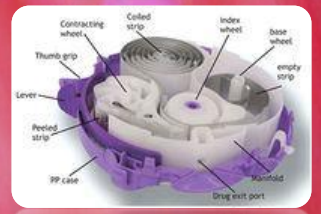
Why the device is importance for Asthma treatment?



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Introduction

- **Inhaled therapy** as the primary route for administering β2-agonists, anticholinergics, and corticosteroids.
- **Inhalation technique** : All inhalers are effective; therapeutic effect; different doses.
- **Drug formulation properties**: Particle size distribution, delivery system, inhalation device (appropriate particle size)
- **Inhalation technique**: Inspiratory flow rate,inspiratory volume, breathing hold time
- **Lung deposition**

Introduction

- **The degree of airway narrowing**, which varies with the type and severity of the lung disease, also influences the distribution of the dose within the lung and potentially, the response to the therapy.

Factors That Affect Aerosol Deposition

- **Physical factors** : Particle size distribution
- **Ventilatory factors** : Inspiratory flow rate and breath hold
- **Anatomical factors** : Airway caliber and distortion due to disease
- **Pateint-related factors** : Ability to correctly use the delivery system and compliance

Aerosol Medication (1)

Advantages

- Aerosol drug delivery is **noninvasive and painless**.
- Unlike oral and intravenous therapy, aerosolized therapy delivers drugs **directly to the airway surfaces and into receptor sites**.
- The aerosol route allows delivery of high drug concentrations to the airway.
- Systemic dose of most aerosolized drug is reduced compared with oral and intravenous treatments.
- Inhales B2-agonist bronchodilators produce a more **rapid onset of action** than with oral delivery.

From Dolovich M. Aerosols and aerosol delivery devices. Middleton's allergy : principles and practice. 7th ed.Philadelphia: Mosby; 2009,p.679-700

Aerosol Medication (2)

Disadvantages

- Less-than-optimal **technique** decreases drug delivery and potentially reduces efficacy.
- Techniques differ between **device categories** and device within a specific category, so there is no one technique to learn for all the medication that are available.
- The proliferation of inhalation devices has resulted in a **confusing number of choices.**
- Inhaler devices are **less convenient than oral drug** administration : **more time is required** for drug administration

From Dolovich M. Aerosols and aerosol delivery devices. Middleton's allergy : principles and practice. 7th ed.Philadelphia: Mosby; 2009,p.679-700

Pressurized Metered-Dose Inhalers (pMDIs)

Points to consider in selection of device

- ✓ MMAD
- ✓ FPF
- ✓ Age of patient use
- ✓ Ability of patient to inhale and actuate at the same time
- ✓ Delivery efficiency
- ✓ Dose counter

FPF, Fine particle fraction ; MMAD, mass median aerodynamic diameter.

Drug in Powder Form

Dry powder inhalers

- Aerosol of dry powder are created by directing air through an aliquot of loose powder. Because **DPIs are breath-actuated**, the need to **synchronize inhalation** with actuation is eliminate. Howover, the dispersion of the powder into respirable particles is depend on the creation of **turbulent flow** in the haler.

- Creation of this turbulent flow is the function of both the patient's ability to inhale the powder at a sufficiently high inspiratory flow rate and the design of the powder device.

Drug in Powder form

Dry powder inhalers

- Most powder-dispensing systems require the use of a carrier substance. The carriers that used include **lactose and glucose.**

- The size and surface characteristics of the particles in the powder blend effect how the formulation “flows” out of the device. Allergic reaction to lactose and glucose appear to be fewer than to the surfactants and propellants used in pMDIs.

- The particle size of dry powder particles is on the order of 1-2 *u*m, but the size of the lactose or glucose particles can range from approximately 20-65 *u*m. Consequently, most of the carrier deposits in the oropharynx.

Drug in Powder form

Design and Performance (1)

- DPIs that are currently commercially available are passive, or **patients driven**, and **rely on the patient's inspiration effort** to dispense the dose from the device.

- The specific **resistance of a DPI device affects the maximal inspiration flow rate** (**IFR**) that can be drawn through the device. Although high resistance decrease the ability to draw air through the inhaler, *inhalation at the optimal IFR and a fast initiate acceleration rate help to produce an aerosol with a greater FPF.*

Drug in Powder form

Design and Performance (2)

- Thus an *advantage high-resistance device* is the potential for increasing delivery of drug to the *lower respiratory tract.*
- The resistance of a DPI can be classified with respect to the inhalation flow required to produce a pressure drop of 4 kPa across device.
- DPIs that are currently commercially available are passive, or patients driven, and rely on the patient's inspiration effort to dispense the dose from the device.

Drug in Powder form

Design and Performance (3)

- The specific resistance of a DPI device affects the maximal inspiration flow rate (IFR) that can be drawn through the device. Although high resistance decrease the ability to draw air through the inhaler, inhalation at the optimal IFR and a fast initiate acceleration rate help to produce an aerosol with a greater FPF.

- Thus an advantage high-resistance device is the potential for increasing delivery of drug to the lower respiratory tract.

- The resistance of a DPI can be classified with respect to the inhalation flow required to produce a pressure drop of 4 kPa across device.

Drug in Powder form

Design and Performance (4)

- A **low-resistance device** allows an inspiration flow of more than 90 L/min to produce a pressure drop of 4 kPa. A **medium-resistance device** allows an inspiration flow of 60-90 L/min , whereas a **medium-high resistance device** allows an inspiration flow of 50-60 L/min and A **high-resistance** device allows flows less than 50 L/min.

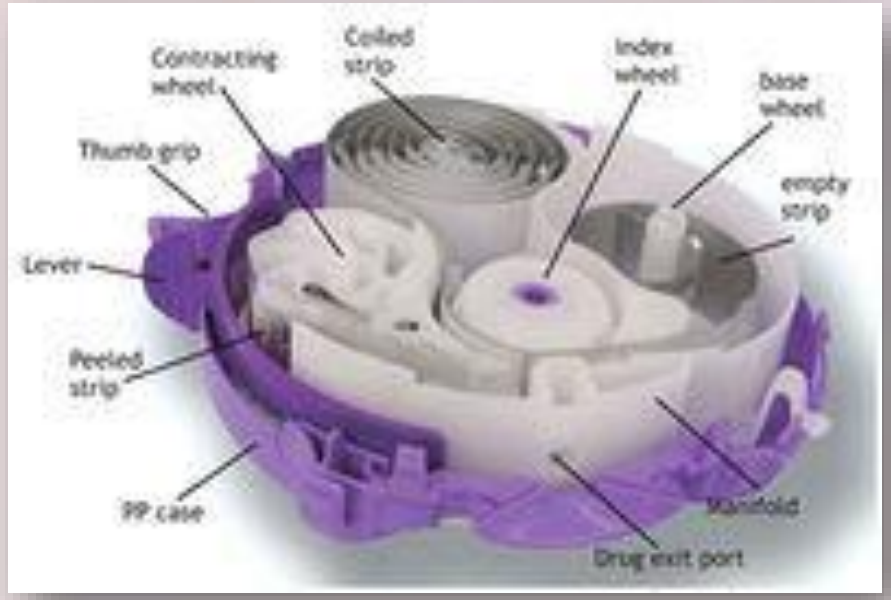
- Although DPIs with a high resistance tend to produce greater lung deposition than those with a lower resistance, the clinical sidnificance of this is not known.

Drug in Powder form

Design and Performance (5)

- Some study has shown that preschool-age chidren with asthma and patient with COPD may have problems achieving minimum flow some DPIs. Inhalation flow also appears to be reduced during acute exacerbations.
- Wide variability has been documented in the FPF of drug poweders from existing DPIs, ranging from 10-60% of the nominal dose. This variability may potentially result in marked different in lung deposition between the different devices.
- It’s important to store DPIs in a cool, dry environment.

Diskus : Accuhaler



Diskus

- The device should be discarded after removal from the moisture-protective foil overwrap pouch
- Diskus itself does NOT contain desiccant

Handihaler


Open on other
side only
Open blister
immediately
Inhalation only

Turbuhaler

Turbuhaler

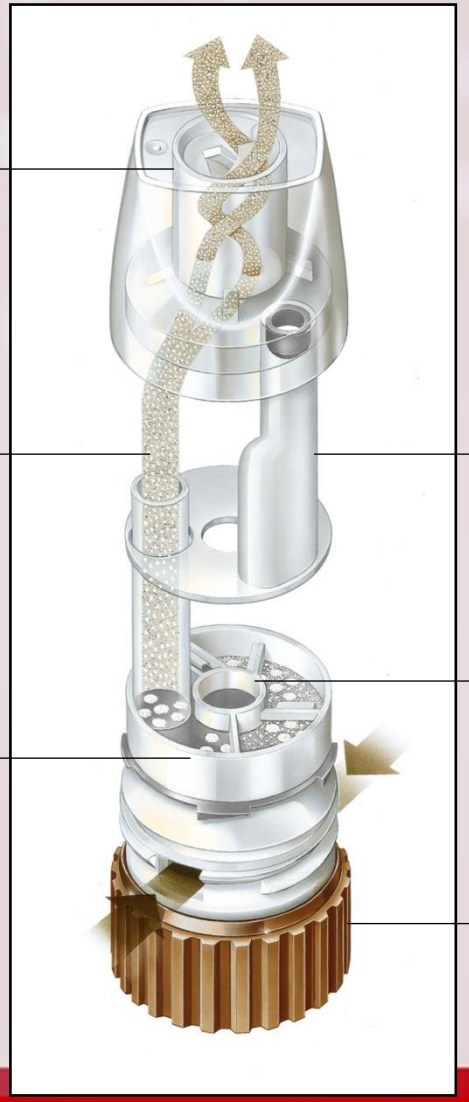
- The air enters through air inlets and passes through desiccant store to keep humidity out

Turbuhaler – design and operation

Mouthpiece is specially designed with spiral channels to deaggregate the dose to respirable particles

Inhalation channel transports dosage of drug aggregates to the mouthpiece

Rotating dosing disc determines the dose of medication for delivery to the inhalation channel

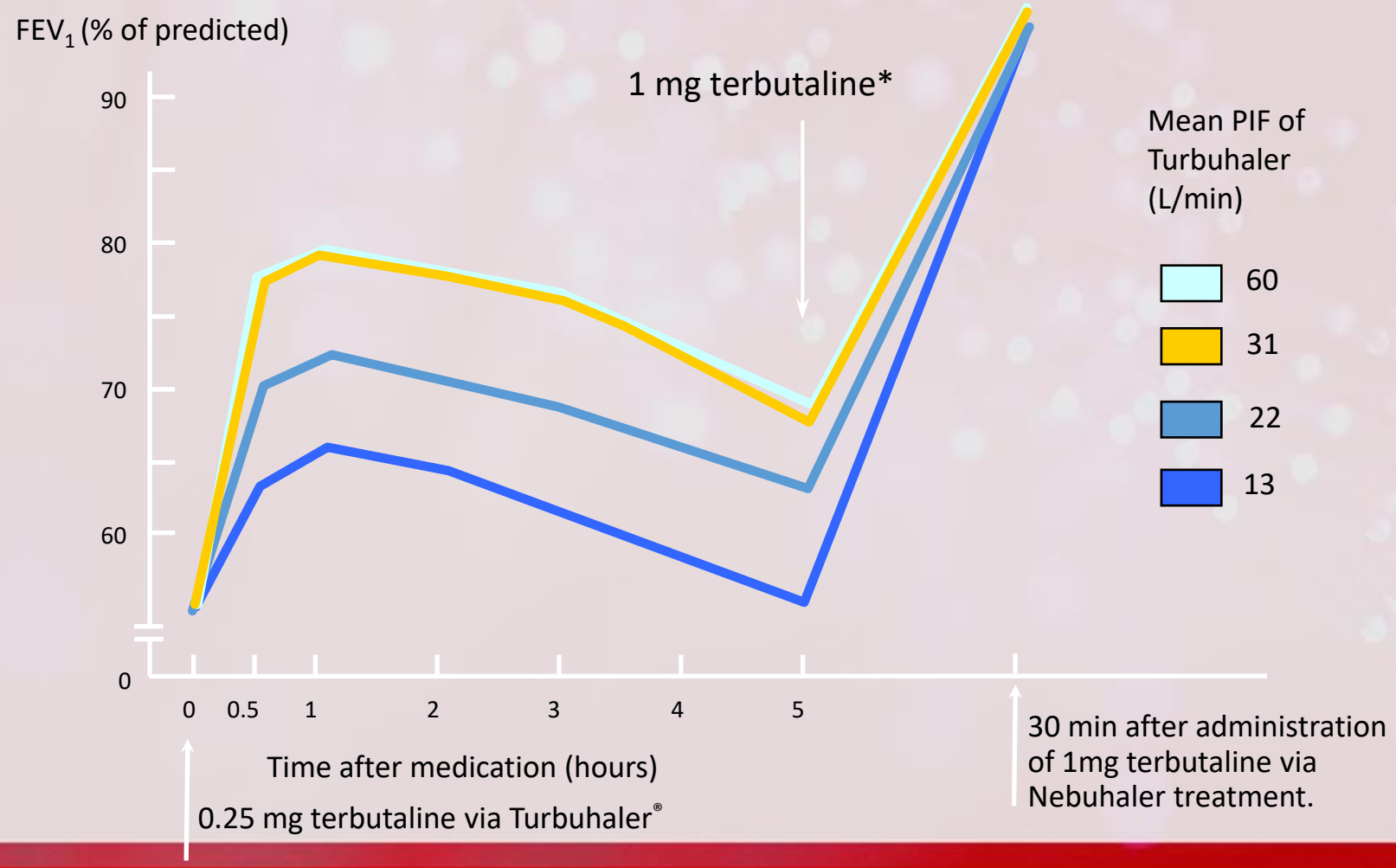


Drug reservoir holds 60 or 120 doses of medication

Dosing scrapers ensures precise dosing by removing excess amounts of drug

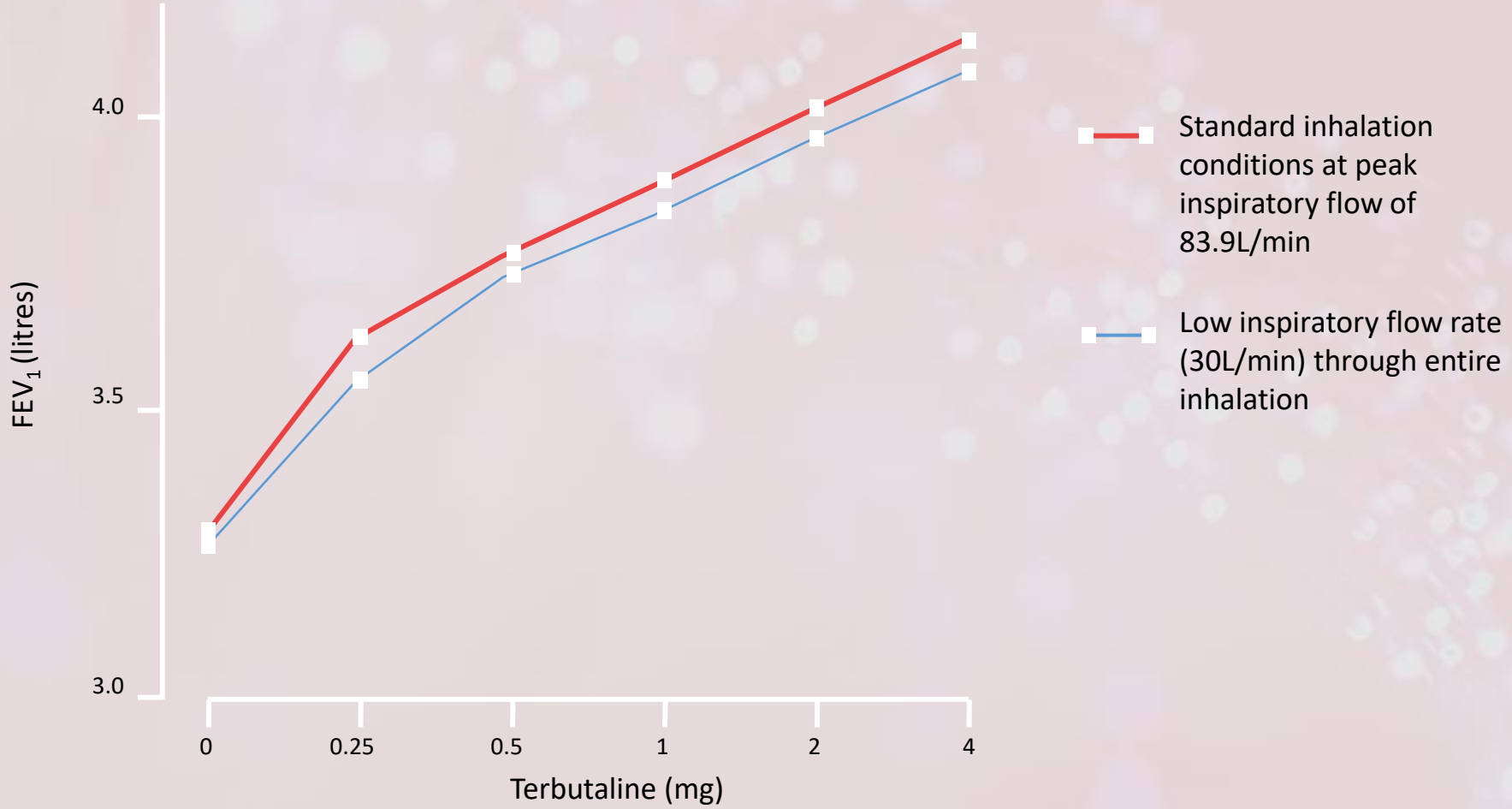
Twist grip loads a single dose when turned completely in one direction and then back again

Turbuhaler is fully effecitve at flow rate **≥ 30 L/min** at patients aged ≥ 6 years



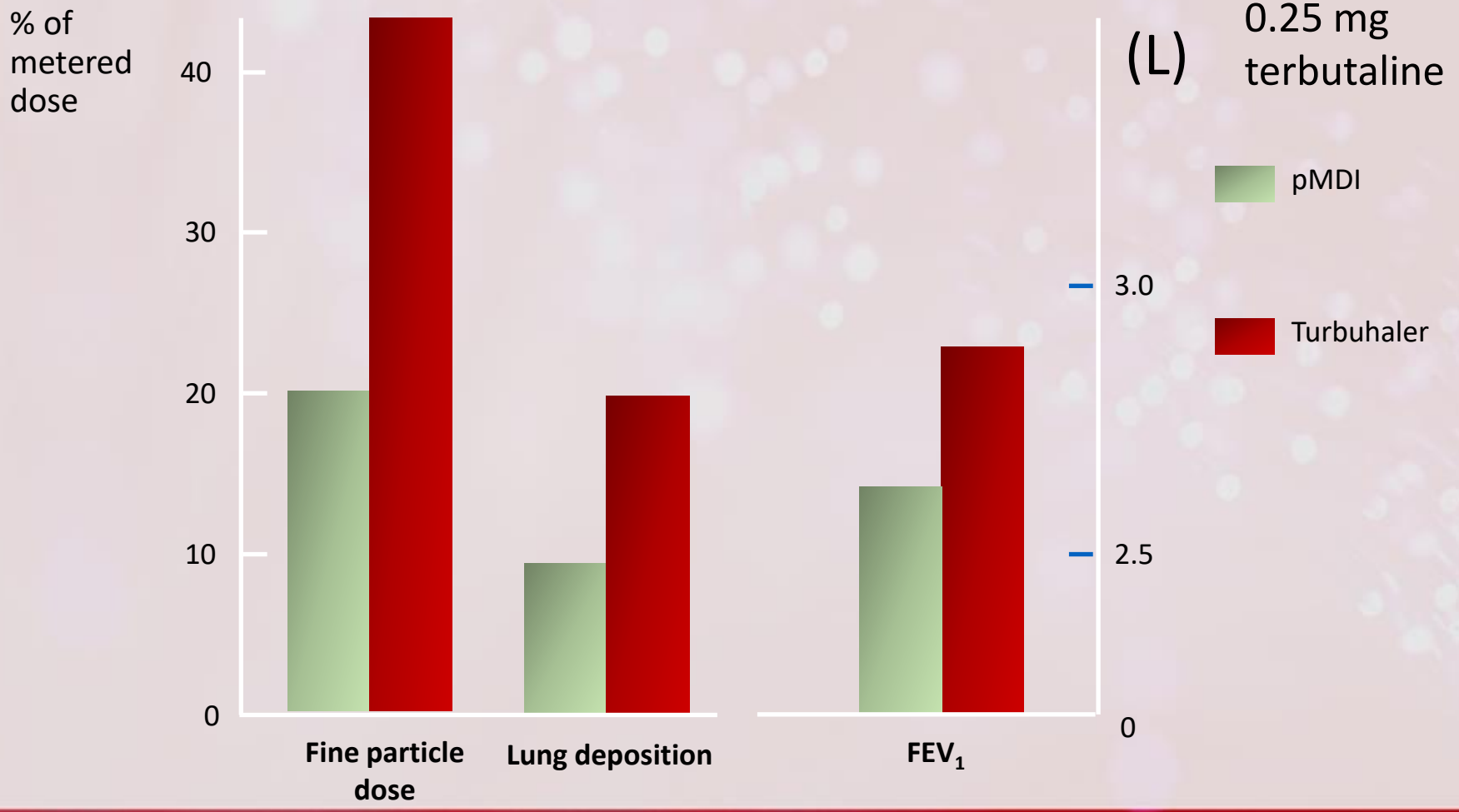
Pederson S, et al. *Arch Dis Child* 1990; 65: 308-310

Turbuhaler is clinically effecitve at both standard & low inspiratory flow rate similar level of bronchodilation & FEV_1



Meijer RJ, et al. *Thorax* 1996; 51: 433-434

Higher proportion fine particle dose and lung deposition leads to better efficacy



Borgström L, et al. *Am J Respir Crit Care Med* 1996; 153: 1636-1640

Dry Powder Inhalers

Device	Drug	Dose available	Type	Resistance
Diskus	Fluticasone Salbutamol Salmeterol	50, 100,250,500 200 50	Individual dose in a blister inside the device	Medium
Handihaler	Tiotropium	18	Capsule	High
Turbuhaler	Budesonide Formoterol Terbutaline Budesonide/Formoterol	100,200,400 6,12 500 100/6,200/6,400/12	Multidose reservoir	Medium/High

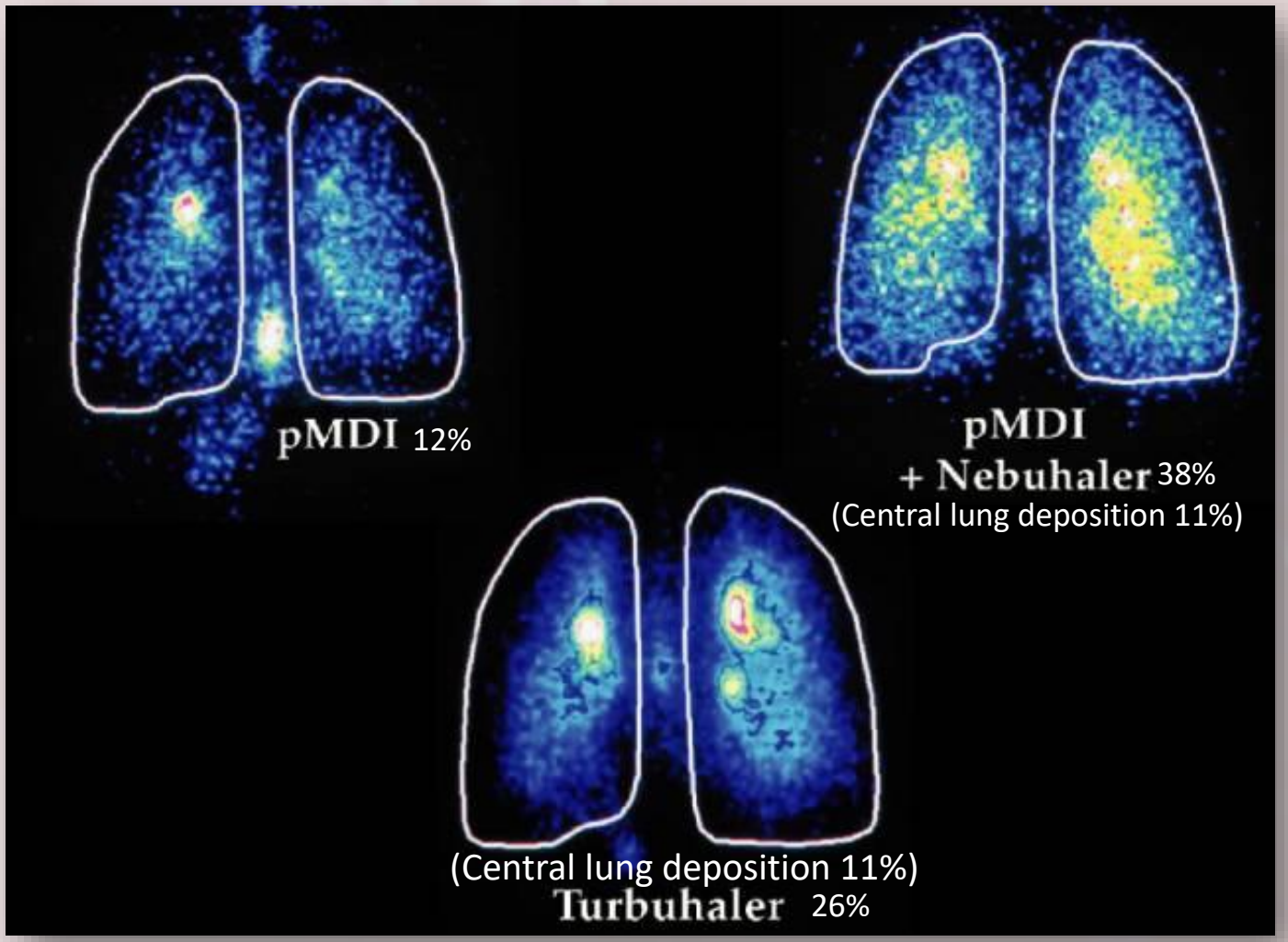
BUD/FOR turbuhaler delivers higher % of fine particle dose on both budesonide & formoterol

		Fine particle dose (% of labeled dose)	MMAD (µm)
BUD/FOR Turbuhaler	Budesonide	63	2.2
	Formoterol	55	2.4
SAL/FLU Disku	Fluticasone	22	4.4
	Salmeterol	22	4.4

MMAD = mass median aerodynamic diameter

Granlund KM, et al. *Eur Respir J* 2000; 16 (suppl. 31): 455s

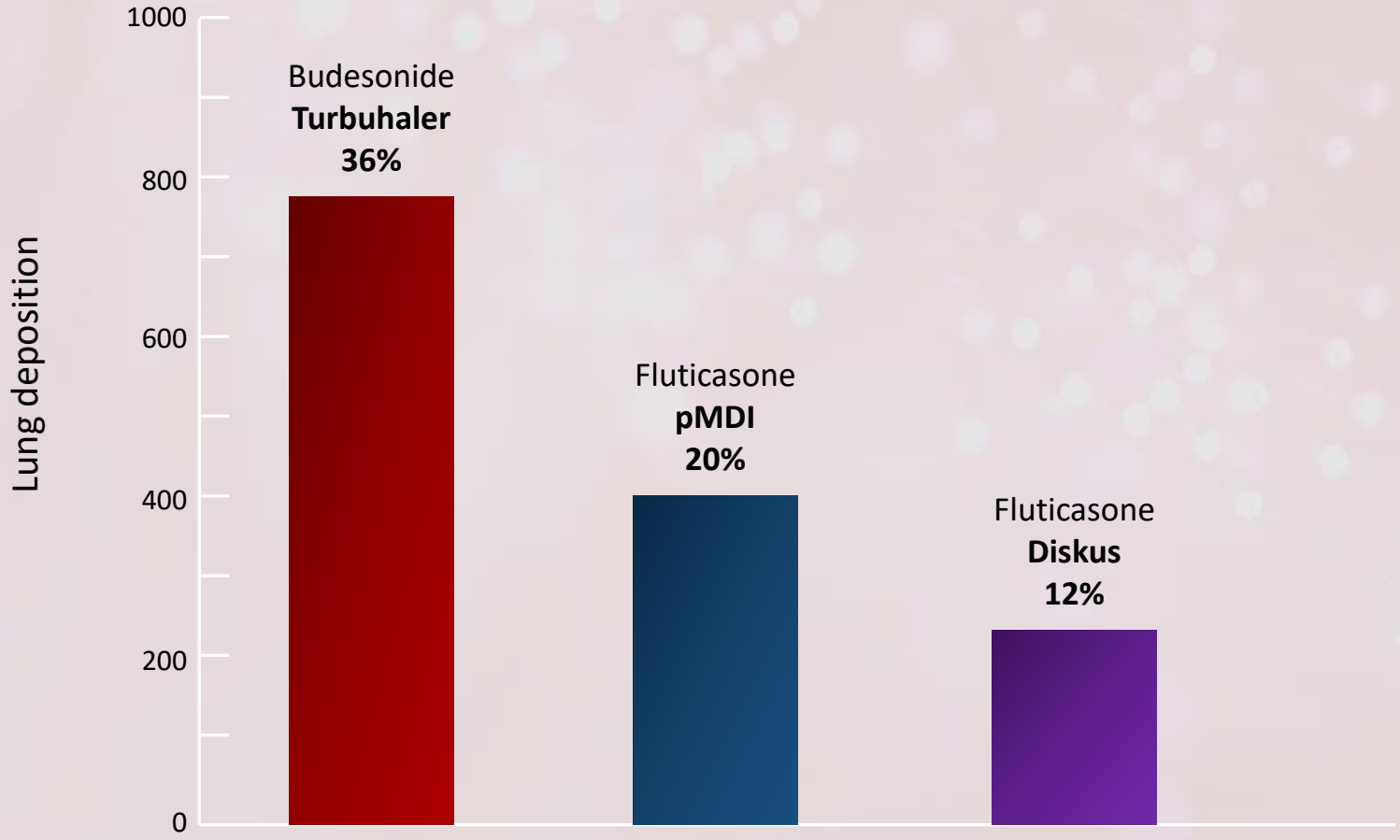
Turbuhaler : gives better central lung deposition as same as pMDI with spacer



Thorsson et al*, 1998b*

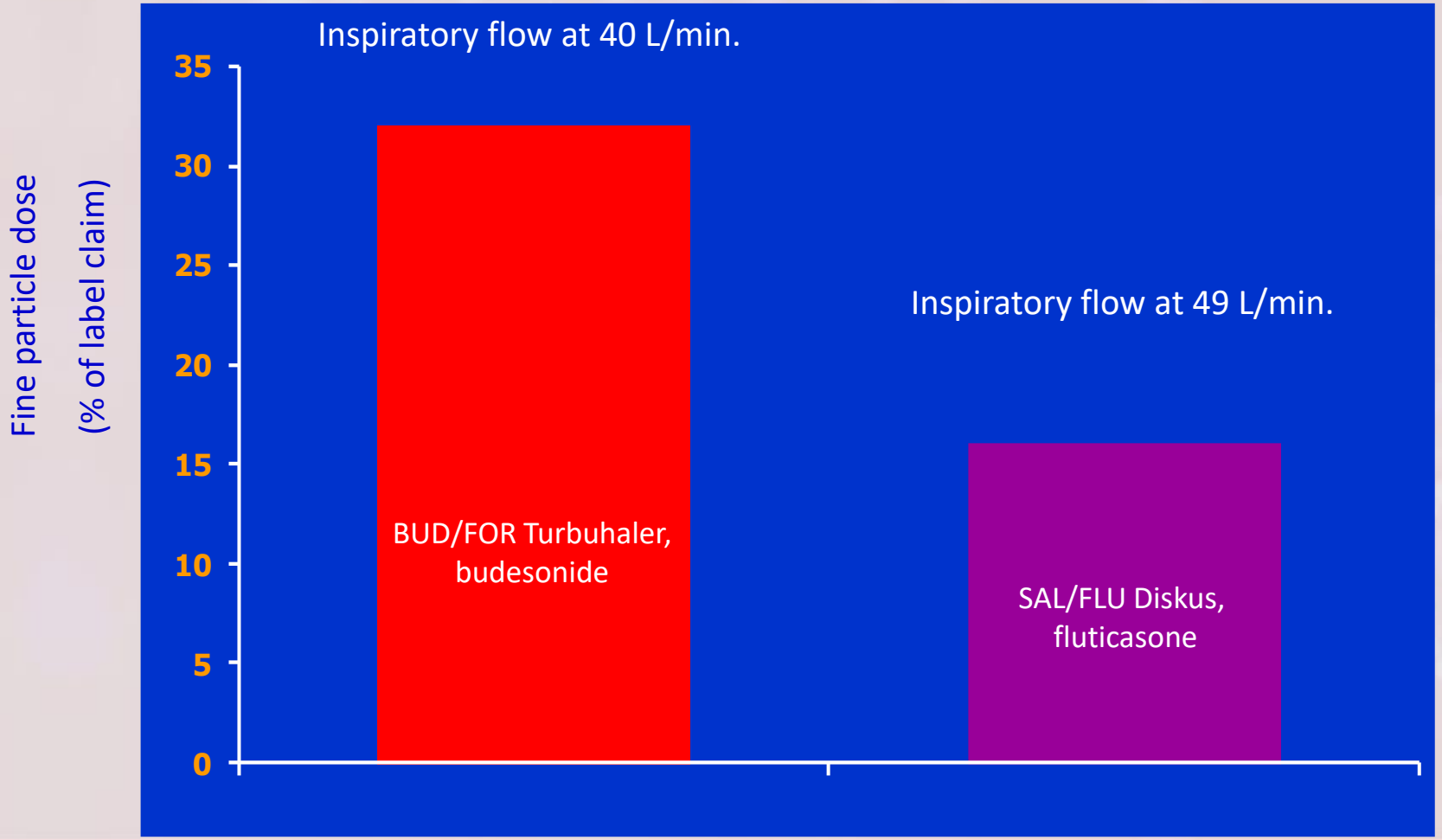
Thorsson L, et al. *Int J Pharmaceut* 1998; 168: 119-127

Lung deposition of budesonide is greater than that of fluticasone via Diskus or pMDI



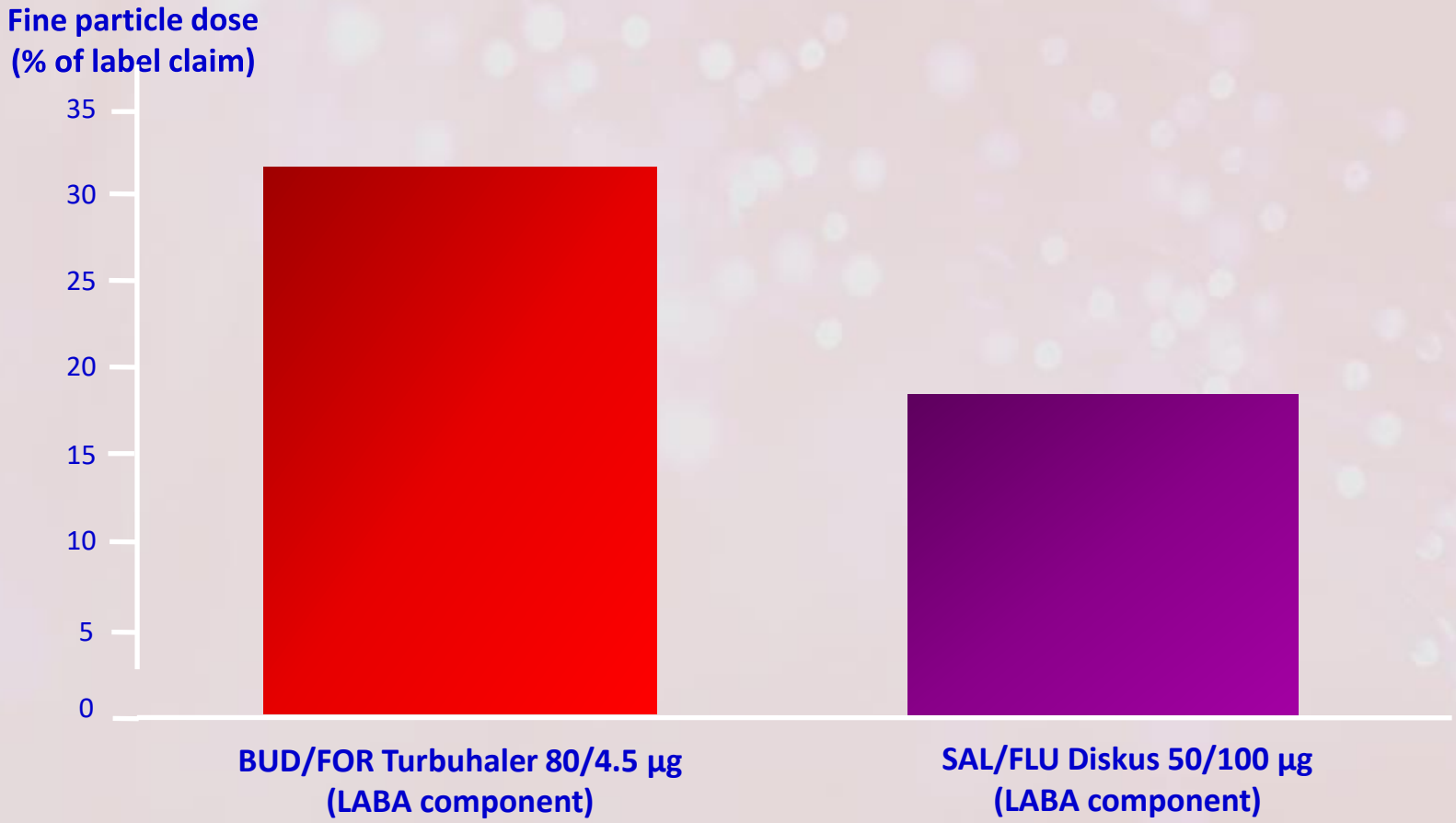
Thorsson L, et al. *Br J Clin Pharmacol* 2001; 52: 529-538

Higher % of fine particle dose with BUD/FOR turbuhaler even at low inspiratory flow



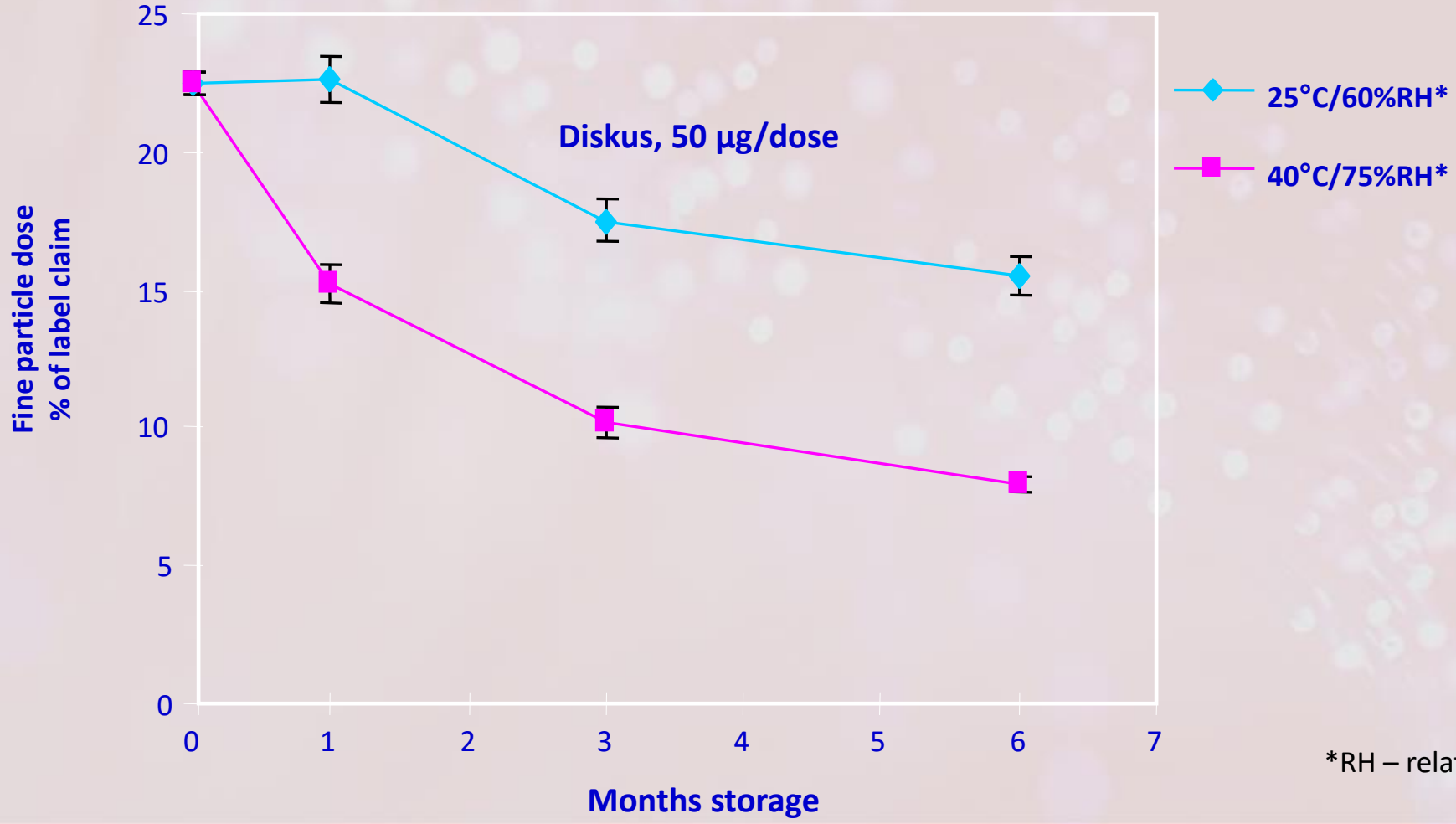
Asking L, et al. *J Aerosol M* 2001; 14: 502

% Fine particle mass at low flow rates in young asthmatic children aged ≥ 4 years is also higher with **Turbuhaler**



Gustafsson PM, et al. *Am J Respir Crit Care Med* 2003; 167: A117

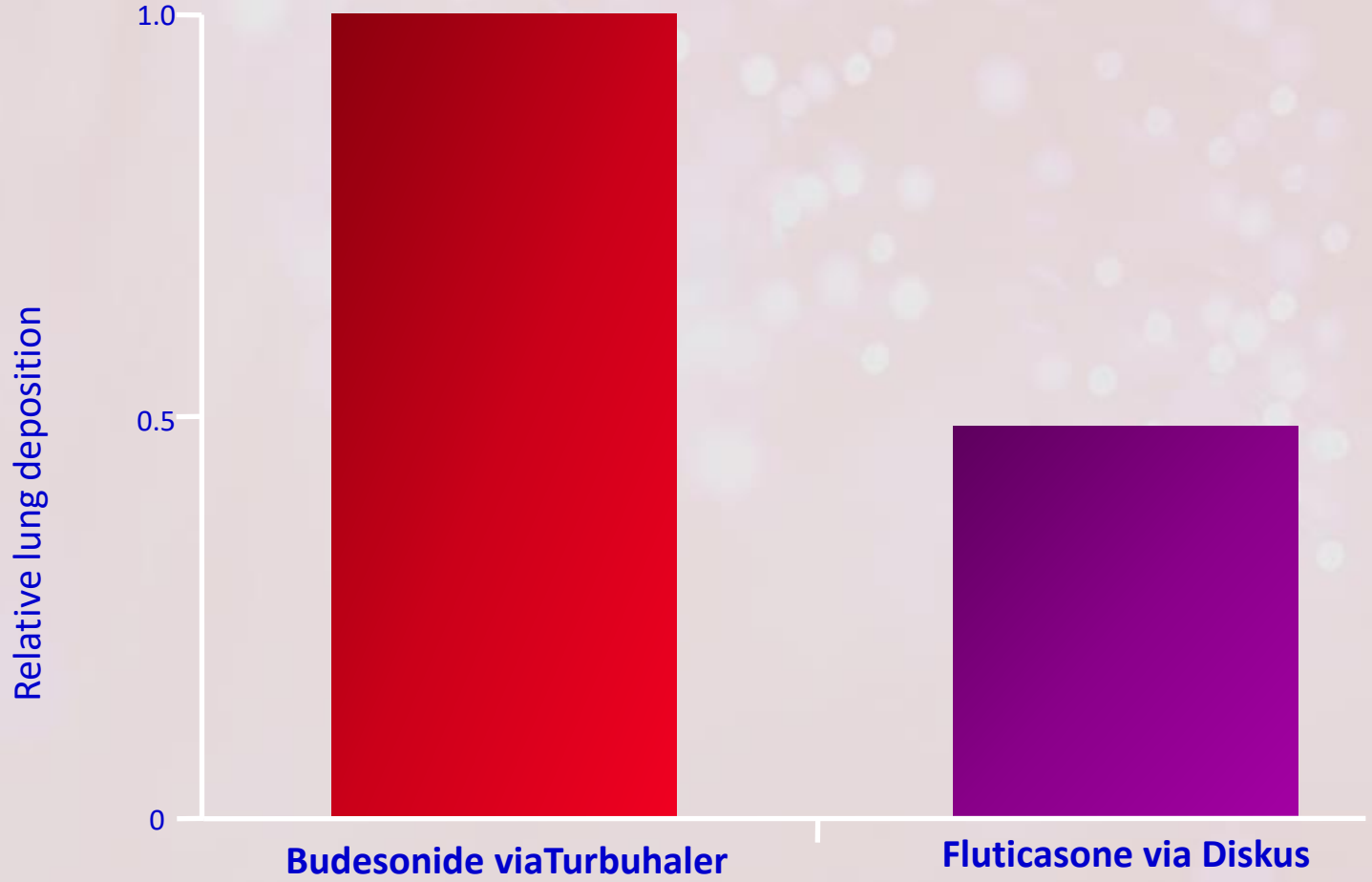
Aluminum blisters may fail to protect against humidity in Diskus



*RH – relative humidity

Asking L, et al. *J Aerosol Med* 1999; 12 (No 3): 204

in vivo lung deposition of budesonide via **Turbuhaler** is higher even when the inhaler is stored under hot & humid condition (40˚/75%)

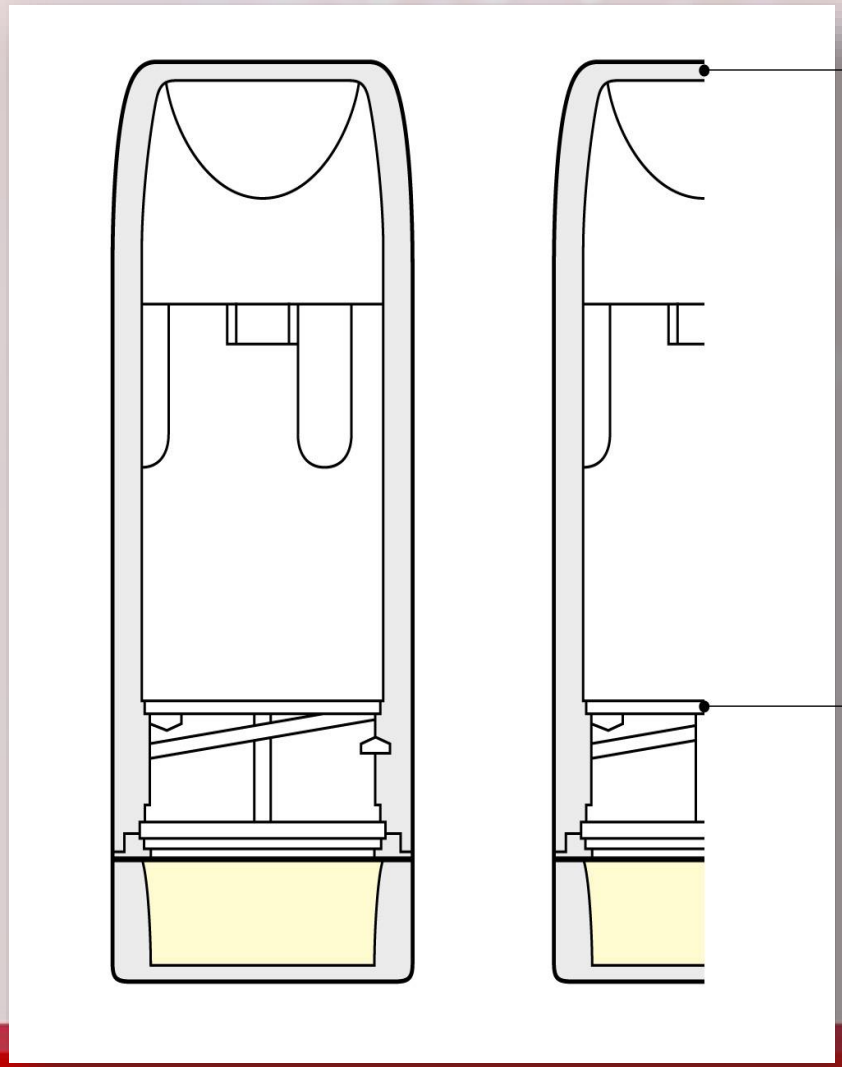


Borgström L, et al. *Am J Respir Crit Care Med* 2003; 167(suppl. 7): A896

Turbuhaler is

- Convenient : no need of mouth-hand coordination
- Effective : deliver dose at as Low inspiratory flow of 30L/min for patients ≥ 6 years of age; and 30L/min delivers similar level of drug as 60L/min
- Higher % of fine particle size & lung deposition rate than pMDI, Diskus in patients ≥ 4 years of age
- Low dose variability with Turbuhaler
- No problem with Hot/Humandity as Hot/Humandity does not effect lung deposition and fine particle dose via Turbuhaler.
- Safe- Low otopharyngeal deposition, no propellants, no preservatives

Distinction between metered dose and delivered dose



Summary of Important concepts

- Deposition of aerosols in the lung depends on the combination of aerosols/inhaler-specific physical factors, patient-relate ventilatory factors, and the nature of the airways/lung disease.

- Some Hydrofluoroalkane (HFA) propellant pressurized metered dose inhalers (pMDIs) provide a different quality and quantity of aerosolized medication, but with revised dosage regimens, a similar response is achieved to that obtained with the original chlorofluorocarbon (CFC) pMDIs.

Summary of Important concepts

- Physicians and health care workers need to know what devices are available to deliver the drug they wish to prescribe for their patients.
- Physicians need to know the features of each type of delivery system and how to use them before they prescribe for their patients.
- Physicians and health care workers need to educate their patients how to use the prescribed aerosol deliver system.

Thank you