AEROSOLS

DEFINITION:

- An aerosol comprises of solid or liquid particles suspended in a gas

- GOALS :
  - High efficiency of drug delivery
  - Reproducible dosing
  - Targeted delivery to site of action
  - Ease of device operation
  - Short duration of treatment
  - Minimized risk to the patient and clinician
  - Cost - effectiveness

CLASSIFICATION OF AEROSOLS

- BLAND:

  include heated or cooled sterile water/ saline

- MEDICATED:

  bronchodilators, steroids, mucokinetic agents , ant allergic agents, local anesthesia, antimicrobials, surfactant, insulin , vosopressin

AEROSOL PHYSICS

- The depth of aerosol delivery is a function of many variables--
  - -size and physical characteristics of the aerosol
  - - amount of aerosol
  - - anatomy and geometry of the airway
  - - ventilatory pattern

DEPOSITION OF AEROSOLS

- Deposited by 3 mechanisms: diffusion, inertial impaction and sedimentation

SIZE (MMAD)	SITE
<0.5 U	**Stable (no deposition)**
0.5-2 U	**Alveoli**
2-5 U	**Bronchi & bronchioles**
5-100 u	**Mouth, nose & upper airway**
>100 u	**Filtered by URT**

INDICATIONS OF AEROSALS

- DIAGNOSTIC :
  - Ventilation scans
  - Airway responsiveness & bronchodilator reversibility
  - Dosimetry

- THERAPEUTIC:
  - Treatment of airway and lung parenchymal diseases
  - Systemic diseases (D.M , D.I)

INHALED THERAPIES

DIAGNOSIS	THERAPY
ARDS	Surfactant, anti-inflammatories
Pneumonia / sepsis	Antibiotics, surfactant
COPD exacerbation	Bronchodilators, anti-inflammatories
Pulm. HTN	Vasodilators
Asthma	Bronchodilators, anti-inf.

METHODS OF AEROSOL GENERATION

- NEBULIZERS:

  Pneumatic : - small volume, large volume small particle generator

  Ultrasonic

- METERED DOSE INHALERS:- (+ accessory device: spacer / chamber / spring loaded actuator)

- DRY POWDER INHALERS :– Rotahaler/ spinhaler/ turbohaler/ diskhaler

NEBULIZERS

- Pneumatic/ Jet nebulizers :- work on Bernoulli's principle
- Small volume nebulizer (SVN): Hand-hold nebulizers / ventilator circuits

-gas flow rates : 6-8 l / m

-optimal volume : 4-5ml

-particle size : 1-5 u

-10% of aerosol reaches its site of action

-not ideal mode of aerosol delivery

Pneumatic/ Jet nebulisers

ADVANTAGES

- Patient coordination not required
- Effective with tidal breathing
- High dose possible
- Dose modification
- Can be used with supplemental oxygen
- Can deliver combination therapies if compatible

DISADVANTAGES

- Lack of portability
- Pressurized gas source required
- Lengthy treatment time
- Doesn’t aerosolize suspension well
- Device preparation required
- Performance variability

ULTRASONIC NEBULISERS

- Electric charge is applied to a piezo electric crystal (transducer)- ultrasonic vibrations are generated
- Size of aerosol particles depend on frequency of the transducer while the volume is related to the amplitude of the sound waves
- Suitable for long duration aerosol delivery for relief of bronchospasm, upper airway edema & for humidification in tracheostomised patients

ULTRASONIC NEBULISERS

ADVANTAGES

- Patient coordination not required
- High dose possible
- No CFC release
- Quiet, faster delivery than jet nebuliszers
- Newer designs are portable and small

DISADVANTAGES

- Expensive
- Need for electricity/batteries
- Possible drug degradation
- Contamination possible
- Drug preparation required

DRY POWDER INHALERS

COMPONENTS:

DEVICE: (Rotahaler /Spinhaler /
Turbuhaler/ Diskhaler)

DRUG RESERVIOR:- discrete gelatin capsules,
multidose strips

DRY POWDER INHALERS

ADVANTAGES

- Breath- actuated
- Less patient co-ordination required
- Propellant not required
- Small & portable
- Short treatment time
- Dose counters in newer designs

DISADVANTAGES

- Requires moderate to high inspiratory flow
- Some units are single dose
- Can result in high pharyngeal deposition
- Not all medications available

METERED DOSE INHALERS

ADVANTAGES

- Portable &compact
- Rx time is short
- No drug preparation required
- Dose-dose reproducibility high
- No contamination of contents

DISADVANTAGES

- Coordination of breathing and actuation needed
- High pharyngeal deposition
- Upper limit to unit dose content
- Remaining doses difficult to determine
- Potential for abuse
- Many use CFC

Holding chamber, Reverse flow spacer, or spacer

ADVANTAGES

- Reduces need for patient co-ordination
- Reduces pharyngeal deposition

DISADVANTAGES

- More expensive
- Less portable
- Can reduce dose available if not used properly
- Inhalation can be more complex for some patients

Table 2—*General Age Requirements for Correct Use of Aerosol Delivery Device Types**

Aerosol Delivery Method	Minimum Age
Small-volume nebulizer	≤ 2 yr
MDI	> 5 yr
MDI with chamber	> 4 yr
MDI with chamber and mask	≤ 4 yr
MDI with endotracheal tube	Neonate
Breath-actuated MDI	> 5 yr
DPI	≥ 5 yr

*Based on National Asthma Education and Prevention Program.[2]

ACCP / ACAAI RECOMMENDATIONS

EMERGENCY DEPT		RECOMMEND	LIMITED DATA
	SHORT ACTING BETA 2 AGONISTS	❑Nebulizers ❑MDI with spacer/ holding chambers	❑DPI ❑MDI with out spacer/ holding chambers/ ❑Breath actuated MDI

ACCP / ACAAI RECOMMENDATIONS

INPATIENT		RECOMMEND	LIMITED DATA
	BETA2 AGONISTS	❑Nebulizers ❑MDI with spacer/ holding chambers	❑DPI ❑MDI with out spacer/ holding chambers/ ❑Breath actuated MDI

ACCP / ACAAI RECOMMENDATIONS

OUT PATIENT	ASTHMA	RECOMMEND
	SHORT ACTING BETA 2 AGONISTS	❑MDI with or without spacer/ holding chambers ❑DPI
	CORTICOSTEROIDS	❑MDI with or without spacer/ holding chambers ❑DPI

ACCP / ACAAI RECOMMENDATIONS

OUT PATIENT	COPD	RECOMMEND
	BETA2 AGONISTS ANTICHOLINERGICS	❑MDI with or without spacer/ holding chambers ❑DPI ❑Nebulizers

ACCP / ACAAI RECOMMENDATIONS

- Frequent intermittent nebulization and continuous nebulizations are appropriate alternatives in severely dyspneic patients in ED / ICU

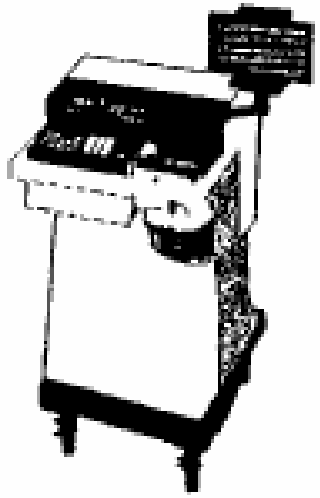
- MECHANICAL VENTILATION: Both nebulization and MDI's can be used but careful attention to the technique is necessary

AEROSOLS IN MECHANICAL VENTILATION

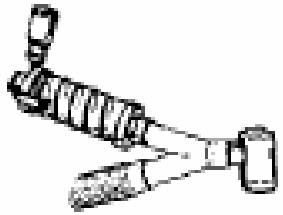
Table 1. Factors That Influence Lower-Respiratory-Tract-Deposition During Mechanical Ventilation

Physical and chemical properties of the medication
Characteristics of the aerosol-generating device
Position of the aerosol-generating device in the circuit
Ventilator settings
Characteristics of the ventilator circuit and endotracheal tube
Humidity of the inspired air
Airway anatomy and secretions

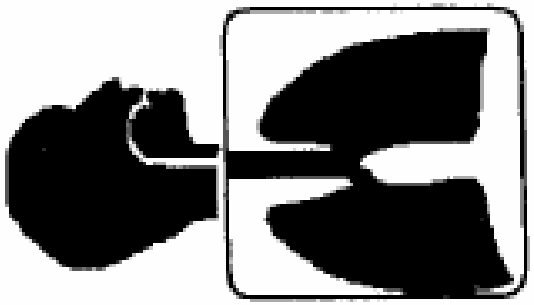
Ventilator-Related
- Ventilation mode
- Tidal volume
- Respiratory rate
- Duty cycle
- Inspiratory waveform
- Breath-triggering mechanism



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



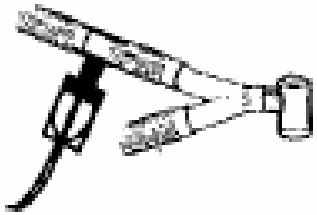
Drug-Related
- Dose
- Formulation
- Aerosol particle size
- Targeted site for delivery
- Duration of action



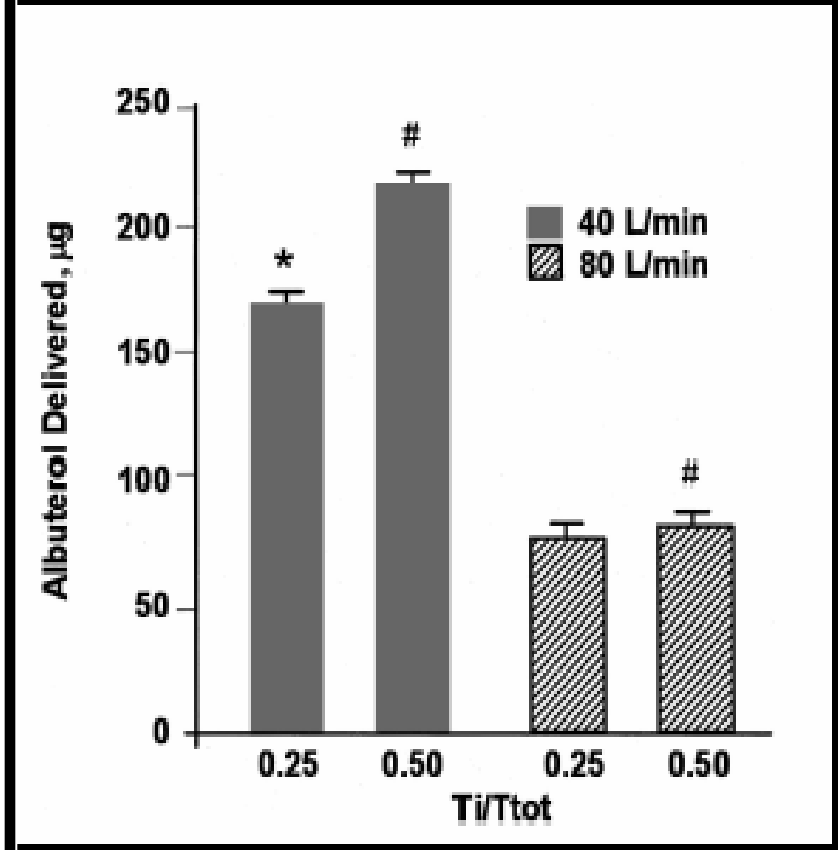
Device-Related - Nebulizer
- Type of nebulizer
- Fill volume
- Gas flow
- Cycling: inspiration vs continuous
- Duration of nebulization
- Position in the circuit

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

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

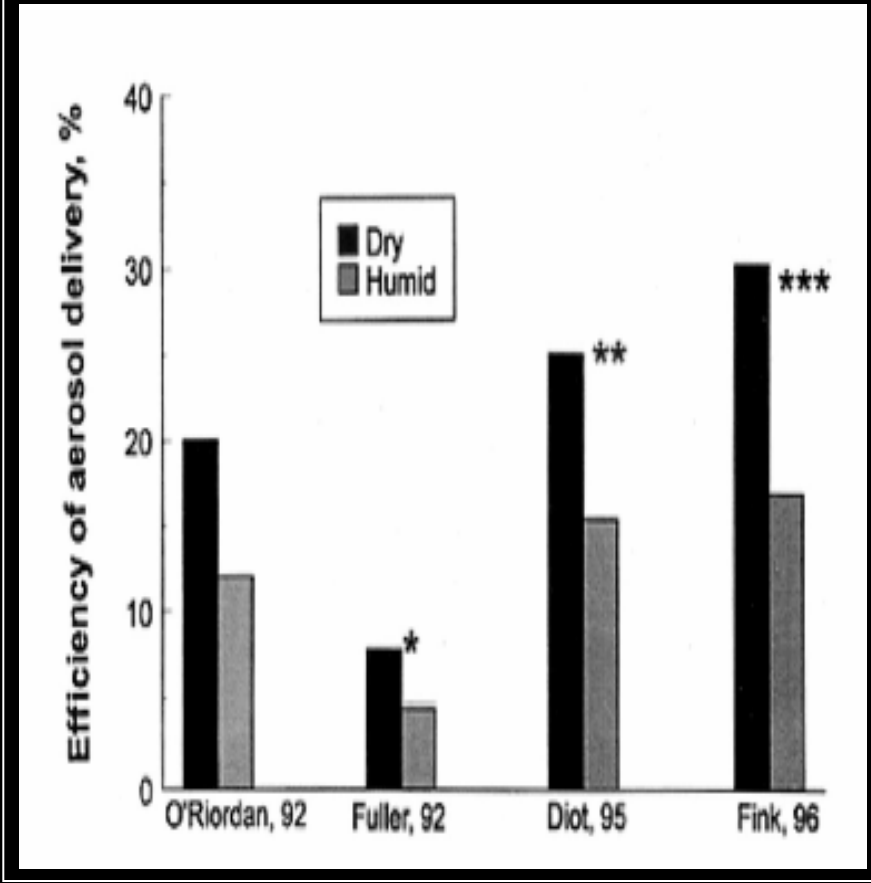


AEROSOLS IN M.V



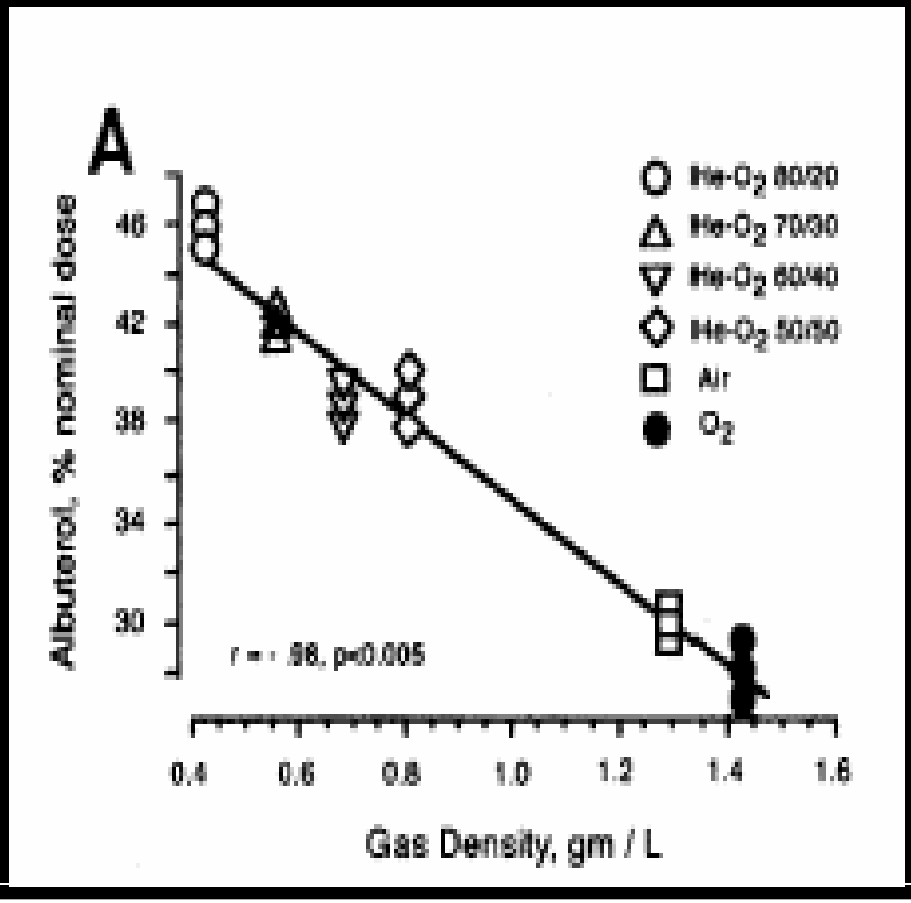
- Tidal volume >500ml
- Slow inspiratory flow
- Long inspiratory time
- In simulated spontaneous breath than controlled m.v
- Connection to the circuit at app 15 cm from ETT

HUMIDITY:



- 40% reduction – increased impaction in ventilatory circuits
- Dry gas for longer times harm the mucosa
- Disconnection – VAP

GAS DENSITY



- High inspiratory flow-turbulence-drug particle impaction losses
- MDI- Drug delivery was inversely correlated with density
- NEBULIZER-Drug output correlated positively with density

Table 2. Using a Nebulizer During Mechanical Ventilation

1. Clear secretions from the endotracheal tube
2. Be sure the tidal volume is > 500 mL
3. If possible, decrease the inspiratory flow to ≤ 60 L/min
4. Place the drug solution in the nebulizer. Total volume in the nebulizer should be 4–6 mL
5. Place the nebulizer in the inspiratory limb, 30 cm from the Y-piece
6. Be sure the gas flow to the nebulizer is ≥ 6 L/min
7. If possible, nebulize the solution only during inspiration
8. Tap the nebulizer intermittently during operation
9. When nebulization ends, disconnect the nebulizer from the ventilator circuit

Table 3. Using a Metered-Dose Inhaler During Mechanical Ventilation

1. Clear secretions from the endotracheal tube
2. Be sure the tidal volume is > 500 mL
3. If possible, decrease the inspiratory flow to ≤ 60 L/min
4. Be sure the actuator-spacer device is in the inspiratory limb
5. Shake the MDI and place it into the actuator-spacer device
6. Actuate the MDI at the onset of inspiration
7. Wait 20–30 s before administering the next MDI actuation

AEROSOLS IN M.V

- MDI:
- Easy to administer
- Less personnel time
- Reliable dose
- No risk of bacterial contamination

- NEBULIZER:
- Aerosol production is variable
- Particle size is variable
- Bacterial contamination
- Ventilatory settings

NEW FRONTIERS

NEW DEVICES

- Vibrating plate technology
- Intratracheal catheter

NEW DRUG FORMULATIONS

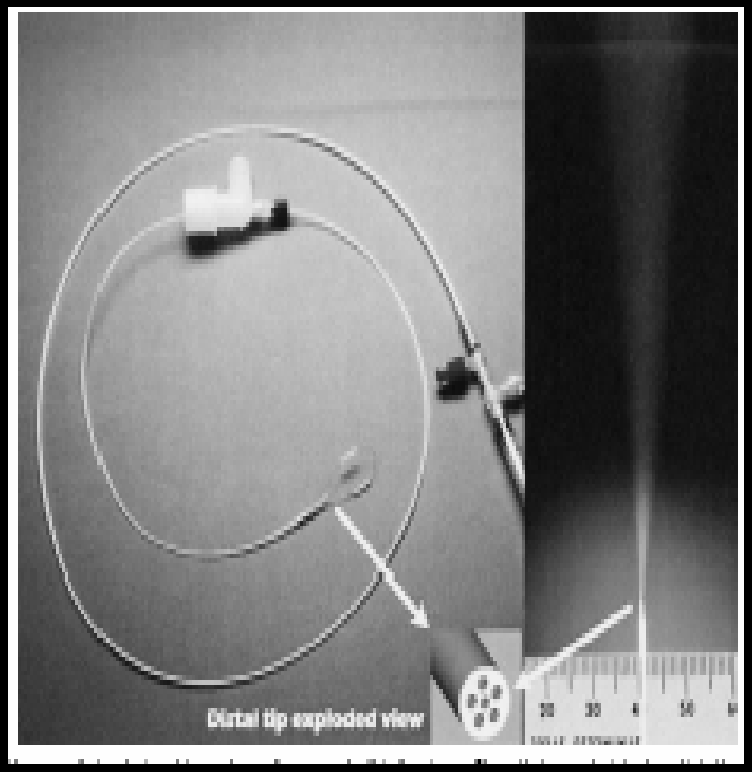
- Liposomal formulations
- Surfactant therapy
- GM-CSF

VIBRATING PLATES

Fig. 1. The Aerosolb Pro (shown with battery pack) is placed in the inspiratory limb of the ventilator circuit. (Courtesy of Aerogen)

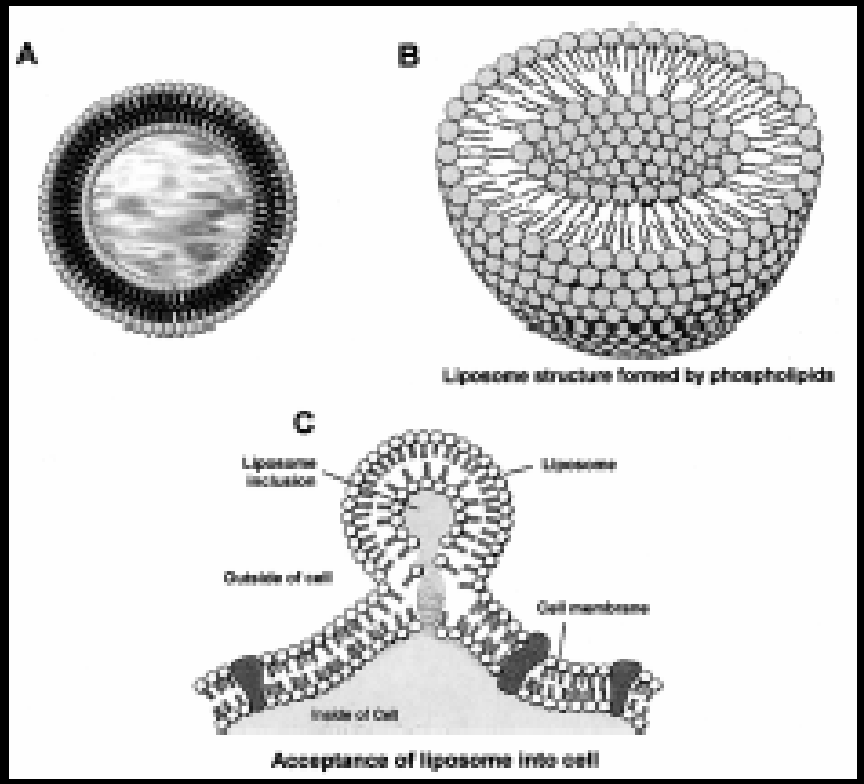
- Aerosols with fine particle fraction
- Portable, quiet, battery operated
- Higher efficiency of drug delivery
- Minimal residual drug left
- Short nebulization time
- Doesn’t denature proteins/ peptides

INTRATRACHEAL CATHETER



- Can be passed into trachea via an endotracheal tube/ bronchoscope
- Ideal for targeted aerosol therapy within lung
- Surfactants,antibiotics, DNA,suspensions can be aerosolized

LIPOSOME FORMULATIONS



- Closed concentric bilayer, nanometer in size
- Extended therapeutic response (slow release depot effect)
- Delivers hydrophilic, hydrophobic drugs
- Nucleic acids for gene therapy

SURFACTANT THERAPY

- Deficiency of endogenous surfactant in neonates
- Adults with ALI
- Appears promising as a treatment for various other disorders in critically ill –

  asthma, bronchiolitis, pneumonia, sepsis and interstitial lung disease

GM-CSF

- PULMONARY ALVEOLAR PROTEINOSIS:

  Patients pulmonary functions improved over 6 months of intermittent therapy(250 mic.g bd)

- METASTATIC CANCER:

  Low toxicity and promising antitumor effect against lung metastases

HAZARDS OF AEROSOL THERAPY

PATIENT:

- Bronchospasm
- Infection
- Airway obstruction(sputum induction in patients with poor cough reflex)
- Over hydration (infants)
- Thermal injury (heated aerosols)
- Device malfunction
- Cardio toxicity (CFC)

CARE GIVER:

- Asthma in subjects with hyper-reactive airways
- Infection
- Rash
- Bronchospasm
- Conjunctivitis

ENVIRONMENT:

- Ozone layer depletion by CFCs