

# A Guide to **Aerosol Delivery Devices for Respiratory Therapists**

5<sup>th</sup> Edition



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**With a Foreword by**

The American Association for Respiratory Care

**Disclosure**

Douglas S. Gardenhire, EdD, RRT, RRT-NPS, FAARC discloses relationship with Aerogen.

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# FOREWORD

Aerosol therapy is a cornerstone 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, their ability to manage patients with both acute and 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 behavior 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 with 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 fifth 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.

# CONTINUING RESPIRATORY CARE EDUCATION (CRCE)

## American Association for Respiratory Care

As part of your membership benefits in the American Association for Respiratory Care® (AARC), the Association:

- provides you with continuing education opportunities;
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The contents of this book are approved for six CRCE contact hours. To earn those CRCE contact hours, please visit the AARC web site at:

<http://c.aarc.org/go/edu>

Further instructions will be given on that web site, including:

- how to register to take an examination to assess your mastery of course objectives

## 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, 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.

# ACRONYMS

<b>CDC</b>	Centers for Disease Control and Prevention
<b>CDER</b>	Center for Drug Evaluation and Research
<b>CDRH</b>	Center for Devices and Radiological Health
<b>CF</b>	cystic fibrosis
<b>DPI</b>	dry-powder inhaler
<b>FDA</b>	U.S. Food and Drug Administration
<b>FPF</b>	fine-particle fraction
<b>GSD</b>	Geometric Standard Deviation
<b>HFA</b>	hydrofluoroalkane
<b>IC</b>	infection control
<b>MMAD</b>	mass median aerodynamic diameter
<b>MMD</b>	mass median diameter
<b>pMDI</b>	pressurized metered-dose inhaler
<b>SPAG</b>	small particle aerosol generator
<b>SVN</b>	small-volume nebulizer
<b>VHC</b>	valved holding chamber

# THE SCIENCE OF AEROSOL DRUG DELIVERY

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.<sup>1</sup> 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
- 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  $\mu\text{m}$  (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  $\mu\text{m}$  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  $\mu\text{m}$
- 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 ( $>3\ \mu\text{m}$ ), 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  $1\ \mu\text{m}$ . These mechanisms come into play as aerosol particles are inhaled orally or through the nose. Larger particles ( $>10\ \mu\text{m}$ ) are filtered in the nose and/or the oropharynx, largely by inertial impaction; particles of  $5\text{--}10\ \mu\text{m}$  generally reach the proximal generations of the lower respiratory tract, and particles of  $1\text{--}5\ \mu\text{m}$  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  $3\ \mu\text{m}$ , aerosol deposition shifts from the periphery of the lung to the conducting airways. Oropharyngeal deposition increases as particle size increases above  $6\ \mu\text{m}$ . Exhaled loss is high with very small particles of  $1\ \mu\text{m}$  or less. Consequently, particle sizes of  $1\text{--}5\ \mu\text{m}$  are best for reaching the lung periphery, whereas  $5\text{--}10\ \mu\text{m}$  particles deposit mostly in the conducting airways, and  $10\text{--}100\ \mu\text{m}$  particles deposit mostly in the nose.

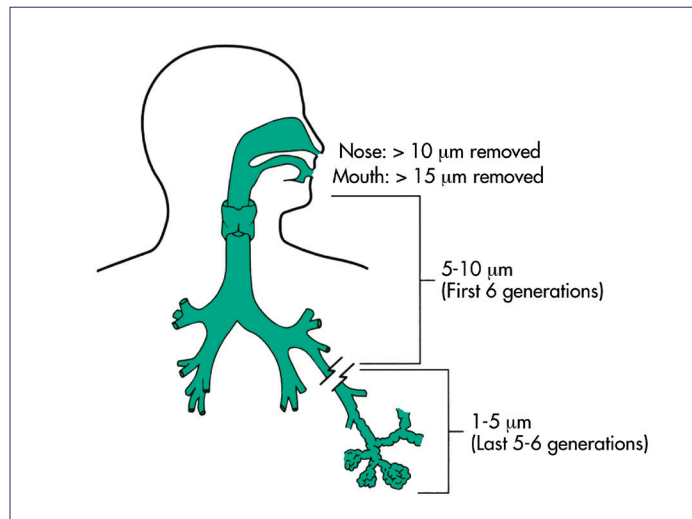
Aerosol devices in clinical use produce *heterodisperse* (also termed *polydisperse*) particle sizes, meaning that there is a mix of sizes in the aerosol. *Monodisperse* aerosols, which consist of a single particle size, are rare in nature and medicine. A measure that quantifies a polydisperse aerosol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

As seen in Figure 1, larger particles between  $10\text{--}15\ \mu\text{m}$  deposit mostly in the upper airways, particles within the  $5\text{--}10\ \mu\text{m}$  range reach the large bronchi, and particles of  $1\text{--}5\ \mu\text{m}$  penetrate to the lower airways and lung periphery.<sup>2</sup>

## 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.



**Figure 1.** A simplified view of the effect of aerosol particle size on the site of preferential deposition in the airways. (From Reference 2, with permission)

- **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 value. 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  $1\text{--}50\%$  with clinical aerosol delivery systems.<sup>3-7</sup> Deposition is dependent on a variety of factors such as the device, the patient, the drug, and the disease. For example, out of  $200\ \mu\text{g}$  of albuterol in two actuations or puffs from a pMDI, only about  $20\text{--}40\ \mu\text{g}$  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.

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

Drug	pMDI Nominal Dose	SVN Nominal Dose
Albuterol	0.2 mg (200 µg)	2.5 mg
Ipratropium	0.04 mg (40 µg)	0.5 mg
Levalbuterol	0.045 mg - 0.09 mg	0.31 mg - 1.25 mg

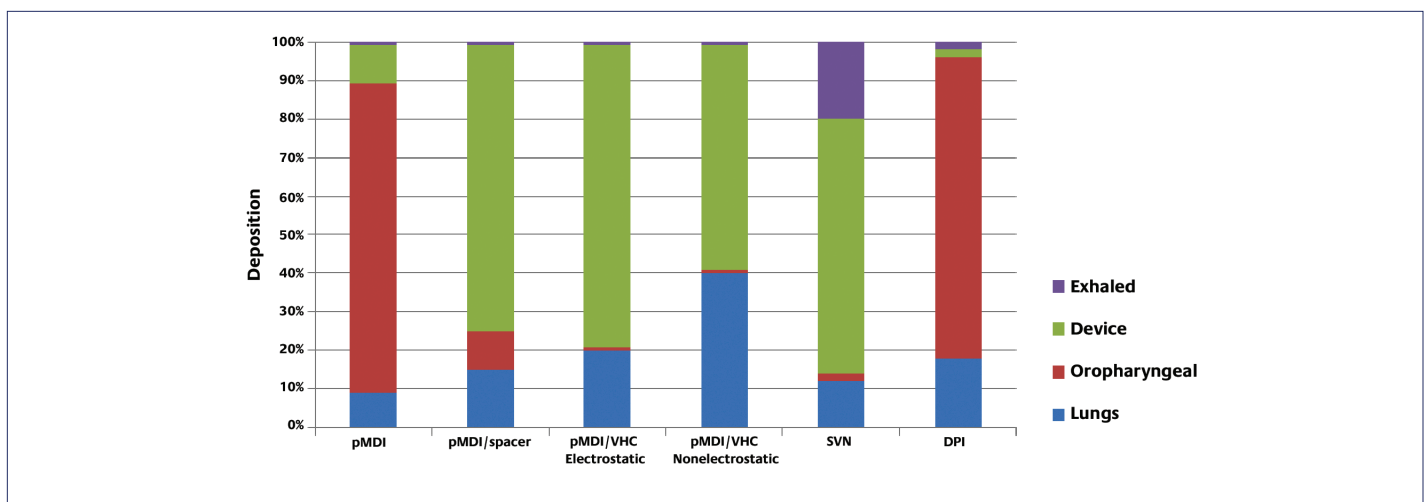
It is important to realize that different types of aerosol devices deposit a different fraction of the total dose of a given drug (also termed “nominal” dose) in the lungs. In addition, different types of aerosol devices such as nebulizers and pMDIs do not have the same nominal dose. Using albuterol 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.

### 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*.<sup>8</sup> 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 hydrofluoroalkane propellant, which replaces the older chlorofluorocarbon (CFC) propellants.<sup>9</sup> New devices such as the Respimat® inhaler (Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT) have shown lung depositions of 40%.<sup>10</sup> Although lung dose efficiency varies between devices, inhalers with relatively low lung deposition fraction have been clinically proven to achieve the desired therapeutic effect in the target audience.



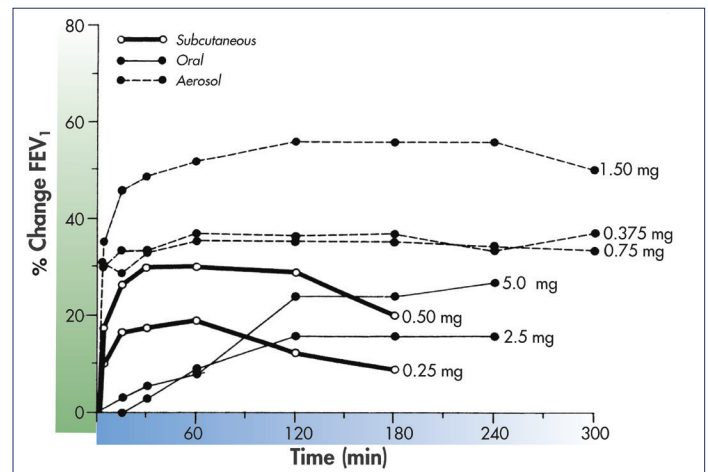
**Figure 2.** Drug deposition with common aerosol inhaler devices. Shown by color are the varying percentages of drug lung deposition and drug loss in the oropharynx, device, and exhaled breath

pMDI = pressurized metered-dose inhaler; VHC = valved holding chamber; SVN = small-volume nebulizer; DPI = dry-powder inhaler

(Modified, with permission, from Reference 1 and Reference 7)

## 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.<sup>11</sup> 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.



**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)

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

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

## 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.<sup>12,13</sup> 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.<sup>13-15</sup> 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.<sup>16-18</sup> An increase in drug concentration may be due to evaporation, heating, or the inability to efficiently nebulize suspensions.<sup>13,16,18,19</sup> 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.<sup>20-25</sup> 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,<sup>26</sup> it may also increase the risk of asthma-like symptoms and cause occupational asthma.<sup>27-29</sup> 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.<sup>30-32</sup>

## 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.

**Table 3.** Currently available aerosol drug formulations with corresponding inhaler devices and costs for use in the United States.

**HFA** = hydrofluoroalkane; **pMDI** = pressurized metered-dose inhaler; **SVN** = small-volume nebulizer; **DPI** = dry-powder inhaler  
 Cost information from [www.goodrx.com](http://www.goodrx.com). Prices used were from WalMart in 2023.

Short-Acting Bronchodilator							
Drug	Brand	Device	Strength	Doses	Cost	Cost/ Dose	
Albuterol Sulfate	Generic	SVN	0.63	25	\$11.89	\$0.48	
			1.25	25	\$15.51	\$0.62	
			2.5	25	\$6.61	\$0.26	
			pMDI	90 mcg	200	\$11.01	\$0.06
	ProAir® HFA	pMDI	90 mcg	200	\$84.29	\$0.43	
	ProAir RespiClick®	DPI	90 mcg	200	\$77.30	\$0.39	
	ProAir Digihaler	DPI	90 mcg	200	\$99.93	\$0.50	
	Proventil® HFA	pMDI	90 mcg	200	\$91.17	\$0.46	
Ventolin® HFA	pMDI	90 mcg	200	\$66.53	\$0.33		
Levalbuterol	Xopenex® Inhalation Solution	SVN	0.31/3ml	24	\$499.39	\$20.81	
			0.63/3ml	24	\$252.95	\$10.54	
			1.25/3ml	24	\$252.95	\$10.54	
			1.25/0.5ml	24	\$449.67	\$18.74	
	Generic			0.31/3ml	25	\$22.59	\$0.90
				0.63/3ml	25	\$27.74	\$1.11
				1.25/3ml	25	\$23.30	\$0.93
				1.25/0.5ml	60	\$148.20	\$2.47
	Xopenex HFA™	pMDI	45 mcg	200	\$77.34	\$0.39	
	Generic	pMDI	45 mcg	200	\$19.45	\$0.10	
Ipratropium Bromide	Ipratropium Bromide	SVN	vial	25	\$8.98	\$0.36	
	Atrovent HFA®	pMDI	17 mcg	200	\$482.23	\$2.41	
Ipratropium Bromide and Albuterol Sulfate	Ipratropium Bromide and Albuterol Sulfate	SVN	.5/2.5ml	120	\$32.52	\$0.27	
	Combivent® Respimat®	SMI	20/100 mcg	120	\$499.66	\$4.16	

**HFA = hydrofluoroalkane; pMDI = pressurized metered-dose inhaler; SVN = small-volume nebulizer; DPI = dry-powder inhaler**  
 Cost information from [www.goodrx.com](http://www.goodrx.com). Prices used were from WalMart in 2023.

### Long-Acting Bronchodilator

Drug	Brand	Device	Strength	Doses	Cost	Cost/ Dose
Acclidinium Bromide	Tudorza Pressair®	DPI	400 mcg	60	\$318.10	\$5.30
Arformoterol	Brovana®	SVN	15 mcg/2ml	30	\$457.06	\$15.24
				60	\$907.12	\$15.12
Formoterol	Perforomist®	SVN	20 mcg/2ml	60	\$873.92	\$9.57
Salmeterol	Serevent®	DPI	50 mcg	60	\$340.31	\$5.67
Tiotropium	Spiriva®	DPI	18 mcg	30	\$359.25	\$11.98
	Spiriva Respimat®	pMDI	1.5 mcg	30	\$359.25	\$11.98
	Spiriva Respimat®	pMDI	2.5 mcg	30	\$359.25	\$11.98
Olodaterol	Striverdi Respimat®	pMDI	2.5 mcg	60	\$180.74	\$3.01
Umeclidinium	Incruse® Ellipta®	DPI	62.5 mcg	30	\$314.17	\$10.47
Glycopyrrolate	Lonhala Magnair	VMN	25 mcg	60	\$1189.85	\$19.80

### Mucoactive Drugs

Drug	Brand	Device	Strength	Doses	Cost	Cost/ Dose
Dornase Alpha	Pulmozyme®	SVN	2.5mg/2.5ml	30	\$3,918.00	\$130.60
N-Acetylcysteine		SVN	4ml/10%	1	\$2.06	\$2.06
			10ml/10%	1	\$7.95	\$3.18
			30ml/10%	1	\$14.24	\$1.90
			4ml/20%	1	\$7.11	\$7.11
			10ml/20%	1	\$14.77	\$5.91
			30ml/20%	1	\$22.65	\$3.02
Hyperosmolar Saline	HyperSal®	SVN	3.5%	60	\$197.40	\$3.29
			7%	60	\$197.40	\$3.29
	PulmoSal™ (ph 7.4)	SVN	7%	60	\$194.6	\$3.21

**HFA** = hydrofluoroalkane; **pMDI** = pressurized metered-dose inhaler; **SVN** = small-volume nebulizer; **DPI** = dry-powder inhaler  
 Cost information from www. goodrx.com. Prices used were from WalMart in 2023.

**Corticosteroids**

Drug	Brand	Device	Strength	Doses	Cost	Cost/ Dose
Beclomethasone	QVAR™ 40 Redihaler	pMDI	40 mcg	120	\$181.61	\$1.51
	QVAR™ 80 Redihaler	pMDI	80 mcg	120	\$239.82	\$2.00
Budesonide	Pulmicort Respules	SVN	0.25 mg	30	\$277.90	\$9.26
			0.5 mg	30	\$325.92	\$10.86
			1.0 mg	30	\$645.38	\$21.51
	Generic	SVN	0.25 mg	30	\$54.97	\$1.83
			0.5 mg	30	\$44.45	\$1.48
			1.0 mg	30	\$211.93	\$7.06
	Pulmicort® Flexhaler®	DPI	90 mcg	120	\$197.94	\$1.65
			180 mcg	120	\$262.88	\$2.19
Ciclesonide	Alvesco®	pMDI	80 mcg	60	\$108.54	\$1.81
			160 mcg	60	\$108.54	\$1.81
Fluticasone propionate	Flovent Diskus®	DPI	50 mcg	60	\$207.31	\$3.46
			100 mcg	60	\$124.59	\$2.07
			250 mcg	60	\$290.75	\$4.84
	Flovent HFA®	pMDI	44 mcg	120	\$218.82	\$1.83
			110 mcg	120	\$277.56	\$2.31
			220 mcg	120	\$412.65	\$3.51
	Generic	pMDI	44 mcg	120	\$135.36	\$1.13
			110 mcg	120	\$180.21	\$1.50
			220 mcg	120	\$270.58	\$2.26
	ArmonAir® Digihaler®	DPI	55 mcg	60	\$279.50	\$4.66
113 mcg			60	\$279.50	\$4.66	
232 mcg			60	\$348.03	\$5.80	
Fluticasone furoate	Arnuity® Ellipta®	DPI	50 mcg	30	\$222.92	\$7.43
			100 mcg	30	\$222.92	\$7.43
			200 mcg	30	\$296.26	\$9.88
Mometasone furoate	Asmanex® HFA	pMDI	50 mcg	120	\$195.46	\$1.63
			100 mcg	120	\$214.87	\$1.79
			200 mcg	120	\$251.39	\$2.10
	Asmanex®	DPI	110 mcg	30	\$199.66	\$6.65
			220 mcg	30	\$215.08	\$7.17

**HFA** = hydrofluoroalkane; **pMDI** = pressurized metered-dose inhaler; **SVN** = small-volume nebulizer; **DPI** = dry-powder inhaler  
 Cost information from www. goodrx.com. Prices used were from WalMart in 2023.

### Combination Drugs

Drug	Brand	Device	Strength	Doses	Cost	Cost/ Dose
Albuterol and Budesonide	AIRSUPRA	pMDI	90/80 mcg	120	Newly approved. No pricing available	
Fluticasone and Salmeterol	Advair HFA®	pMDI	45/21 mcg	120	\$345.48	\$2.88
			115/21 mcg	120	\$414.77	\$3.46
			230/21 mcg	120	\$543.01	\$4.53
	Advair Diskus®	DPI	100/50 mcg	60	\$355.61	\$5.59
			250/50 mcg	60	\$415.41	\$6.92
			500/50 mcg	60	\$544.39	\$9.07
	AirDuo RespiClick® Authorized Generic	DPI	55/14 mcg	60	\$100.86	\$1.68
			113/14 mcg	60	\$41.56	\$0.69
			232/14 mcg	60	\$41.56	\$0.69
	AirDuo Digihaler	DPI	55/14 mcg	60	\$462.25	\$7.70
			113/14 mcg	60	\$462.25	\$7.70
			232/14 mcg	60	\$519.37	\$8.86
	Wixela	DPI	100/50 mcg	60	\$98.82	\$1.65
			250/50 mcg	60	\$112.48	\$1.87
			500/50 mcg	60	\$182.20	\$3.09
Generic	DPI	100/50 mcg	60	\$98.82	\$1.65	
		250/50 mcg	60	\$112.48	\$1.87	
		500/50 mcg	60	\$187.65	\$3.13	
Budesonide and Formoterol	Symbicort®	pMDI	80/4.5 mcg	120	\$332.34	\$2.77
			160/4.5 mcg	120	\$378.74	\$3.16
	Breyna	pMDI	80/4.5 mcg	120	\$93.13	\$0.78
			160/4.5 mcg	120	\$90.74	\$0.77
Mometasone/Formoterol	Dulera®	pMDI	50/5 mcg	120	\$330.53	\$2.75
			100/5 mcg	120	\$362.14	\$3.17
			200/5 mcg	120	\$362.14	\$3.17
Fluticasone furoate/ Vilanterol	Breo® Ellipta®	DPI	100/25 mcg	60	\$252.30	\$4.21
			200/25 mcg	60	\$242.30	\$4.04



HFA = hydrofluoroalkane; pMDI = pressurized metered-dose inhaler; SVN = small-volume nebulizer; DPI = dry-powder inhaler  
 Cost information from www. goodrx.com. Prices used were from WalMart in 2023.

### Combination Drugs (continued)

Drug	Brand	Device	Strength	Doses	Cost	Cost/ Dose
Tiotropium/Olodaterol	Stiolto® Respimat®	SMI	2.5/2.5 mcg	60	\$459.53	\$7.66
Umeclidinium/Vilanterol	Anoro® Ellipta®	DPI	62.5/25 mcg	60	\$485.04	\$8.08
Acclidinium Bormide/ Formoterol	Duaklir Pressair®	DPI	400/12 mcg	60	\$653.93	\$10.90
Formoterol/ Gylcopyrrolate	Bevespi Aerosphere®	pMDI	9/4.8 mcg	120	\$441.62	\$3.68
Budesonide/Formoterol/ Gylcopyrrolate	Breztri Aerosphere®	pMDI	160/9/4.8 mcg	120	\$578.98	\$4.82
Fluticasone furate/ Umeclidinium/Vilanterol	Trelegy	DPI	100/62.5/25 mcg	60	\$657.87	\$10.96
			200/62.5/25 mcg	60	\$657.87	\$10.96

### Other Drugs

Drug	Brand	Device	Strength	Doses	Cost	Cost/ Dose
Zanamivir	Relenza®	DPI	5 mg	20	\$67.75	\$3.39
Tobramycin generic Bethkis Tobi Podhaler	TOBI®	SVN	300mg/5ml	56	\$8,682.00	\$155.04
			300mg/5ml	56	\$6,041.63	\$107.89
			300mg/4ml	56	\$6,672.96	\$2119.16
		DPI	28 mg	224	\$2,464.00	\$11.00
Aztreonam	Cayston®	SVN	75 mg	84	Specialty drug, no price available	
Cromolyn Sodium		SVN	20mg/2ml	60	\$302.00	\$5.03
Ribavirin	Virazole®	SPAG	6g	1	\$19,783.00	\$19,783.00
Mannitol	Aridol®	DP	Bronchial Challenge Test Kit, No pricing available			

# SMALL-VOLUME NEBULIZERS

Small-volume nebulizers (SVNs) are popular aerosol generators in acute care settings with clinicians and patients as they convert drug solutions or suspensions into aerosols that deposit into the patient's lower respiratory tract while requiring 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 that require active participation and hand-eye-breath coordination. 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, and 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)

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

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 that operate at a higher efficiency and require shorter treatment durations tend to be 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 5. Drug formulations and approved nebulizers for that formulation (Modified, with permission, from Reference 1)**

Drug Formulation	Approved Nebulizer
Acetylcysteine (Mucomyst®)	Nebulizer type not specified
Arformoterol (Brovana®)	Nebulizer type not specified
Formoterol (Perforomist®)	Nebulizer type not specified
Budesonide (Pulmicort Respules®)	Should not be used with ultrasonic nebulizer, hand-held PARI LC PLUS™ Reusable Nebulizer
Tobramycin (TOBI®)	Pari LC®, Sidestream Plus
Dornase alfa (Pulmozyme®)	Hudson T Up-draft II, Marquest Acorn® II, Pari LC®, Durable Sidestream®, Pari Baby™
Pentamidine (NebuPent)	Marquest Respirgard II
Ribavirin (Virazole®)	Small Particle Aerosol Generator
Iloprost (Ventavis®)	I-neb Adaptive Aerosol (AAD) System
Aztreonam (Cayston®)	Altera™ Nebulizer System
Treprostinil (Tyvaso®)	Tyvaso® Inhalation System

**Table 6. Relative costs of different nebulizer systems (Modified, with permission, from Reference 1)**

Nebulizer Type	Approximate Cost Range
Pneumatic compressor nebulizer	\$30–\$200
Ultrasonic nebulizer	\$70–\$250
Vibrating mesh/horn nebulizer	\$50–\$1,200
Microprocessor-controlled breath-actuated nebulizer	\$750–\$2,000

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

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

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

Technical Factors	Patient Factors
Design and model of nebulizer	Breathing pattern
Flow used to power nebulizer	Nose vs. mouth breathing
Fill volume of nebulizer	Composition of inspired gas
Solution characteristics	Airway obstruction
Composition of driving gas	Positive pressure delivery
Designs to enhance nebulizer output	Artificial airway and mechanical ventilation
Continuous vs. breath-actuated	

## 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 located in the aerosol stream impacts these droplets, producing smaller particles. The operating 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 is a key determining factor in the size of particles 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.<sup>1,33,34</sup>

- **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:** Altering the fill volume is another factor that impacts the efficiency of jet nebulizers. Studies report increased efficiency with this due to nebulizers with a fixed dead volume, and thus an increase in fill volume reduces the proportion of dead volume within the nebulizer. Although efficiency increases with a greater fill volume, there is also an increase in nebulization time.<sup>34</sup> Likewise, 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.<sup>1,34</sup> 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 helium-oxygen (heliox) gas mixtures 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,

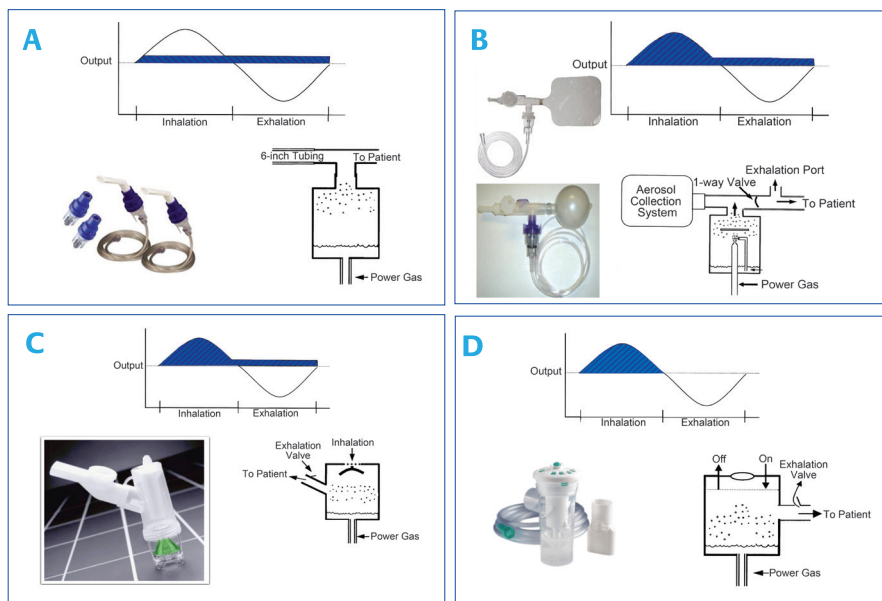
ultimately increasing treatment times. Consequently, the flow with heliox should be increased by 1.5–2 times to bring particle size and output back to levels achieved with air or oxygen.

- **Humidity and Temperature:**

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



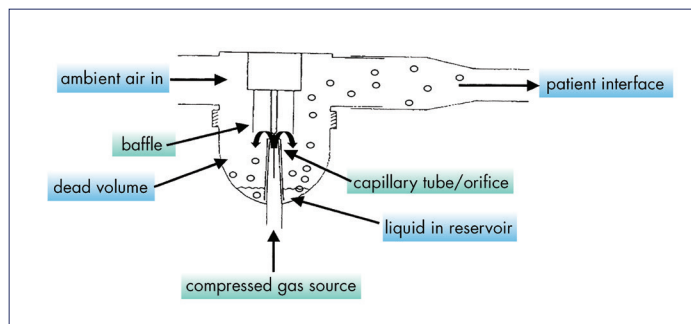
**Figure 4.** Different types of pneumatic jet nebulizer designs and their aerosol output indicated by the shaded area: **A.** pneumatic jet nebulizer with reservoir tube; **B.** jet nebulizer with collection bag; **C.** breath-enhanced jet nebulizer; **D.** breath-actuated jet nebulizer. (From Reference 1, with permission)

air during exhalation and anytime when the patient is not breathing (Figure 4-A).<sup>36-37</sup> Consequently, only 8-15% 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.<sup>38</sup> Figure 5 illustrates the functioning of a jet nebulizer. Examples of a jet nebulizer with a reservoir tube model include the Sidestream Nebulizers™ (Philips, Murrysville, PA) and the Micro Mist® (Teleflex Medical, Research Triangle Park, NC).

### Types of Pneumatic Jet Nebulizer Designs

Nebulizer design changes over the past decade have created different nebulizer categories.<sup>35,36</sup> 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.

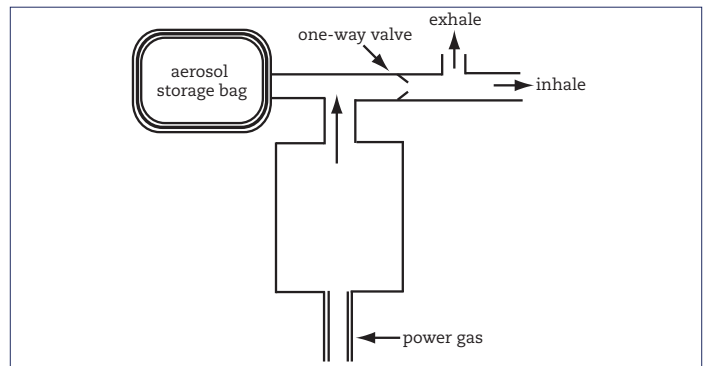
- A. Jet Nebulizer with a Reservoir Tube:** This is the least expensive and most widely used nebulizer. It provides continuous aerosol during inhalation, exhalation, and breath-hold, causing the release of aerosol to ambient



**Figure 5.** Schematic illustration of the function of a jet nebulizer (From Reference 1, with permission)

**B. Jet Nebulizer with Collection Bag or Elastomeric Reservoir Ball:**

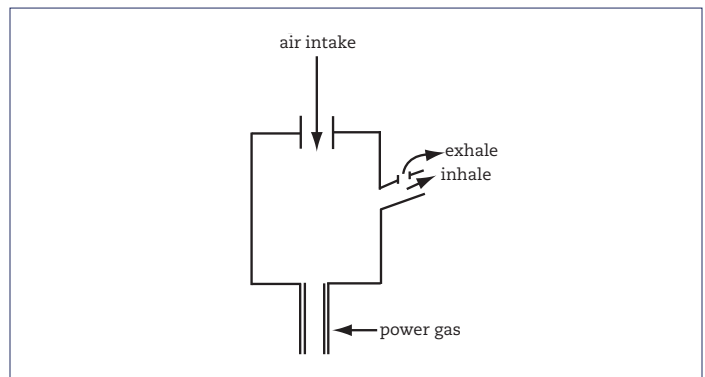
These types of nebulizers generate aerosol by continuously filling a reservoir (Figure 4-B). The patient inhales aerosol from the reservoir through a one-way inspiratory valve and exhales to the atmosphere through an exhalation port between the one-way inspiratory valve and the mouthpiece.<sup>35,37</sup> Figure 6 illustrates the principle of operation and patterns of gas flow during inhalation and exhalation with the Circulaire® II (Westmed, Tucson, AZ) which is one model of the nebulizer with a collection bag or elastomeric reservoir ball.



**Figure 6.** Schematic illustration of the function of a jet nebulizer with collecting bag. (From Reference 37, with permission)

**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® Sprint (PARI, Midlothian, VA), NebuTech HDN® (Salter Labs, Arvin, CA), and SideStream Plus® (Philips, Murrysville, PA) are the breath-enhanced nebulizers available on the market.

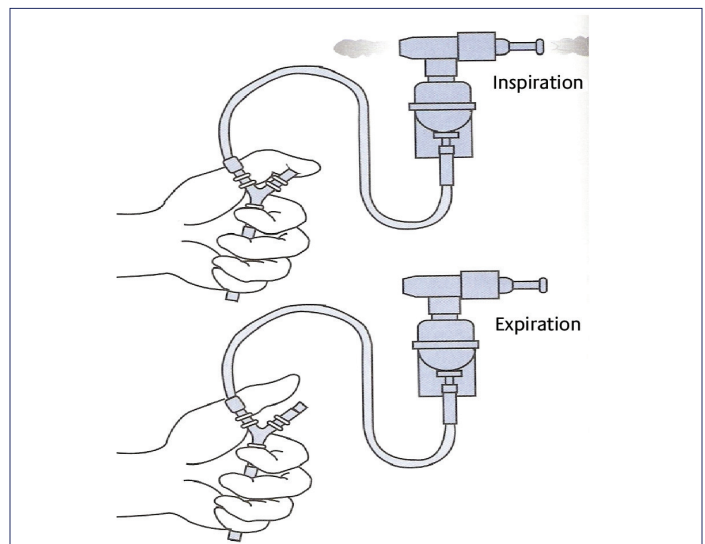


**Figure 7.** Schematic illustration of the function of a breath-enhanced jet nebulizer (From Reference 37, with permission)

**D. Breath-Actuated Jet Nebulizer:**

Breath-actuated nebulizers are designed to increase aerosol drug delivery to patients by generating aerosol only during active inspiration. Consequently, loss of medication during the expiration phase is greatly reduced, as shown in Figure 4-D.<sup>37</sup> 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)

2. **Mechanical Breath-Actuated:** The AeroEclipse® II BAN (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 active inspiration and eliminates the need for a storage bag or reservoir. Patients must be able to generate a sufficient inspiratory flow to trigger the nebulizer. Therefore, the sensitivity of this mechanism makes it suitable only for some children and adults. The AeroEclipse II BAN can deliver aerosolized medication in both a breath actuated or continuous mode. This device has not been tested for use with Pentamidine.
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

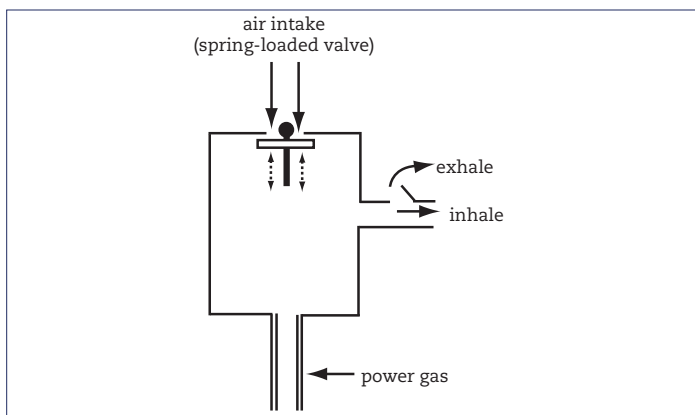
I-neb AAD® system (Philips) is one model of the microprocessor, breath-actuated nebulizer that uses vibrating mesh nebulization.

### Ultrasonic Nebulizers

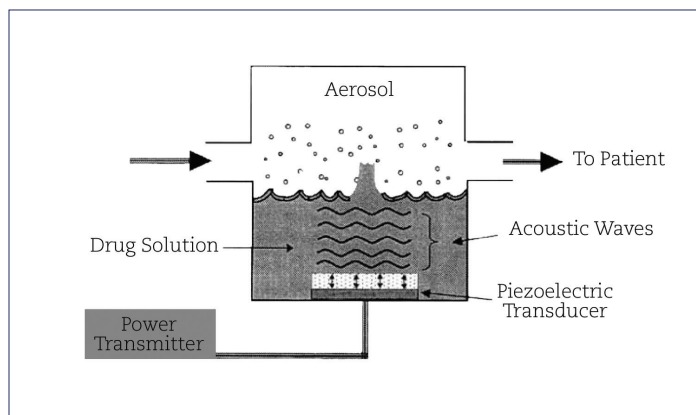
Ultrasonic nebulizers convert electrical energy to high-frequency vibrations using a transducer. These vibrations are transferred to the surface of the solution, creating a standing wave that generates aerosol (Figure 10). Ultrasonic nebulizers were initially introduced as large-volume nebulizers most 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 Tyvaso Inhalation System, MABIS® NebPak™, and MiniBreeze™ Ultrasonic Nebulizers (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.



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



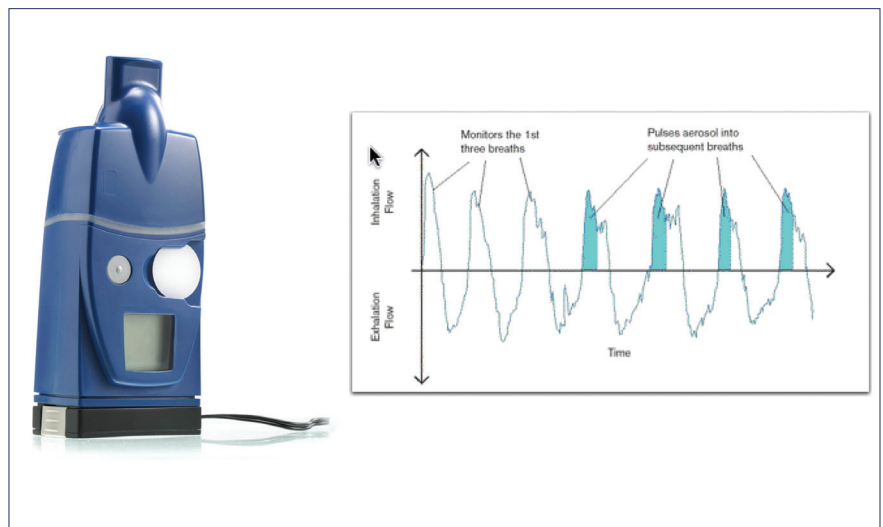
**Figure 10.** Components and operation principle of an ultrasonic nebulizer. (From Reference 1, with permission)

**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 Aerogen® Ultra and Solo (Aerogen, Galway, Ireland), Akita® Jet (Inamed, Germany), and eRapid® (PARI, Midlothian, VA) are models of the active vibrating mesh nebulizers (Figure 11).

**Passive Mesh:** These types of nebulizers utilize an ultrasonic horn to push fluid through a mesh (Figure 11). I-neb® AAD System® (Philips) and MicroAir™ NE-U100 (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. The 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 11.** Basic configurations of mesh nebulizers. Image by Allergy & Asthma Network via <https://allergyasthmanetwork.org/>.



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



## 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  $\mu\text{m}$ . Because of teratogenic characteristics of ribavirin, a scavenging system is strongly recommended for use during its administration.

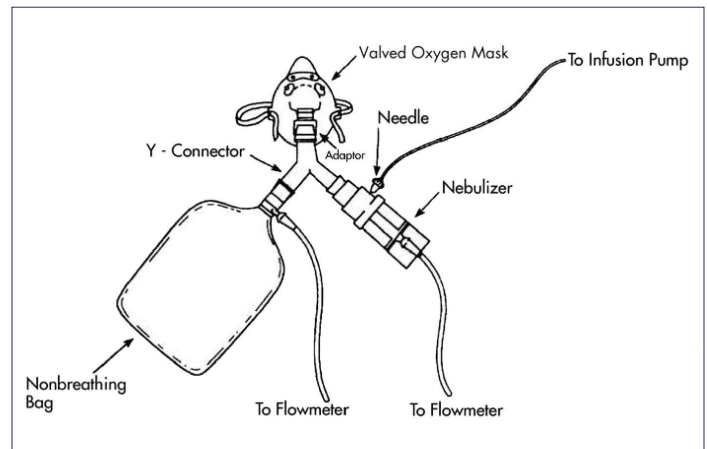
### Nebulizer for Aerosolized Pentamidine Administration

When administering aerosolized pentamidine, an SVN fitted with inspiratory and expiratory one-way valves and an expiratory filter is used. These valves prevent exposure of secondhand pentamidine aerosol and contamination of the ambient environment with exhaled aerosol. In 2014, the National Institute for Occupational Safety and Health (NIOSH) removed pentamidine from its hazardous drug list, indicating it no longer requires these devices or aerosol treatments to be delivered in a negative pressure room.

## Continuous Aerosol Therapy

Continuous aerosol drug administration is a safe treatment modality and is used to treat patients suffering acute asthma exacerbations. 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.<sup>39</sup> 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.

In regards to COVID-19 patients, the virus can stay sustainable and infectious in aerosols for hours and on surfaces up to days (depending on the inoculum shed). Nebulization is linked with release of aerosols during the patient's exhalation and is a cause of concern in COVID patients. The exhaled aerosols (fugitive emissions) contain particles ranging from 0.860 to 1.437  $\mu\text{m}$ , and up to 50% of the generated aerosol may continue to be deferred as airborne particles in the indoor environment for several hours. If aerosolized medication is required and has to be given to the patient, such patients should be isolated in an airborne infection isolation room (AIIR) or negative pressure rooms with minimum 12 air changes per hour or at least 160 L/min in areas with



**Figure 13.** Setup for continuous aerosol therapy (From Reference 1, with permission)

natural ventilation. It is important that health care workers wear PPEs, including a gown overall, face shield, gloves, and an N 95 respirator mask.<sup>172</sup> Admittance into these areas should be limited, and those who are not involved in direct bedside care with the patient should not be allowed.

The MAGNAIR (Figure 14) is a closed-system nebulizer utilizing eFlow® technology developed by PARI. Traditionally, nebulizers use an open system that allows medication from the vial to be placed directly into the medication cup of the nebulizer. MAGNAIR uses a sealed unit dose vial that is inserted into the cap of the MAGNAIR handset and pierced open once the cap is closed. This eliminates manual filling, reducing the chance for medication to be wasted or spilled. The MAGNAIR is a vibrating mesh nebulizer producing a MMAD (mass median aerodynamic



**Figure 14.** The Magnair is a vibrating mesh nebulizer (With permission from Sunovion)

diameter) of 3.7  $\mu\text{m}$  with a total administration time less than 3 minutes. Patients are initially prescribed a LONHALA MAGNAIR starter kit that contains a 30-day supply of LONHALA unit dose vials and the MAGNAIR nebulizer system.

Future prescriptions are supplied as a refill kit containing a 30-day supply of medication and a new nebulizer. The old nebulizer should be discarded at the end of each 30-day cycle. The nebulizer should only be used to nebulize LONHALA; no other medication should be used with the MAGNAIR nebulizer system. The MAGNAIR nebulizer is portable and powered by 4AA batteries or an AC adapter.

LONHALA (glycopyrrolate) is a long-acting muscarinic antagonist (LAMA) used to treat COPD twice daily. A one milliliter LONHALA unit dose vial contains 25 mcg and must be used with the MAGNAIR nebulizer system. Advise the patient to read the FDA patient information and instructions of use (FDA-approved patient labeling found in starter kit) prior to use. Inform patients that LONHALA MAGNAIR is not meant to relieve acute symptoms of COPD and extra doses should not be used for that purpose.

### **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 aerosol delivery. 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. Place 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.
6. Keep the nebulizer vertical during treatment.
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 per manufacturer's specifications.
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 are 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.

#### 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 and all connections are secured tightly.
3. Make sure that the nebulizer is cleaned and dried between uses.
4. Make sure that the nebulizer is operated in its proper orientation.

### Technique Box 1. Steps for Correct Use of Nebulizers (continued)

#### Troubleshooting

##### Problem with Jet Nebulizers: Absent or Low Aerosol

Causes	Solutions
<ul style="list-style-type: none"> <li>Loose or unattached connections</li> <li>Inappropriate flowmeter setting</li> <li>Obstruction in the orifice of the jet nebulizer</li> <li>If the treatment must be interrupted</li> </ul>	<ul style="list-style-type: none"> <li>Check the connections and make sure that they are properly attached.</li> <li>Check the flowmeter setting and adjust the flow if it is not appropriate.</li> <li>Check the orifice of the jet nebulizer and clear obstructions when needed.</li> <li>Turn off the unit to avoid waste.</li> </ul>

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

Causes	Solutions
<ul style="list-style-type: none"> <li>Incorrect battery installation (seen in both mesh and ultrasonic nebulizers)</li> <li>External power source connection (seen in both mesh and ultrasonic nebulizers)</li> <li>Overheated unit (seen in ultrasonic restart nebulizers)</li> <li>Incorrect connection of the control module cable (seen in mesh nebulizers)</li> <li>Malfunctioning electronics (seen in both mesh nebulizers and ultrasonic nebulizers)</li> </ul>	<ul style="list-style-type: none"> <li>Check the battery installation and reinstall if needed.</li> <li>Check the connections with the AC adapter and the electrical output.</li> <li>Turn off the unit, wait until it cools down, and turn the unit on again.</li> <li>Check the connections with the control module cable and attach them properly, if needed.</li> <li>Replace the unit.</li> </ul>

##### 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.<sup>18</sup> Whereas some respiratory therapists and patients tap the nebulizer in order to reduce dead volume and increase nebulizer output,<sup>40</sup> others continue aerosol therapy past the point of sputtering in an effort to decrease dead volume.<sup>18</sup> 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.<sup>18,41</sup> 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 50-53 for the cleaning instructions of small-volume nebulizers.

# INHALERS

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 15). Patients are commonly prescribed several types of inhalers with different instructions for operation. Without explaining the purpose for each prescribed inhaler confusion can take place, resulting in decreased adherence. Also, 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.

Figure 15. Common Inhalers Available in the United States



# Respiratory Treatments



Allergy & Asthma Network is a national nonprofit organization dedicated to ending needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.

AllergyAsthmaNetwork.org  
800.878.4403

1234 = DOSE INDICATOR G = GENERIC AVAILABLE DISEASE STATES: A = ASTHMA C = COPD

## SHORT-ACTING BETA<sub>2</sub>-AGONIST BRONCHODILATORS

relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours

<b>ProAir® Digihaler™</b> 90 mcg albuterol sulfate inhalation powder 1234 A	<b>ProAir® RespiClick®</b> 90 mcg albuterol sulfate inhalation powder 1234 A	<b>Proventil® HFA</b> 90 mcg albuterol sulfate 1234 A G	<b>Ventolin® HFA</b> 90 mcg albuterol sulfate 1234 A G	<b>Xopenex® HFA</b> 45 mcg levalbuterol tartrate A G
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## LONG-ACTING BETA<sub>2</sub>-AGONIST BRONCHODILATORS

relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath for at least 12 hours

<b>Serevent® Diskus®</b> 50 mcg salmeterol xinafoate inhalation powder 1234 A C	<b>Striverdi® RespiMat®</b> 2.5 mcg olodaterol hydrochloride 1234 C
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## INHALED CORTICOSTEROIDS

reduce and prevent swelling of airway tissue; they do not relieve sudden symptoms of coughing, wheezing or shortness of breath

<b>Alvesco® HFA</b> 80, 160 mcg ciclesonide 1234 A	<b>ArmonAir® Digihaler™</b> 55, 113, 232 mcg fluticasone propionate inhalation powder 1234 A	<b>Arnuity® Ellipta®</b> 50, 100, 200 mcg fluticasone furoate inhalation powder 1234 A	<b>Asmanex® HFA</b> 50, 100, 200 mcg mometasone furoate 1234 A	<b>Asmanex® Twisthaler®</b> 110, 220 mcg mometasone furoate inhalation powder 1234 A	<b>Flovent® Diskus®</b> 50, 100, 250 mcg fluticasone propionate inhalation powder 1234 A	<b>Flovent® HFA</b> 44, 110, 220 mcg fluticasone propionate 1234 A	<b>Pulmicort Flexhaler®</b> 90, 180 mcg budesonide inhalation powder 1234 A	<b>QVAR® Redihaler™</b> 40, 80 mcg beclomethasone dipropionate 1234 A
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## MUSCARINIC ANTAGONISTS (ANTICHOLINERGIC)

relieve cough, sputum production, wheeze and chest tightness associated with chronic lung diseases

<b>Short-acting</b> <b>Atrovent® HFA</b> 17 mcg ipratropium bromide 1234 C	<b>Long-acting</b> <b>Incruse® Ellipta®</b> 62.5 mcg umeclidinium inhalation powder 1234 C	<b>Spiriva® HandiHaler®</b> 18 mcg tiotropium bromide inhalation powder G	<b>Spiriva® RespiMat®</b> 1.25, 2.5 mcg tiotropium bromide 1234 A C	<b>Tudorza® Pressair™</b> 400 mcg acclidinium bromide inhalation powder 1234 C
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## COMBINATION MEDICATIONS

contain both short-acting beta<sub>2</sub>-agonist and short-acting muscarinic antagonist

<b>Combivent® RespiMat®</b> 20/100 mcg ipratropium bromide and albuterol 1234 C
---

## COMBINATION MEDICATIONS

contain both inhaled corticosteroid and long-acting beta<sub>2</sub>-agonist (LABA)

<b>Advair Diskus®</b> 100/50, 250/50, 500/50 mcg fluticasone propionate and salmeterol inhalation powder 1234 A C G	<b>Advair® HFA</b> 45/21, 115/21, 230/21 mcg fluticasone propionate and salmeterol xinafoate inhalation powder A G	<b>AirDuo® Digihaler™</b> 55/14, 113/14, 232/14 mcg fluticasone propionate and salmeterol inhalation powder 1234 A	<b>AirDuo® RespiClick®</b> 55/14, 113/14, 232/14 mcg fluticasone propionate and salmeterol inhalation powder 1234 A G	<b>Breo® Ellipta®</b> 100/25, 200/25 mcg fluticasone furoate and vilanterol inhalation powder 1234 A C	<b>Dulera®</b> 50/5, 100/5, 200/5 mcg mometasone furoate and formoterol fumarate dihydrate 1234 A	<b>Symbicort®</b> 80/4.5, 160/4.5 mcg budesonide and formoterol fumarate dihydrate 1234 A C G	<b>Wixela® Inhub™</b> 100/50, 250/50, 500/50 mcg fluticasone propionate and salmeterol xinafoate (approved generic of Advair Diskus®) 1234 A C G
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## COMBINATION MEDICATIONS

contain both long-acting beta<sub>2</sub>-agonist (LABA) and long-acting muscarinic antagonist (LAMA)

<b>Anoro® Ellipta®</b> 62.5/25 mcg umeclidinium and vilanterol inhalation powder 1234 C	<b>Bevespi Aerosphere®</b> 3/4.8 mcg glycopyrrolate and formoterol fumarate 1234 C	<b>Duakir® Pressair™</b> 400, 12 mcg acclidinium bromide and formoterol fumarate 1234 C
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## COMBINATION MEDICATIONS

contain inhaled corticosteroid, long-acting beta<sub>2</sub>-agonist (LABA) and long-acting muscarinic antagonist (LAMA)

<b>Trelegy® Ellipta®</b> 200/62.5/25 mcg, 100/62.5/25 mcg fluticasone furoate, umeclidinium and vilanterol inhalation powder 1234 A C	<b>Breztri Aerosphere™</b> 160/9/4.8 mcg budesonide, glycopyrrolate and formoterol fumarate 1234 A
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## BIOLOGICS

target cells and pathways that cause airway inflammation; delivered by injection or IV

<b>Cinqair®</b> realizumab A	<b>Dupixent®</b> dupilumab A	<b>Fasenra™</b> bemralizumab A	<b>Nucala®</b> mepolizumab A	<b>Tezspire™</b> tezepelumab-ekko A	<b>Xolair®</b> omalizumab A
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## BRONCHIAL THERMOPLASTY

A minimally invasive procedure that uses mild heat to reduce airway smooth muscle, leading to fewer severe asthma flares, ER visits, and days lost from activities.  
www.aafp.org/asthma.com  
A



## PDE4 INHIBITORS

ease lung inflammation and reduce exacerbations

<b>Daliresp®</b> 250, 500 mcg roflumilast C
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Reviewed by Dennis Williams, PharmD

Generic versions of brand name inhalers are not included on this poster. Generic inhalers may be a different color.

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# PRESSURIZED METERED-DOSE INHALERS

Since its development by Dr. George Maisson 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. Ensuring device effectiveness and safety in the time of COVID-19 depends on choosing the right device for the right patient after a careful evaluation of device features, the potential risk for device contamination, and viral transmission. It is vital for respiratory therapists to train patients on the risk of contamination during device preparation and viral transmission<sup>178</sup>. Table 9 gives the advantages and disadvantages associated with the use of pMDIs.

## Types of pMDIs

There are two major types of pMDIs: conventional 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.

### Conventional pMDI

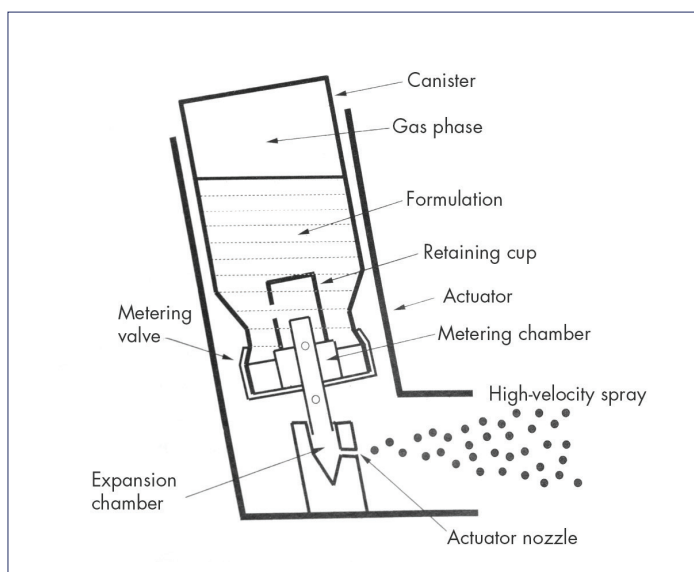
As seen in Figure 16, the pMDI consists of a canister, the medication, the propellant/excipient, a metering valve, the mouthpiece, and actuator.<sup>42</sup> The medication represents only 1–2% of the mixture emitted from the pMDI and is either suspended or dissolved in the propellant/excipient mixture. The propellant of the pMDI makes up 80% of the mixture. 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 ranges from 25–100  $\mu\text{L}$  and provides 50  $\mu\text{g}$  to 5 mg of drug per actuation, depending on the drug formulation.

**Table 9.** Advantages and disadvantages of pMDIs (Modified, with permission, from Reference 1)

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

**Table 10.** Basic components of the pMDI (From Reference 1 with permission)

Component	Particulars
Canister	Inert, able to withstand high internal pressures and utilize a coating to prevent drug adherence
Propellants	Liquefied compressed gases in which the drug is dissolved or suspended
Drug Formulary	Particulate suspensions or solutions in the presence of surfactants or alcohol that allocate the drug dose and the specific particle size
Metering Valve	Most critical component that is crimped onto the container and is responsible for metering a reproducible volume or dose, elastomeric valves for sealing and preventing drug loss or leakage
Actuator	Frequently referred to as the 'boot' and 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)
Dose Counter	This component provides a visual tracking of the number of doses remaining in the pMDI



**Figure 16.** Standard components of pMDI (Modified with permission from Reference 42)

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 propellants used with pMDIs are HFAs. HFAs are pharmacologically inert and do not contain surfactant or use alcohol for this purpose.

#### 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 the 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 17 shows the standard components of the Respimat®.





Figure 17. Soft-mist inhaler

### Currently Available pMDI Formulations

A number of aerosol formulations are available for use in pMDIs today (Figure 15). 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  $\mu\text{m}$  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 pMDI is in the fine particle fraction range in which the aerodynamic diameter of aerosols is less than 5  $\mu\text{m}$ . 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 factors:

**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.<sup>43</sup> 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.<sup>12</sup>

**Storage Temperature:** Outdoor use of pMDIs in very cold weather may significantly decrease aerosol drug delivery. Dose delivery was constant with HFA pMDIs over the range of  $-20^{\circ}$  to  $20^{\circ}\text{C}$ .

**Nozzle Size and Cleanliness:** The amount of medication delivered to the patient is dependent upon nozzle size, cleanliness, and lack of moisture. The 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.<sup>44</sup> A nozzle extension with an inner diameter  $<1$  mm increases drug delivery.<sup>44</sup> 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.<sup>43</sup> A pause between puffs may improve bronchodilation, especially during asthma exacerbations with episodes of wheezing and poor control of symptoms.<sup>45</sup> In other cases, such as in the day-to-day management of pre-adolescents with a beta agonist (terbutaline) and a corticosteroid (budesonide), pauses between puffs have not been found to be beneficial.<sup>46</sup> 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.<sup>1,7,13</sup>

**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

**Table 11.** Priming requirements for common commercially available pMDIs

Short-Acting Bronchodilators			
Generic Name	Brand Name	Time to Prime	No. of Sprays
Albuterol Sulfate HFA	Proventil® HFA	New and when not used for 2 weeks	4
	Ventolin® HFA	New and when not used for 14 days	4
Levalbuterol HCl	Xopenex® HFA	New and when not used for 3 days	4
Ipratropium Bromide HFA	Atrovent® HFA	New and when not used for 3 days	2
Ipratropium Bromide/Albuterol Sulfate Combination	Combivent® HFA	New and when not used for 24 hours	3
Inhaled Corticosteroids			
Generic Name	Brand Name	Time to Prime	No. of Sprays
Beclomethasone Propionate HFA	QVAR™ Redihaler	New and when not used for 10 days	2
Ciclesonide	Alvesco®	New and when not used for 10 days	3
Fluticasone Propionate	Flovent® HFA	New	4
		Not used more than 7 days or if dropped	1
Combination Drugs			
Generic Name	Brand Name	Time to Prime	No. of Sprays
Budesonide combined with Formoterol	Symbicort® HFA	New and not used more than 7 days or if dropped	2

for a while. Because shaking the pMDI will mix the suspension in the canister but not the metering chamber, priming of the pMDI is required. Table 11 provides the recommended guidelines for priming the various pMDIs available on the market.

**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 during 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.<sup>47,48</sup>

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.<sup>47,49</sup> In contrast, other researchers suggest that the open-mouth technique does not offer any advantage over the closed-mouth technique,<sup>50,51</sup> but that it does create additional hazards such as the aerosol plume being misdirected from the mouth and into the eye or elsewhere.<sup>52</sup> 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.

**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.<sup>53-55</sup> 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

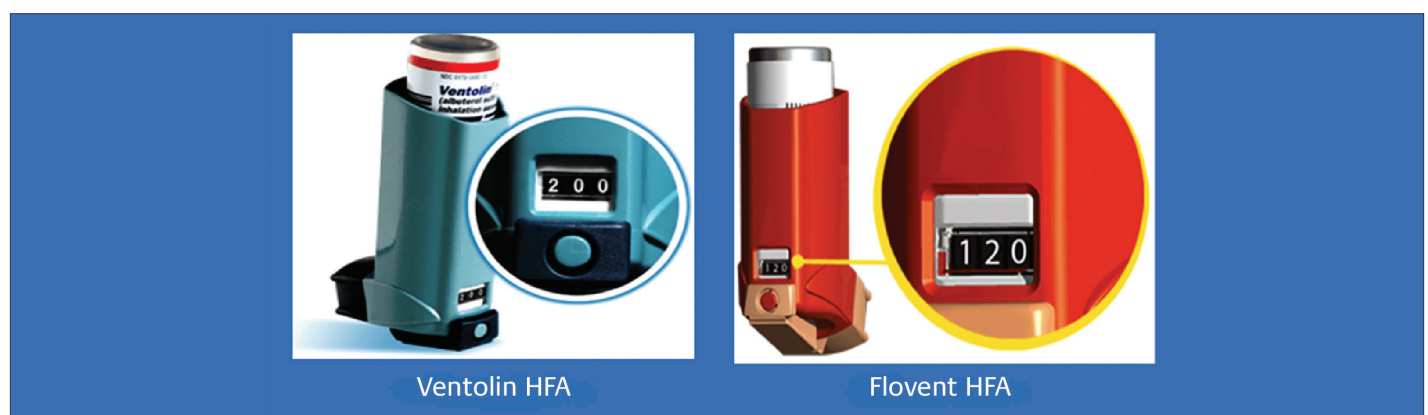
after the pMDI is "empty of drug."<sup>13,56</sup> Also, the pMDI without a dose counter could lead to waste if the inhaler is discarded prematurely. Indirect methods such as floating the canister in water are misleading and can reduce the ability of the pMDI to work properly.<sup>55,57,58</sup> Therefore, 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.<sup>59</sup> 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<sup>®</sup> HFA (GlaxoSmithKline, Research Triangle Park, NC) and Flovent<sup>®</sup> HFA (GlaxoSmithKline) have built-in dose counters (Figure 18).

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 of and patient satisfaction with dose counters,<sup>60-62</sup> care must be

*(continued on page 31)*



**Figure 18.** Counter on Ventolin<sup>®</sup> HFA and Flovent<sup>®</sup> HFA pMDIs

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

### Technique for pMDIs

#### Open-Mouth Technique: The patient should be instructed to:

1. Remove the mouthpiece cover and shake the pMDI thoroughly.
2. Prime the pMDI into the air if it is new or has not been used for several days.
3. Sit up straight or stand up.
4. Breathe all the way out.
5. Place the pMDI two finger widths away from their lips.
6. 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.
7. Actuate the pMDI as they begin to breathe in slowly.
8. Breathe slowly and deeply through the mouth and hold their breath for 10 seconds. If they cannot hold their breath for 10 seconds, then for as long as possible.
9. Wait one minute if another puff of medicine is needed.
10. Repeat Steps 2–10 until the dosage prescribed by the physician is reached.
11. If taking a corticosteroid, they should rinse their mouth after the last puff of medicine, spit out the water, and not swallow it.
12. Replace the mouthpiece cover on the pMDI after each use.

#### Closed-Mouth Technique: The patient should be instructed to:

1. Remove the mouthpiece cover and shake the inhaler thoroughly.
2. Prime the pMDI into the air if it is new or has not been used for several days.
3. Sit up straight or stand up.
4. Breathe all the way out.
5. Place the pMDI between their teeth; make sure that their tongue is flat under the mouthpiece and does not block the pMDI.
6. Seal their lips.
7. Actuate the pMDI as they begin to breathe in slowly.
8. Hold their breath for 10 seconds. If they cannot hold their breath for 10 seconds, then for as long as possible.
9. Wait one minute if another puff of medicine is needed.
10. Repeat Steps 2–10 until the dosage prescribed by the patient's physician is reached.
11. If taking a corticosteroid, they should rinse their mouth after the last puff of medicine, spit out the water, and not swallow it.
12. Replace the mouthpiece cover on the pMDI after each use.

#### Breath-Actuated pMDI (RediHaler™) Technique: When using the RediHaler™, the patient should be instructed to:

1. Remove the white cap cover over the mouthpiece and check for foreign objects.
2. Keep the RediHaler™ in an upright position.
3. Breathe out normally, away from the RediHaler™.
4. Place the pMDI between their teeth. Make sure that their tongue is flat under the mouthpiece and does not block the pMDI.
5. Seal their lips around the mouthpiece and do not block the air vent on top of the inhaler.
6. Inhale deeply through the mouthpiece with steady moderate force.
7. Remove the mouthpiece from the mouth.
8. Hold breath for 5 to 10 seconds or as long as possible.
9. Repeat steps above until the dosage prescribed by the patient's physician is reached.
10. Replace the mouthpiece cover and rinse mouth.

## Technique Box 2. Steps for Correct Use of pMDIs (continued)

### Technique for pMDIs

#### Preparation:

1. With the 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 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 cap until it snaps fully open.
10. Point the inhaler toward the ground. Press the dose-release button. Close the cap.
11. Repeat steps 7–10 until a spray is visible.
12. Once the spray is visible, repeat steps 7–10 three more times to make sure the inhaler is ready for use.

#### Patient-Use Instructions:

1. Hold the inhaler upright with the 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 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 cap until next prescribed dose.

#### General Steps To Avoid Reduced or No Dosing for pMDIs: The patient should:

1. Remove the cap of the pMDI from the boot.
2. Prime as directed (Table 11 on page 27).
3. Clean and dry the boot of the pMDI based on the manufacturer's guidelines.
4. Track remaining doses.

## Technique Box 2. Steps for Correct Use of pMDIs (continued)

### Troubleshooting

#### Problem with Jet Nebulizers: Absent or Low Aerosol

Causes	Solutions
<ul style="list-style-type: none"> <li>• Incorrect pMDI assembly</li> <li>• Incorrect pMDI and spacer assembly</li> <li>• Empty pMDI</li> </ul>	<ul style="list-style-type: none"> <li>• Check the assembly and reassemble when needed.</li> <li>• Check the assembly of the pMDI/spacer and reassemble if needed.</li> <li>• Check the dose counter or daily log sheet to ensure there is enough medicine in the canister. Otherwise, replace the pMDI.</li> </ul>

(continued from page 28)

taken to assure that a third-party dose counter works with the specific pMDI being used.<sup>18,63</sup> 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.<sup>63</sup> Using a third-party dose-counting device increases the cost of aerosol therapy, which may limit its wide acceptance. Figure 19 shows currently available pMDI dose counters in the U.S..

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 doses remaining in the pMDI, Table 12 contains recommendations for keeping track of the number of doses with and without integrated dose counters.

**Cleaning:** Please refer to the Infection Control section on page 50 for the cleaning instructions for inhalers.



Figure 19. Currently available pMDI dose counters on the market

**Table 12. Monitoring remaining pMDI doses**

<b>Without Dose Counter: The user should:</b>
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. 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 are administered on a daily log sheet and subtract them from the total number 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.
<b>With Dose Counter: The user should:</b>
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.

# METERED-DOSE INHALER ACCESSORY DEVICES

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.

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 that 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 U.S. 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), and OptiChamber Diamond® and the OptiChamber® Advantage (Philips) are examples of forward sprays. 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

**Table 13.** Advantages and disadvantages of holding chambers or spacers ("add-on" devices) used with pMDIs (Modified, with permission, from Reference 64)

Advantages	Disadvantages
Reduces oropharyngeal drug impaction and loss	Large and cumbersome compared to the pMDI alone
Increases inhaled drug by two to four times over the pMDI alone	More expensive and bulky than a pMDI alone
Allows use of the pMDI during acute airflow obstruction with dyspnea	Some assembly may be needed
No drug preparation required	Patient errors in firing multiple puffs into chamber prior to inhaling or there is a delay between actuation and inhalation
Simplifies coordination of pMDI actuation and inhalation	Possible contamination with inadequate cleaning
Helps reduce local and systemic side effects <sup>64</sup>	





**Figure 20.** Examples of VHCs and spacers

ACE<sup>®</sup> has a canister nozzle receptacle, while the AeroChamber<sup>®</sup>, OptiChamber Advantage<sup>®</sup>, and OptiChamber Diamond<sup>®</sup> 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 20 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. Some 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. It's important to assure the valve works properly, as dysfunctional valves can cause ineffective delivery of medication.<sup>65</sup> 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, delay between actuation and inhaling the dose, or improper insertion of actuator into spacer and/or VHC.<sup>66</sup> It has been shown that improper insertion of the actuator can contribute to a spray of medication not following the optimal axis of the chamber and a good portion of medicine ending up deposited on the inside of

the chamber.<sup>67</sup> Also, it has been suggested that spacer size and shape may be related to deposition of specific particle sizes.<sup>66</sup> More research is needed on length, shape, and volume of spacers. 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 50 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. Remove the mouthpiece cover and shake the inhaler thoroughly.
2. Prime the pMDI into the air if it is new or has not been used for several days.
3. Assemble the apparatus and check for foreign objects.
4. Keep the canister in a vertical position.
5. Sit up straight or stand up.
6. Breathe all the way out.
7. Follow the instructions below based on the type of device interface used:

With the mouthpiece:	With the mask:
<ol style="list-style-type: none"> <li>a. Place the mouthpiece of the spacer between their teeth and seal their lips. Make sure that their tongue is flat under the mouthpiece and does not block the pMDI.</li> <li>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.</li> <li>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.</li> </ol>	<ol style="list-style-type: none"> <li>a. Place the mask completely over the nose and mouth and make sure it fits firmly against the face.</li> <li>b. 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.</li> <li>c. 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.</li> <li>d. Wait 15–30 seconds if another puff of medicine is needed.</li> <li>e. Repeat steps above until the dosage prescribed by the patient’s physician is reached.</li> <li>f. If taking a corticosteroid, rinse the mouth after the last puff of medicine, spit out the water, and do not swallow it.</li> <li>g. Replace the mouthpiece cover on the pMDI after each use.</li> </ol>

#### General Steps To Avoid Reduced or No Dosing for pMDIs with Spacer/VHC: 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

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 intention 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.

## Types of DPIs

Currently, DPIs can be classified into three categories based on the design of their dose containers: single-dose DPIs, multiple unit-dose DPIs, and multiple-dose DPIs (Figure 21). 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 premeasured 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 within 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

**Table 14.** Advantages and disadvantages of DPIs (Modified, with permission, from Reference 1)

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

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 HandiHaler® (Boehringer Ingelheim), and The TOBI Podhaler® (Novartis) are examples of single-dose DPIs (Figure 21). While the HandiHaler® is used for the delivery of tiotropium bromide, the TOBI Podhaler is utilized for the administration of tobramycin. 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 swallow 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 RespiClick®, the Flexhaler® (Organon LLC), and the Pressair® (AstraZeneca, Wilmington, DE), and the Diskus® and Ellipta® (GlaxoSmithKline). The Twisthaler® 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.



**Figure 21.** Currently available dry-powder aerosol formulations in the United States categorized by design features (see text description of design features)

In the Twisthaler® 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 Twisthaler® 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 Twisthaler®, no priming is necessary with the Diskus®.

The Ellipta® is similar to the Diskus® and is used in the delivery of various long-acting beta agonists and combination medications such as Brea® and Anoro® (GlaxoSmithKline) as well as other drugs such as Incruse®, an ultra-long-acting anticholinergic, and Arnuity® (Mylan), a corticosteroid. Similar to the Diskus®, this multi-dose DPI utilizes two coiled blister strips containing individually wrapped doses of dry-powder medication. Opening the mouthpiece cover peels the foil to expose the medication dosage. After inhaling the medication, the mouthpiece cover is returned to its closed position. It is important to note that if the mouthpiece cover is opened and the dose is prepared, closing the mouthpiece cover without inhalation of the medication will result in a lost dose.

The Pressair® is multi-dose dry power inhaler that administers acclidinium bromide in 30 or 60 doses. The device utilizes a button that once depressed loads the medication. This can be confirmed visually by checking the control window that changes from red to green once a new dose is ready. Once the patient inhales a click can be heard, noting the dose was inhaled. The individual may confirm by looking at the control window that changes from green to red to indicate a dose has been taken. Patients will need to have a minimum peak inspiratory flow of 35 L/min to effectively use this device.

The Inhub® is also similar to the Diskus® as a multi-dose dry powder inhaler. It is used to deliver Wixela® (Mylan), which is the equivalent generic for Advair Diskus® and has the same steps for usage. It is a pre-metered/pre-filled multiple-dose inhaler containing 60 doses of fluticasone propionate and salmeterol inhalation powder. After opening the mouthpiece cover from

top to bottom and pushing the lever down to release a dose the individual may inhale the medication. Once the mouthpiece cover is pushed back on top the lever will return to the start position and the dose counter will count down one dose. There is a red indicator that will appear after taking 51 doses.

The Digihaler® (Teva) is a smart inhaler system that contains a built-in electronic module that records and stores information about the inhaler events. It may be used with, and transmits information to, an app through Bluetooth® wireless technology. It is used in the delivery of various medications such as ProAir®AirDuo® (Teva), and Armonair®. In using the Digihaler®, the inhaler must be held upright while opening the cap and shouldn't be opened until the user is ready for a dose. The cap will click and that means the medication is available for inhalation. The cap needs to be placed back in closed position and opened again if another dose is needed. Digihaler® has a dose counter and individuals do not need to be wirelessly connected to the mobile app for it to work or to take the medication. It does not need to be primed and cannot be used with a spacer or volume holding chamber.

### Currently Available DPI Formulations

As seen in Figure 21, 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 factors:

**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<sup>®</sup> has a higher resistance than the Diskus<sup>®</sup> and therefore requires a greater inspiratory effort. When the patient inhales through the DPI, they create 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. A respiratory therapist should utilize an In Check Dial (Figure 22) to measure inspiratory flow of the DPI to be used. Noting that each DPI requires different flows, the respiratory therapist may need to make suggestions based on the patient's 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<sup>®</sup> and Pressair<sup>®</sup> should be protected from humidity and moisture as much as possible. Whereas it is easy to keep the Twisthaler<sup>®</sup> and Pressair<sup>®</sup> 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 mouthpiece, especially after the device is cocked and loaded and when the powder is exposed. Therefore, patients must be instructed to exhale away from the DPI prior to inhalation.

## 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.

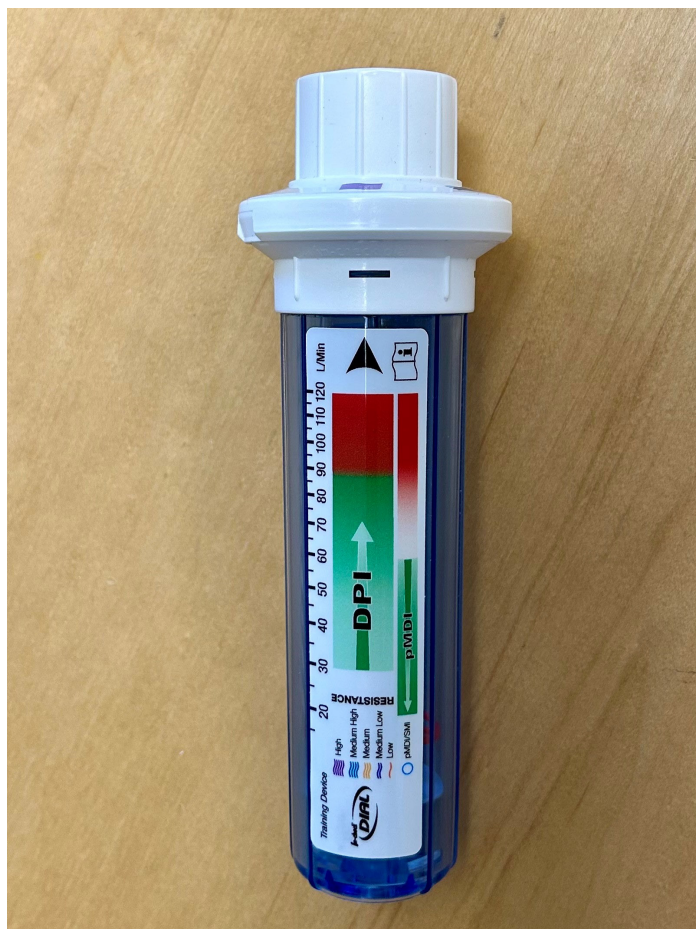


Figure 22. In Check Dial

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

### Technique for Single-Dose DPIs

#### 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 during inhalation.
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.

#### Podhaler: The patient should be instructed to:

1. Hold the base of the Podhaler and unscrew the lid in a counter-clockwise direction, setting aside the lid once complete.
2. Stand the Podhaler upright in the base of the case.
3. Hold the body of the Podhaler and unscrew the mouthpiece in a counter-clockwise direction, setting aside the mouthpiece on a clean, dry surface.
4. Take the blister card and tear the pre-cut lines along the length and width.
5. Peel the foil that covers one Podhaler capsule on the blister card.
6. Remove the capsule one at a time and place in the capsule chamber at the top of the Podhaler.
7. Place the mouthpiece back on the Podhaler and screw the mouthpiece in a clockwise direction until tight.
8. Hold the Podhaler pointing the mouthpiece down.
9. Placing the thumb on the blue button, press the blue button all the way down once.
10. Exhale as completely as possible away from the inhaler.
11. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece.
12. Breathe in a full breath deeply and slowly and perform a 10-second breath hold (or as long as comfortable).
13. Exhale away from the device.
14. To ensure the entire dose has been inhaled, repeat steps 10 through 12.
15. Unscrew the mouthpiece and remove the capsule from the chamber and throw away.
16. Repeat steps 4 to 15 three more times until all four doses (4 capsules) have been used.

#### 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.
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 the 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 perform a 10-second breath hold or as long as comfortable.
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 perform a 10-second breath hold 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 and close the lips tightly around the mouthpiece.
8. Inhale the dose with a rapid and steady flow while holding the Twisthaler® horizontal.
9. Remove the mouthpiece from the mouth and perform a five to 10-second breath hold or as long as comfortable.
10. Do not exhale into the device.
11. Immediately replace the cap, turn in a clockwise direction, and gently press down until a click is heard.
12. Firmly close the Twisthaler® to assure that the next dose is properly loaded.
13. Be sure that the arrow is in line with the dose-counter window.
14. Store device in cool, dry place.



#### Technique Box 4. Steps for Correct Use of Each Model of DPIs (continued)

##### Technique for Multiple-Dose DPIs (continued)

###### 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 is turned 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. Do not exhale into the device.
8. Place the mouthpiece into the mouth, close the lips tightly around the mouthpiece, and inhale deeply and forcefully through the inhaler.
9. Remove the inhaler from the mouth and exhale.
10. Do not exhale into the device.
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 the mouth with water after each dose to reduce the risk of developing thrush. Do not swallow the rinse water.

###### Pressair: The patient should be instructed to:

1. Wash and dry 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 the patient and the green button on top. DO NOT place in the 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 the mouth.
7. Place the mouthpiece into the mouth and breathe in quickly and deeply.
8. A click is heard when the dose is delivered, but continue the deep breath until at full capacity.
9. Remove the device from the 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.

###### RespiClick®: The patient should be instructed to:

1. Hold the inhaler upright with the red mouthpiece cover facing the patient.
2. Remove the red mouthpiece cover in the upright position until a click is heard. This exposes the mouthpiece as well as loads the medication. The dose counter on the back of the device will count down one number each time the medication is delivered.
3. Exhale away from the device.
4. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece.
5. Do not block the air vent above the mouthpiece.
6. Inhale deeply through the RespiClick®.
7. Remove the mouthpiece from the mouth and perform a 10-second breath hold or as long as comfortable.
8. Check the dose counter on the back of the device to make sure the dose was delivered.
9. Firmly close the cap over the mouthpiece.
10. Store the device in a cool dry place.
11. Observe the counter for the number of doses remaining and replace when appropriate.

#### Technique Box 4. Steps for Correct Use of Each Model of DPIs (continued)

##### Technique for Multiple-Dose DPIs (continued)

###### Inhub®: The patient should be instructed to:

1. Hold the Inhub in one hand and with your other hand on the grip lower the mouthpiece cover from top to bottom.
2. Hold the inhaler in the vertical position. Push the yellow lever down to the end of the purple arrows (you will hear a click) and the Inhub is now ready to use.
3. Exhale away from the device.
4. Put the mouthpiece to your lips. Breathe in quickly and deeply through the Inhub.
5. Remove the Inhub from the mouth and perform a 10-second breath hold or as long as comfortable.
6. Check the dose counter on the back of the device to make sure the dose was delivered.
7. Push the mouthpiece cover up to the closed position; this will automatically return the yellow lever to the start position. Make sure the Inhub is shut and you cannot see the mouthpiece.
8. The dose counter will count down one dose as you close the mouthpiece cover. This will now tell you how many doses are left.
9. Remember to rinse your mouth with water after breathing in the medicine. Spit out the water. Do not swallow it.
10. Store the device in a cool dry place.
11. After 51 doses, a red indicator will be present. This indicator warns you there are 9 or fewer doses left and is a reminder to get a refill.

###### Digihaler®: The patient should be instructed to:

1. Hold the inhaler upright with the bright colored (different color depending on the brand) mouthpiece cover facing the patient.
2. Remove the bright colored mouthpiece cover in the upright position until a click is heard. This exposes the mouthpiece as well as loads the medication. The dose counter on the back of the device will count down one number each time the medication is delivered.
3. Exhale away from the device.
4. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece.
5. Do not block the air vent above the mouthpiece.
6. Inhale deeply through the Digihaler®.
7. Remove the mouthpiece from the mouth and perform a 10-second breath hold or as long as comfortable.
8. Check the dose counter on the back of the device to make sure the dose was delivered.
9. Firmly close the cap over the mouthpiece.
10. For ICS medications remember to rinse your mouth with water after breathing in the medicine. Spit out the water. Do not swallow it.
11. Store the device in a cool dry place.
12. Observe the counter for the number of doses remaining and replace when appropriate.
13. Inhaler use is recorded as an event when you open the cap or inhale and the data can only be viewed by your doctor and their team if you choose to share it with them.

## Technique Box 4. Steps for Correct Use of Each Model of DPIs (continued)

### Technique for Multiple-Dose DPIs (continued)

#### Ellipta®: The patient should be instructed to:

1. Open the device by sliding the mouthpiece cover down until a click is heard. This exposes the mouthpiece as well as loads the medication. The center dose counter will count down one number each time the mouthpiece cover is opened.
2. Hold the Ellipta® in an upright position.
3. Exhale away from the Ellipta®.
4. Place the mouthpiece into the mouth and close lips tightly around the mouthpiece. Do not block the air vent on the device.
5. Keep the device horizontal while inhaling the dose with a rapid and steady breath.
6. Remove the mouthpiece from the mouth and perform a 10-second breath hold or as long as comfortable.
7. Do not exhale into the device.
8. Close the mouthpiece cover.
9. Store the device in a cool dry place.
10. Observe the counter for the number of doses remaining and replace when appropriate.

#### General Steps to Avoid Reduced or No Dosing for DPIs: 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

Causes	Solutions
<ul style="list-style-type: none"><li>• Incorrect DPI assembly</li><li>• Failure to discharge medicine</li><li>• Empty DPI</li></ul>	<ul style="list-style-type: none"><li>• Replace the unit.</li><li>• Check the dose counter to ensure that it is not empty.</li><li>• Otherwise, replace the DPI.</li></ul>

## How To Know the DPI Is Empty

**Single-Dose DPI:** Single-dose DPIs such as 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.<sup>68</sup> 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.<sup>69</sup> 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.<sup>68</sup> 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 Table 15.

**Cleaning:** Please refer to the Infection Control section on page 50 for the cleaning instructions for DPIs.

**Table 15. Monitoring remaining doses of multiple-dose DPI**

	Dose Container	No. of Doses	Type of Indicator	Meaning of Dose Indicator
Flexhaler®	Reservoir	60 or 120	"0"	Although the indicator counts down every time a dose is loaded, it will not move with each individual dose but in 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.
Twisthaler®	Reservoir	30	"01"	The dose display showing "01" indicates the last dose of medicine in the Twisthaler®, and the medicine must be refilled.
Diskus®	Blister Strip	60	Red numbers	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.
RespiClick®/ Digihaler®	Reservoir	60 or 200	"0"	When the dose counter displays "0," there is no medicine left and the device should be disposed.
Ellipta®	Blister Strip	30	"0"	When the dose counter displays "0," this is the last dose. Discard the device after inhalation.
Pressair®	Reservoir	30 or 60	"0"	When dose counter displays "0," there is no medicine left and the device should be disposed.
Inhub®	Blister Strip	60	Red numbers	The numbers turning red in the dose display indicates that there are nine doses left. When the dose window shows "0," there is no medicine left, and the discus should be disposed.
Digihaler®	Reservoir	60 or 200	"0"	When the dose counter displays "0," there is no medicine left and the device should be disposed.

# CRITERIA TO SELECT AN AEROSOL GENERATOR

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.<sup>8</sup> 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.<sup>13,69-76</sup> The patient's cognitive ability to understand how and when to use a device and drug as well as their physical ability and coordination in using an aerosol generator should guide the selection of an aerosol generator.<sup>8,13,18,69,75,77-79</sup> 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 pages 48-49.

As for adults and the elderly who cannot manage hand-held coordination or proper inhalation technique,<sup>77,80-82</sup> 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.<sup>77,83</sup>

### 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.<sup>84-87</sup> 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.<sup>8,18,79,87</sup> 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.<sup>8,18,87-88</sup>

## 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.<sup>69,79</sup> Also, nebulizers may be less preferable to deliver inhaled medications as they are more expensive, require a power source, and need regular maintenance.<sup>69,87,89-90</sup> 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.<sup>91-93</sup> 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.<sup>79</sup> 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.

# NEONATAL AND PEDIATRIC AEROSOL DRUG DELIVERY

Children 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.<sup>70-73,77,94-95</sup> 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 children.

## Age and Physical Ability

Selection of an aerosol device is critical to successful aerosol therapy in infants and children.<sup>70,78,95,169,171</sup> Children under the age of three may not reliably use a mouthpiece, making delivery via mask necessary for both nebulizers and pMDIs.<sup>95-99,169</sup> Especially at low tidal volumes, VHCs are the preferred method for pMDI

delivery in infants and small children.<sup>97-98,169,170</sup> 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.<sup>73,100</sup>

## 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 16 presents the recommended ages for introducing different types of aerosol generators to children.<sup>69-71,99-103</sup> Small-volume nebulizers and pMDIs with VHCs are recommended for use with infants and children up to five years of age.<sup>70-71,100</sup> 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.<sup>70,97-99</sup> 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

**Table 16.** Age guidelines for use of aerosol delivery device types

Aerosol Generator	Age
SVN with mask or hood	Infant <sup>94</sup>
SVN with mask	≤ 3 years
SVN with mouthpiece	≥ 3 years
pMDI with valved holding chamber/spacer and mask	< 4 years
pMDI with valved holding chamber/spacer	≥ 4 years
Dry-powder inhaler	≥ 4 years
Metered-dose inhaler	≥ 5 years
Breath-actuated MDI (e.g., Autohaler®)	≥ 5 years
Breath-actuated nebulizer	≥ 5 years

techniques.<sup>70-71,100</sup> With low tidal volumes and short inspiratory times, breath-actuated nebulizers may increase inhaled dose compared to continuous nebulization.<sup>104</sup> 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.<sup>70</sup> It is generally accepted that the cognitive ability to control breathing and hand/breath coordination develops by age five or six.<sup>69,70,101</sup> Once children reach age four and above, they may have a sufficient understanding of how to use a pMDI or DPI successfully.<sup>73,100</sup>

### **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,<sup>94,96,102,105-106</sup> with most of the inhaled dose depositing in the upper airways or pharynx, which is then swallowed.<sup>71-72,94,106-107</sup> 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 infants, 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,<sup>108</sup> an in-vivo study showed that 69% of the children woke up during aerosol administration and 75% of them were distressed.<sup>109</sup>

### **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.<sup>173,174</sup>

### **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<sup>104,110</sup> and is effective in the clinical treatment of children.<sup>104,111-112,178</sup> 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%.<sup>113-117</sup> 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.<sup>97,113,118-119</sup>

### **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.<sup>120-121,172</sup> 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.



# INFECTION CONTROL

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),<sup>20-22,177</sup> asthma,<sup>23-24</sup> and immunodeficiency.<sup>122,174</sup> A survey of respiratory therapists and cystic fibrosis patients found a wide disparity of nebulizer cleaning methods.<sup>123</sup> In another survey, it was shown that only 60% of cystic fibrosis caregivers were aware of infection control guidelines.<sup>124</sup> In the absence of infection control (IC), an aerosol generator will be contaminated and may cause bacterial colonization in the respiratory tract.<sup>20-22,25,125</sup> 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.<sup>24,125-126</sup>

## 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.<sup>23-24,127-128</sup> Therefore, the importance of cleaning and maintaining aerosol equipment should be emphasized in IC education programs<sup>129,176</sup> 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.<sup>130</sup> 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.<sup>131,176</sup> Furthermore, a majority of cystic fibrosis health care workers reported a low self-efficacy with using infection control guidelines, which can be linked to poor adherence.<sup>124</sup> Changing aerosol generators every 24 hours, using disposable equipment with health insurance approval, and partnering with patients to increase adherence<sup>85</sup> can increase patient compliance to IC and minimize the risk of infection.

## Cleaning and Maintenance of 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<sup>132-133</sup> as shown in Table 17.
- *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 manufacturer's suggestions. Table 18 provides the steps for cleaning the pMDI accessory devices.
- *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.

**Table 17.** Cleaning instructions for the pMDI

Cleaning the pMDI
Clean once a week and as needed. Look at the hole where the drug sprays out from the inhaler.
Clean the inhaler if you see powder in or around the hole.
Remove the pMDI canister from the plastic container so it does not get wet.
Rinse the plastic container with warm water and shake out to remove excess water.
Dry overnight.
Replace the canister back inside the mouthpiece and recap the mouthpiece.

**Table 18. 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.

- **Nebulizers:** In the home, nebulizers should be cleaned after every treatment. A study showed that 73% of nebulizers were contaminated with microorganisms and 30% had potentially pathogenic bacteria.<sup>134</sup> Moreover, there was a significant increased risk of COPD exacerbation in COPD patients that had nebulizers with pathogens versus those with non-pathogenic bacteria. However, nebulizer contamination can be significantly improved with proper instruction on infection control.<sup>135</sup> 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,<sup>136</sup> 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 19 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:

**Heat methods:**

1. Boil or microwave<sup>137</sup> the nebulizer parts in water for five minutes. This disinfection process does not require a final rinse.
2. Wash in a dishwasher if the dishwasher achieves a temperature of > 158°F or 70°C for 30 min.<sup>137</sup>

**Cold Methods:**

1. Soak them in solution of one-part household bleach and 50-parts water for three minutes.
2. Soak the parts in 70% isopropyl alcohol for five minutes.
3. Soak them in 3% hydrogen peroxide for 30 minutes.
4. 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 suggests 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.<sup>138</sup>

**Final Rinse:** The patient should use sterile water (not distilled or bottled) for the final rinse.<sup>136</sup> 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.<sup>139</sup> 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.

**Table 19. Cleaning instructions for the jet nebulizer**

Cleaning After Each Use	Cleaning Once or Twice a Week
Wash hands before handling equipment.	Wash hands before handling equipment.
Disassemble parts after every treatment.	Disassemble parts after every treatment.
Remove the tubing from the compressor and set it aside. The tubing should not be washed or rinsed.	Remove the tubing from the compressor and set it aside. The tubing should not be washed or rinsed.
Rinse the nebulizer cup and mouthpiece with either sterile water or distilled water.	Wash nebulizer parts in warm water with liquid dish soap.
Shake off excess water.	Disinfect the nebulizer based on the manufacturer's recommendations. The nebulizer parts may be soaked in one of the following solutions: <ol style="list-style-type: none"> <li>1. One-part household bleach and 50-parts water for three minutes</li> <li>2. 70% isopropyl alcohol for five minutes</li> <li>3. 3% hydrogen peroxide for 30 minutes</li> <li>4. One-part distilled white vinegar in three-parts hot water for one hour (not recommended for CF patients).</li> </ol>
Air dry on an absorbent towel.	Rinse parts with sterile or distilled water.
Store the nebulizer cup in a zippered plastic bag.	Shake off excess water and place all parts on a clean paper towel.
	Allow them to air dry completely on an absorbent towel.
	Reassemble the nebulizer and store in a clean, dry bag container.

### 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.<sup>140-141</sup> The Centers for Disease Control and Prevention (CDC) recommends that nebulizers be cleaned, rinsed with sterile water, and air-dried between treatments.<sup>142</sup> 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.<sup>143-144</sup> If an aerosol generator is labeled "For Single Patient Use," it should be used on a single patient and then discarded.

**MDI – Common Canister Use:** Many hospital pharmacies see a robust number of MDI canisters still containing medication returned, leading to strategies for reducing cost.<sup>10</sup> As a result, some hospitals practice common canister protocol for specific patient populations. A review focusing on common canister protocol and the risk of infection found some evidence of cross-contamination.<sup>145</sup> However, the evidence from the studies in this review is weak since none of the research is in the form of peer-reviewed publications. A recent study indicated a common canister protocol was associated with significant cost savings when compared to single-patient MDI, and reported similar rates of ventilator associated pneumonia, mortality, and length of stay.<sup>146</sup> Hospital decision makers must perform a full risk-benefit evaluation before incorporating a common canister protocol in their institution,

as more work needs to be done in this area before best-practices can be suggested with a high degree of confidence.

**Inhaled Drugs:** Multi-dose drug containers have been associated with contaminated nebulizers and are a potential source of spreading nosocomial infections.<sup>149-151</sup> Therefore, unit-dose medications are recommended when possible.<sup>142</sup> 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.<sup>151-152</sup> 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.<sup>30,153</sup> 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.<sup>31,152,154-156</sup> Also, the World Health Organization's guidelines suggest that inadequate hand hygiene is the leading cause of nosocomial infection and spread of multidrug resistant organisms.<sup>157</sup> Health care workers who self-reported hand washing during patient care had a lower risk of having respiratory infections.<sup>31,154-156</sup>

**Protective Equipment:** Respiratory therapists must have access to the appropriate personal protective equipment, such as masks and eye protectors, when needed.<sup>30</sup>

**Ventilation System:** These systems exchange room air six to 10 times per hour<sup>31</sup> and create a negative-pressure environment in patient rooms that is effective in removing 99.9% of airborne contaminants in 69 minutes.<sup>32</sup>

**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.

# EDUCATING PATIENTS IN CORRECT USE OF AEROSOL DEVICES

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. Lack of adherence can result in poor health outcomes and increased health care costs.<sup>72,158</sup> Both long- and short-term adherence may be influenced by patient and social factors.<sup>158-159</sup> 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%.<sup>160</sup> Therapists should be aware that patients tend to over-report use of inhaled drugs compared to data obtained from device monitors. Failure to adhere to prescribed therapy is categorized as "unintentional" or "intentional." Table 20 lists both types of non-adherence with definitions and examples.<sup>131</sup>

**Table 20.** General types of non-adherence to prescribed aerosol therapy and potential factors that can predispose to each type (Modified, with permission, from Reference 1 and Reference 131)

<b>Unintentional Factors:</b> Not Understanding Therapy Correctly	<b>Intentional Factors:</b> Understanding Therapy But Not Adhering Correctly
Misunderstanding prescribed drug regimen: <ul style="list-style-type: none"> <li>• Poor physician-patient communication</li> <li>• Poor therapist-patient communication</li> </ul>	Patient beliefs: <ul style="list-style-type: none"> <li>• Do not really require regular medication</li> <li>• Are not really sick</li> <li>• Gain attention from parents and kept at home (children)</li> <li>• Medication too expensive</li> <li>• Concern about side effects</li> <li>• Perceived lack of effect from medication</li> </ul>
Language barriers	Patient forgetfulness
	Patient stress and busy lifestyle
	Complex and demanding aerosol regimens
	Psychological factors (e.g., depression)

Upon assessing poor patient adherence, a strategy incorporating patient-centered care may help the caregiver understand patient beliefs, views, and concerns about their treatment. Goal setting and action plans are two motivational tools that may improve patient adherence and can be discussed in a supportive bi-directional conversation with the patient during the patient-centered approach.

Note that one example of unintentional non-adherence is incorrect aerosol device technique due to misunderstanding the 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 (Table 21). DPIs were also introduced, in part, with the

**Table 21. Common problems, disadvantages, and errors with each type of aerosol generator (Modified, with permission, from References 1 and 132)**

Pressurized Metered-Dose Inhalers	Dry-Powder Inhalers
<p>Errors in technique</p> <ul style="list-style-type: none"> <li>• Failure to coordinate pMDI actuation on inhalation</li> <li>• Too short a period of breath hold after inhalation</li> <li>• Too rapid an inspiratory flow rate</li> <li>• Inadequate priming/shaking/mixing before use</li> <li>• Abrupt discontinuation of inspiration as aerosol hits throat</li> <li>• Actuating pMDI at total lung capacity</li> <li>• Actuating pMDI prior to inhalation</li> <li>• Firing pMDI multiple times during single inhalation</li> <li>• Firing pMDI into mouth but inhaling through nose</li> <li>• Exhaling during actuation</li> <li>• Putting wrong end of inhaler in mouth</li> <li>• Holding canister in the wrong position</li> <li>• Failing to remove cap before use</li> <li>• Excessive use of pMDI beyond rated capacity (loss of dose count)</li> <li>• Failure to clean boot</li> <li>• Wasting remaining doses</li> </ul>	<p>Errors in technique</p> <ul style="list-style-type: none"> <li>• Not holding device correctly while loading dose</li> <li>• Failure to pierce or open drug package</li> <li>• Using the inhaler in wrong orientation</li> <li>• Failure to prime</li> <li>• Exhaling through the mouthpiece</li> <li>• Not exhaling to residual volume before inhaling</li> <li>• Not inhaling forcefully enough</li> <li>• Inadequate or no breath hold</li> <li>• Exhaling into mouthpiece after inhaling</li> </ul>
Lack of adequate patient training in use of pMDI	Use of multi-dose reservoir designs in high ambient humidity, which can reduce fine-particle dose
Cognitive impairment of users	Lack of patient instruction in assembly or use
Lack of adequate hand strength or flexibility to activate pMDI	<b>Nebulizers</b>
Ideomotor dyspraxia	Failure to assemble equipment properly
	Spillage of dose by tilting some nebulizers
	Failure to keep mouthpiece in mouth during nebulization
	Failure to mouth breathe
	<b>Valved Holding Chambers/Spacers</b>
	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

rationale that their use would be simpler than with a pMDI.<sup>161-162</sup> 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 21 lists the common errors and mistakes that can occur with each type of device.<sup>131,161-162</sup>

### 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 21). A large systematic review on errors in inhaler use revealed that incorrect inhaler technique is frequent and has not improved over the last 40 years.<sup>163</sup> Lack of coordination, improper inhalation (speed and/or depth), and no post-inhalation breath hold were the most frequent MDI technique errors.<sup>163</sup> Also, 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.<sup>94</sup> 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 counting the number of doses remaining in the pMDI (see page 28). It has been shown that using MDIs without a counter results in significantly poorer adherence (underuse and overuse) when compared to MDIs with a counter.<sup>164</sup> Furthermore, significantly more asthma and COPD patients visited the ED when not using a dose counter when compared to a group using a dose counter.<sup>165</sup>

### Common Patient Errors with Holding Chambers/Spacers

Common errors that can occur with holding chambers/spacers are also listed in Table 21. 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.<sup>33,166</sup> 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 21). Error rates, defined as failure to correctly perform an essential step, have been shown to be similar for pMDIs and DPIs.<sup>167</sup> In contrast, another study revealed that the DPI had a significantly lower rate of improper handling compared to the MDI.<sup>167</sup> A large study on asthma patient errors with a DPI showed that the most common mistakes included failure to exhale prior to inhalation, insufficient breath hold at end of inhalation, and lack of forceful inhalation.<sup>168</sup> Moreover, factors significantly associated with one or more of these major errors included an asthma-related hospitalization or no inhaler technique review during the previous year.<sup>167</sup> One of the unfortunate aspects of DPIs is that the models currently available in the U.S. all have a somewhat different design. They look different, and there are differences in the details of cocking and loading the DPIs.<sup>161</sup> 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 21). Disadvantages include bulk and size of equipment, need for external power source (compressed gas or electricity), and lengthy treatment times. Also, aerosol generators can function at suboptimal levels for providing adequate medication delivery.<sup>169</sup> 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 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). 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.



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