

Inhalational Devices

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Introduction

- Basics of aerosolized therapy
- Issues in delivery devices
 - Which Device Work Best for Which Patient?

Aerosol Medications

Advantages

- Direct treatment of lungs
 - High drug concentrations in the airway
 - Reduced systemic adverse effects
- Inhaled β_2 -agonist bronchodilators produce a more rapid onset of action than oral delivery
- Some drugs are only active with aerosol delivery
- Aerosol drug delivery is painless and convenient

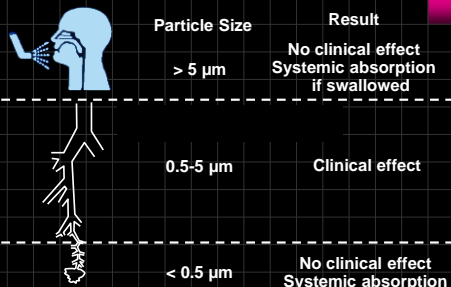
Disadvantages

- Less than optimal technique decreases drug delivery and potentially reduces efficacy
- The proliferation of inhalation devices has resulted in a confusing number of choices
- Inhaler devices are less convenient than oral drug administration
 - Greater time required for drug administration
 - Some patients may find the device less portable

Clinical Response to Aerosolized Therapy

- Aerosol size characteristics
 - Respiratory fraction—Dose reaching the Lungs
 - In general, the Mass Median Aerodynamic Diameter (MMAD) between 0.5 and 5.0 μm
 - Larger particles impact upper airways
 - Smaller particles are exhaled on next breath

Particle Size and Airway Deposition



Clinical Response to Aerosolized Therapy (cont.)

- Ventilatory parameters
 - Higher inspiratory rates—less distribution to peripheral airways
- Airway size
 - Obstruction and edema—less distribution to peripheral airways



Delivery Devices

Delivery Devices

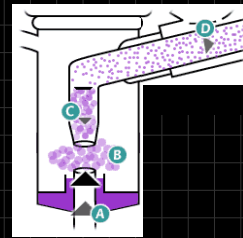
- Nebulizers
 - Jet
 - Ultrasonic
- pMDIs
 - HFA
 - With or without spacers/holding chambers
- DPIs

Nebulizers



- Jet
 - Function by Bernoulli principle
 - Compressed gas passes through a constriction undergoes a small reduction in pressure
 - Thus causing drug solution to be drawn up a feed tube from a reservoir and fragmented into droplets (15-500 μm)
 - Most of the droplets generated impact on the baffles producing smaller particles which are inhaled or returned to reservoir
- Ultrasonic
 - Work by spray formation from high frequency ultrasonic signal (1-3 MHz) by a piezoelectric transducer

Jet Nebulizers: Operating Principles



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“The Good” with nebulizers

- No need for coordination
- Effective with tidal breathing
- High dose possible

“The Bad” with nebulizers

- Size
- Cost
- Patient compliance
- Lengthy treatment time
- Device cleaning required
- 2/3 of medicine lost

pMDIs



- Propellants
 - HFA
- Suspension or solutions
- Surfactants (alcohol, oleic acid, lecithin)
 - Reduce particle agglomeration
- Press and Breathe

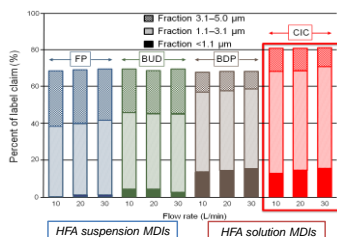
“The Good” with pMDIs

- Size
- Quick to use
- Direct delivery to needed site
- Rapid onset of action
- Dose required—much less than systemic agents
- Good dose-dose reproducibility

“The Bad” with pMDIs

- Highly technique dependent
 - Coordination between actuating and inhaling
 - Inspiratory flow rate too fast (0.4 L/min)
 - Breath-hold too short (≥ 10 seconds)
 - Failure to shake canister
 - Drug floats to top of canister
- Remaining doses difficult to determine if no counter

MDIs are able to produce a high proportion of small particles



FP: fluticasone; BUD: budesonide; BDP: beclomethasone; CIC: ciclesonide; MDI: metered dose inhaler; DPI: dry powder inhaler

Spacers and Holding Chambers



Source: Pharmacotherapy © 2004 Pharmacotherapy Publications

What Is a Valved Holding Chamber?

A *Valved Holding Chamber (VHC)* is a device used with a pMDI (pressurized Metered Dose Inhaler) to improve the delivery of aerosol medication into the lungs.

- VHCs are cylinder-like devices that work by:
 - Slowing down the velocity of the medication coming from a pMDI to allow better deposition into the lungs rather than the mouth and throat
 - Improving drug delivery for those who might have difficulty using a pMDI
 - Removing larger particles of medication before they settle in the mouth or throat

Spacers and Holding Chambers

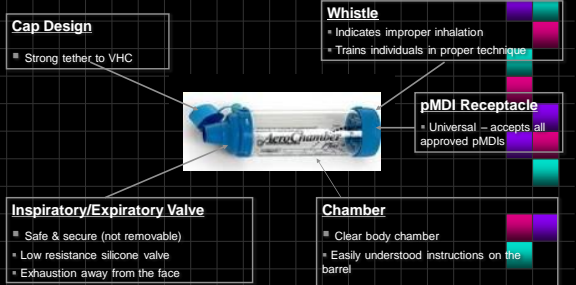


- No need to coordinate inhaling and actuating
- Decreased deposition of medication in oropharynx
- Decreased side effects
 - Important with inhaled corticosteroids
 - Oral candidiasis
 - Dysphonia

Points about spacers and MDIs

- Flow characteristics
 - Each MDI and spacer has different flow dynamics
- Spacer volume
- Number of actuations
 - More actuations in spacer, the less respirable dose
- Delay in actuation and inhalation
 - A 20 second delay reduce fine particle size 80%
- Static charge

Valve Holding Chamber Features Without a Mask



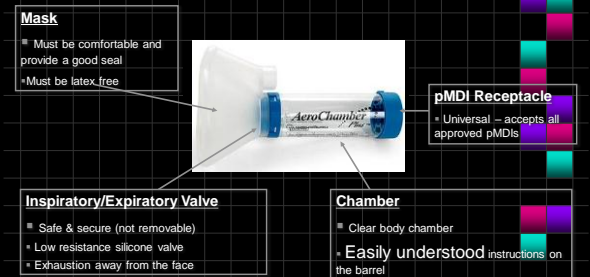
MDI with Valved-Holding Chamber

How to Use the MDI with a Valved Holding Chamber:

1. Remove the cap from the MDI and shake for 5 seconds.
2. Insert the mouthpiece of the inhaler into the open end of the chamber.
3. Have the child exhale all of the way out.
4. Have child place the chamber mouthpiece into their mouth and push down on the inhaler to release the medication.
5. Have the child inhale slowly and deeply.
6. Have the child hold their breath and count to 10.
7. Then have the child exhale normally.
8. If using a quick-relief medication, wait one minute before taking the second puff.



VHC Features with a Mask



VHC Sizes

- Valved holding chambers (VHCs) come in different sizes.

Individuals should consult with their physician for appropriate sizing.

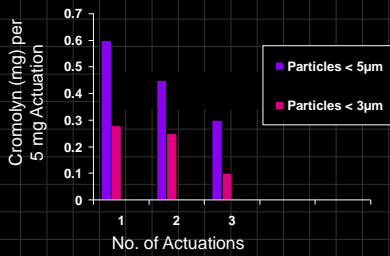


Not All VHC Masks Are the Same

- How to select the best-fitting mask for a child... consult with a physician.



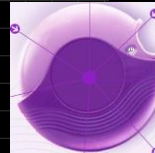
Effect of Multiple MDI Actuations into Spacer



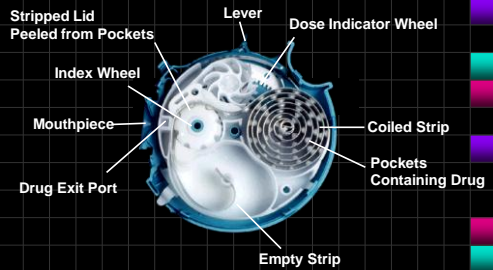
From O'Callaghan et al. Thorax 1993

DPIs

- Discrete Drug Containment Systems
- Reservoir Drug Containment Systems



DISKUS



“The Good” with DPIs

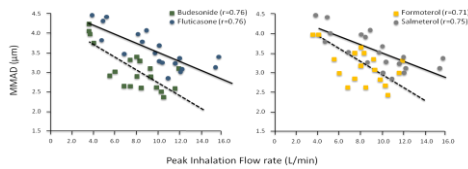
- Breath actuated
- Less patient coordination required
- No propellant
- Small and portable
- Dose counters

“The Bad” with DPIs

- Requires moderate to high inspiratory flow
- Some units are single dose
- Can result in high pharyngeal deposition

DPI particle size distribution is dependent on PIF with both Turbuhaler® and Diskus®

- Flow during the initial part of the inspiratory effort is important in determining the characteristics of the particle size distribution generated by a dry powder inhaler



MMAD with PIF rate for: BUD and FP, and formoterol and salmeterol. The continuous line represents the line of regression for FP and salmeterol (Diskus®) and the dashed line for BUD and formoterol (Turbuhaler®)

DPI: dry powder inhaler; MMAD: mass median aerodynamic diameter; PIF: peak inspiratory flow; BUD: budesonide; FP: fluticasone propionate

I. Tassin-WY et al. Int J Pharm 2006;316:131-7.

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Respimat

- Functions like pMDI
- Propellant-free
- Multi-dose reservoir
- Uses a spring to push drug solution through a nozzle
- Delivers a stream of liquid forming a mist
- High drug deposition in the lung
 - 30% to 40%



Figure 3-3: Choosing an Inhaler Device for Children with Asthma^a

Age Group	Preferred Device	Alternate Device
Younger than 4 years	Pressurized metered-dose inhaler plus dedicated spacer with face mask	Nebulizer with face mask
4–6 years	Pressurized metered-dose inhaler plus dedicated spacer with mouthpiece	Nebulizer with mouthpiece
Older than 6 years	Dry powder inhaler, or breath-actuated pressurized metered-dose inhaler, or pressurized metered-dose inhaler with spacer and mouthpiece	Nebulizer with mouthpiece

^aBased on efficacy of drug delivery, cost effectiveness, safety, ease of use, and convenience.

GINA Guidelines November 2006

Challenges: The Problems with Young Children

- Small tidal volume
- Small airways
- Rapid respiration
- Inability to hold breath with inhaled medication
- Nose breathing
- Aversion to masks
- Cognitive ability
- Fussiness and crying



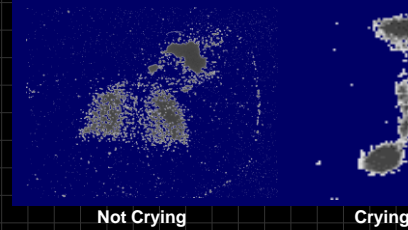
Everard. Adv Drug Del Rev. 2003;55:969-78; Marikani. Ann Allergy. 1990;64:383-397; Geller. Curr Opin Pulm Med. 1997;3:414-419; Newhouse. Chest. 1982;82:395-415.

Nebulizers vs MDIs with spacer and face mask

- Some studies show equal efficacy, while others show one device is better than the other
 - Peters J, Stevenson M, Beverley C, Lim JN, Smith S. The clinical effectiveness and cost-effectiveness of inhaler devices used in the routine management of chronic asthma in older children: a systematic review and economic evaluation. *Health Technol Assess* 2002; 6:1-167.
- My opinion: Parent preference



The Effect of Crying on Lung Deposition



G Murakami Ann Allergy 1990; 64:383-7

Selection of Delivery Device

- Patient's ability to use device correctly
- Preference of the patient for the device
- Availability of the drug/device combination
- Compatibility between the drug and delivery device
- Lack of time or skill to properly instruct patient
- Cost of the therapy
- Potential for reimbursement

Use of Delivery Devices

- Technique is paramount in efficacy of use
- Each device requires a different learning curve
- Numerous studies have demonstrated that medical personnel do not accurately know the proper technique for commonly used delivery devices

Does introduction of new "easy to use" inhalational devices improve medical personnel's knowledge of their proper use?

Nagesh Chopra, MD*, Nicolae Oprea, MD*, Alan Fark, PhD†, and John Oppenheimer, MD‡

- Test knowledge of RTs, RNs, PCPs, pharmacists, and medical residents in community-based hospital surroundings
- Compare pMDI, Turbuhaler, and Diskus

Annals Allergy 2002

Table 1. Six Correct Steps in Using MDI, Turbuhaler, and Diskus, and Percentage of All Medical Personnel Omitting or Not Performing the Individual Steps Correctly

6 Correct steps to use a MDI	Percentage of medical personnel omitting the steps
1. Remove the cap	0
2. Shake canister thoroughly	30
3. Breathe out steadily to FRC or RV	36
4. Insert or place the mouthpiece 2-4 cm away from the mouth keeping the canister upright	4
5. Discharge the inhaler while taking a slow, deep breath	24
6. Hold your breath in full inspiration for 5-10 seconds, exhale	20
Correct Steps to use a Turbuhaler	
1. Remove the cover	0
2. Turn the bottom clockwise until it clicks while keeping the inhaler upright	80
3. Then turn the bottom anticlockwise to the maximum while keeping the inhaler upright	98
4. Turn your head away from the inhaler and exhale to FRC or RV	54
5. Place the mouthpiece between your lips horizontally or vertically and inhale deeply and forcefully	30
6. Hold your breath in full inspiration for 5-10 seconds, exhale	38
Correct steps to use a Diskus	
1. Put the thumb of your hand on the thumb grip and push your thumb away from you as far as it will go until the mouthpiece appears and snaps into position	2
2. Slide the lever away from you as far as it will go until it clicks while keeping the Diskus horizontal	84
3. Holding the Diskus horizontal and away from your mouth, breathe out to FRC or RV	56
4. Put the mouthpiece to your lips and breathe in steadily and deeply	24
5. Remove the Diskus from your mouth. Hold your breath in full inspiration for 5-10 seconds and exhale	34
6. Put your thumb on the thumb grip and slide the thumb grip back towards you as far as it will go to click it shut	34

Table 3a. Mean Percentage Demonstration Scores for the Three Inhalational Devices by All Medical Personnel

	RT	RN	Residents	PCP	Pharmacists	Combined
MDI	98.33	73.30	64.97	93.32	74.99	80.9
Turbuhaler	63.29	43.31	38.30	61.62	43.29	49.9
Diskus	83.31	46.62	58.29	78.30	54.96	64.2
Combined	81.6	54.4	53.8	77.7	57.7	

Conclusions

- Delivery of medication by inhalation can vary depending upon the device and the patient
- Both need to be considered in determining the best way to administer the medication to the lung
- It doesn't matter how efficacious the medication is if it doesn't get into the lungs!!!