





Inhalation devices in the Far East

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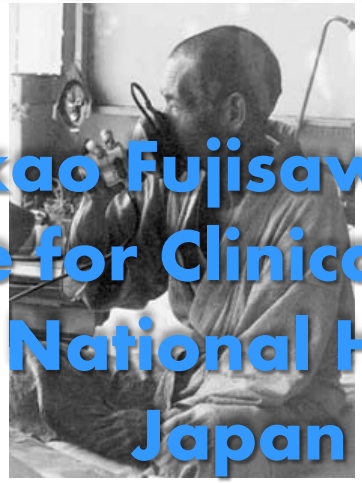



Inhalation devices in the Far East

- Basics of inhalation therapy
- Characteristics of various inhalation devices
- A tidbid of nebulizers

Inhalation is the mainstay of drug delivery in asthma

- Bronchodilators, corticosteroids and other anti-asthma drugs can be effectively delivered to the airways by inhalation.
- Efficiency of the delivery system is the key to success in the treatment of asthma.
- Choice and proper use of inhalation devices are very important.

Factors influencing lung delivery

Lung delivery =

Drug factors

1. Dose
2. Formulation (aerosol/dry powder/ suspension/solution)
3. Size of particles

+ Device factors

1. DPI/pMDI/Nebulizer
2. Size of particles
3. Spacer/VHC

+ Inhalation skills

1. Inhalation technique
2. Adherence

+ Respiratory factors

1. Breathing patterns
   - respiratory rate
   - crying
   - asthma symptoms
2. Body size
3. Anatomical characteristics

Inhalation devices :MDIs and Nebulizers

Type of device		Advantages	Shortcomings
Metered-dose inhalers (MDIs)	Pressurized MDI (pMDI) Dry powder (DPI)	Small/handy No electricity Quick	Dependent on patient's skill Lung delivery varies between devices
Nebulizers	Jet Vibrating mesh Ultrasonic	Less dependent on patient's coordination and cooperation.	Expensive Time consuming Bulky Output is dependent on devices

Inhalation devices :Nebulizers

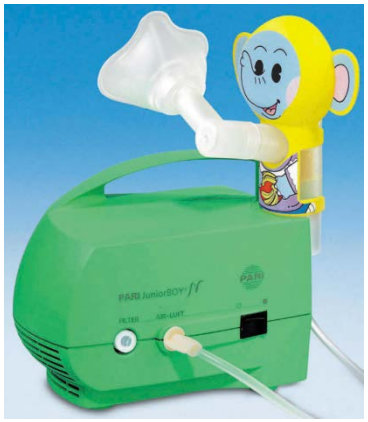
Type of nebulizers	Aerosol generation methods	Advantages	Shortcomings
Jet	Compressed gas flow disperses a liquid into a fine mist.	Sturdy	Noisy Heavy/bulky AC-powered

Mechanism of a jet nebulizer

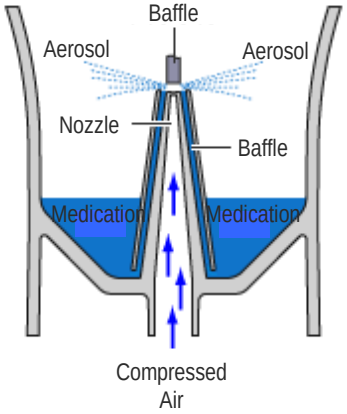
<Configuration>

Nebulizer kit
(to turn liquid medication into a fine mist)

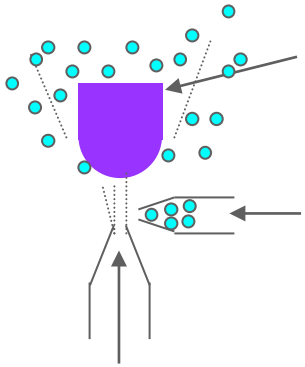
Compressor
(to make a compressed air)



<Configuration of Nebulizer Kit>



<Nebulization>



Advantages:

- **Almost every solutions can be nebulized**

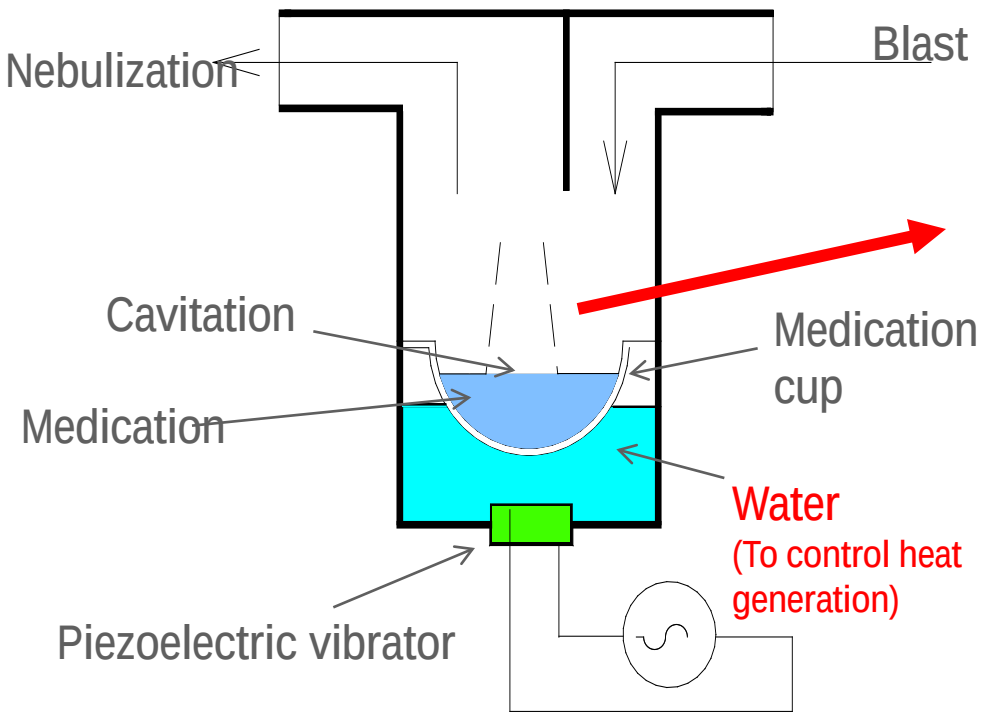
Disadvantages:

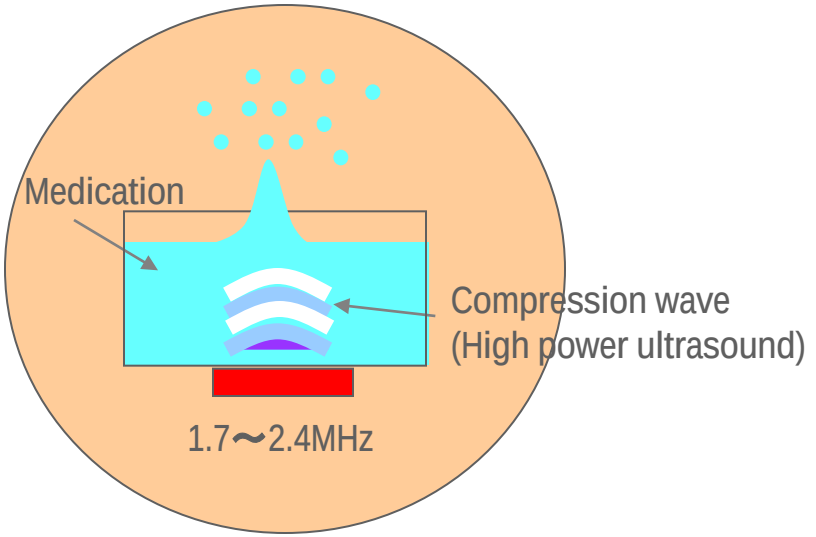
- **Noisy**
- **Bulky**

Inhalation devices :Nebulizers

Type of nebulizers	Aerosol generation methods	Advantages	Shortcomings
Jet	Compressed gas flow disperses a liquid into a fine mist.	Sturdy	Noisy Heavy/bulky AC-powered
Ultrasonic	Piezoelectric crystal oscillation at high frequency vibrates the surface of a solution and releases liquid droplets to form an aerosol	Quiet Large volume	Not for suspension formulation Possible denaturation of drug

Mechanism of ultrasonic nebulizer





High-frequency oscillation: 1.7 ～ 2.4MHZ

Advantages:

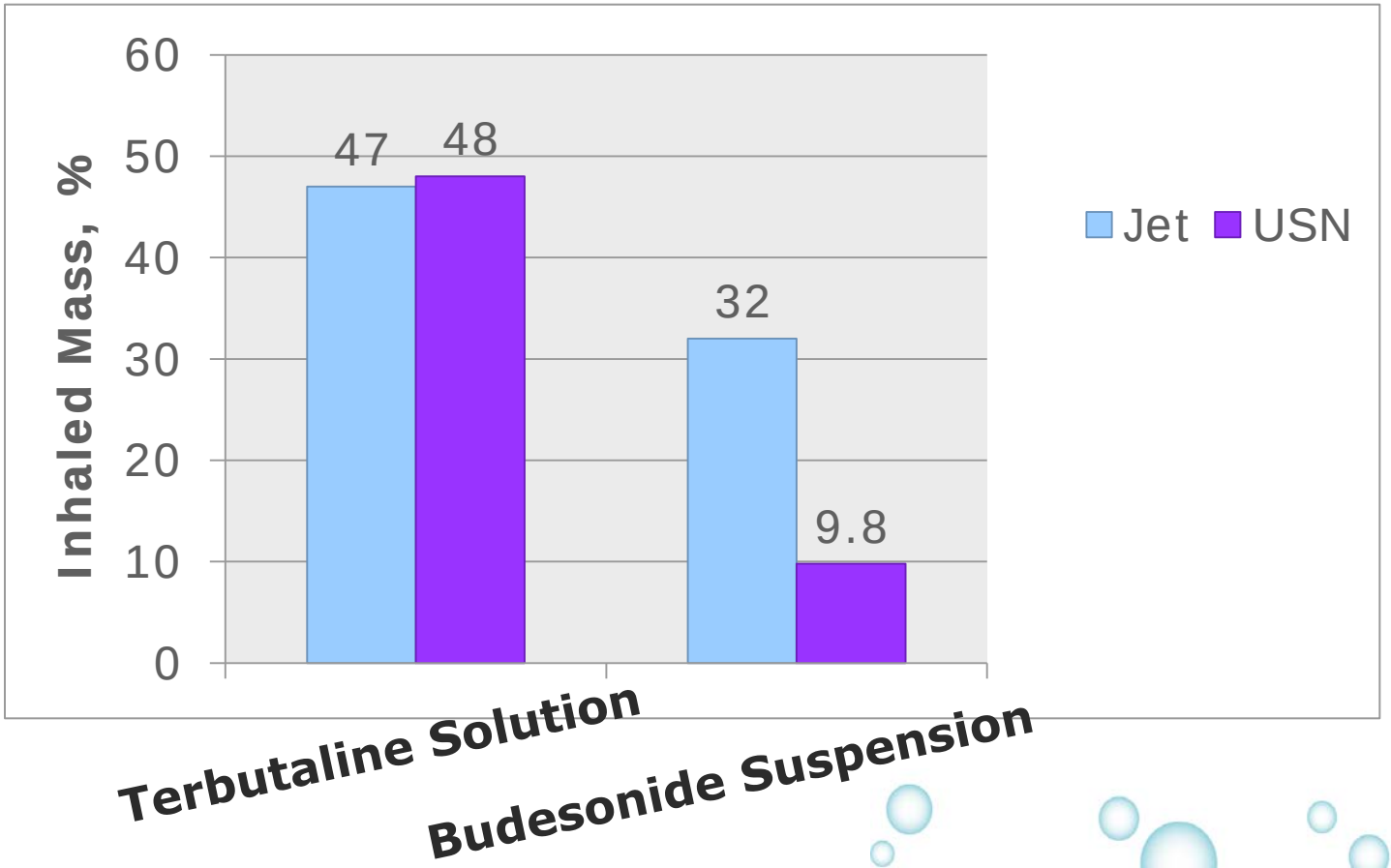
- Large amount of nebulization volume
- Noiseless

Disadvantages:

- Large amount of residual volume
- Some solution can not be nebulized

Ultrasonic is not for budesonide inhalation suspension

Jet = Spira E4 jet nebulizer
USN = Spira Ultrasonic nebulizer



Nikander K. J Aerosol Med 1994;7(Suppl 1):S19-S24

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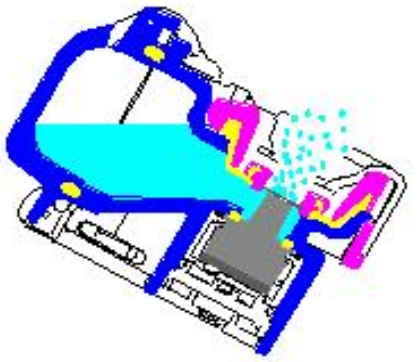
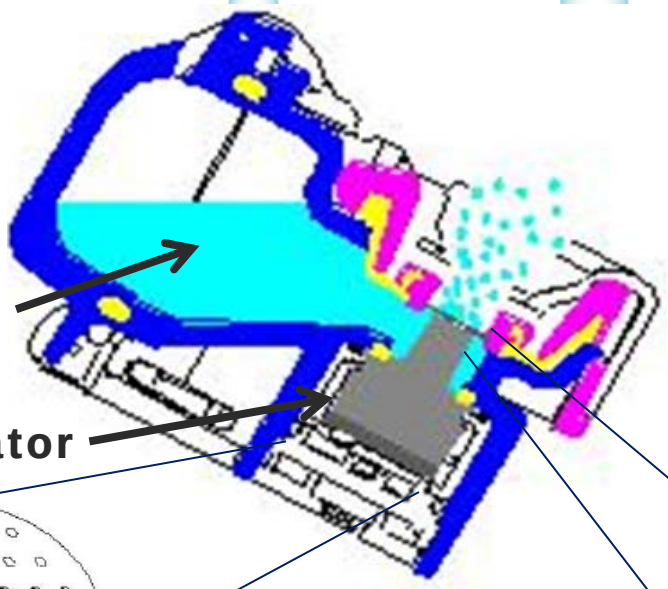
Vibrating mesh	Vibration mesh with numerous (1000~6000) tapered holes creates an aerosol by a micro-pumping action	Quiet Less bulky DC-powered	Sturdy?? Not many manufacturers

Mechanism of a mesh nebulizer



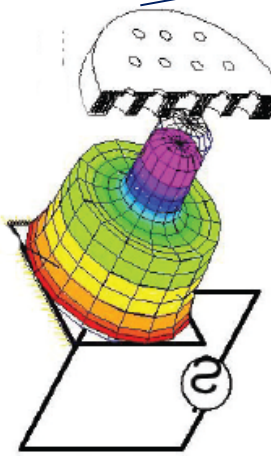
Any direction
Minimal residual volume

Mechanism of a mesh nebulizer



Medication

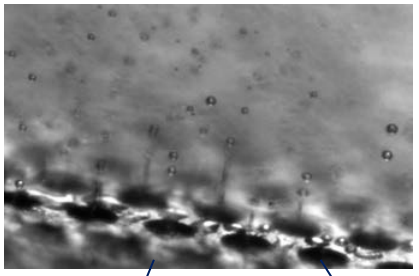
Horn oscillator

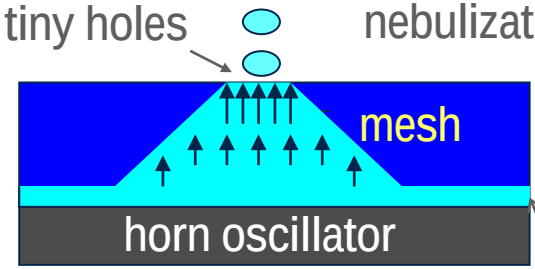


High frequency vibration

Piezoelectric crystal

Electrical current





Advantages:

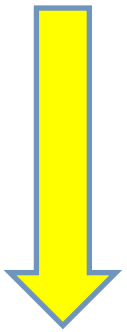
- Small
- Quiet
- Minimal residual volume

Disadvantages:

- Expensive
- Side effect due to larger lung delivery??

High efficiency of drug delivery to the lung

High clinical efficacy



Overdose → side effect?

Reduction of nominal dose?

Comparison of jet and mesh nebulizers

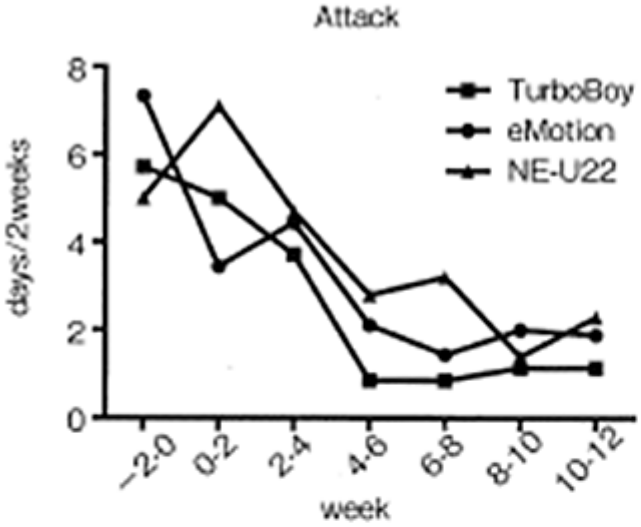
Thirty children, 6m-4y, with asthma were randomly assigned to one of 3 nebulizer devices for budesonide inhalation suspension (Pulmicort Respule) at 05mg/day for 12 weeks.

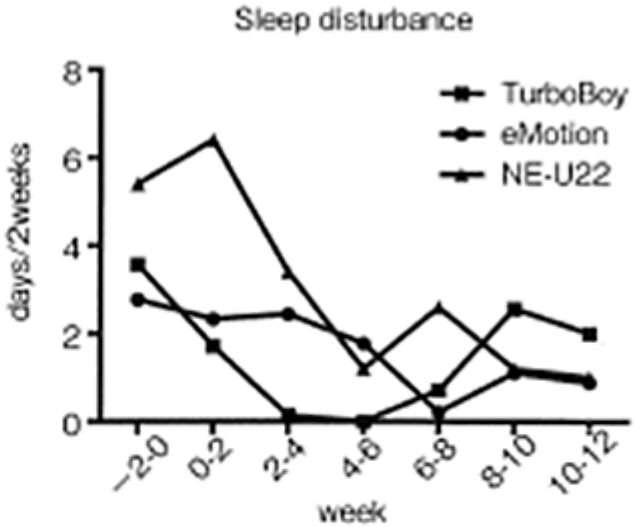
	Jet	Mesh 1	Mesh 2
	PARI TurboBOY®+ LC Plus®	PARI eMotion®	OMRON NE-U22®
			
MMD	3.8 μm	4.4 μm	≒5 μm
%RF	65 %	61 %	73.7 %
TOR	0.44 g/min	0.70 g/min	≧0.25 g/min

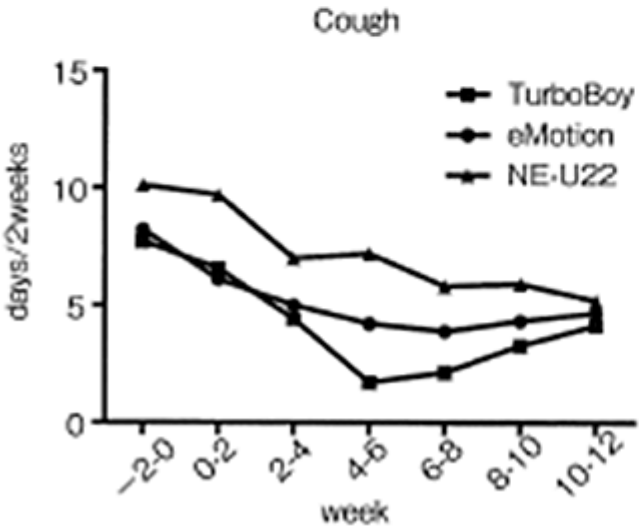
MMD: Mass Median Diameter, %RF: Percentage Respirable Fraction, TOR: Total Output Rate

Tezuka, Arerugi 57:1034-42, 2008

Comparison of jet and mesh nebulizers :efficacy

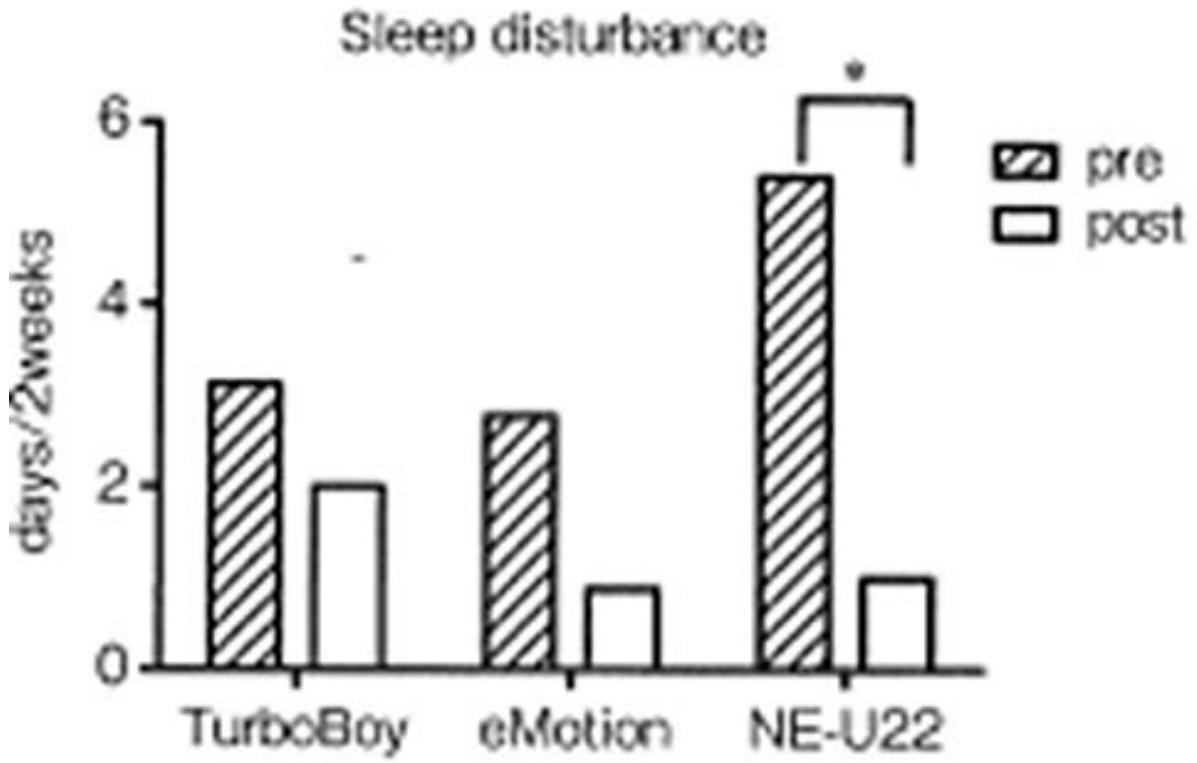






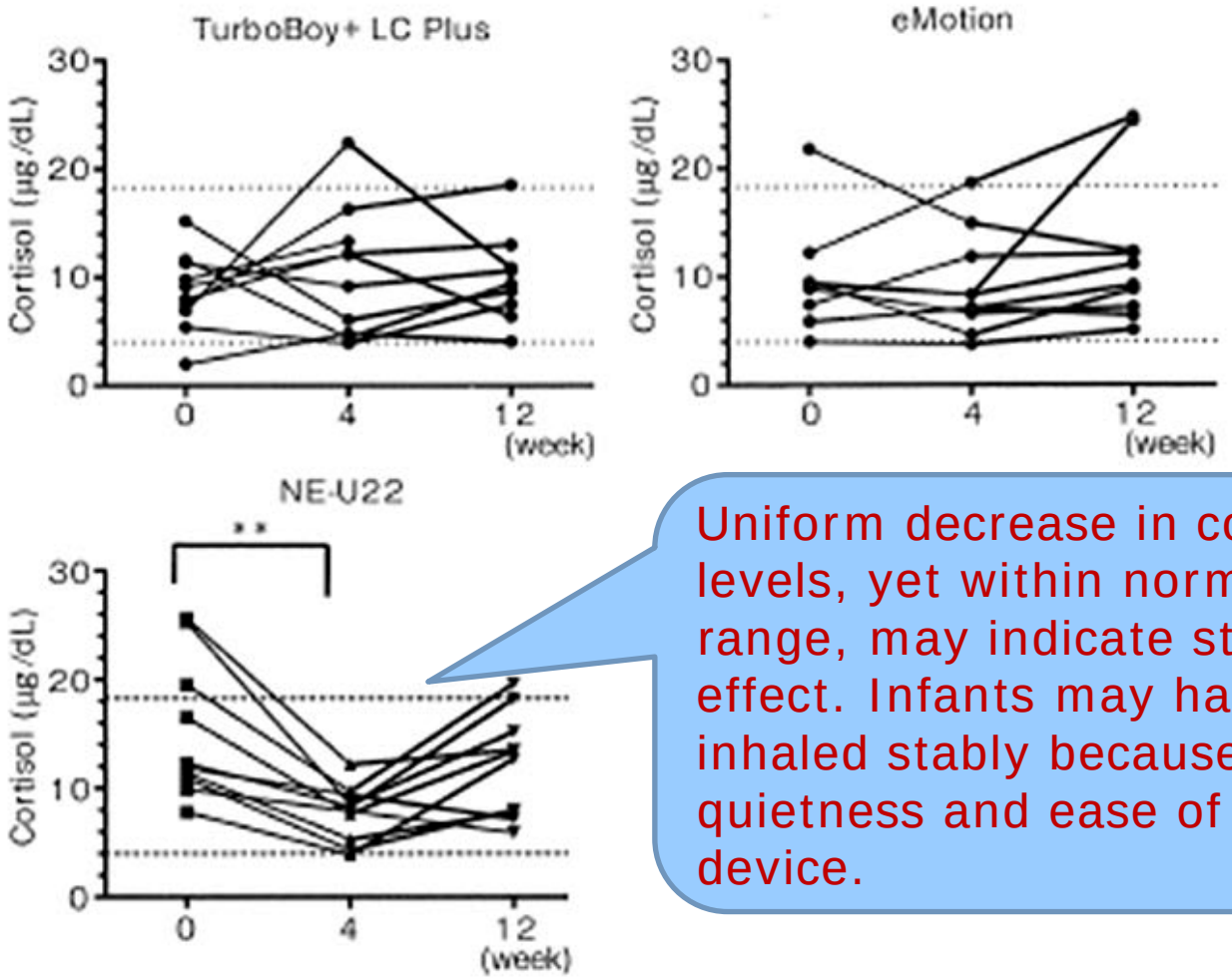
Tezuka, Arerugi 57:1034-42, 2008

Comparison of jet and mesh nebulizers :efficacy



Tezuka, Arerugi 57:1034-42, 2008

Comparison of jet and mesh nebulizers :plasma cortisol levels



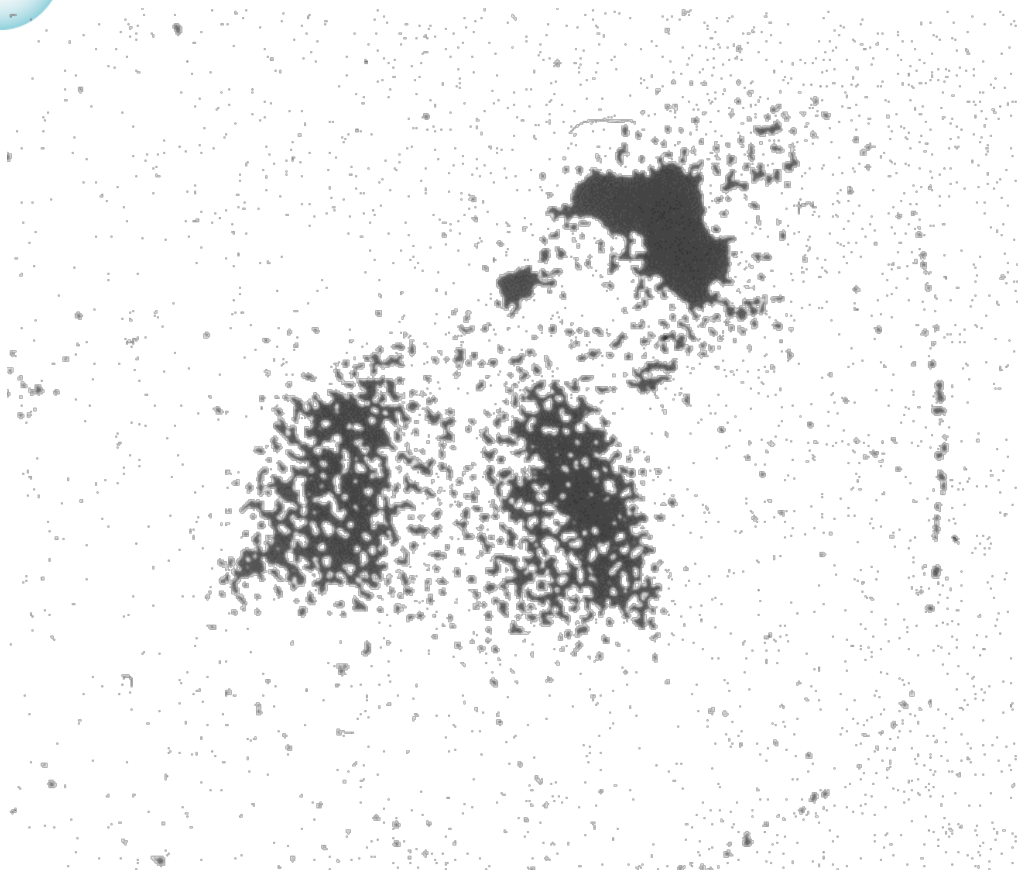
Uniform decrease in cortisol levels, yet within normal range, may indicate stable effect. Infants may have inhaled stably because of quietness and ease of the device.

Tezuka, Arerugi 57:1034-42, 2008

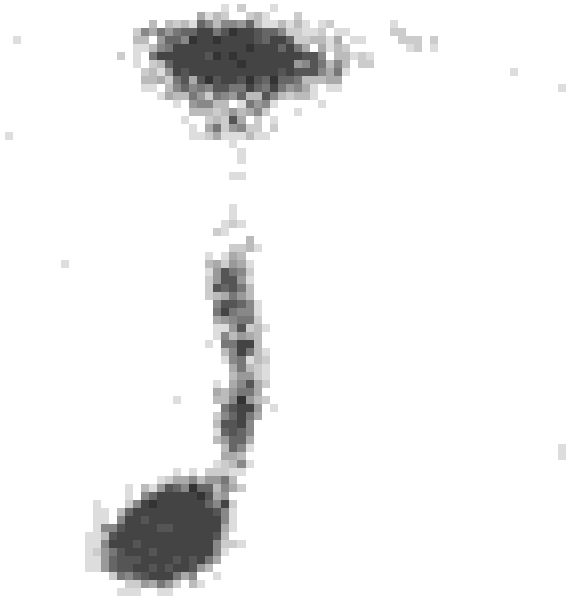
Choice of inhalation devices for children

Age	Device / Drug	Adjunctive device
Infants	1. Suspension/solution	Nebulizer + mask
	2. pMDI	Spacer/valved holding chamber (VHC) + mask
Toddlers	1. pMDI	Spacer/VHC
	2. Suspension/solution	Nebulizer
School children	1. DPI	none
	2. pMDI	Spacer/VHC
	3. Suspension/solution	Nebulizer

The Effect of Crying on Lung Deposition



Not Crying

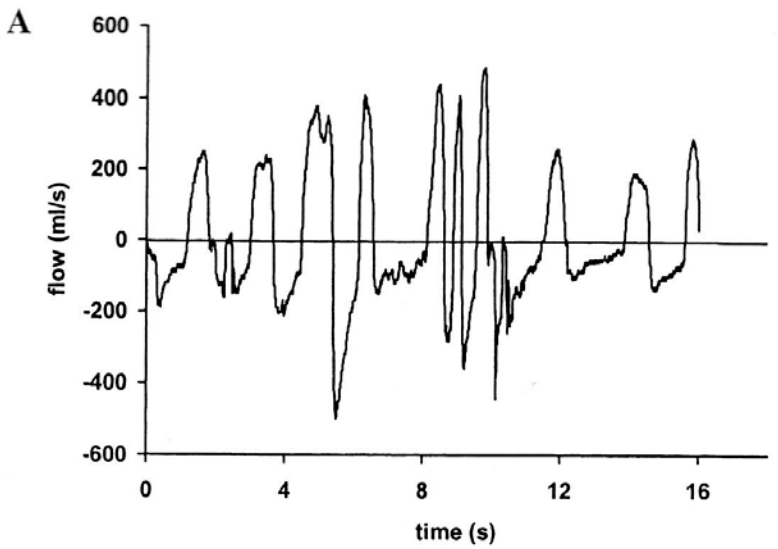


Crying

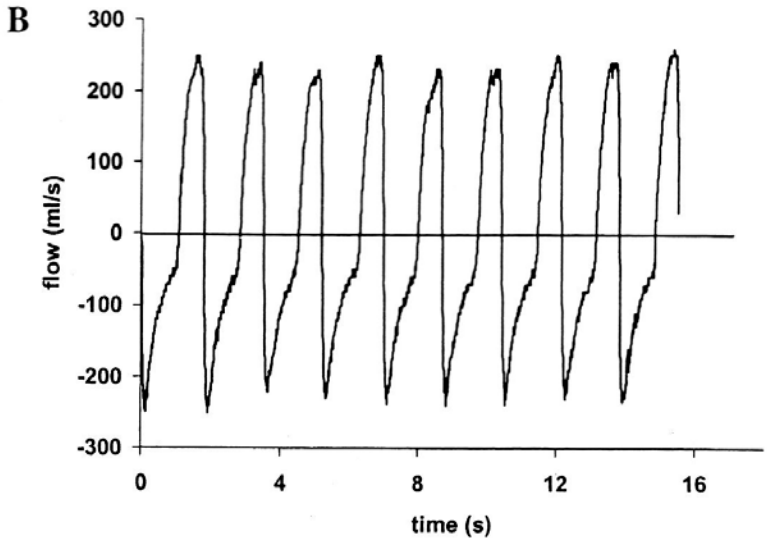
G Murakami Ann Allergy 1990;64:383-7

Tidal breathing patterns of infants

Awake



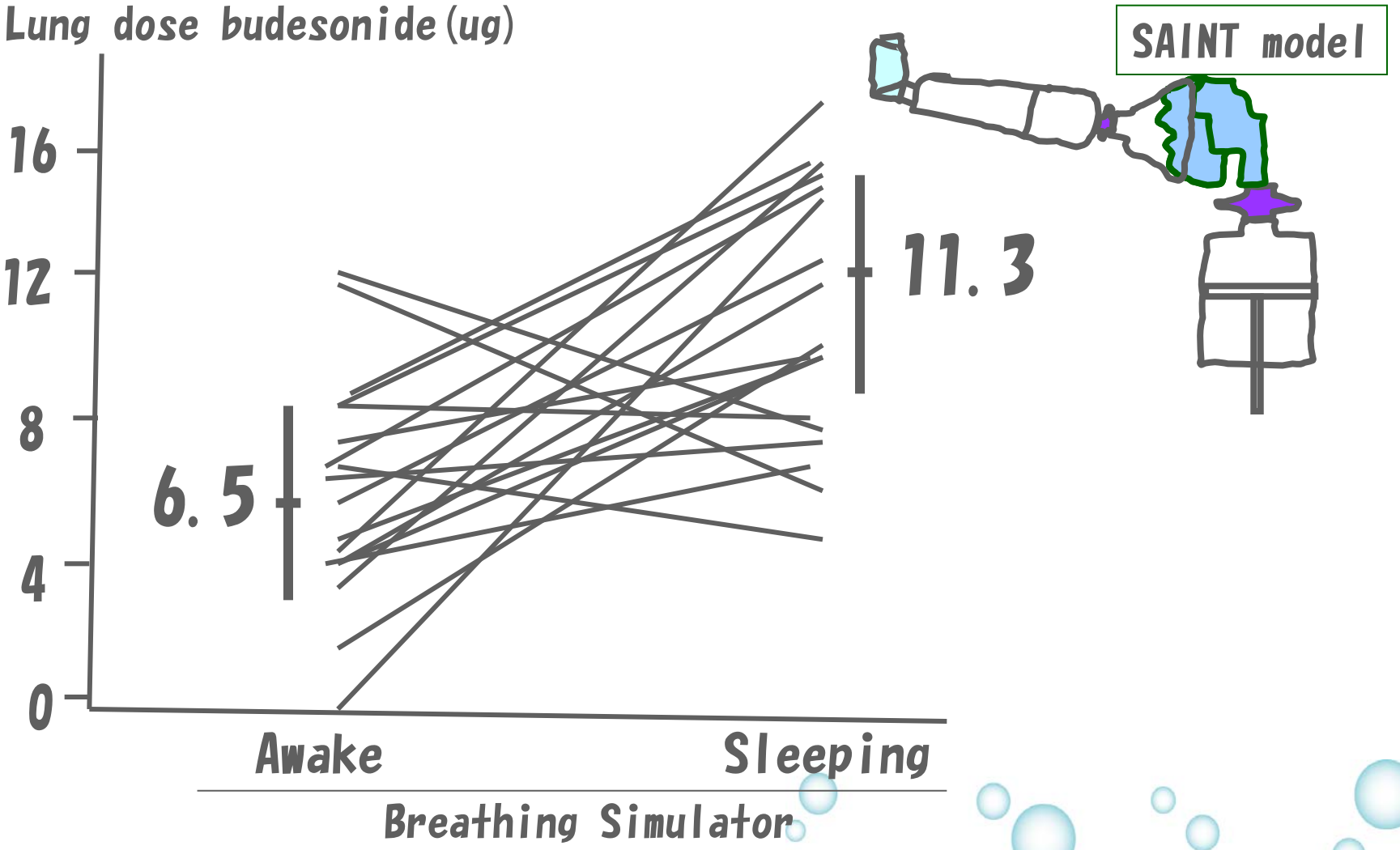
Sleeping



By pneumotachograph

Janssen HM, J Aerosol Med 2003, 16:395-400

For infants who do not coordinate, nebulize during sleep



Janssen HM, J Aerosol Med 2003, 16:395-400

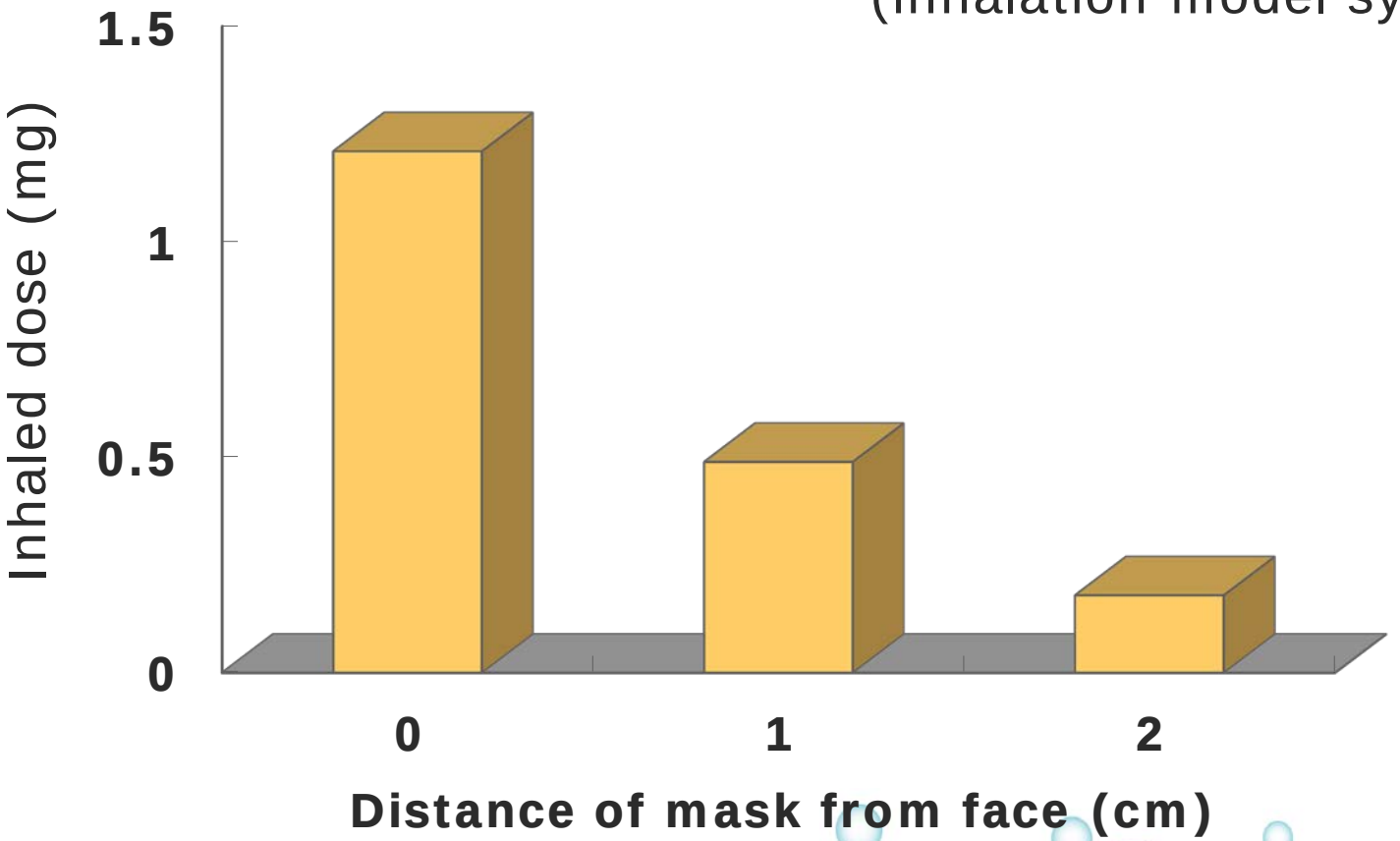
Check points for nebulizers

- Mouthpiece
  - Patient properly hold mouthpiece in his/her mouth
  - No backflow of saliva
  - Mouth-breathing while holding mouthpiece

- Mask
  - No leak between mask and face
  - No crying, quiet breathing
  - Wipe around the mouth after inhalation

Loose contact of mask causes huge loss

(inhalation model system)



Everand ML, et al. Arch Did Child 67:586;1992.

Check points for pMDI

- Without adjunctive device
  - Synchronize actuation and inhalation
  - Mouth breathing (not inhale from nose)
  - Slow and deep breathing
  - Breath holding after inhalation
- With spacer/VHC
  - No leak between mask and face
  - No crying, quiet breathing
  - Wipe around the mouth after inhalation

Check points for DPI

- Hold a device in proper direction to avoid loss of powders
- Proper inhalation flow
- Deep inhalation/breath-holding
- Gurgle and wash mouth after inhalation (ICS)

Recommended devices in JPGL 2012

Spacers

エアロチャンバー・プラス®　オプティヘラー®　ボアテックス®

Nebulizers

NE-U22（オムロン）　NE-C28（オムロン）　ボヤージ（東京エムアイ商会）

ターボボーイN（パリ）　ジュニアボーイN（パリ）　ボーイN（パリ）　ボーイモバイルS（パリ）

Summary

- Multiple factors influence the lung delivery of inhalation drugs in asthma.
- Among them, proper choice and use of inhalation devices are very important.
- More clinical study is necessary to give appropriate positioning of new generation nebulizers.