related Factors

Age, Physical, and Cognitive Ability of Patients
An aerosol generator should be selected in accord with the patient’s age, physical, and cognitive ability. Age changes anatomic and physiologic factors such as airway size, respiratory rate, and lung volume. The patient’s cognitive ability to understand how and when to use a device and drug as well as his/her physical ability and coordination in using an aerosol generator should guide the selection of an aerosol generator. Aerosol devices have different requirements for proper use. For guidance about the device selection in infants and pediatrics, see “Neonatal and Pediatric Aerosol Drug Delivery” on page 46.

As for adults and the elderly who cannot manage hand-held coordination or proper inhalation technique, pMDIs may not be a good option. Also, the inability to generate sufficient inspiratory flow (>40–60 L/min) eliminates the use of aerosol generators such as DPIs.

Preference of Patients
Patient preference is a critical factor in the selection of an aerosol generator and the effectiveness of aerosol therapy. Patients tend to use devices they prefer more regularly than devices they dislike. Therefore, the selection of an aerosol generator should be tailored according to the patient’s needs and preferences.

Drug-related Factors

Availability of Drug
Some drug formulations are available with only one type of aerosol generator. If a drug can be administered with the three types of aerosol generators, the clinician should select an aerosol generator based on the patient’s needs and preference. Otherwise, a drug formulation that can be used with only a single aerosol generator dictates which aerosol generator to choose.

Combination of Aerosol Treatments
Many patients are prescribed more than one inhaled drug. In that case, using the same type of aerosol generator may increase the patient’s adherence to therapy while minimizing the patient’s confusion caused by the use of different aerosol devices.

Device-related Factors

Convenience of Aerosol Generator
Selecting the most convenient aerosol generator for the patient is very important to adherence. Ease of use, treatment time, portability, cleaning, and maintenance required for
each device should guide the selection process. For example, a rescue medication needs to be small, light, and portable so the patient can easily have it available when needed. Also, nebulizers may be less preferable to deliver inhaled medications as they are more expensive, require a power source, and need regular maintenance. When all other factors are equal, the most convenient device should be chosen for patients.

**Durability of Aerosol Generator**

A selected aerosol generator should have good durability so that it can withstand rigorous treatment and cleaning procedures every day. Devices that require extensive cleaning are not a good choice for patients unwilling to routinely clean and maintain the device.

**Cost and Reimbursement of Aerosol Generator**

It is very important to select an aerosol generator that is the least out-of-pocket expense for the patient. Patients do not use drugs and devices they cannot afford. As shown in Table 3, Table 6, and Table 7, costs of aerosol generators and drug formulations vary widely. The cost to the patient will depend on the presence and type of medical insurance they have. If the “best” device/drug is not one that the patient can afford, the least costly aerosol generator and drug combination should be identified in order to meet the patient’s needs. Therefore, it is important to work with the patient to identify strategies to access affordable drug/device options in order to meet their clinical needs. If all the other factors are constant, the least costly aerosol generator and drug combination should be selected.

**Environmental and Clinical Factors**

When and where the aerosol therapy is required can impact device selection. For example, therapy that is given routinely, once or twice a day, before or after bedtime does not need to be as portable as rescue medications that may be required at anytime. Also, noisy compressors may not be good in small homes where a late-night treatment might awaken other members of the family. In environments where patients are in close proximity to other people, secondhand exposure to aerosols may be a factor, and devices that limit or filter exhaled aerosol should be selected.
Infants are not simply anatomically scaled-down adults. Therefore, aerosol drug administration differs fundamentally in infants and children. Cognitive ability (i.e., understanding how and when to use a device and drug) and physical ability (i.e., coordination to use that device) as well as age-related anatomic and physiologic factors (i.e., airway size, respiratory rate, lung volumes) create substantial challenges for effective aerosol delivery at each stage of development.\textsuperscript{68-71,91} When respiratory therapists gain a clear understanding of these challenges, they can optimize aerosol drug delivery and its therapeutic outcomes in less developed patients. This section explores the challenges and solutions that may optimize aerosol drug delivery in infants and pediatrics.

### Age and Physical Ability

Selection of an aerosol device is critical to successful aerosol therapy in infants and children.\textsuperscript{68,76,91} Children under the age of three may not reliably use a mouthpiece, making delivery via mask necessary for both nebulizers and pMDIs.\textsuperscript{91-95} Especially at low tidal volumes, VHCs are the preferred method for pMDI delivery in infants and small children.\textsuperscript{93,94} Breathing patterns, inspiratory flow rates, and tidal volumes change with age. Even healthy children below four years of age cannot reliably generate sustained inspiratory flow rates of 60–90 L/min required for optimal use of many DPIs. Thus, the use of breath-actuated nebulizers or DPIs may not be reliable in children younger than four years.\textsuperscript{71,96}

### Age and Cognitive Ability

The choice of aerosol device should be tailored to the patient’s age and to cognitive ability to use the device correctly. Table 15 presents the recommended ages for introducing different types of aerosol generators to children.\textsuperscript{68-70,96-99} Small-volume nebulizers and pMDIs with VHCs are recommended for use with infants and children up to five years of age.\textsuperscript{69,70,96} Since children up to three years of age typically cannot use a mouthpiece, both nebulizers and pMDIs with holding chambers should be administered via masks.\textsuperscript{69,93,94} Independent of age, a face mask should be used until the child can comfortably use a mouthpiece. A child below five years of age may not be able to master specific breathing techniques.\textsuperscript{69,70,96} With low tidal volumes and short inspiratory times, breath-actuated nebulizers may increase inhaled dose compared to continuous nebulization.\textsuperscript{100} However, it may take three-fold more time to administer that dose. Also, time constraints and portability of compressor nebulizers make them less desirable for preschool children.\textsuperscript{69} It is generally accepted that the cognitive ability to control breathing and hand/breath coordination develops by age five or six.\textsuperscript{68,69,97} Once children reach age four and above, they may have a sufficient understanding of how to use a pMDI or DPI successfully.\textsuperscript{71,96}

<table>
<thead>
<tr>
<th>Aerosol Generator</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVN with mask</td>
<td>≤ 3 years</td>
</tr>
<tr>
<td>SVN with mouthpiece</td>
<td>≥ 3 years</td>
</tr>
<tr>
<td>pMDI with holding chamber/spacer and mask</td>
<td>&lt; 4 years</td>
</tr>
<tr>
<td>pMDI with holding chamber/spacer</td>
<td>≥ 4 years</td>
</tr>
<tr>
<td>Dry-powder inhaler</td>
<td>≥ 4 years</td>
</tr>
<tr>
<td>Metered-dose inhaler</td>
<td>≥ 5 years</td>
</tr>
<tr>
<td>Breath-actuated MDI (e.g., Autohaler™)</td>
<td>≥ 5 years</td>
</tr>
<tr>
<td>Breath-actuated nebulizers</td>
<td>≥ 5 years</td>
</tr>
</tbody>
</table>
Aerosol Drug Delivery in Distressed or Crying Infants

Inhaled drugs should be given to infants when they are settled and breathing quietly. Crying children receive virtually no aerosol drug to the lungs,\textsuperscript{92,98,101,102} with most of the inhaled dose depositing in the upper airways or pharynx, which is then swallowed.\textsuperscript{69,70,102,103} Therefore, it is essential to develop approaches that minimize distress before administering aerosol drugs. These approaches include, but are not limited to, playing games, comforting babies, and providing other effective forms of distraction. Also, aerosol drugs can be administered while the infant is asleep as long as administration does not wake up or agitate the infant. Although sleep breathing patterns indicated a higher lung dose in an infant-model study,\textsuperscript{104} an in-vivo study showed that 69% of the children woke up during aerosol administration and 75% of them were distressed.\textsuperscript{105}

Patient-device Interface

Even infants and small children can make known their preferences for specific devices. This should be a consideration in device selection. Using a device that is preferred by the child and parent can increase adherence, inhaled dose, and desired clinical response.

Mouthpiece or Face Mask?

Mouthpieces and face masks are commonly used for aerosol drug delivery in children above three years of age. Studies suggest that the mouthpiece provides greater lung dose than a standard pediatric aerosol mask\textsuperscript{100,106} and is effective in the clinical treatment of children.\textsuperscript{100,107,108} Consequently, the use of mouthpieces should be encouraged, but a mask that is consistently used is better than a mouthpiece that is not.

Importance of a Closely Fitting Face Mask

A good face mask seal is a critical factor in achieving optimal drug deposition and avoiding getting aerosol into eyes. Even small leaks of 0.5 cm around the face mask decrease drug inhaled by children and infants by more than 50%.\textsuperscript{109-113} Initially, a small child may refuse to use a face mask when feeling sick or irritable. However, parental education, play activities, encouragement to hold the mask firmly against the child’s face, and close supervision can reduce poor tolerance of face masks and improve aerosol drug delivery.

Face Mask or Blow-by?

Blow-by is the administration of aerosolized drug through the nebulization port of a nebulizer that is directed toward the patient’s face. Although blow-by is a technique commonly used for crying babies or uncooperative children, it has been documented that it is less efficient compared with a face mask as aerosol drug deposition decreases significantly as the distance from the device to the child’s face is increased. Therefore, evidence suggests blow-by to be ineffective and use should be discouraged.\textsuperscript{93,109,114,115}

Parent and Patient Education

As children grow and their aerosol device needs to be changed, they and their care providers should be taught the best techniques for the use and maintenance of aerosol devices. Also, children may demonstrate poor adherence to aerosol drug delivery because they lack the ability to use a device correctly or contrive to use it ineffectively.\textsuperscript{116,117} Therefore, respiratory therapists should explain the effects of medications prescribed, the importance of aerosol therapy, and the proper use of aerosol generators to the patient and the parent. After initial training is provided, frequent follow-up demonstration is essential to optimize aerosol drug delivery and adherence to prescribed therapy in infants and children.
Aerosol generators can become contaminated with pathogens from the patient, the care provider, and the environment. The contamination of nebulizers has been documented in patients with cystic fibrosis (CF), asthma, and immunodeficiency. In the absence of infection control (IC), an aerosol generator will be contaminated and may cause bacterial colonization in the respiratory tract. Therefore, it is essential to establish an IC management system that will reduce nosocomial infections, length of stay in the hospital, and costs associated with hospitalization.

IC Management System in Aerosol Drug Delivery

Patient Education and Awareness

Patient Education: It has been documented that aerosol generators used at home are frequently contaminated with bacteria. Therefore, the importance of cleaning and maintaining aerosol equipment should be emphasized in IC education programs with patients and caregivers through repeated oral and written instructions.

Patient Adherence: Approximately 85% of patients with CF fail to disinfect their nebulizers at home. It has been determined that, in addition to the constraints of cleaning and disinfecting instructions provided by the manufacturers, adherence can be influenced by personal, socio-cultural, and psychological factors. Changing aerosol generators every 24 hours, using disposable equipment with health insurance approval, and partnering with patients to increase adherence can increase patient compliance to IC and minimize the risk of infection.

Cleaning and Maintenance of Aerosol Generators

Preventing Infection and Malfunction of Home Aerosol Generators

Cleaning: The cleaning instructions for the different types of aerosol generators are given below.

- Pressurized Metered-dose Inhalers: The plastic container of pMDIs should be cleaned at least once a week as shown in Table 16.

<table>
<thead>
<tr>
<th>Cleaning the pMDI</th>
<th>Cleaning the Autohaler™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean once a week and as needed.</td>
<td>Clean once a week and as needed.</td>
</tr>
<tr>
<td>Look at the hole where the drug sprays out from the inhaler.</td>
<td>Remove the mouthpiece cover.</td>
</tr>
<tr>
<td>Clean the inhaler if you see powder in or around the hole.</td>
<td>Turn the Autohaler™ upside down.</td>
</tr>
<tr>
<td>Remove the pMDI canister from the plastic container so it does not get wet.</td>
<td>Wipe the mouthpiece with a clean dry cloth.</td>
</tr>
<tr>
<td>Rinse the plastic container with warm water and shake out to remove excess water.</td>
<td>Gently tap the back of the Autohaler™ so the flap comes down and the spray hole can be seen.</td>
</tr>
<tr>
<td>Dry overnight.</td>
<td>Clean the surface of the flap with a dry cotton swab.</td>
</tr>
<tr>
<td>Replace the canister back inside the mouthpiece and recap the mouthpiece.</td>
<td>Recap the mouthpiece and make sure the lever is down.</td>
</tr>
</tbody>
</table>
• **Metered-dose Inhalers Accessory Devices**: When a spacer is used with a pMDI, it should be cleaned before first use and then periodically cleaned based on the manufacturers’ suggestions. Table 17 provides the steps for cleaning the pMDI accessory devices.

**Table 17. Cleaning Instructions for the pMDI Chamber**

**Cleaning the Chamber Device**

- Clean every two weeks and as needed.
- Disassemble the device for cleaning.
- Soak the spacer parts in warm water with liquid detergent and gently shake both pieces back and forth.
- Shake out to remove excess water.
- Air dry spacer parts in the vertical position overnight.
- Do not towel dry the spacer as this will reduce dose delivery because of static charge.
- Replace the back piece on the spacer when it is completely dry.

• **Dry-powder Inhaler**: It is important to note that DPIs should not be submerged in water. Also, they should be kept dry as moisture will decrease drug delivery. Although there is no clear evidence about the DPI cleaning practice, each manufacturing company has recommendations for periodic cleaning and suggests wiping the mouthpiece of the DPI with a clean dry cloth.

• **Nebulizers**: In the home, nebulizers should be cleaned after every treatment. The longer a dirty nebulizer sits and is allowed to dry, the harder it is to thoroughly clean. Rinsing and washing the nebulizer immediately after each treatment can go a long way in reducing infection risk. According to the Cystic Fibrosis Foundation guidelines, parts of aerosol generators should be washed with soap and hot water after each treatment, with care taken not to damage any parts of the aerosol generator. Table 18 provides the cleaning instructions for the jet nebulizer. Mesh and ultrasonic nebulizers should be cleaned and disinfected based on the manufacturer’s recommendations. Also, it is important to remember not to touch the mesh during the cleaning of mesh nebulizers because this will damage the unit.
Disinfection: Periodic disinfection and nebulizer replacement is highly recommended to minimize contamination. Each manufacturer suggests a different method of disinfection for its product. Therefore, the manufacturer’s specific instructions on disinfecting aerosol generators should be followed. It is also important to note that all solutions should be discarded after disinfection. The varied methods for disinfection include having the patient:

1. Boil the nebulizer parts for five minutes. This disinfection process does not require a final rinse.
2. Soak them in solution of one-part household bleach and 50-parts water for three minutes.
3. Soak the parts in 70% isopropyl alcohol for five minutes.
4. Soak them in 3% hydrogen peroxide for 30 minutes.
5. Soak them in one-part distilled white vinegar in three-parts hot water for one hour (not recommended for CF patients).

The patient should disinfect the nebulizer once or twice a week by using one of the methods for disinfection listed above. Evidence suggest that a quaternary ammonium compound can also be used for disinfecting jet nebulizers as it has comparable effectiveness with the combined disinfection procedure of a detergent pre-wash and 1.25% acetic acid soak. Also, a quaternary ammonium compound soak need only be 10 minutes, while the acetic acid soak should not be less than one hour. Another advantage of using the quaternary solution is that it can be reused for up to one week, as opposed to the acetic acid solution that cannot be reused.129

<table>
<thead>
<tr>
<th>Table 18. Cleaning Instructions for the Jet Nebulizer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cleaning After Each Use</strong></td>
</tr>
<tr>
<td>Wash hands before handling equipment.</td>
</tr>
<tr>
<td>Disassemble parts after every treatment.</td>
</tr>
<tr>
<td>Remove the tubing from the compressor and set it aside. The tubing should not be washed or rinsed.</td>
</tr>
<tr>
<td>Rinse the nebulizer cup and mouthpiece with either sterile water or distilled water.</td>
</tr>
<tr>
<td>Shake off excess water.</td>
</tr>
<tr>
<td>Air dry on an absorbent towel.</td>
</tr>
<tr>
<td>Store the nebulizer cup in a zippered plastic bag.</td>
</tr>
<tr>
<td><strong>Cleaning Once or Twice a Week</strong></td>
</tr>
<tr>
<td>Wash hands before handling equipment.</td>
</tr>
<tr>
<td>Disassemble parts after every treatment.</td>
</tr>
<tr>
<td>Remove the tubing from the compressor and set it aside. The tubing should not be washed or rinsed.</td>
</tr>
<tr>
<td>Wash nebulizer parts in warm water with liquid dish soap.</td>
</tr>
<tr>
<td>Disinfect the nebulizer based on the manufacturer’s recommendations. The nebulizer parts may be soaked in one of the following solutions:</td>
</tr>
<tr>
<td>1. One-part household bleach and 50-parts water for three minutes</td>
</tr>
<tr>
<td>2. 70% isopropyl alcohol for five minutes</td>
</tr>
<tr>
<td>3. 3% hydrogen peroxide for 30 minutes</td>
</tr>
<tr>
<td>4. One-part distilled white vinegar in three-parts hot water for one hour (not recommended for CF patients).</td>
</tr>
<tr>
<td>Rinse parts with sterile or distilled water.</td>
</tr>
<tr>
<td>Shake off excess water and place all parts on a clean paper towel.</td>
</tr>
<tr>
<td>Allow them to air dry completely on an absorbent towel.</td>
</tr>
<tr>
<td>Reassemble the nebulizer and store in a clean, dry bag container.</td>
</tr>
</tbody>
</table>
**Final Rinse:** The patient should use sterile water (not distilled or bottled) for the final rinse. Sterile water can be made by boiling tap water for five minutes.

**Drying and Maintenance:** Because bacteria grow in wet, moist places, nebulizers should be thoroughly dried and stored in a clean dry place between treatments. Drying can be enhanced by attaching gas flow to the nebulizer for a short time after it is rinsed. It has been reported that nebulizer performance may change in time due to incorrect cleaning, maintenance, and disinfection procedures. Nebulizers must be kept from being contaminated by following the manufacturer's instructions for care and cleaning. This is necessary for all aerosol generators used for inhaled medication.

**Preventing Infection and Malfunction of Aerosol Generators at Hospitals or Clinics**

**Aerosol Generators:** Bacterial contamination of nebulizers at the hospital has been associated with nosocomial infections. The Centers for Disease Control and Prevention (CDC) recommends that nebulizers be cleaned, rinsed with sterile water, and air-dried between treatments. Also, each hospital or out-patient clinic should have an infection surveillance program that can determine local IC practices based on the continuous and systematic collection, analysis, and interpretation of infection data. Nebulizers should be changed every 24 hours. If an aerosol generator is labeled “For Single Patient Use,” it should be used on a single patient and then discarded.

**Inhaled Drugs:** Multi-dose drug containers have been associated with contaminated nebulizers and are a potential source of spreading nosocomial infections. Therefore, unit-dose medications are recommended when possible. Also, it is important to avoid contaminating drug solutions.

**Infection Transmission:** The transmission of infection from therapist to patient can be reduced by therapists washing their hands with water and soap or cleaning hands with hand sanitizers before and after treatment. The use of gloves should be considered an adjunct to hand hygiene. A respiratory therapist must change gloves between patients and clean hands after gloves are removed due to the fact that gloves create a warm and moist environment that supports the growth of microbial contamination and, thereby, the transmission of infection. Goggles, face masks, and face shields should be used alone or in combination to seal out airborne pathogens that therapists may inhale with aerosol drug therapy.

**Compliance to IC Management System:** The IC management system can be effective only with the practice of the dedicated and knowledgeable respiratory therapists who implement it. Therefore, respiratory therapists should be trained appropriately in using set protocols established by the IC management system in aerosol drug delivery.

**Infection Surveillance:** It is essential for hospitals to establish simple and sensible infection surveillance measures to periodically evaluate the IC activities used by respiratory therapists.

**Occupational Health and Safety of Respiratory Therapists**

Respiratory therapists undergo not only the risk of exposure to inhaled medications but are also faced with the risk of inhaling pathogens during aerosol therapy. The elements of occupational health and safety for the respiratory therapist are shown below.
**Health Assessment and Immunization:** Screening respiratory therapists for infection and immunization must occur from the beginning to the end of employment.

**Hand Hygiene:** It has been documented that hand hygiene is effective in decreasing the transmission of respiratory viruses\(^{31,141,143-145}\). Health care workers who self-reported hand-washing during patient care had a lower risk of having respiratory infections.\(^{31,143-145}\)

**Protective Equipment:** Respiratory therapists must have access to the appropriate personal protective equipment, such as masks and eye protectors, when needed.\(^{30}\)

**Ventilation System:** These systems exchange room air six to 10 times per hour\(^{31}\) and create a negative-pressure environment in patient rooms that is effective in removing 99.9% of airborne contaminants in 69 minutes.\(^{32}\)

**Filtered Nebulizers:** Placing a filter on the exhalation part of a nebulizer may protect respiratory therapists from infection and reduce secondhand aerosol breathing in hospitals and out-patient clinics.
A number of problems occur with patient use of aerosol devices. Knowledge of these problems can help the respiratory therapist better instruct patients. Understanding 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 devices 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 their 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. 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 pMDI monitor reported only 48%. 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 19 lists both types of non-adherence with definitions and examples.

<table>
<thead>
<tr>
<th>Unintentional Factors: Not Understanding Therapy Correctly</th>
<th>Intentional Factors: Understanding Therapy But Not Adhering Correctly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Misunderstanding prescribed drug regimen:</td>
<td>Patient beliefs:</td>
</tr>
<tr>
<td>• Poor physician-patient communication</td>
<td>• Does not really require regular medication</td>
</tr>
<tr>
<td>• Poor therapist-patient communication</td>
<td>• Is not really sick</td>
</tr>
<tr>
<td>Language barriers</td>
<td>• Gain attention from parents and kept at home (children)</td>
</tr>
<tr>
<td></td>
<td>• Medication too expensive</td>
</tr>
<tr>
<td></td>
<td>• Concern about side effects</td>
</tr>
<tr>
<td></td>
<td>• Perceived lack of effect from medication</td>
</tr>
<tr>
<td></td>
<td>Patient forgetfulness</td>
</tr>
<tr>
<td></td>
<td>Patient stress and busy lifestyle</td>
</tr>
<tr>
<td></td>
<td>Complex and demanding aerosol regimens</td>
</tr>
<tr>
<td></td>
<td>Psychological factors (e.g., depression)</td>
</tr>
</tbody>
</table>

Note that one example of unintentional non-adherence is incorrect aerosol device technique due to misunderstanding prescribed drug regimen, which can be corrected through patient training. There is no perfect, fail-safe, error-proof inhaler on the market today. The pMDI is recognized as a difficult inhaler for patients to use without proper training. Even holding chambers and spacers introduced to address these issues present additional problems...
DPIs were also introduced, in part, with the rationale that their use would be simpler than with a pMDI.\textsuperscript{147,148} Nebulizers are probably the simplest inhaler type for a patient to use if we assume that assembly, proper cleaning, and maintenance is not a problem. However, there can be problems with all types of inhaler devices. Table 20 lists the common errors and mistakes that can occur with each type of device.\textsuperscript{125,147,148}

**Table 20. Common problems, disadvantages, and errors with each type of aerosol generator**

*Modified, with permission, from References 1 and 126*

### Pressurized Metered-dose Inhalers

**Errors in technique**
- Failure to coordinate pMDI actuation on inhalation
- Too short a period of breathhold after inhalation
- Too rapid an inspiratory flow rate
- Inadequate priming/shaking/mixing before use
- Abrupt discontinuation of inspiration as aerosol hits throat
- Actuating pMDI at total lung capacity
- Actuating pMDI prior to inhalation
- Firing pMDI multiple times during single inhalation
- Firing pMDI 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 pMDI beyond rated capacity (loss of dose count)
- Failure to clean boot
- Wasting remaining doses

Lack of adequate patient training in use of pMDI
Cognitive impairment of users
Lack of adequate hand strength or flexibility to activate pMDI
Ideomotor dyspraxia

### Valved Holding Chambers/Spacers

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

### Dry-powder Inhalers

**Errors in technique**
- Not holding device correctly while loading dose
- Failure to pierce or open drug package
- Using the inhaler in wrong orientation
- Failure to prime
- Exhaling through the mouthpiece
- Not exhaling to residual volume before inhaling
- Not inhaling forcefully enough
- Inadequate or no breath hold
- Exhaling into mouthpiece after inhaling

Use of multi-dose reservoir designs in high ambient humidity, which can reduce fine-particle dose
Lack of patient instruction in assembly or use
Common Patient Errors with pMDIs

Although hand-breath coordination with a pMDI has long been recognized as a problem, there are a number of other potential mistakes a patient can make when using a pMDI (Table 20). Failure to shake a pMDI before each use can interfere with correct drug release. Failure to prime a pMDI 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 a pMDI 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 pMDI until there was no sound when it was actuated. A pMDI 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 pMDI (see pages 31-32).

Common Patient Errors with Holding Chambers/Spacers

Common errors that can occur with holding chambers/spacers are also listed in Table 20. 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 pMDI 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 pMDI through the chamber. An alternative is to purchase a non-electrostatic holding chamber/spacer.

Common Patient Errors with DPIs

Problems have also been identified with patient use of DPIs (Table 20). Error rates, defined as failure to correctly perform an essential step, have been shown to be similar for pMDIs and DPIs. 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 SVNs

The usual problems cited with SVNs are not problems of patient use but rather general disadvantages with this type of aerosol device (Table 20). 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. In addition, newer nebulizer technology is directed at reducing the overall

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Table 20. Common problems, disadvantages, and errors with each type of aerosol generator (continued)

<table>
<thead>
<tr>
<th>Nebulizers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to assemble equipment properly</td>
</tr>
<tr>
<td>Spillage of dose by tilting some nebulizers</td>
</tr>
<tr>
<td>Failure to keep mouthpiece in mouth during nebulization</td>
</tr>
<tr>
<td>Failure to mouth breathe</td>
</tr>
</tbody>
</table>

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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 (e.g., DPIs). Confusion and errors of use can result. The following general steps are recommended for clinicians to ensure correct patient use:

1. Review device instructions carefully and practice with a placebo device prior to teaching others.
2. Demonstrate assembly and correct use of device to patients using a checklist.
3. 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).
   a. Written instructions should be accompanied by pictures for patients with low literacy.
4. Have the patient practice use of the device while being observed by the clinician.
5. Review patient use of the device at each return visit.
6. Review the patient’s understanding of the inhaled medications at each return visit (when to use, purpose of drug, prescribed frequency).
7. Have a high index of suspicion for incorrect use or non-adherence if poor management of airway disease occurs.


71. Ahrens RC. The role of the MDI and DPI in pediatric patients: “Children are not just miniature adults”. Respir Care 2005; 50(10):1323–1328.


75. Rau JL. Practical problems with aerosol therapy in COPD. Respir Care 2006; 51(2):158-172.


84. Fink JB. Inhalers in asthma management: is demonstration the key to compliance? Respir Care 2005; 50(5):598-600.


90. Rubin BK. What does it mean when a patient says, “my asthma medication is not working?” Chest 2004; 126(3):972-981.


139. U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Public health advisory: contamination of multi-dose bottles of Albuterol Sulfate Solution for Inhalation (0.5%), 2002.


