

DM SEMINAR
Aerosol therapy in ICU

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Aerosol therapy

Aerosol therapy refers to the delivery of a drug to the body via the airways by delivering it in an aerosolised form

An aerosol is a stable suspension of solid or liquid particles dispersed in air as a fine mist

Physiological basis for aerosol delivery

- Impaction : Particle having a size $> 3\mu$ deposit in oropharynx and larger airways
- Diffusion : diffusion by way of Brownian motion is the dominant mechanism for the smaller sized aerosols ($<0.5\mu$)
- *Sedimentation* : particle size in the range of $1-3\mu$ are subject to gravitational sedimentation in the small airways and tends to be enhanced by breath holding

Physical Characteristics of Aerosol

- Size of the aerosol droplets is generally characterised by mass median aerodynamic diameter (MMAD)
- The MMAD of an aerosol refers to the particle diameter that has 50% of the aerosol mass residing above and 50% of its mass below it
- Any droplet with MMAD larger than 5μ is likely to be filtered out in the upper airways and fail to reach even the larger airways

- **Aerosol particles less than 5μ in size readily reach the distal areas of the respiratory tract**
- **A particle size less than 2μ is ideal and is able to percolate right up to the peripheral airways**
- **Aerosols containing drugs with hygroscopic properties are likely to increase in size in humid conditions that may adversely impact the delivery of the drug**
- **Aerosols that are generated at a very high velocity tend to get deposited in the upper airways and consequently the delivery to the lower airways is compromised**

Pros & Cons

Advantages

Aerosol doses are generally smaller than systemic doses.

Onset of effect with inhaled drugs is faster than with oral dosing.

Drug is delivered directly to the lungs, with minimal systemic exposure.

Systemic side effects are less frequent and severe with inhalation when compared to systemic delivery.

Inhaled drug therapy is less painful than injection and is relatively comfortable.

Disadvantages

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

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

The difficulty of coordinating hand action and inhalation with the pMDIs reduces effectiveness.

The lack of knowledge of correct or optimal use of aerosol devices by patients and clinicians decreases effectiveness.

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

The lack of standardized technical information on inhalers for clinicians reduces effectiveness.

Types of aerosols

Bland aerosol

**Sterile water or
hypotonic, normotonic, and
hypertonic saline
delivered with or without
oxygen**

Pharmacologically active

**Aerosols which deliver drugs
to the lungs**

Bland aerosol

- Humidify inspired gas,
- Hydrate dry mucosal surfaces in patients with inflamed upper airways
- Enhance expectoration of lower-airway secretions
- Induce sputum expectoration for diagnostic purposes

- Routine use of bland aerosols is usually discouraged

- ✧ ineffective in liquefying the secretions as sufficient volume fail to reach the lower airways

Gallon AM. Thorax 51:429,1996.

- ✧ the use of bland aerosols in the treatment of COPD has not been shown to be of any benefit

- ✧ Bland aerosols may provoke bronchospasm and place patients at risk for nosocomial pneumonia

*American Thoracic Society/European Respiratory Society :
Am J Respir Crit Care Med 152:577,1995*

Pharmacologically active aerosols

- **Inhaled therapy has been used clinically since the early days of medical history**
 - Drug is delivered directly to its targeted site of action
 - Fewer side effects, and the onset of action is generally faster
 - Broad range of drugs is available as aerosols to treat lung diseases
 - β adrenergic agonist
 - anticholinergics
 - antiinflammatory agents
 - antiinfectives

- **Potential hazards of aerosol drug therapy include**
 - ✧ **reaction to the drug being administered**
 - ✧ **risk of infection**
 - ✧ **bronchospasm**
 - ✧ **potential for delivering too much or too little of the drug**

Factors affecting drug delivery

Ventilator-related

- Ventilation mode
- Tidal volume
- Respiratory rate
- Duty cycle
- Inspiratory waveform
- Breath-triggering mechanism



Device-related - MDI

- Type of spacer or adapter
- Position of spacer in circuit
- Timing of MDI actuation
- Type of MDI



Device-related - nebulizer

- Type of nebulizer
- Fill volume
- Gas flow
- Cycling: inspiration vs continuous
- Duration of nebulization
- Position in the circuit

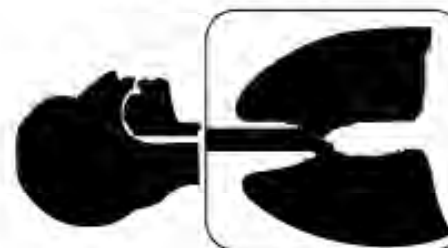


Circuit-related

- Endotracheal tube size
- Humidity of inhaled gas
- Density of inhaled gas

Drug-related

- Dose
- Formulation
- Aerosol particle size
- Targeted site for delivery
- Duration of action



Patient-related

- Severity of airway obstruction
- Mechanism of airway obstruction
- Presence of dynamic hyperinflation
- Patient-ventilator synchrony

Inhalation therapy in patients receiving invasive mechanical ventilation

- **Drugs administered as aerosols in mechanically ventilated patients:**
 - **Bronchodilators**
 - b-agonists (albuterol, metaproteronol, fenoterol)
 - anticholinergic agents (ipratropium bromide);
 - **Prostaglandins**
 - alprostadiol, prostacyclin, iloprost, treprostonil
 - **Mucolytics**
 - acetylcysteine
 - **Proteins**
 - Pulmozyme, surfactant
 - **Antibiotics**
 - antibacterials (aminoglycosides); antivirals (ribavirin);
 - antifungals (amphotericin);
 - **Corticosteroids**
 - beclomethasone; budesonide

Bronchodilators

- **Indications for using bronchodilator therapy in ventilator-supported patients are as follows**
 1. **asthma**
 2. **COPD**
 3. **acute bronchospasm or wheezing**
 4. **elevated airway resistance**
 5. **dynamic hyperinflation**
 6. **difficulty in weaning**
 7. **chronic ventilator dependence**

Goals of bronchodilator therapy

- **Reverse bronchoconstriction**
- **Decrease the work of breathing**
- **Relieve dyspnea**

Bronchodilators

- **B₂ adrenergics**

Short acting

Long acting



Bronchodilating properties

Augmentation of mucociliary clearance

Metabolic responses

Inhibition of mediator release from

Mast cells, basophils, and possibly other cells

Tremor is the principal side effect of β_2 agonists

Hyperglycemia, hypokalemia and hypomagnesemia

- **Anticholinergics**

Short acting

Long acting



Appear to have a role in acute asthma when combined with sympathomimetic drugs

In intubated patients to prevent bradycardia induced by suctioning

In patients with severe bronchorrhea

first-line therapy for the critically ill needing bronchodilatation

Prostanoids

- **Administration of prostacyclin by inhalation provides targeted pulmonary vasodilation**
- **Aerosolized vasodilators selectively increase blood flow to well ventilated but poorly perfused lung regions**

- **Inhaled prostacyclin and prostaglandin E1 are as effective as nitric oxide in improving oxygenation and hemodynamics**
- **Inhaled iloprost or treprostonil could be employed for treatment of acute pulmonary hypertension in mechanically ventilated patients**

Are Inhaled Vasodilators Useful in Acute Lung Injury and Acute Respiratory Distress Syndrome?

Mark S Siobal RRT FAARC and Dean R Hess PhD RRT FAARC

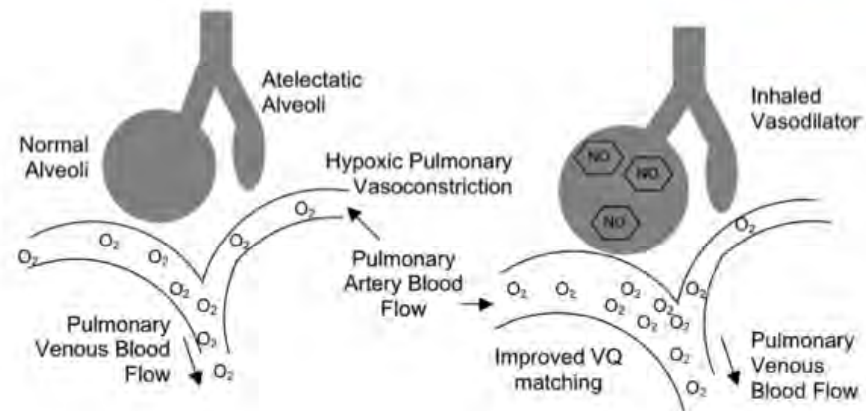
In patients with acute respiratory distress syndrome (ARDS), inhaled vasodilator can result in important physiologic benefits (eg, improved hypoxemia, lower pulmonary arterial pressure, and improved right-ventricular function and cardiac output) without systemic hemodynamic effects. Inhaled nitric oxide (INO) and aerosolized prostacyclins are currently the most frequently used inhaled vasodilators. Inhaled prostacyclins are as effective physiologically as INO and cost less. Randomized controlled trials of INO in the treatment of ARDS have shown short-term physiologic benefits, but no benefit in long-term outcomes. No outcome studies have been reported on the use of prostacyclin in patients with ARDS. There is no role for the routine use of inhaled vasodilators in patients with ARDS. Inhaled vasodilator as a rescue therapy for severe refractory hypoxemia in patients with ARDS may be reasonable, but is controversial. Key words: acute lung injury; acute

CME

Rescue Therapies for Acute Hypoxemic Respiratory Failure Review

Rescue Therapies for Hypoxemia

Delivery of inhaled nitric oxide (NO) to improve ventilation/perfusion (\dot{V}/\dot{Q}) matching. Note that vasodilation will occur selectively in areas where ventilation with NO occurs.



Although use of neither iNO nor iAP has reduced mortality in patients with ARDS/ALI, both can afford modest, short-term improvements in oxygenation, which can be significant in patients with severe, refractory hypoxemia

Surfactant

- **Surfactant replacement therapy (SRT) has been evaluated to correct deficiency of functional surfactant in neonates and adults with acute lung injury**
- **Exogenous surfactants employed for SRT are mixtures of synthetic phospholipids alone (Exosurf) or they are modified natural surfactants obtained from minced animal lung**

- **These exogenous surfactants lack surfactant protein A and D and differ from natural surfactants with respect to their functional and morphologic properties**
- **Inhaled surfactant administered to animals with non-homogeneous lung injury is preferentially deposited in well ventilated and less injured lung regions**

- **Two prospective multicenter randomized trials evaluated the efficacy of inhaled surfactant (Exosurf) in patients with sepsis-induced ARDS**
- **In both trials, there were no improvements in oxygenation, duration of mechanical ventilation, length of stay in the intensive care unit, or survival**

Among patients with ARDS caused by a direct lung injury, those who received surfactant tended to have a higher survival rate than those who received standard therapy

N Engl J Med 2004;351:884-92

Inhaled Antibiotics

- **High mortality rate associated with VAP**
- **Limited penetration of antibiotics into the lung after i.v administration**



Exploration of alternative routes of administration

Why inhalational route?

- **Delivery of greater antibiotic concentration to the airways**
- **Favorable outcomes in patients with cystic fibrosis**
- **Lesser systemic side effects**

ORIGINAL ARTICLE

N Engl J Med. 1975 Sep 4;293(10):471-5.

Aerosol polymyxin and pneumonia in seriously ill patients.

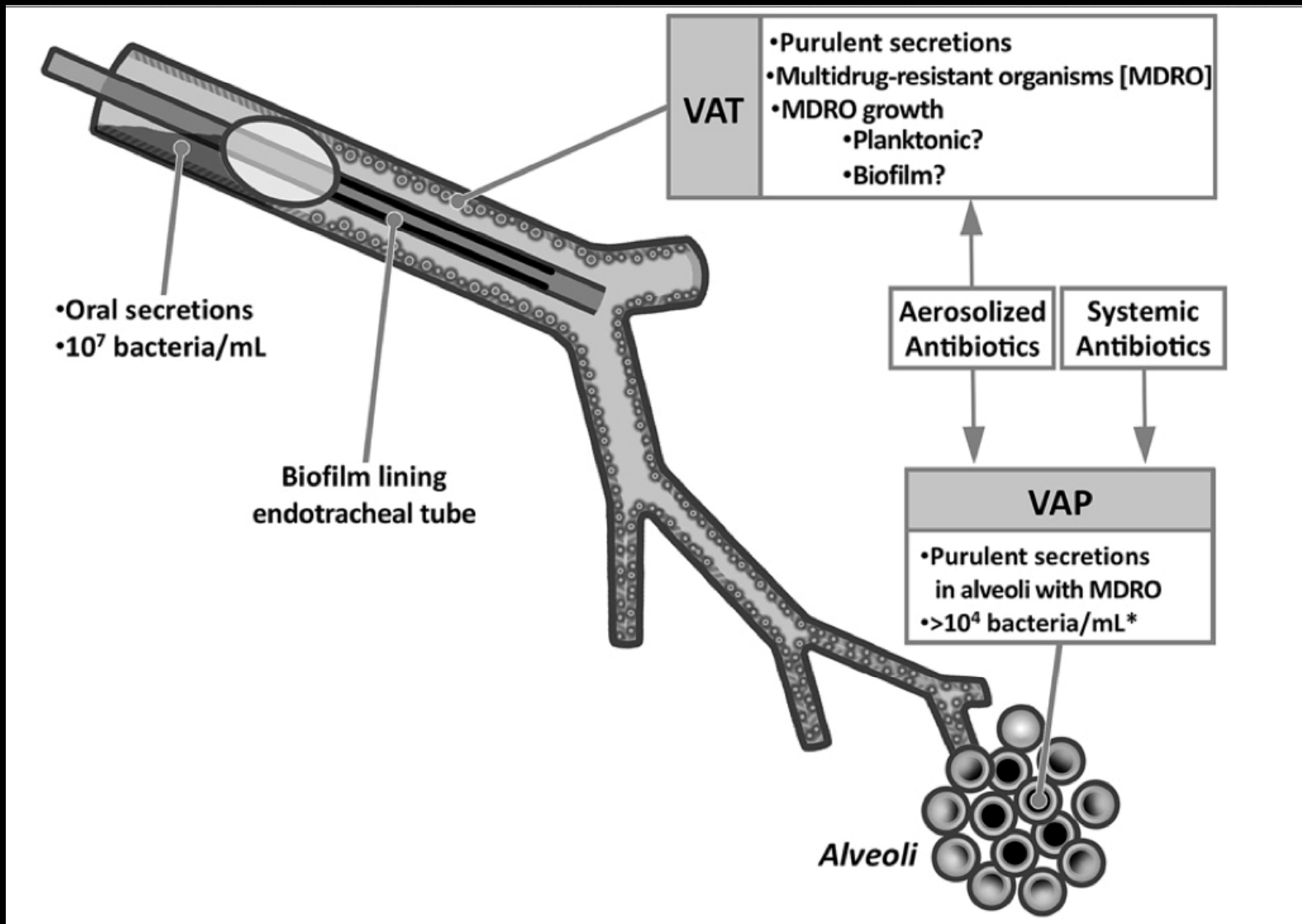
Feeley TW, Du Moulin GC, Hedley-Whyte J, Bushnell LS, Gilbert JP, Feingold DS.

Abstract

Pneumonia caused by *Pseudomonas aeruginosa* occurs frequently in critically ill patients and is associated with a mortality rate of 70 per cent. An aerosol of polymyxin B was administered (2.5 mg per kilogram per day) to the upper airways of 292 patients in a respiratory-surgical intensive-care unit during a seven-month period, in an attempt to prevent *Ps. aeruginosa* pneumonia. Although only one of the patients studied acquired pneumonia due to *Ps. aeruginosa*, 10 others acquired pneumonia caused by a polymyxin-resistant organism. Seven pneumonias were caused by organisms not frequently pathogenic to man (*flavobacteria*, *serratia* and *Streptococcus faecalis*). The mortality rate for acquired pneumonia in this study, 64 per cent, is greater than that in previous studies in which either no polymyxin or cyclic polymyxin therapy was used. Continuous use of polymyxin B aerosol appears to be a dangerous form of therapy.

- **Inhaled antibiotic therapy in mechanically ventilated patients is controversial and less well defined**

Recent work, however, suggests that aerosolized antibiotics can be used in mechanically ventilated patients



Inhaled antibiotic therapy in the mechanically ventilated patient appears promising, but must still be regarded as investigational

Mucolytics

- **Retention of airway secretions is associated with a high risk of pneumonia**
- **Acetylcysteine is often employed to enhance secretion clearance by reducing sputum viscosity**
- **Increase in inspiratory airway resistance after administration of mucolytic agents by aerosol or bolus instillation is a problem with the routine use of these agents**

- **Recombinant human DNase (Pulmozyme) was shown to improve mucus clearance in ventilator-supported patients with spinal cord injury and recurrent atelectasis refractory to conventional treatment**
- **Due to cost constraints, Pulmozyme cannot be recommended for routine use in the management of the ventilator-dependent patients with inspissated secretions**

Corticosteroids

- **Inhaled corticosteroids not recommended for the critically ill with acute exacerbations of obstructive lung disease**
- **When patients are hospitalized for reasons other than acute airway obstruction ,inhaled corticosteroids may be continued if patients have been taking these agents for asthma or COPD maintenance therapy.**

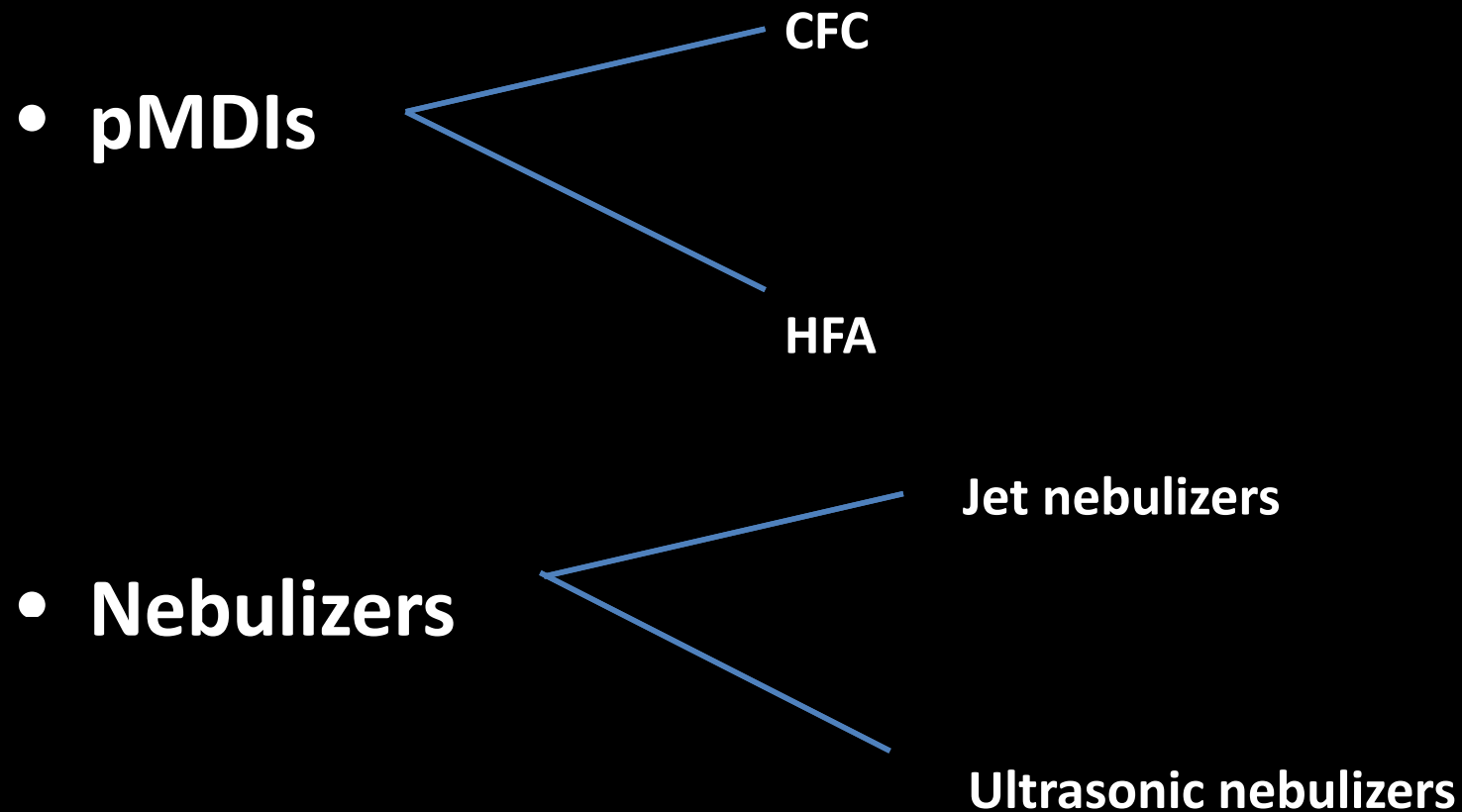
- **The use of inhaled corticosteroids has been recommended for use in neonates and infants with bronchopulmonary dysplasia**
- **Inhaled corticosteroids probably have only a limited role in the treatment of ventilator-supported premature infants.**

Factors governing pulmonary deposition

- **Five major variables need to be considered to optimize aerosol delivery during mechanical ventilation**
 - 1 aerosol generator**
 - 2 aerosol particle size**
 - 3 conditions in the ventilator circuit**
 - 4 artificial airway**
 - 5 ventilator parameters**

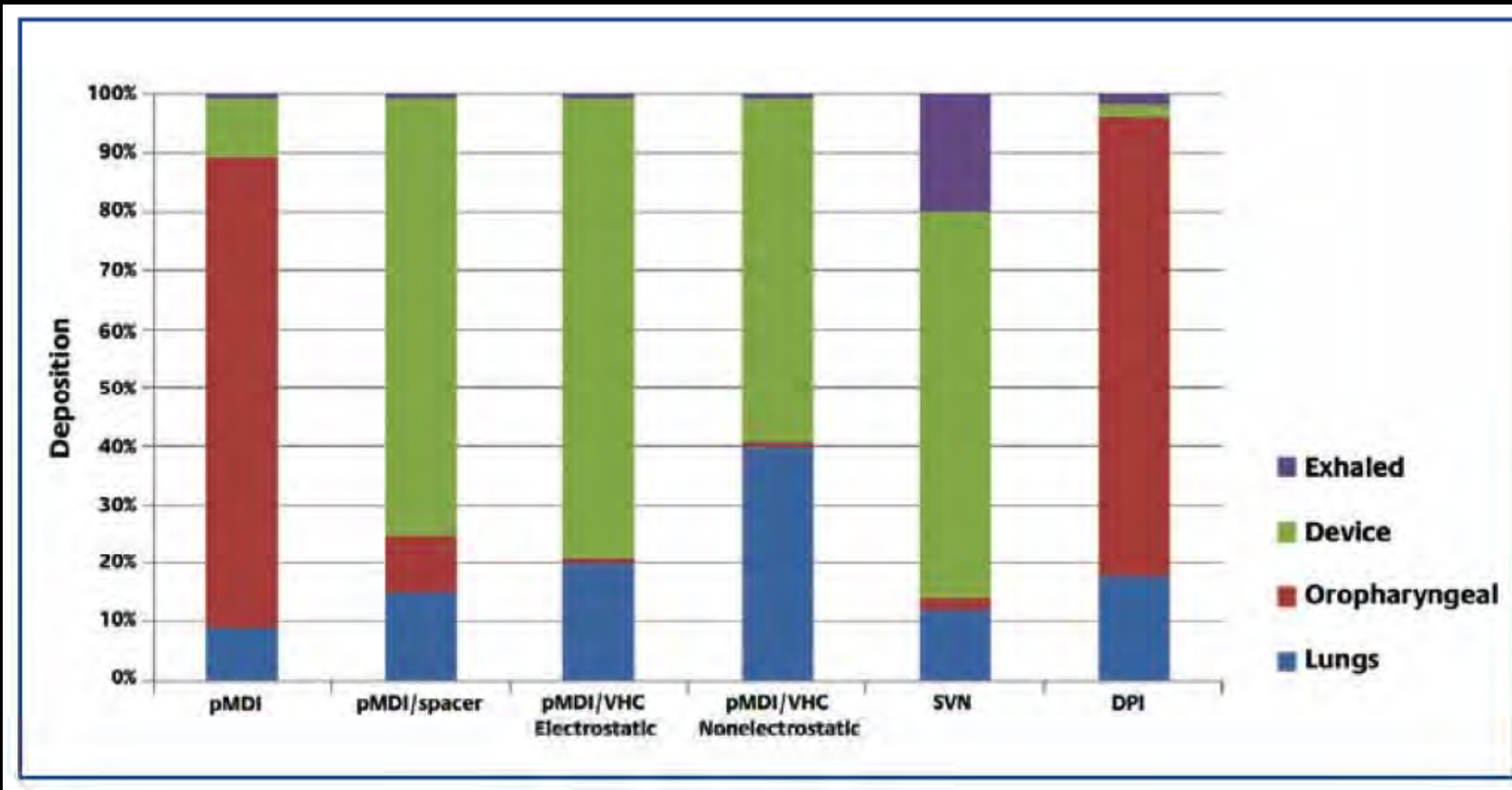
THE AEROSOL GENERATOR

Device which generates aerosol



Choice of aerosol generator

- Better generator-> better size-> better deposition
- Larger particles are trapped in the ventilator circuit and endotracheal tube
- Devices that produce aerosols with MMAD < 2 mm are more efficient during mechanical ventilation



Drug delivery with various devices

Hess DR et al. A guide to aerosol delivery devices for respiratory therapists 2005
 Fink JB. : Mosby's respiratory care equipment. 2010:91-140

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
Cromolyn	2 mg	20 mg
Levalbuterol	0.045 mg – 0.09 mg	0.31 mg – 1.25 mg

Hess DR et al. A guide to aerosol delivery devices for respiratory therapists 2005
Fink JB. : Mosby's respiratory care equipment. 2010:91-140

pMDIs

- **In ventilated patients, pMDIs are chiefly used to deliver bronchodilators**
- **pMDIs more popular than nebulizers for use in the intensive care unit**

PRINCIPLES OF METERED-DOSE INHALER DESIGN

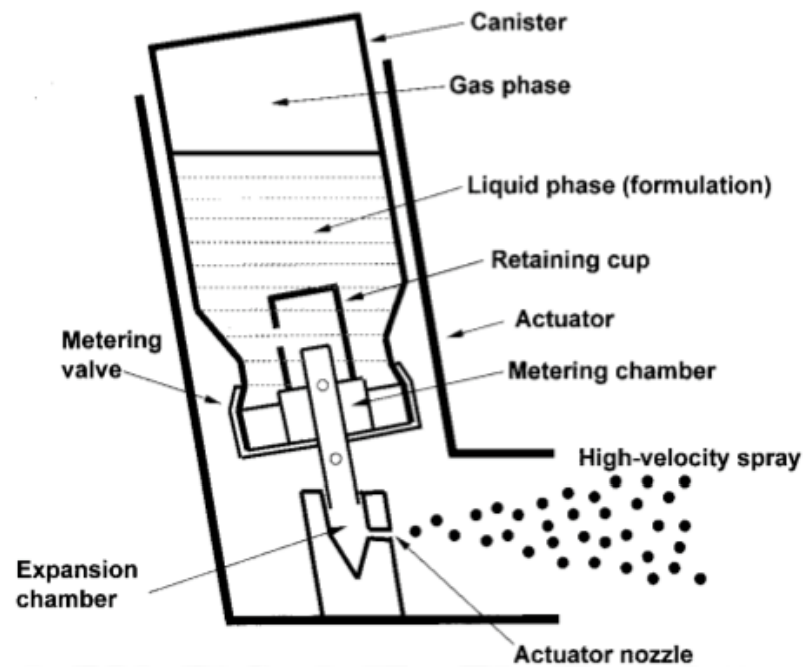


Fig. 1. Schematic of typical pressurized metered-dose inhaler.

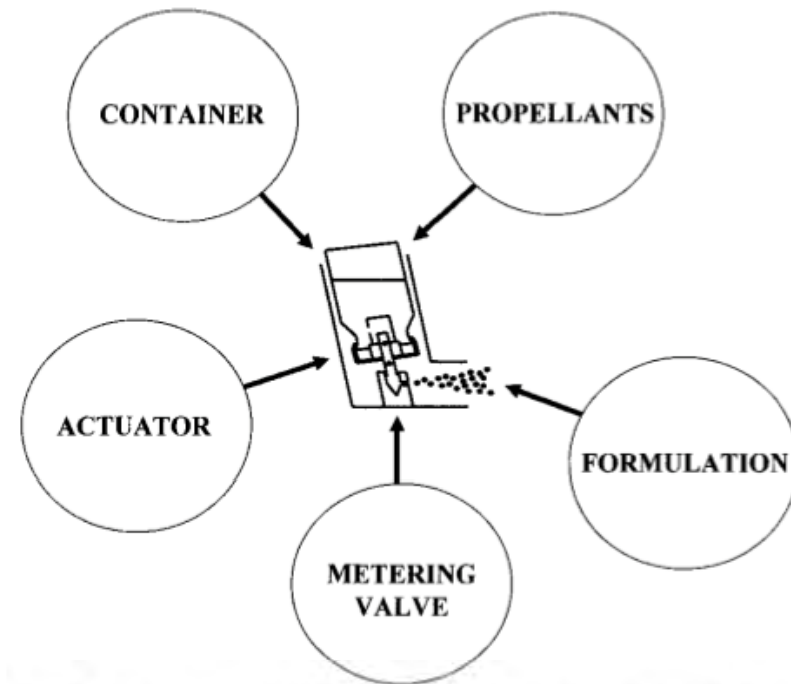


Fig. 2. The key component parts of the pressurized metered-dose inhaler.

**Chlorofluorocarbon (CFC) based MDI s have
been replaced by a newer generation of
hydrofluoroalkane (HFA) based MDI s**

Was CFC better ?

- **In bench models of mechanical ventilation, albuterol HFA- pMDIs employed with an Aerovent spacer provide drug delivery that is lower than that with CFC- pMDIs**
- **Contrarily, beclomethasone HFA- pMDIs employed with an Aerochamber HC MV spacer had a higher efficiency of drug delivery than the beclomethasone CFC-pMDI**

- **Different formulations and types of spacer**
- **The beclomethasone HFA-pMDI is a solution based whereas the albuterol HFA- pMDI is a suspension based**
- **Solution based pMDI produce an extra fine aerosol with MMAD of 1.2 μm**
- **Efficiency of drug delivery depends on how well the canister stem fits into the actuator**

To improve drug delivery with HFA-pMDIs in the setting of mechanical ventilation, the actuators required to connect them in ventilator circuits need to be matched to the size of the pMDI canister stem

Spacer or adapter devices

- **Several commercially available adapters or spacers are used to connect the pMDI canister to the ventilator circuit**
- **The types of adapters available for clinical use include, elbow adapters, inline devices that may be unidirectional or bidirectional, and chamber or reservoir adapters**

A chamber spacer with a pMDI in a ventilator circuit results in four- to sixfold greater aerosol drug delivery compared with either an elbow adapter or a unidirectional inline spacer

CHEST[®]

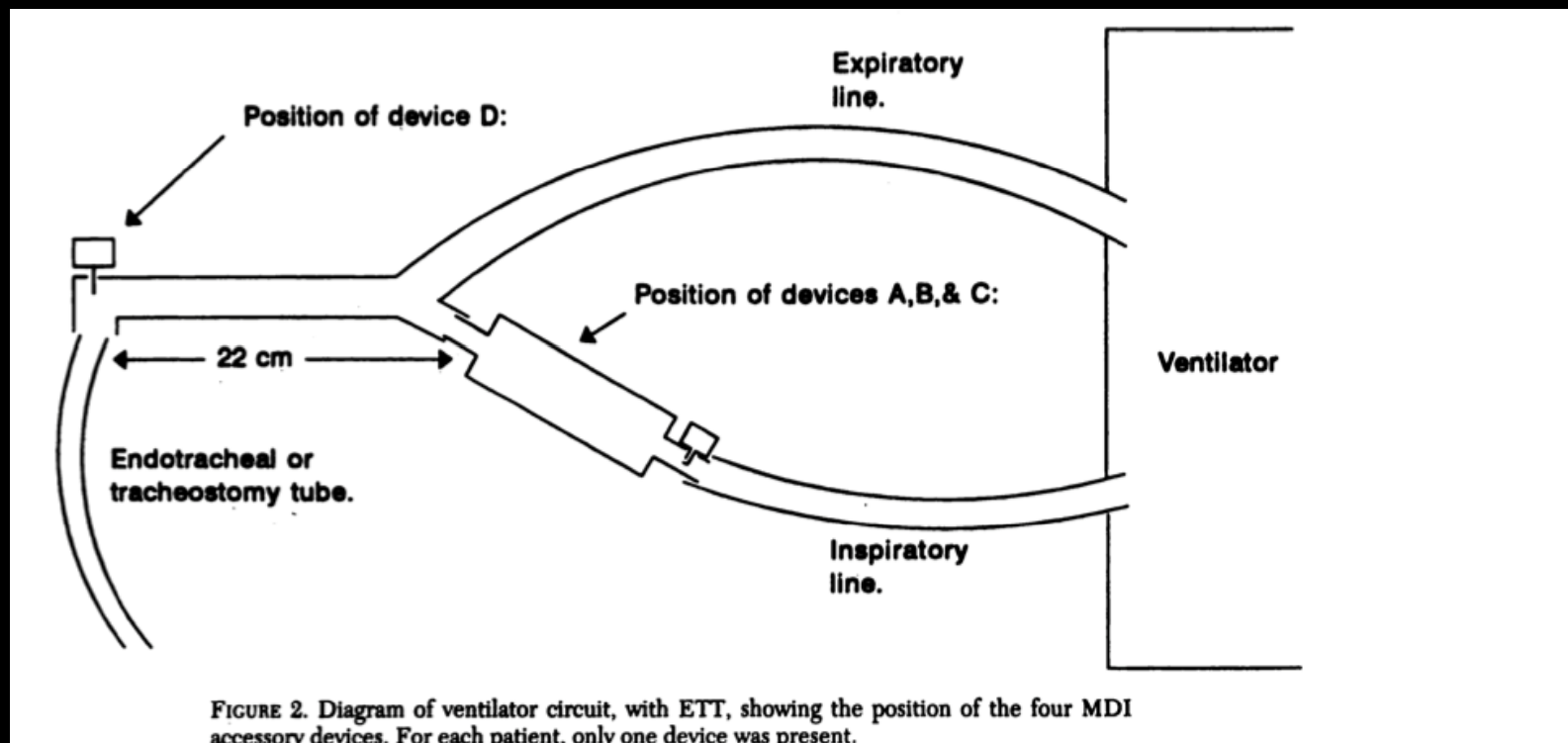
Official publication of the American College of Chest Physicians

CHEST
ONLINE

Efficiency of bronchodilator aerosol delivery to the lungs from the metered dose inhaler in mechanically ventilated patients. A study comparing four different actuator devices.

H D Fuller, M B Dolovich, F H Turpie and M T Newhouse

Chest 1994;105;214-218



Rau et al found that the efficiency of a bidirectional inline spacer was higher than a unidirectional inline spacer, and was comparable to that achieved with chamber spacers; however, the performance of the bidirectional spacer has not been established in clinical studies

The Aerochamber HC MV is another commercially available adapter for aerosol delivery with pMDIs in mechanically ventilated patients

It is more efficient for aerosol delivery with beclomethasone HFA- pMDIs compared to beclomethasone CFC- pMDIs

A pMDI and chamber spacer placed at a distance of approximately 15 cm from the endotracheal tube provides efficient aerosol delivery and elicits a significant bronchodilator response

Nebulizers

- Both jet and ultrasonic nebulizers have been employed for aerosol delivery during mechanical ventilation
- Nebulizers are employed to deliver a variety of agents such as bronchodilators, prostanoids, antibiotics, surfactant, mucolytic agents, and corticosteroids to mechanically ventilated patients

Jet nebulizers

- **A jet of compressed air or oxygen under high pressure is employed to generate an aerosol**
- **Jet nebulizers are connected in the inspiratory limb of the ventilator circuit**
- **They may be operated continuously by pressurized gas from a wall system or gas cylinder**
- **Intermittent delivery by the air flow generated by the ventilator could be employed to run the nebulizer during inspiration**

- **Intermittent operation is more efficient**
- **The rate of aerosol production is highly variable, not only among brands of nebulizers but even in different batches of the same brand**
- **Ventilators with in-built nebulizers facilitate reproducible and consistent dosing with a variety of agents in ventilated patients**

- **The nature of the aerosol produced, particle size, differs among various nebulizer brands**
- **Operational efficiency of a nebulizer changes with the pressure of the driving gas and with different fill volumes**
- **Placing a jet nebulizer at a distance from the endotracheal tube improves its efficiency compared with placing it between the patient Y and endotracheal tube**
- **Addition of a reservoir between the nebulizer and endotracheal tube also modestly increases efficiency of drug delivery**

Ultrasonic nebulizers

- **Vibration frequency and amplitude of vibration of the piezo-electric crystal influence aerosol particle size and drug output, respectively**
- **Most ultrasonic nebulizers have a higher rate of nebulization and require a shorter time of operation than jet nebulizers**
- **Aerosol particle size is larger with ultrasonic nebulizers compared to jet nebulizers**

- **Ultrasonic nebulizers have a higher efficiency for aerosol delivery during mechanical ventilation than jet nebulizers**
- **The cost and bulk of ultrasonic nebulizers and their relative inefficiency in nebulizing drug suspensions are major limitations to their use**

Placement of ultrasonic nebulizers proximal or distal to the Y-piece in the ventilator circuit does not influence the efficiency of aerosol delivery

The efficiency of aerosol delivery with ultrasonic nebulizers can be modestly improved by employing a longer inspiratory time, by reducing the minute ventilation, and by employing a lower respiratory rate

- **When used optimally, MDIs and nebulizers are equally effective in the treatment of patients with obstructive lung disease**
- **MDIs are preferred in ventilated patients over nebulizers**
- **Rate of nebulizer aerosol production is highly variable, not only among brands of nebulizers**
- **Nature of the aerosol produced, especially particle size, is highly variable among different nebulizers**

AEROSOL PARTICLE SIZE

- **During mechanical ventilation, larger particles produced by pMDIs and nebulizers are trapped in the ventilator circuit and endotracheal tube**
- **Devices that produce aerosols with MMAD 2 μm are more efficient during mechanical ventilation than devices that produce aerosols with larger particles**

CONDITIONS IN THE VENTILATOR CIRCUIT

Humidity

- Humidification leads to an increased loss of aerosol in the ventilator circuit
- With careful attention to the technique of administration, the impact of humidity on drug delivery can be overcome by delivering a somewhat higher drug dose

- A dry circuit could be employed for delivery of expensive or those agents for which the amount of drug deposition is critical
- When a dry circuit is employed, drug administration should be achieved within a short period (less than 10 min) to minimize the effects of dry gas on the airway mucosa

The filter in the HME is a barrier to aerosol delivery, and it has to be removed from the circuit during aerosol delivery

Gas density

- **Inhalation of a less dense gas such as helium–oxygen 70/30 mixture, improves drug delivery in both pediatric and adult models of mechanical ventilation**
- **With pMDIs there may be as much as 50% increase in the amount of aerosol delivered to the lower respiratory tract**
- **However nebulizer operation with helium– oxygen reduced drug output and respirable mass**

- **A practical method to achieve maximum pulmonary deposition of aerosol from a nebulizer during mechanical ventilation is to operate the nebulizer with oxygen at a flow rate of 6 to 8 L/min and to entrain the aerosol generated into a ventilator circuit containing helium–oxygen**

ARTIFICIAL AIRWAY

- **Aerosol impaction on the endotracheal tube poses a significant barrier to effective drug delivery**
- **Drug losses within the endotracheal tube could be minimized by placing the aerosol generator at a distance from the endotracheal tube instead of being directly connected to it**
- **When a pMDI and spacer are employed, the presence of humidity in the circuit increased aerosol deposition in the endotracheal tube by approximately threefold**

- ***In vitro* studies show, significant endotracheal tube deposition of aerosol with ultrasonic nebulizers but not with jet nebulizers**
- **Aerosol deposition in tracheostomy tubes has not been studied in as much detail as endotra- cheal tubes**

VENTILATOR PARAMETERS

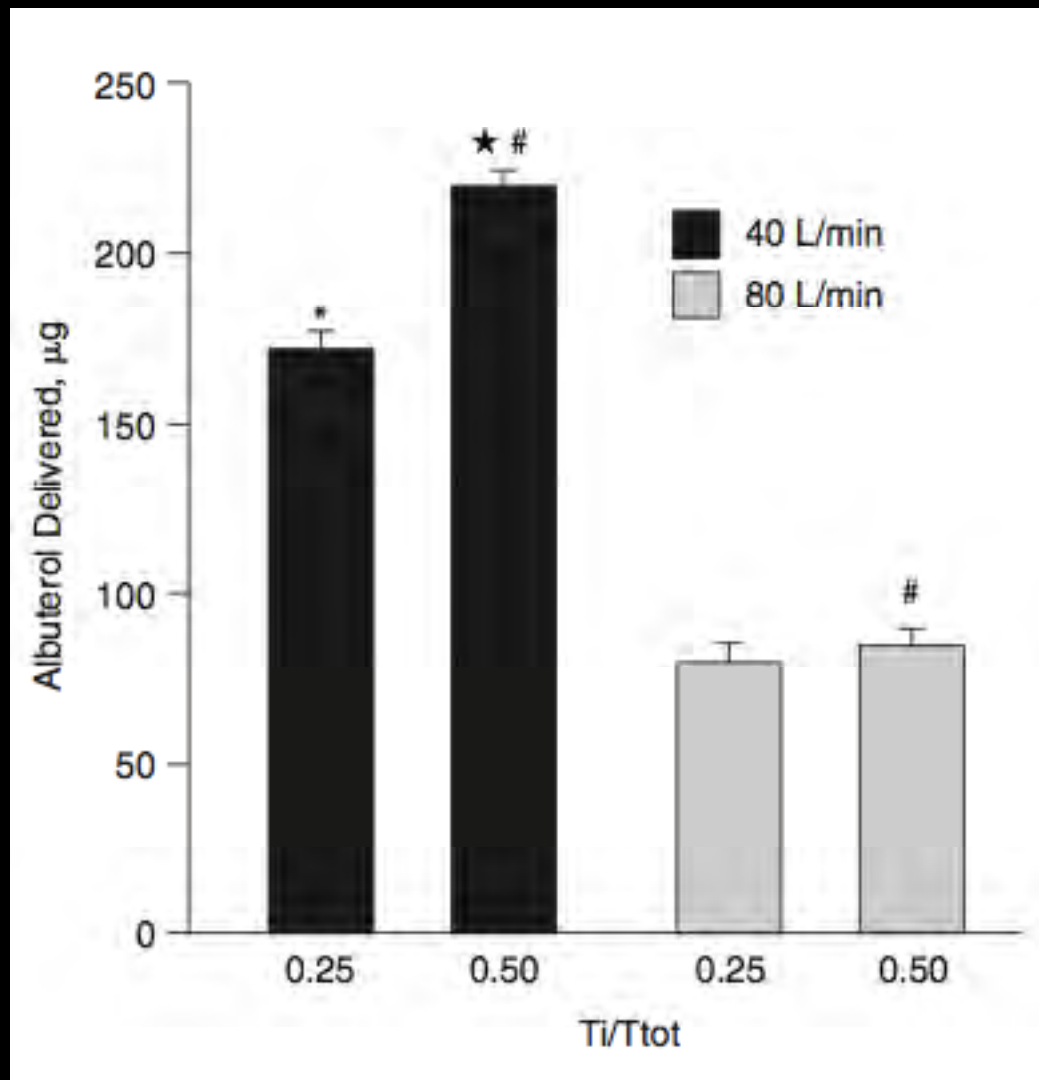
- **The actuation of a metered-dose inhaler (MDI) must be synchronized with the precise onset of inspiratory airflow from the ventilator**
- **As short as 1 to 1.5-sec delay between MDI actuation and a ventilator breath can profoundly reduce the efficiency of drug delivery**

- Intermittent operation of the is more efficient for aerosol delivery compared with continuous aerosol generation because it minimizes aerosol wastage during the exhalation phase of the breathing cycle

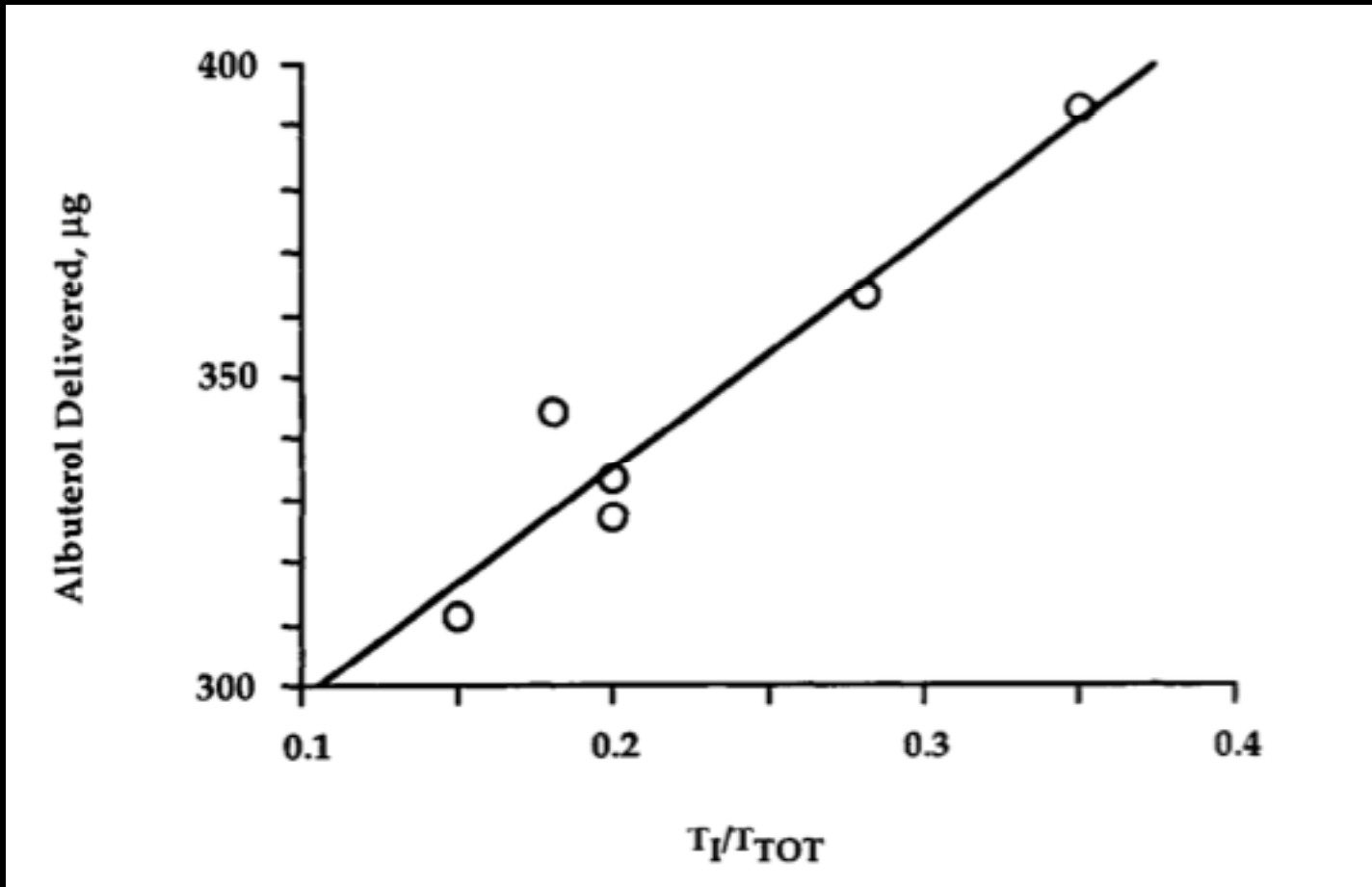
- Lower driving pressure provided by the ventilator (<15 psi) than that provided by pressurized gas (>50 psi) could decrease the efficiency of some nebulizers
- Aerosol generated by a nebulizer operating at the lower pressure may generate particles whose diameter is larger than the 1 to 5 μm that is optimal for aerosol deposition

Characteristics of the ventilator breath

- The characteristics of the ventilator breath have an important influence on aerosol drug delivery
- A tidal volume of 500 mL or more (in an adult) longer inspiratory time, and slower inspiratory flows improve aerosol delivery
- Drug delivery is linearly correlated with a longer duty cycle (T_i/T_{tot}) for both pMDIs and nebulizers
- Drug delivery is improved when a pMDI is synchronized with a simulated spontaneous breath compared with a controlled ventilator breath of similar tidal volume

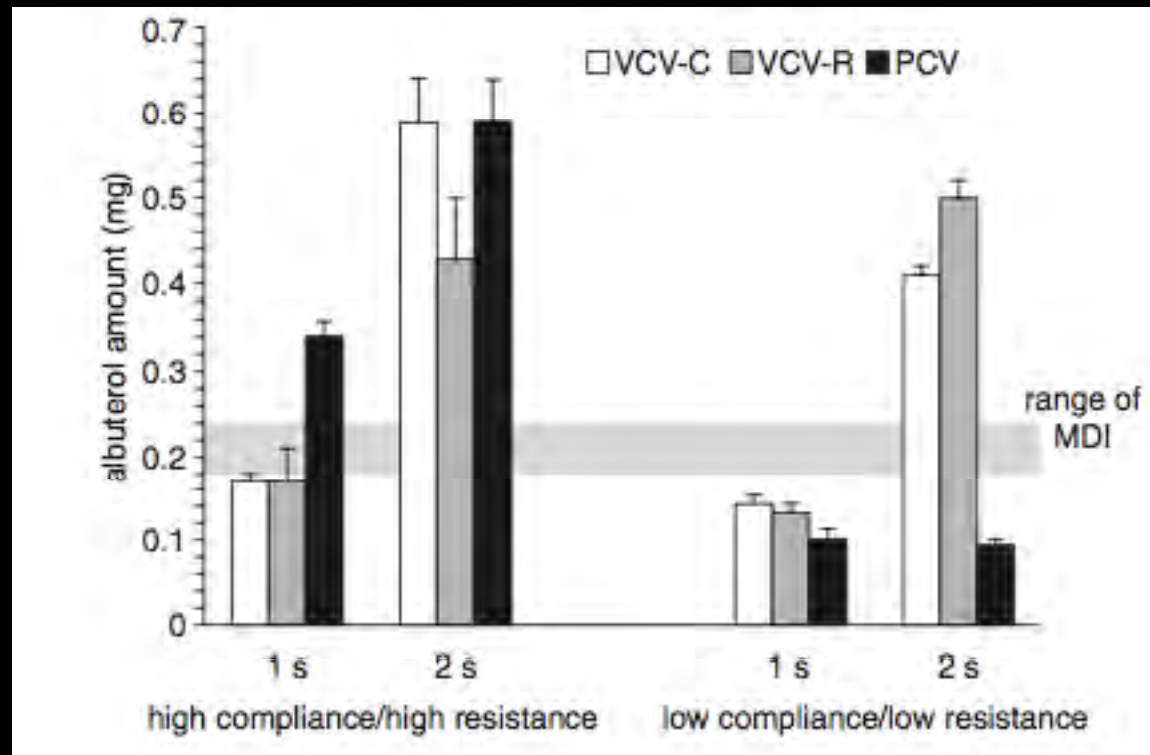


Higher drug delivery with higher Ti/Ttot ratio and at lower flow rates



Linear relationship between drug delivery and inspiratory time

- **Unlike MDIs, nebulizer efficiency is notably lower during pressure-controlled ventilation than during volume-controlled ventilation**
- **Use of a flow trigger with a nebulizer could dilute the aerosol and increase the washout of the aerosol into the expiratory limb between breaths**
- **Delivery to both filters at the bronchi was greater with sinusoidal (362.9 ± 40.4 ug) and decelerating flows (392.9 ± 33.9 ug) than with square flow waveform (327.3 ± 36.8 ug) ($p < 0.01$ in each instance)**



Aerosol delivery in volume v/s pressure controlled modes

- Operational efficiency of a nebulizer changes with the pressure of the driving gas and with different fill volumes
- Unless scrupulously cleaned and disinfected, nebulizers can be a source for aerosolization of bacteria
- Ventilator mode (Pressure v/s Volume) and lung mechanics can influence drug delivery from a nebulizer

Nebulizers	MDI
Highly variable operational efficiency	provide a reliable dose,
Depends on ventilator flow	easy to administer
source for aerosolization of bacteria	do not pose a risk of bacterial contamination
Expensive	Cheaper
Add flow to the ventilator circuit	Do not add additional flow

- **A significant proportion of the inhaled mass deposits in the endotracheal tube and a smaller proportion is exhaled**
- **Efficiency of drug deposition in the lower respiratory tract of ventilated patients is lower with nebulizers than with pMDIs**
- **Higher drug doses are employed with nebulizers to offset their reduced efficiency**
- **The total amount of drug depositing in the lower respiratory tract with jet nebulizers is probably comparable to that achieved with smaller drug doses employed with a pMDI**

Technique of aerosol delivery by pMDI

1. Review order, identify patient, and assess need for bronchodilator.
2. Suction endotracheal tube and airway secretions.
3. Shake pMDI and warm to hand temperature.
4. Place pMDI in space chamber adapter in ventilator circuit.
5. Remove HME. Do not disconnect humidifier.
6. Coordinate pMDI actuation with beginning of inspiration.
7. Wait at least 15 sec between actuations; administer total dose.
8. Monitor for adverse response.
9. Reconnect HME.
10. Document clinical outcome.

pMDI, metered-dose inhaler; HME, heat and moisture exchanger.

Technique for drug delivery by jet nebulizer

1. Review order, identify patient, and assess need for bronchodilator.
2. Suction endotracheal and airway secretions.
3. Place drug in nebulizer to fill volume of 4–6 mL.
4. Place nebulizer in the inspiratory line 18 in (46 cm) from the patient wye connector.
5. Turn off flow-by or continuous flow during nebulizer operation.
6. Remove HME from circuit (do not disconnect humidifier).
7. Set gas flow to nebulizer at 6–8 L/min.
 - a. Use a ventilator if it meets the nebulizer flow requirements and cycles on inspiration, or
 - b. Use continuous flow from external source.
8. Adjust ventilator volume or pressure limit to compensate for added flow.
9. Tap nebulizer periodically until nebulizer begins to sputter.
10. Remove nebulizer from circuit, rinse with sterile water, and run dry; store in safe place.
11. Reconnect humidifier or HME, return ventilator settings and alarms to previous values.
12. Monitor patient for adverse response.
13. Assess outcome and document findings.

Vibrating mesh nebulizers

- 1. Newer generation of nebulizers employ a vibrating mesh or plate with multiple apertures to produce an aerosol**
- 2. These high rate of nebulization and drug output is two to three times higher than with jet nebulizers**
- 3. Temperature of the solution does not change during operation of the vibrating mesh nebulizers, and proteins and peptides can be nebulized with minimal risk of denaturation**

Intratracheal catheter

- A novel device that produces an aerosol in the trachea
- A central lumen transmits the solution to be nebulized and compressed gas is forced under high pressure (100 psi) at a variable flow rate (0.1–3.0 L/min) through several additional lumens that surround the central lumen
- Droplets of drug solution form at the tip of the catheter and aerosol is formed by the pressurized gas breaking up the liquid droplets
- The use of the intratracheal catheter is presently *under investigation*

Inhaled therapy during noninvasive positive pressure ventilation

- **Several investigators have employed in-vitro models to determine the optimal techniques for aerosol delivery in patients receiving NIPPV**
- **Optimum settings required for maximum drug delivery with a pMDI during NIPPV have not been established**
- **In a bench model, 10 cmH₂O continuous positive airway pressure (CPAP) reduced drug delivery from a jet nebulizer**

- **Chart C et al found a fivefold variation (between 5 and 25% of the nominal dose) in the amount of albuterol delivered by a jet nebulizer in vitro;**
- **Delivery was highest (25%) when the nebulizer was close to the patient, inspiratory pressure was high (20 cmH₂O), and expiratory pressure was low (5cmH₂O)**

Both pMDIs and nebulizers could be employed during NIPPV, but further studies are needed to optimize drug delivery from these devices during NIPPV

Conclusion

- **Aerosol therapy is an integral part of management of patients in ICU**
- **Aerosol size of 1 to 5 micron MMAD are better deposited in lungs**
- **Humidity in the ventilator circuit reduces drug delivery**
- **High flow rates , reduced inspiratory time and low tidal volumes hamper drug delivery**

- **Spacer improves drug delivery**
- **pMDI better than nebulizers for drug delivery**
- **Distance of 15 cms from ET in inspiratory limb improves drug delivery**
- **Role of inhaled antibiotics, surfactant & vasodilators needs further validation**