

**XXII Congresso Nazionale
Società Italiana di Pediatria Preventiva e Sociale**

**Il pediatra "advocate"
del bambino e dell'adolescente:
un ruolo Irrinunciabile**

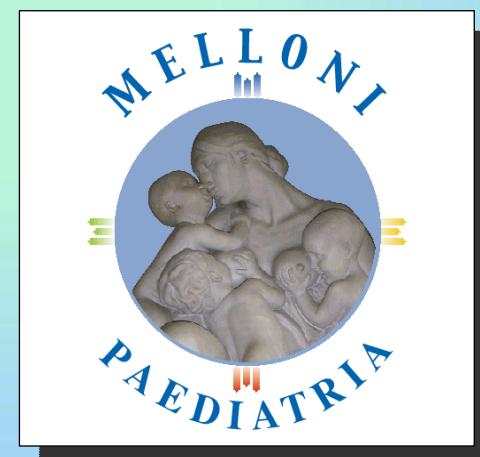


**27 - 29 Maggio 2010
Hotel Villa Diodoro - Taormina**



**Alessandro Fiocchi
May 28th, 2010**

**Aerosolterapia.
Mito e realtà**





Mito

(dal greco μυθος):

- a. Narrazione favolosa di una divinità o di un eroe
- b. Idealizzazione di un fatto straordinario
- c. Cosa creduta esistere ma non frequentata, praticata
- d. Credenza infondata che spinge alla azione

Dizionario Rizzoli-Larousse



Miti in pediatria





Realtà in pediatria





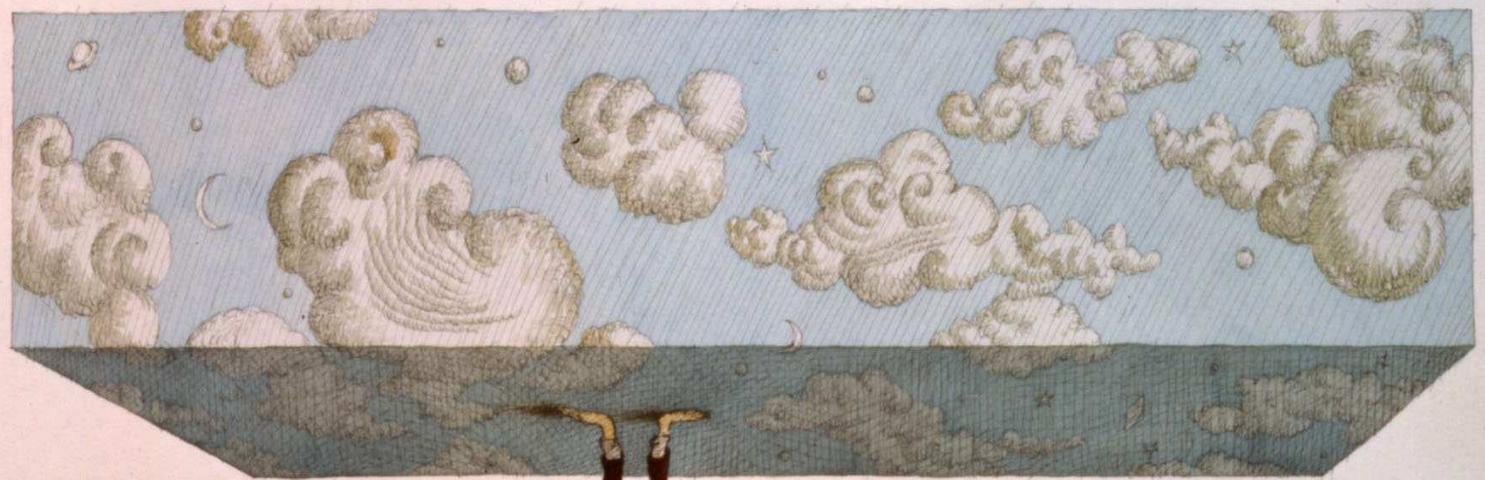
L.M, 8 mesi

- Primogenita, familiarità per allergia negativa
- Socializzata da due mesi
- Da allora, la mamma dice “tossisce sempre”
- Solo episodiche puntate febbrili, al massimo 38,5° rettale
- Trattata con
 - a. un ciclo antibiotico (amoxicillina, 50mg/kg/die per 8 giorni)
 - b. broncodilatatori aerosol (apparecchio ultrasonico)
 - c. Mucolitici
- Ha avuto una volta diagnosi di bronchite asmatica
- Ed una volta diagnosi di broncospasmo



L.M, 8 mesi

- Viene per riacutizzazione con tosse
- Ha temperatura 38,5° rettale
- Riferisce calo dell'appetito, disturbo del sonno
- Obiettivamente ha rantoli sparsi grossolani
- Fischi espiratori.



Brish



Wheezing in età prescolare

1. Fischia. È asmatica?
2. Uso l'aerosol?
3. Ha wheezing. Sarà asmatica?
4. Trattare?



L.M, 8 mesi

Signora, ha una bronchite asmatica.

- Un broncodilatatore!
 - Un antibiotico?
 - Uno steroide inalatorio?
 - Uno steroide per os?
-
- E con che obiettivo:
 - Curare l'episodio certamente!
- Ma anche prevenire successive riesacerbazioni?
 - E se così, steroide od antileucotrienico?



Polverizzatore a vapore per inalazioni (inizio '900)





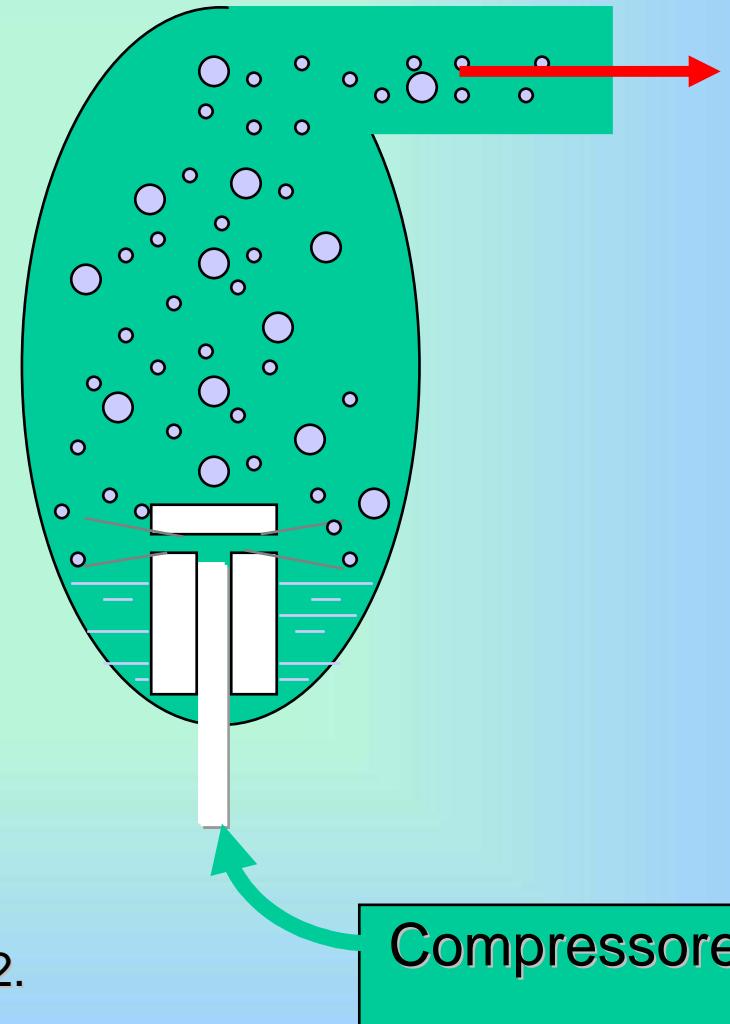
Tutti gli apparecchi per aerosol vanno bene





I nebulizzatori pneumatici.

Sono costituiti da un compressore che eroga un flusso d'aria sufficiente a produrre la nebulizzazione del farmaco in soluzione o in sospensione all'interno della ampolla.



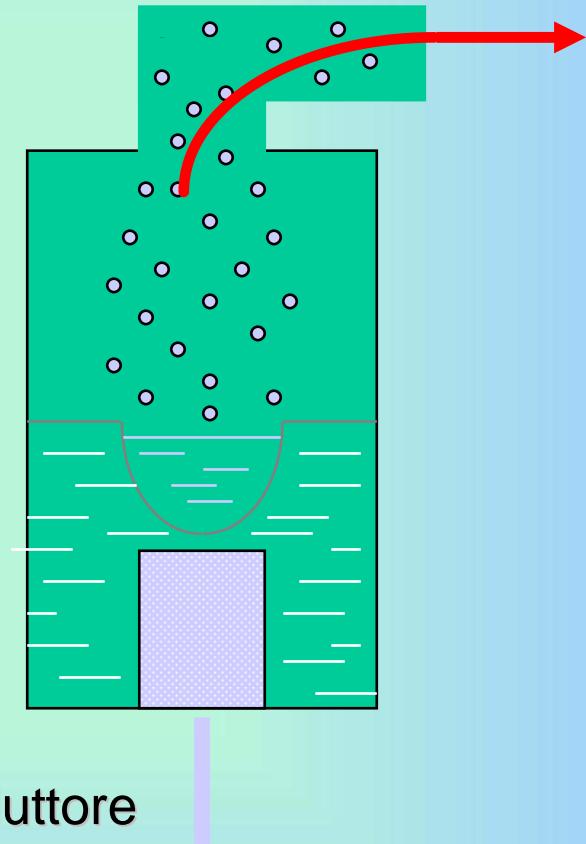
Chantrel G.Eur Respir Rev 2000; 10; 199-202.



I nebulizzatori ad ultrasuoni.

Sono costituiti da un trasduttore piezoelettrico che, generando vibrazioni ultrasoniche (1 MHz) all'interno della vaschetta, aerosolizza il farmaco.

Poiché non è possibile modificare la frequenza delle vibrazioni, questi apparecchi non nebulizzano efficacemente alcuni farmaci, come quelli in sospensione.



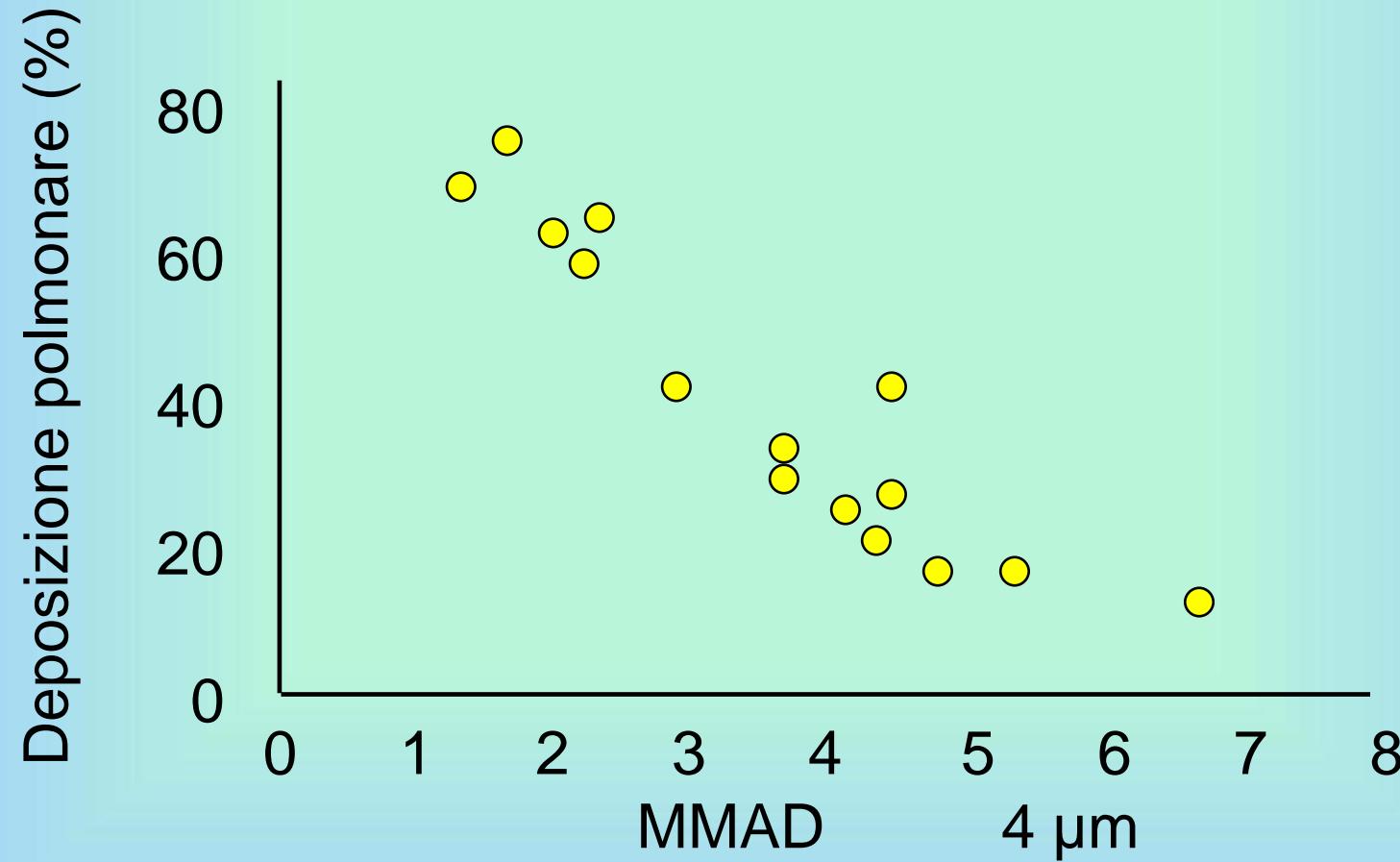


Il diametro delle particelle condiziona la penetrazione nelle vie aeree.

| Dimensione delle particelle | Distretto delle vie aeree |
|-----------------------------|-------------------------------|
| >10 µm | rino-faringe |
| < 10 µm - > 5µm | trachea- grossi bronchi |
| < 5 µm - > 1µm | bronchi-bronchioli |
| < 1 µm | alveoli polmonari |
| < 0,5 µm | espulse durante l'espirazione |



Diametro mediano aerodinamico di massa e deposizione polmonare.



Newman SP. Eur Respir Rev 2000; 10; 224-7-19.



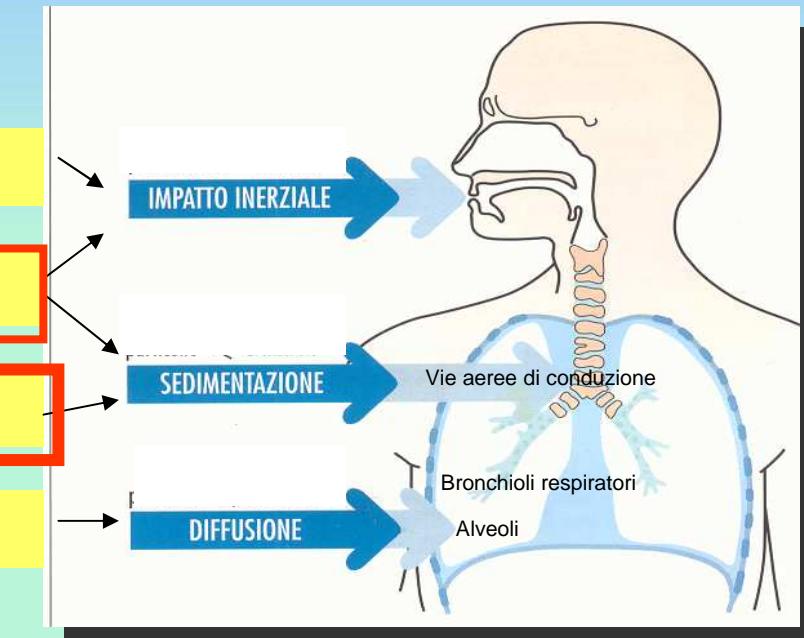
Deposizione del particolato nel polmone

Macroparticelle > 10 micron

Grossolano < 10 micron > 2.5

Fini < 2.5 micron

Ultrafini < 0.1 micron



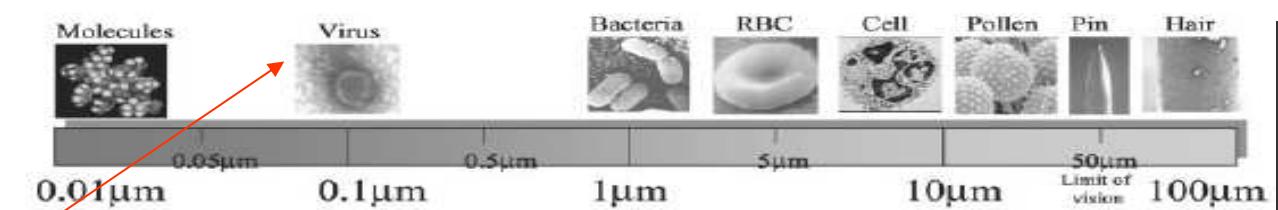
PM

10

2.5

0.1

Le particelle ultrafini possono raggiungere direttamente il circolo per transocitosi



PM₁₀
Thoracic particles

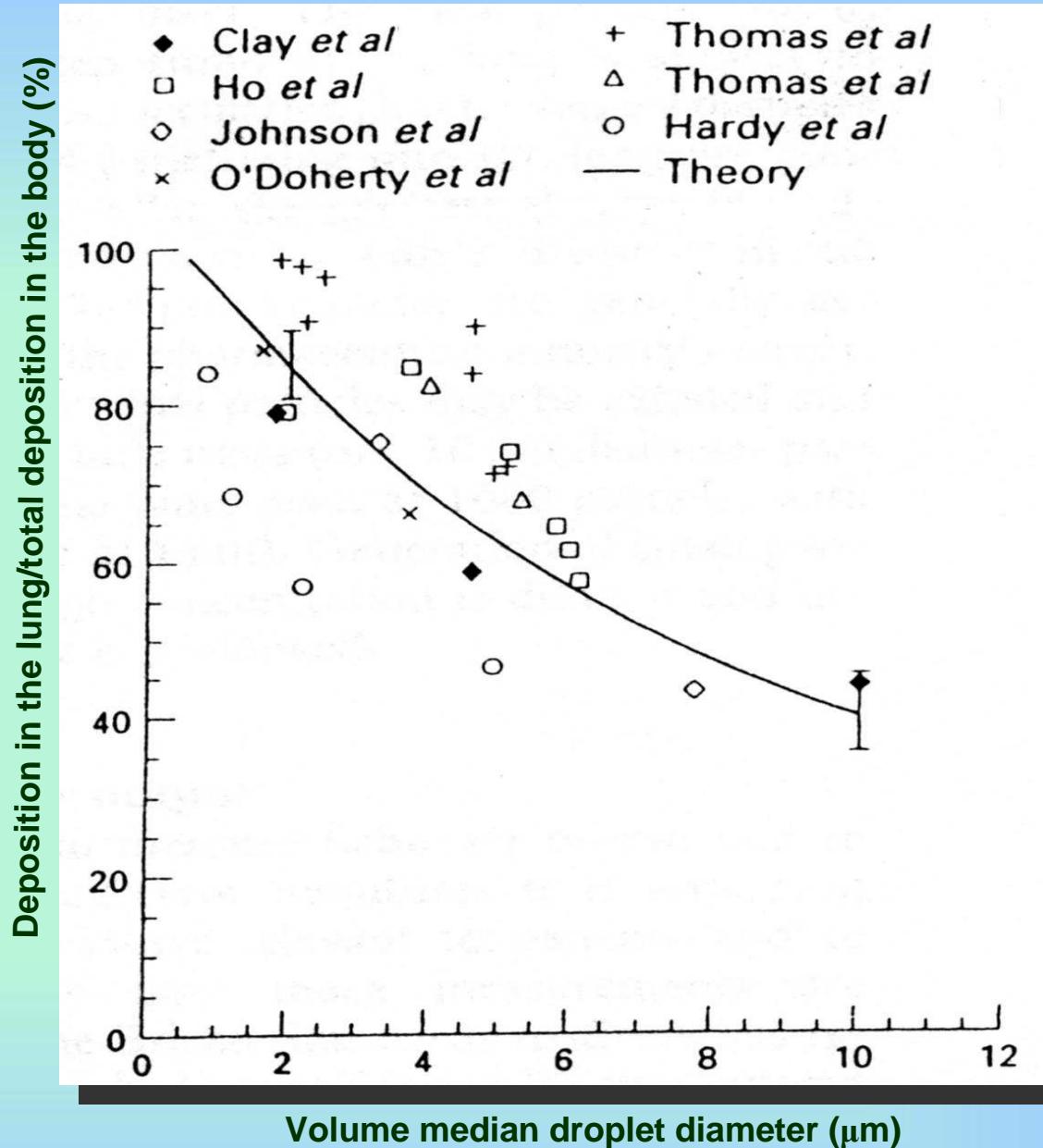
PM_{10-2.5}
Coarse fraction

PM_{2.5}
Fine particles

UFP (PM_{0.1})
Ultrafine particles



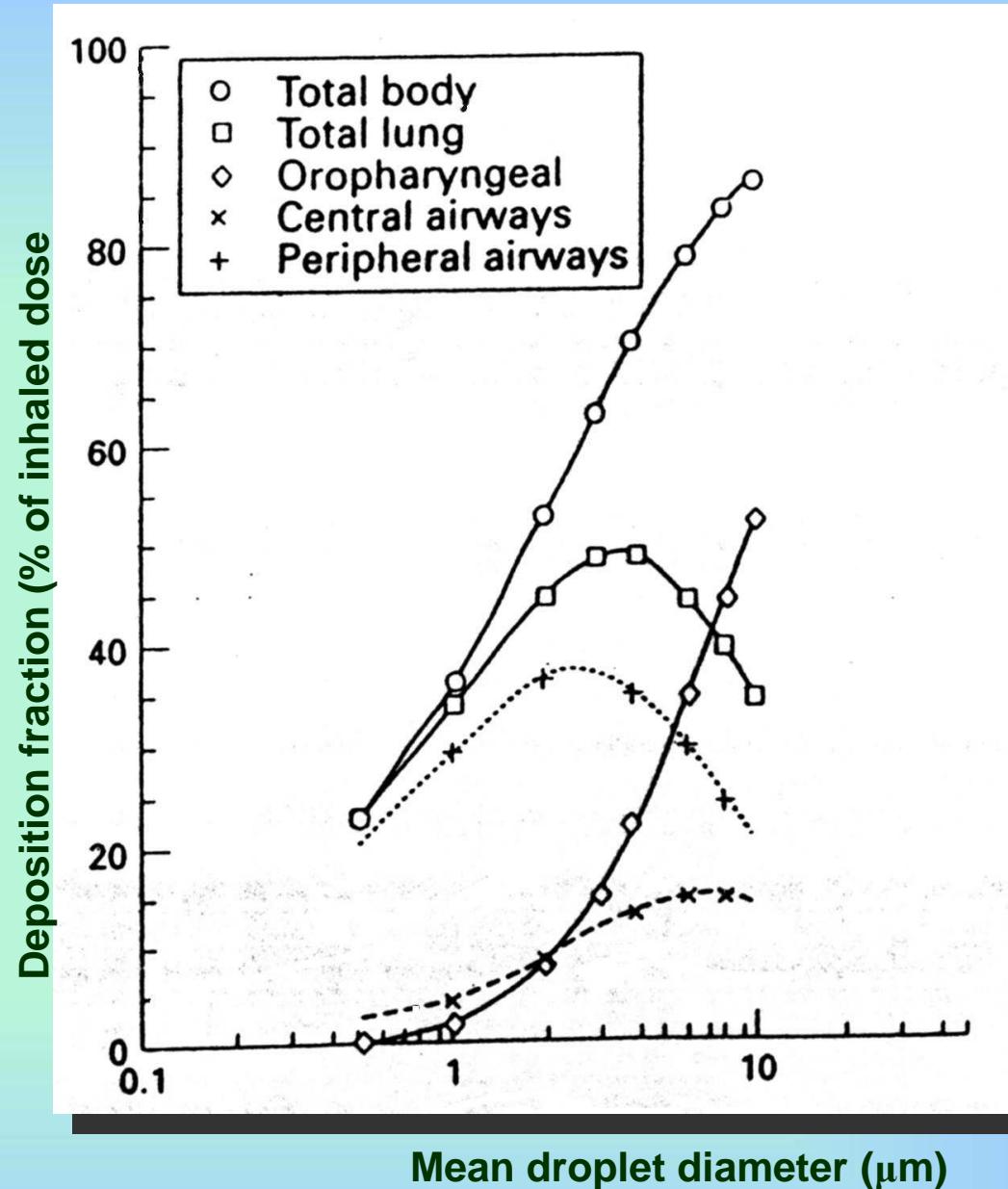
Mass median diameter of an aerosol cloud and percentage thoracic deposition



Clark AR. Int J Pharmacol 1995; 115:69-78



Mean droplet diameter of an aerosol cloud and percentage deposition



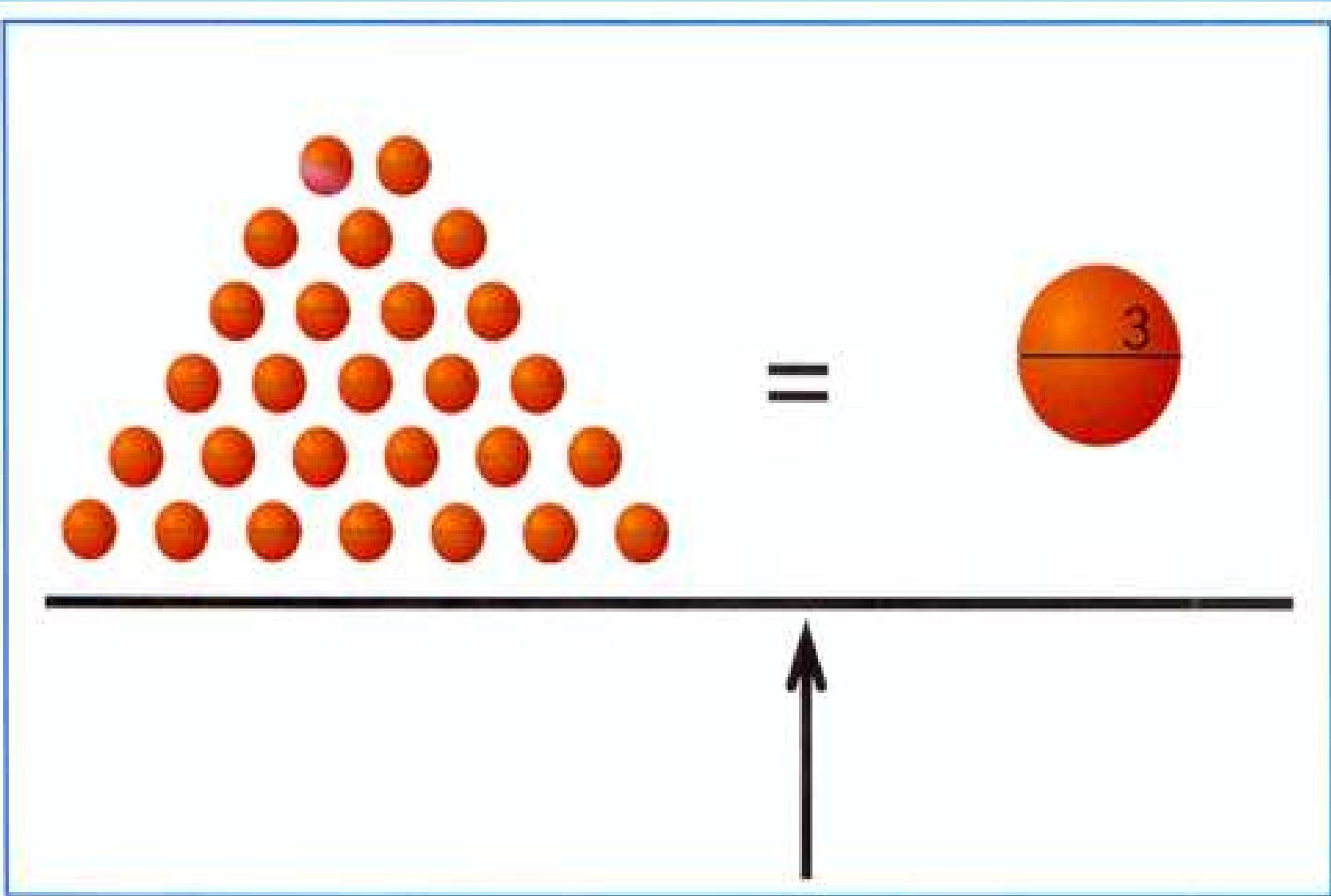
Rudolph G. J Aerosol Sci 1990; 21:s306-s406



Caratteristiche di alcuni nebulizzatori

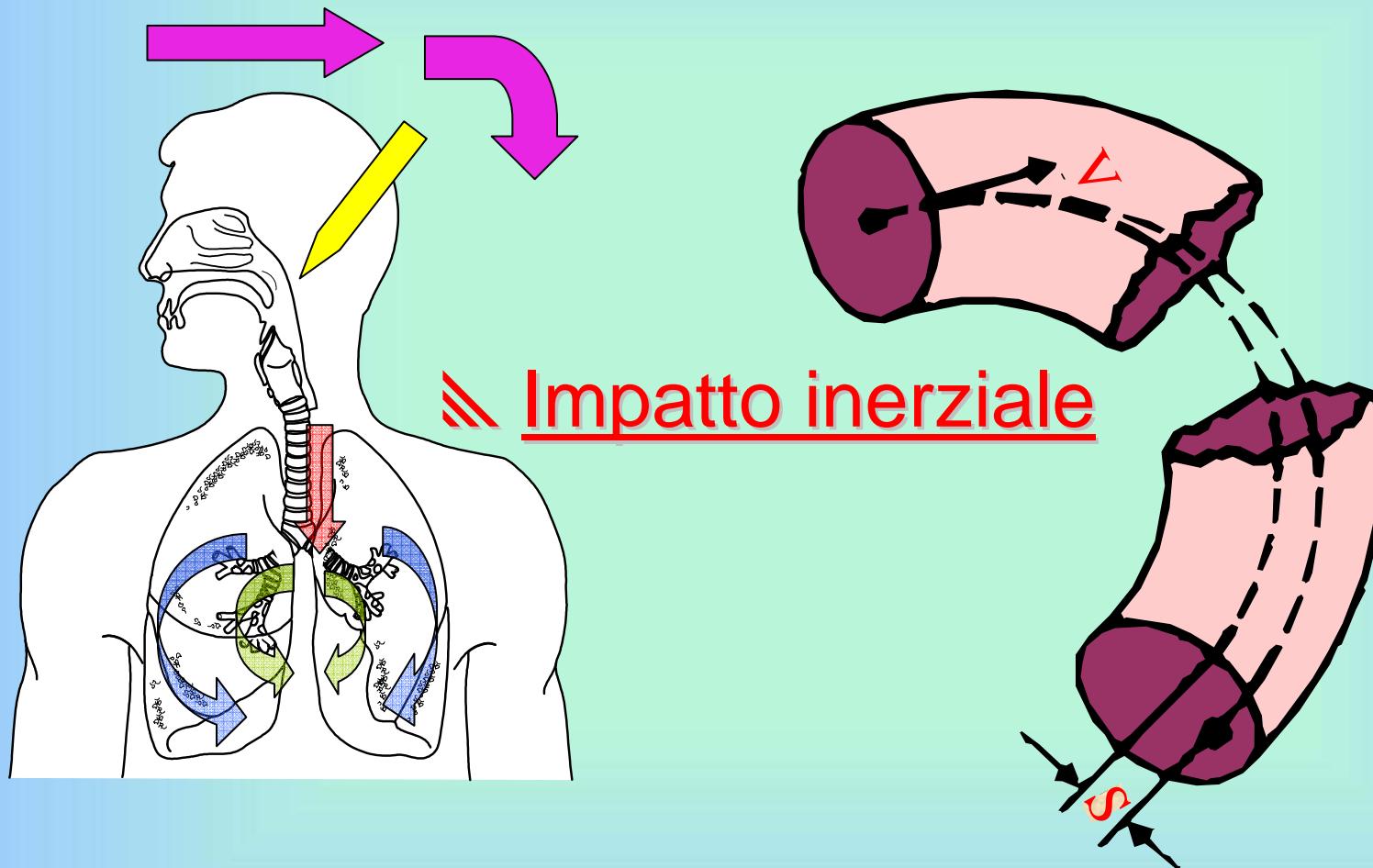
| <u>Ditta</u> | <u>modello</u> | <u>MMAD</u> | <u>tipologia</u> | |
|--------------|----------------|-------------|------------------|------------|
| Markos Mefar | BimboNeb | 2,2 | micron | pneum |
| Markos Mefar | Nebula | 2,3 | micron | pneum |
| Artsana | Project | 0,5-8 | micron | ultrasuoni |
| Pabisch | Ultraneb | 3-4 | micron | ultrasuoni |
| Flaem | Nebulflaem | 0,5-8 | micron | pneum |

Massa delle particelle e farmaco





L'inerzia delle particelle influenza la deposizione oro-faringea



Erogazione del farmaco a velocità contenuta



Lo tratto presto?





Preemptive use of high-dose fluticasone for virus-induced wheezing in young children

- 129 to r flut
- c t
- d 6 to 12

In FP treated children:

- symptoms milder and of shorter duration;
- fewer days of albuterol use
- less negative effect on their parents' quality of life.

Treatment with rescue systemic corticosteroids in upper respiratory infections

OR 0.49

8%

Placebo

Fluticasone

Ducharme FM. Preemptive use of high-dose fluticasone for virus-induced wheezing in young children. N Engl J Med. 2009;360:339-53

AT AGE 6 YRS

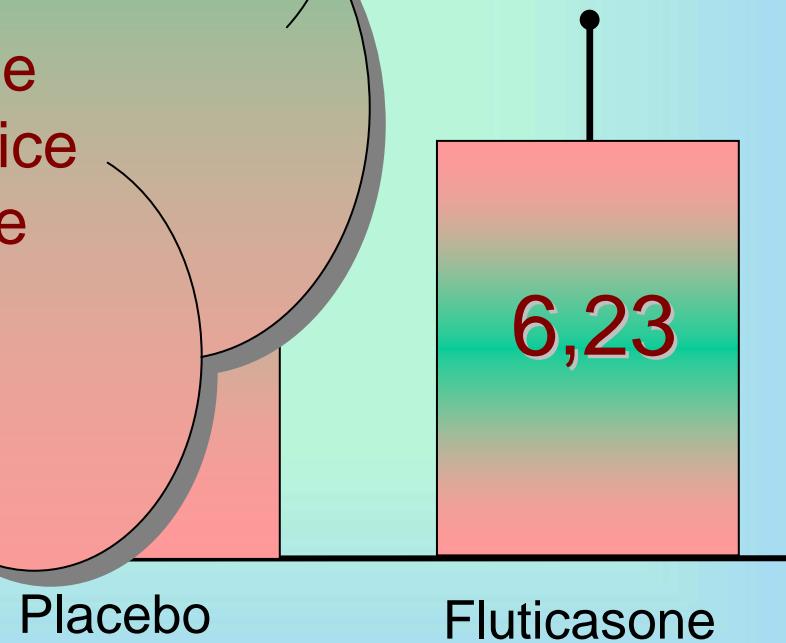


Preemptive use of high-dose fluticasone for virus-induced wheezing in young children

- 129
- to r
- flut
- C
- t
- d
- day
- 6 to 12

Given the potential
for overuse,
this preventive
approach should not be
adopted in clinical practice
until long-term adverse
effects are clarified

gains from baseline in
height in cm



Ducharme FM. Preemptive use of high-dose fluticasone for virus-induced wheezing in young children. N Engl J Med. 2009;360:339-53

AT AGE 6 YRS



Lo tratto a lungo, per prevenire?





Need for answers

Figure 4.3-2: Management Approach Based on Control For Children 5 Years and Younger

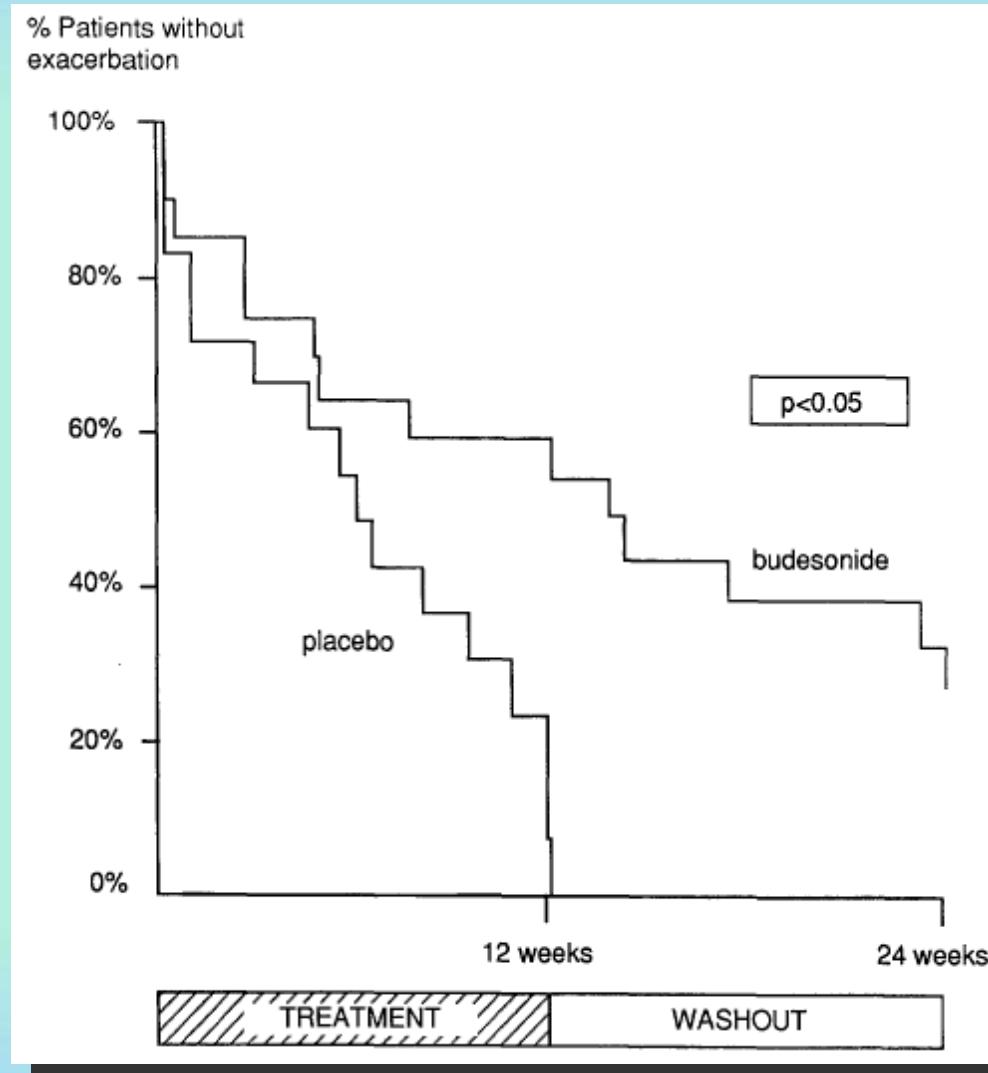
The available literature on treatment of asthma in children 5 years and younger precludes detailed treatment recommendations. The best documented treatment to control asthma in these age groups is inhaled glucocorticosteroids and at Step 2, a low-dose inhaled glucocorticosteroid is recommended as the initial controller treatment. Equivalent doses of inhaled glucocorticosteroids, some of which may be given as a single daily dose, are provided in Chapter 3 (Figure 3-4).

The clinical benefits of intermittent systemic or inhaled glucocorticosteroids for children with intermittent, viral-induced wheeze remain controversial. While some studies in older children have found small benefits, a study in young children found no effects on wheezing symptoms. There is no evidence to support the use of maintenance low-dose inhaled glucocorticosteroids for preventing transient early wheezing.

Leukotriene modifiers: Clinical benefits of monotherapy with leukotriene modifiers have been shown in children older than age 2. Leukotriene modifiers reduce viral-induced asthma exacerbations in children ages 2-5 with a history of intermittent asthma. No safety concerns have been demonstrated from the use of leukotriene modifiers in children.



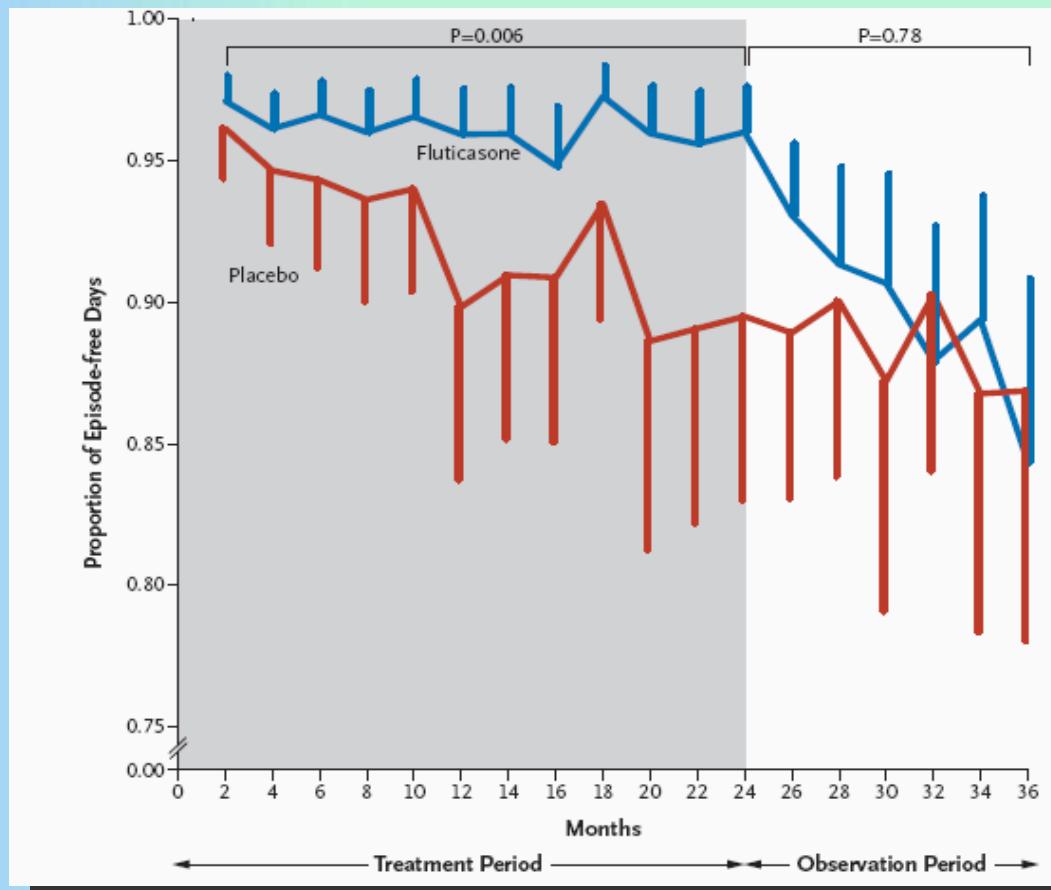
Inhaled steroids in infants



de Blic J. Efficacy of nebulized budesonide in treatment of severe infantile asthma: a double-blind study. *J Allergy Clin Immunol.* 1996; 98:14-20



ICS control but do not cure the disease



285 preschool kids
with wheeze and
high asthma risk
Index

Guilbert, NEJM
2006; 354:1985-97



Does early ICS prevent long term wheezing?

- ICS influence on wheezing

- Guillet G, Szilagyi A, et al. Intermittent inhaled corticosteroid therapy had no effect on the progression from episodic to persistent wheezing and no short-term benefit during episodes of wheezing in the first three years of life.

The early use of inhaled fluticasone prevents long term wheezing

Intermittent inhaled corticosteroid therapy had no effect on the progression from episodic to persistent wheezing and no short-term benefit during episodes of wheezing in the first three years of life.

97

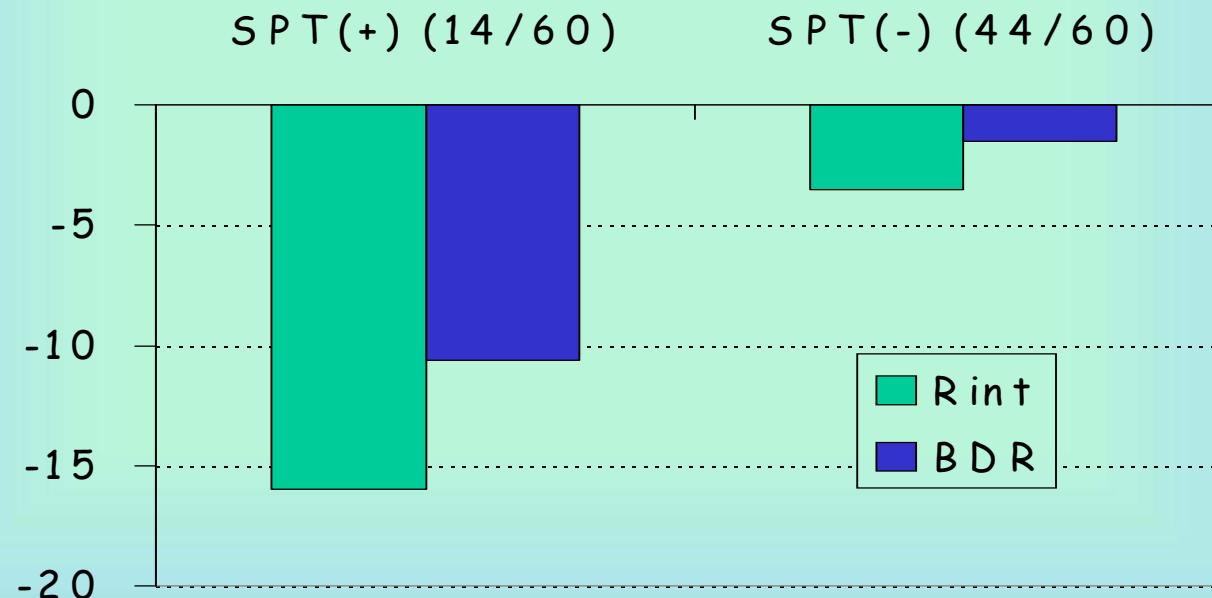
- Murray CS, w, Secondary prevention of propionate in Wheezing, controlled study. Lancet 1997; 349:1111-1115.
 - Bisgaard H, Hermansen MN, Lund L, Halkjaer LB, Buchvald F. Intermittent inhaled corticosteroids in infants with episodic wheezing. N Engl J Med 2006; 354:1998-2005

Murray CS, et al. Intermittent Inhaled Fluticasone (IFWIN): double-blind, randomised, controlled study. Lancet 1997; 349:1111-1115.



Steroid improvement only in atopic children

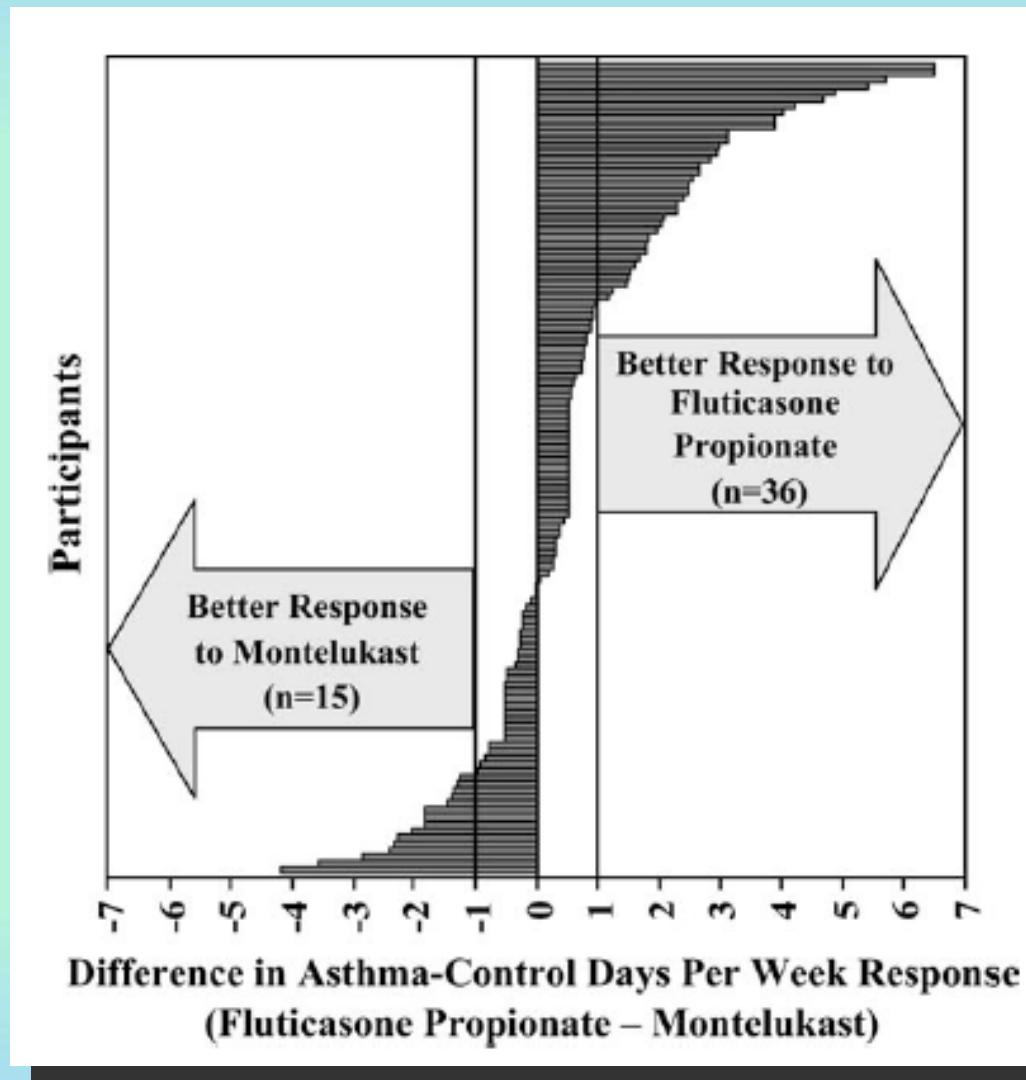
- 61 children with intermittent wheeze
- Fluticasone or placebo for 16 weeks
- Measurement of airway resistance (Rint), bronchodilator responsiveness (BDR)



Pao CS, McKenzie SA. Randomized controlled trial of fluticasone in preschool children with intermittent wheeze. Am J Respir Crit Care Med. 2002; 166:945-9



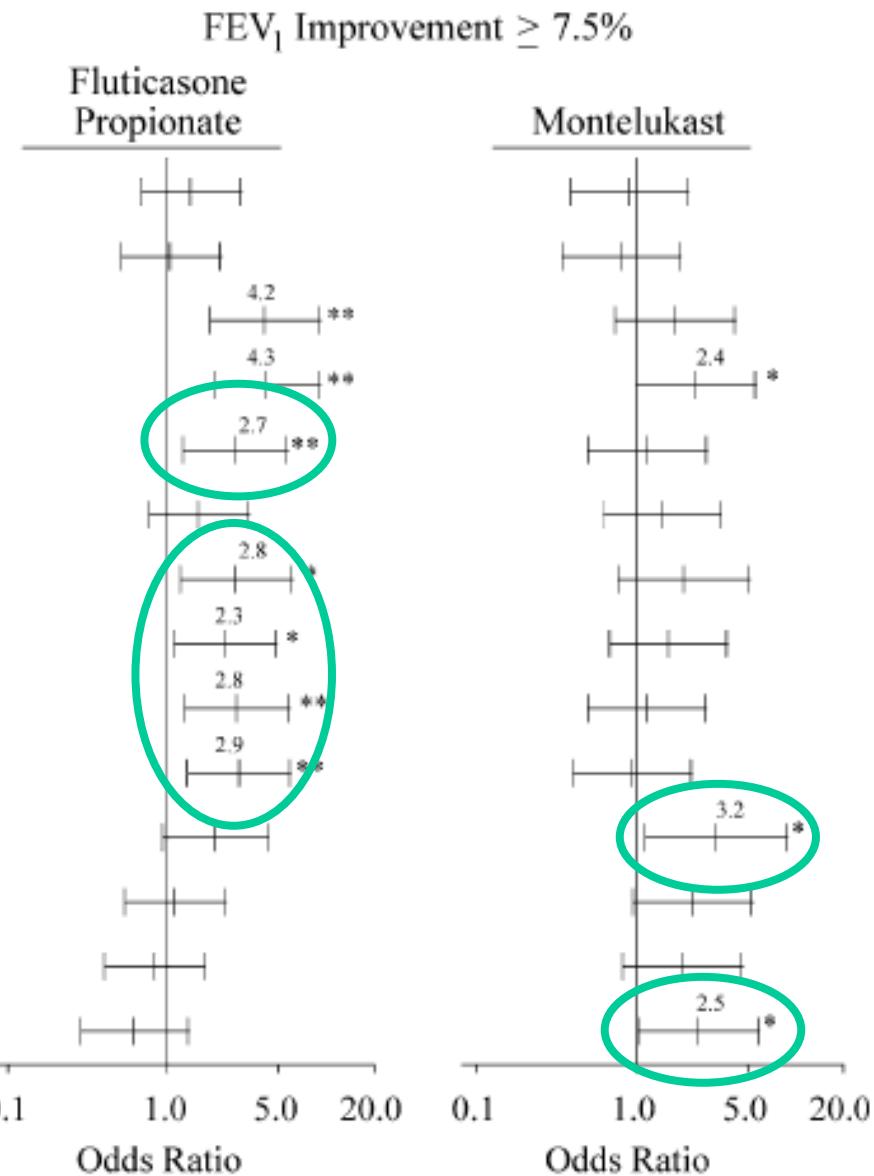
Different response profiles



Zeiger RS. Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma. J Allergy Clin Immunol. 2006;117:45-52



| Baseline Characteristic (N, %) |
|--|
| Bronchodilator use > 4 puffs/week (65, 52%) |
| Asthma-free days \leq 2 days/week (68, 54%) |
| Pre-bronchodilator FEV ₁ % predicted < 90% (41, 33%) |
| Pre-bronchodilator FEV ₁ /FVC < 80% (51, 40%) |
| Methacholine PC ₂₀ \leq 1 mg/ml (54, 45%) |
| Maximum bronchodilator response > 15% (58, 46%) |
| Exhaled nitric oxide > 25 ppb (61, 55%) |
| Blood total eosinophil count > 350 cells/mm ³ (51, 41%) |
| Serum eosinophilic cationic protein > 15 mcg/L (68, 54%) |
| Serum IgE > 200 kU/L (55, 44%) |
| Urinary leukotriene E4 > 100 pg/mg creatinine (59, 50%) |
| Female gender (52, 41%) |
| Minority (60, 48%) |
| Age < 10 (84, 67%) |



Zeiger RS. Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma. J Allergy Clin Immunol. 2006;117:45-52



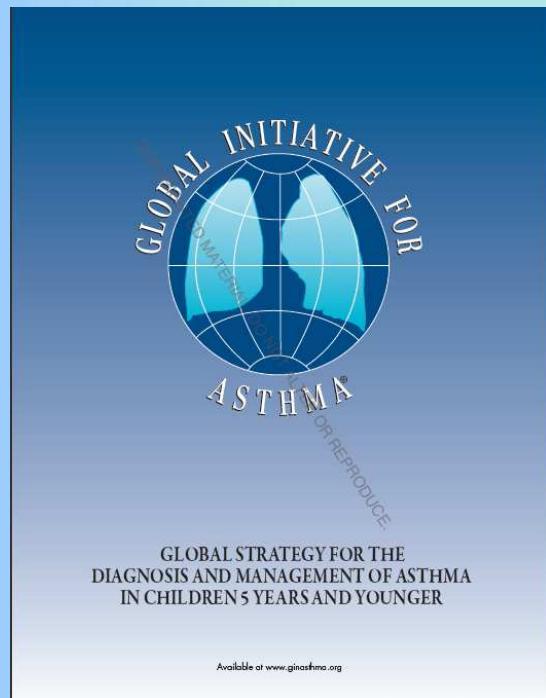
Lo tratto solo al bisogno?





The GINA approach (may 2009)

www.ginasthma.org



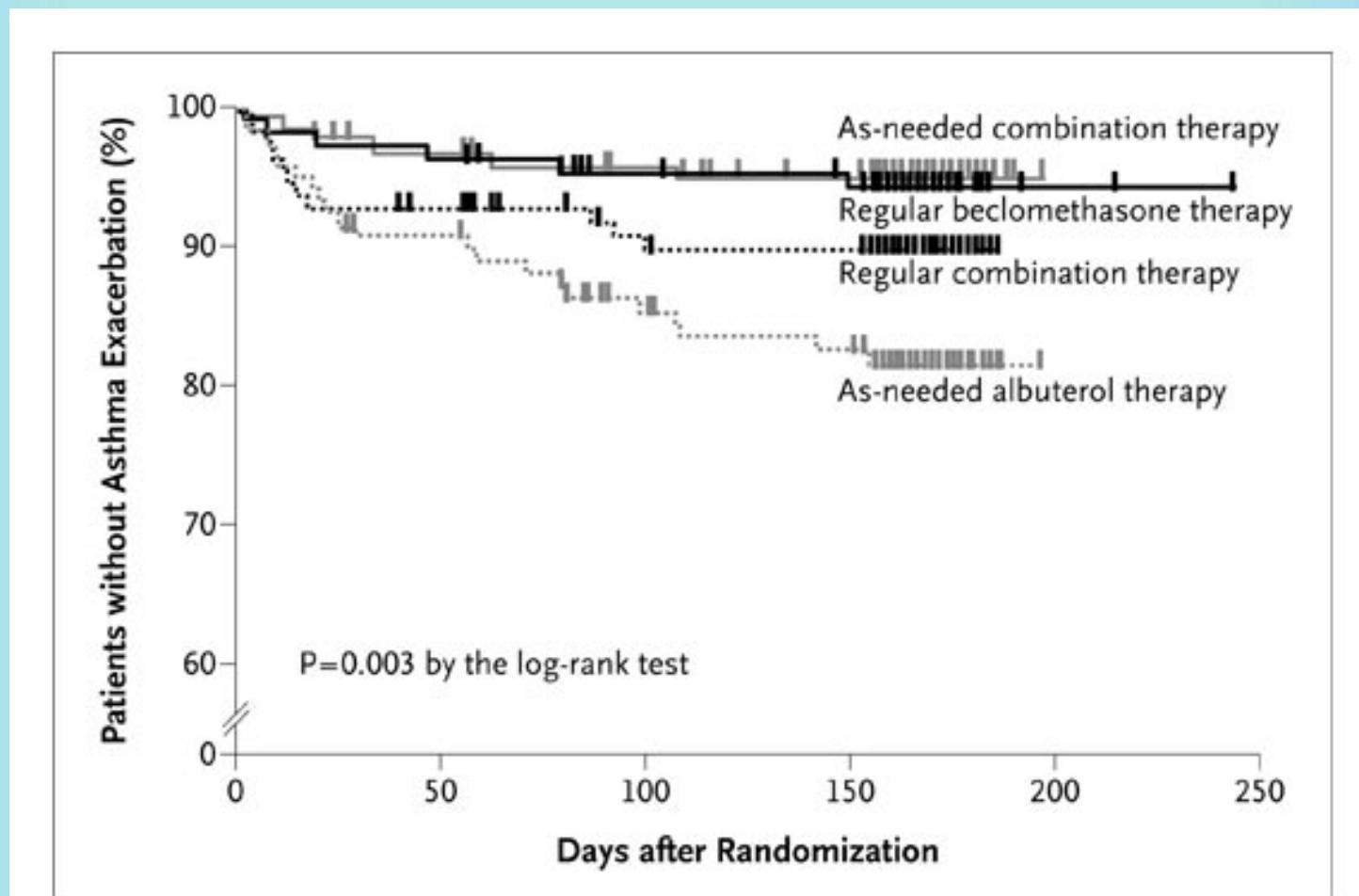
Treatment strategy

Table 5. Asthma Management Approach Based on Control for Children 5 Years and Younger

| Asthma education Environmental control As needed rapid-acting β_2 -agonists | | |
|---|--|--|
| Controlled on as needed rapid-acting β_2 -agonists | Partly controlled on as needed rapid- acting β_2 -agonists | Uncontrolled or only partly controlled on low-dose inhaled glucocorticosteroid |
|  |  |  |
| Controller options | | |
| Continue as needed rapid-acting β_2 -agonists | Low-dose inhaled glucocorticosteroid | Double low-dose inhaled glucocorticosteroid |
| | Leukotriene modifier | Low-dose inhaled glucocorticosteroid plus leukotriene modifier |



Time to First Asthma Exacerbation in patients treated with albuterol and bechlomethasone



Papi A, BEST Study Group. Rescue use of beclomethasone and albuterol in a single inhaler for mild asthma. N Engl J Med. 2007;356:2040-52



BEST is not the best for children

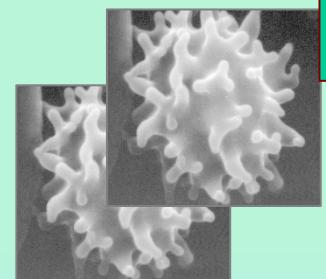
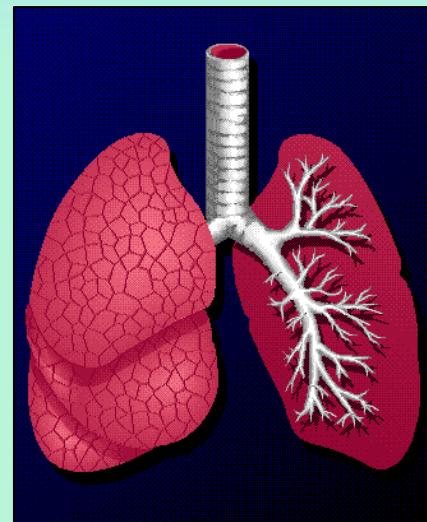
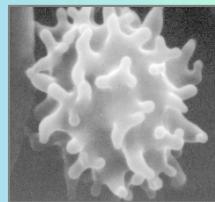
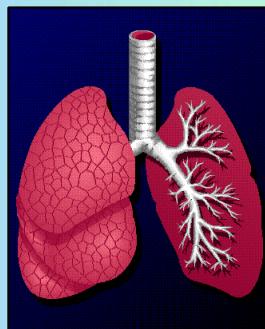
1. The use of morning peak expiratory flow rate as primary outcome does not reliably reflect disease control among children with mild persistent asthma
2. In this adult population trial, **lung growth**, which affects treatment outcomes in children, could obviously not be accounted for
3. **Inflammation**, the major determinant of tissue thickening in children's airways, could not be measured.

Terracciano L, Fiocchi A, Bouygue GR. Beclomethasone and albuterol in mild asthma (letter). N Engl J Med 2007; 357:506-7

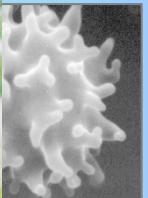
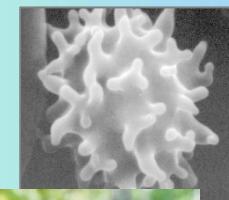
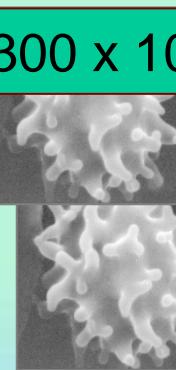


Lung growth

10×10^6

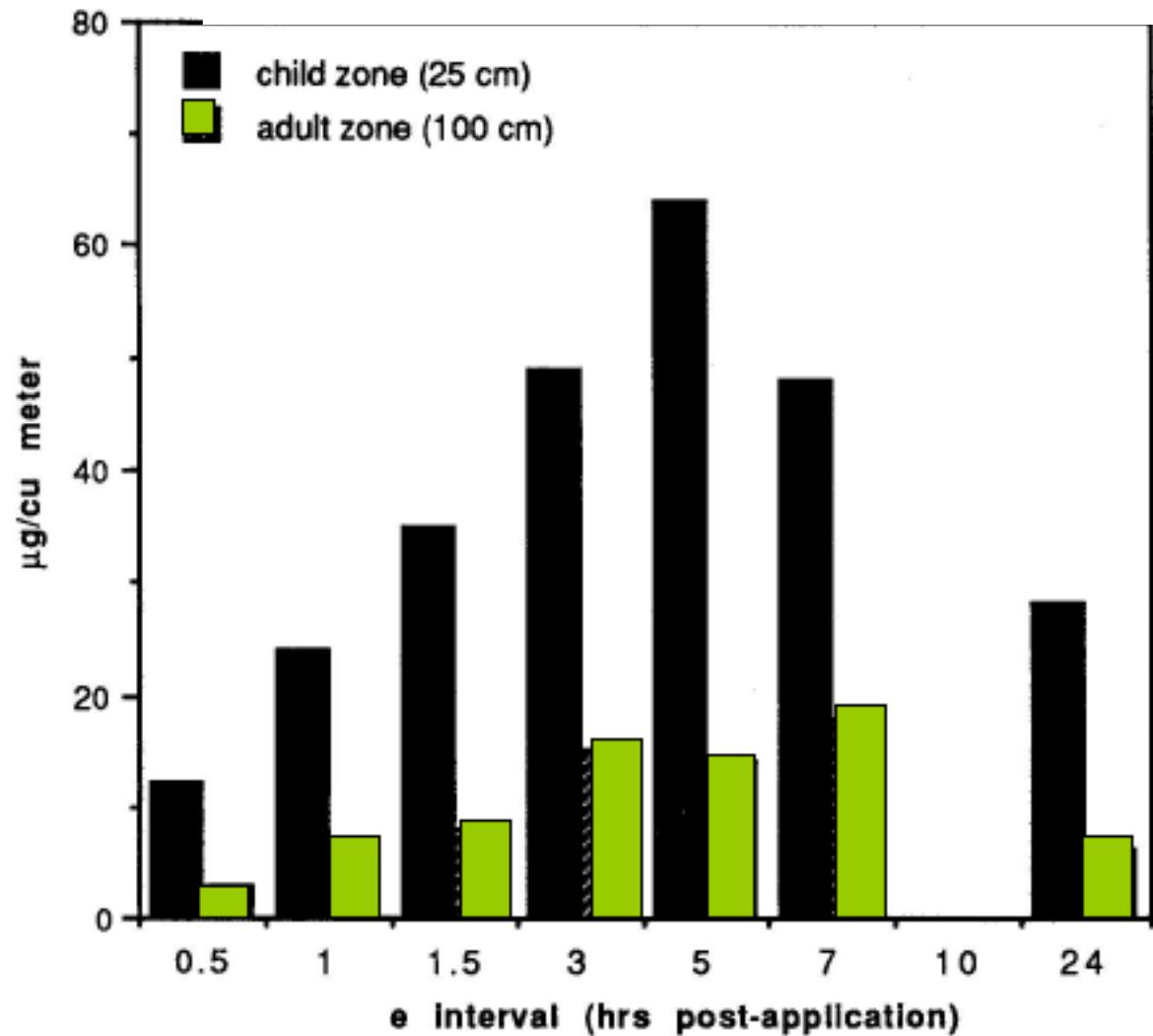


300×10^6





Concentration of contaminants in different zones of the world

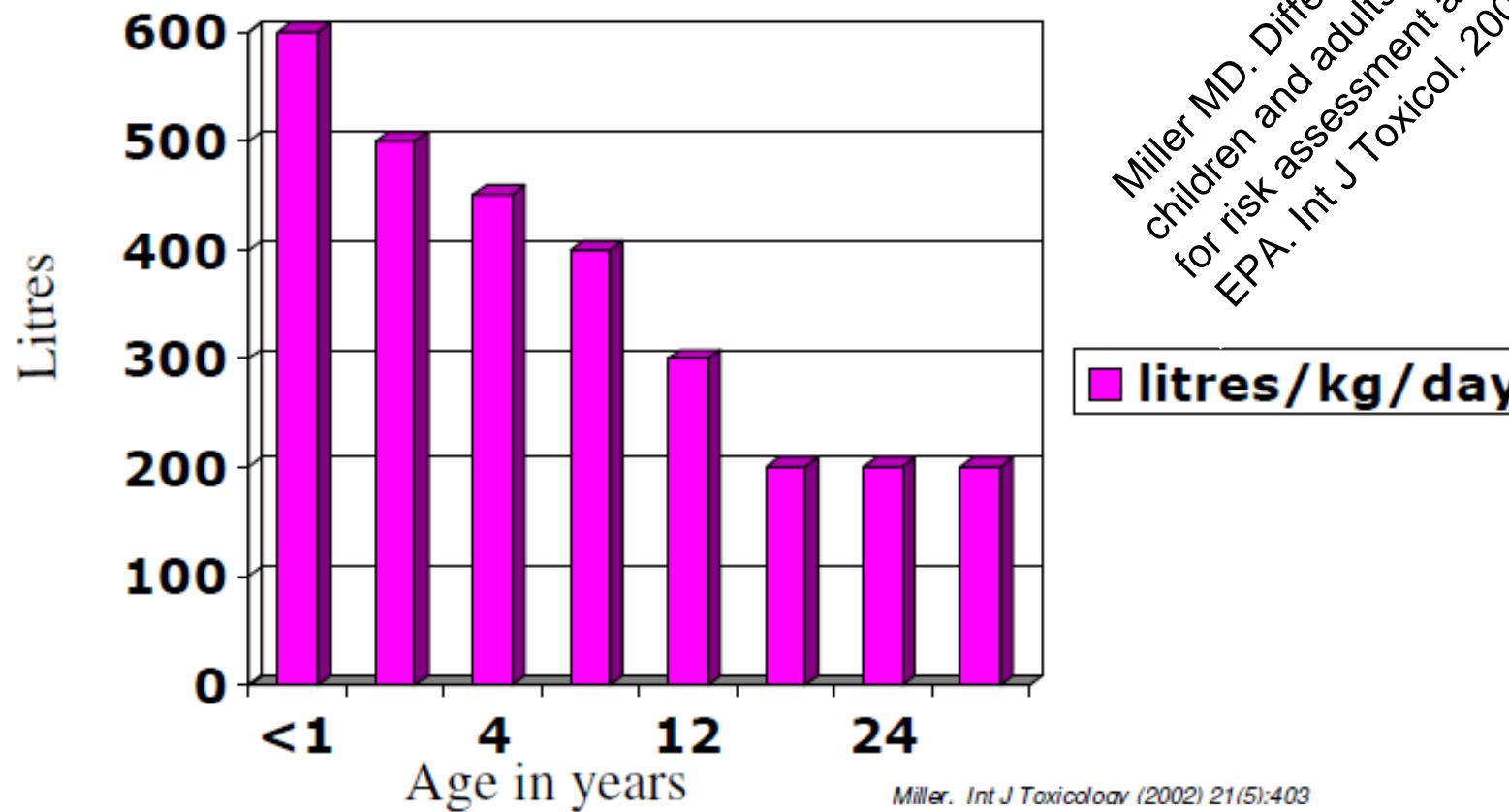


Roberts JR.
Overview of
similarities
and differences
between
children and
adults.
In: risk
assessment,
Guzelian Ed.,
ILSI,
Washington
DC, 1992,
11-18



Minute ventilation per kg body weight/day

OXYGEN DEMAND



Miller MD. Differences between children and adults: implications for risk assessment at California EPA. *Int J Toxicol*. 2002;403-18

Original article

Regular vs prn nebulized treatment in wheeze preschool children

Background: International guidelines recommend regular treatment with inhaled glucocorticoids for children with frequent wheezing; however, prn inhaled bronchodilator alone or in combination with glucocorticoid is also often used in practice. We aimed to evaluate whether regular nebulized glucocorticoid plus a prn bronchodilator or a prn nebulized bronchodilator/glucocorticoid combination is more effective than prn bronchodilator alone in preschool children with frequent wheeze.

Methods: Double-blind, double-dummy, randomized, parallel-group trial. After a 2-week run-in period, 276 symptomatic children with frequent wheeze, aged 1–4 years, were randomly assigned to three groups for a 3-month nebulized treatment: (1) 400 µg beclomethasone bid plus 2500 µg salbutamol prn; (2) placebo bid plus 800 µg beclomethasone/1600 µg salbutamol combination prn; (3) placebo bid plus 2500 µg salbutamol prn. The percentage of symptom-free days was the primary outcome measure. Secondary outcomes included symptom scores, use of relief medication and exacerbation frequency.

Results: As compared with prn salbutamol (61.0 ± 24.83 [SD]), the percentage of symptom-free days was higher with regular beclomethasone (69.6%, SD 20.89; $P = 0.034$) but not with prn combination (64.9%, SD 24.74). Results were no different in children with or without risk factors for developing persistent asthma. The effect of prn combination was no different from that of regular beclomethasone on the primary and on several important secondary outcomes.

Conclusions: Regular inhaled glucocorticoid is the most effective treatment for frequent wheezing in preschool children. However, prn bronchodilator/glucocorticoid combination might be an alternative option, but it requires further study.

A. Papi¹, G. Nicolini², E. Baraldi³,
A. L. Boner⁴, R. Cutrera⁵, G. A. Rossi⁶,
L. M. Fabbri⁷, on behalf of the
**BEclomethasone and Salbutamol
Treatment (BEST) for Children Study
Group**

¹Department of Respiratory Diseases, Research Center on Asthma and COPD, University of Ferrara, Ferrara, Italy; ²Medical Department, Chiesi Farmaceutici, Parma, Italy; ³Department of Pediatrics, Unit of Allergy and Respiratory Medicine, University of Padova, Padova, Italy; ⁴Department of Pediatrics, University of Verona, Verona, Italy;

⁵Respiratory Unit, Department of Pediatrics, Ospedale Pediatrico Bambino Gesù, Rome, Italy;

⁶Department of Pediatrics, Ospedale Gaslini, Genova, Italy; ⁷Department of Respiratory Diseases, University of Modena and Reggio Emilia, Modena, Italy

Key words: asthma; as needed; beclomethasone; salbutamol; wheezing.

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Accepted for publication 28 May 2009



Regular vs prn nebulized treatment in wheeze preschool children

Background: International guidelines recommend regular treatment with inhaled glucocorticoids for children with frequent wheezing; however, prn inhaled bronchodilator alone or in combination with glucocorticoid is also often used in practice.

Aim: regular nebulized glucocorticoid plus a prn bronchodilator vs. prn nebulized bronchodilator/glucocorticoid combination vs. prn bronchodilator alone in preschool children with frequent wheeze.

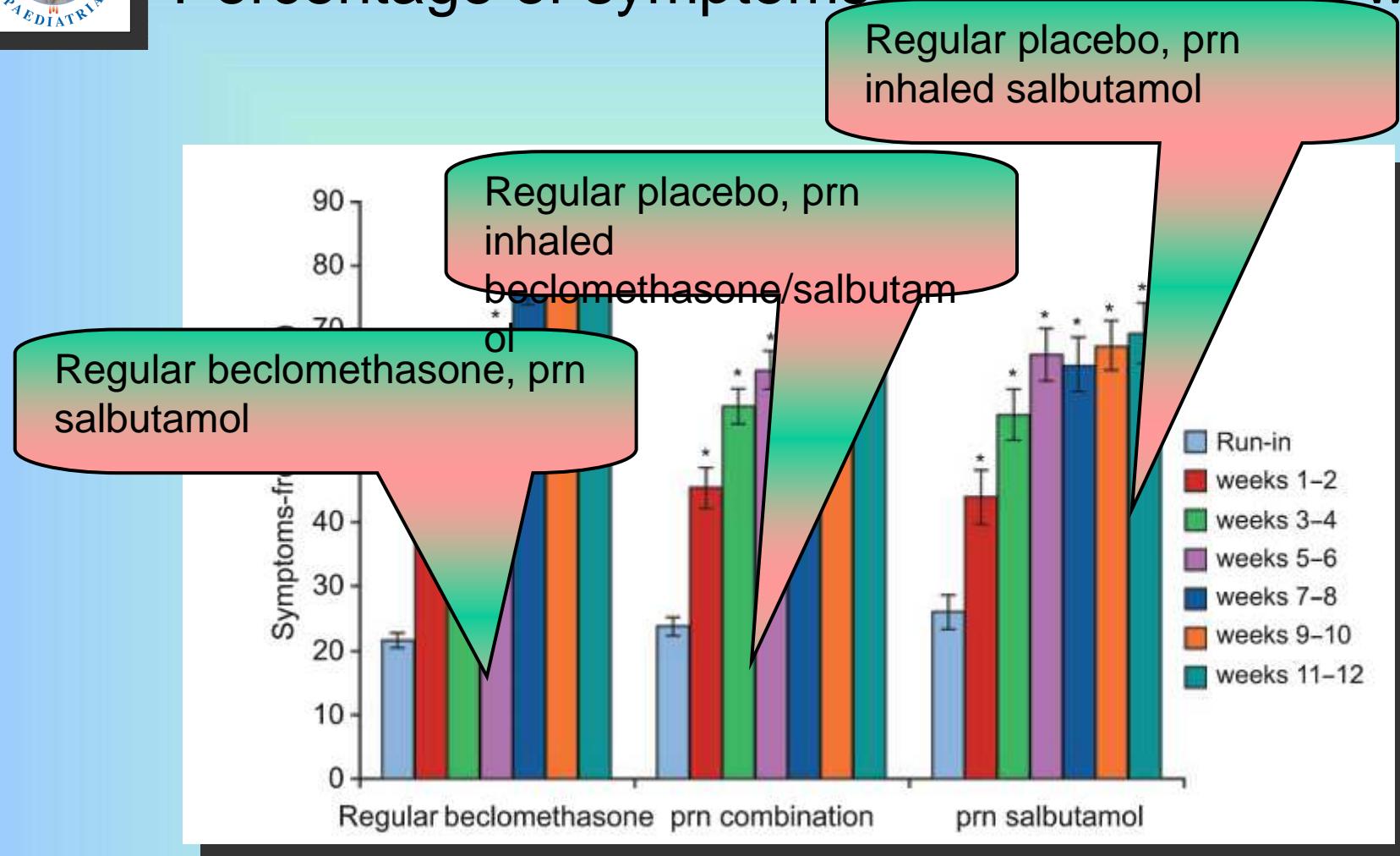
Methods: 276 symptomatic children with frequent wheeze, aged 1–4 years, randomly assigned to three groups for a 3-month nebulized treatment:
(1)400 µg beclomethasone bid plus 2500 µg salbutamol prn;
(2)placebo bid plus 800 µg beclomethasone/1600 µg salbutamol prn;
(3) placebo bid plus 2500 Ig salbutamol prn.

Outcome measure: % of symptom-free days. Symptom scores. Use of relief medication. Exacerbation frequency.

Papi A, BEST Study Group. Regular vs prn nebulized treatment in wheeze preschool children. Allergy 2009; 64: 1463–1471



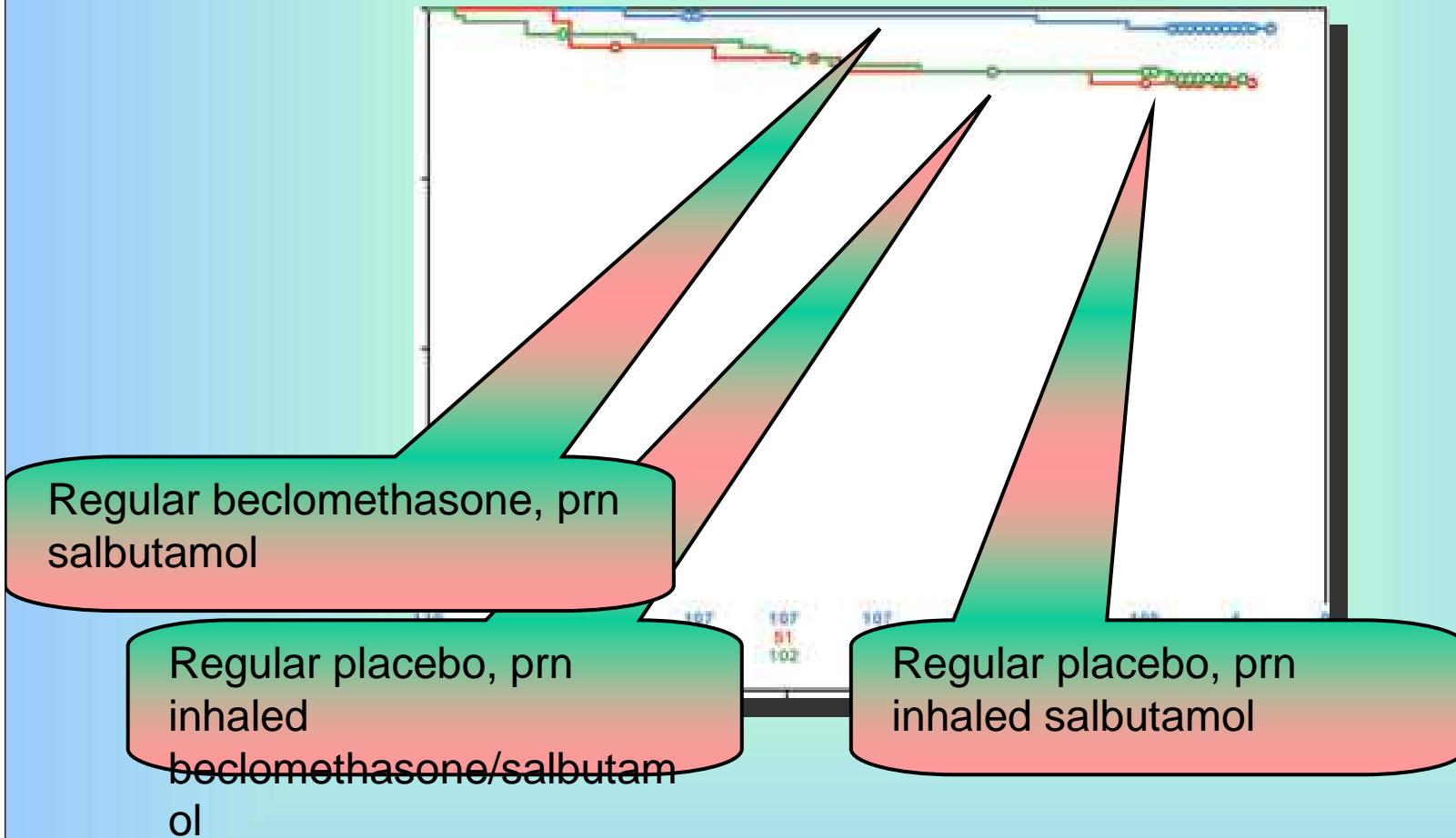
Percentage of symptoms-free days over 2 weeks



Papi A, BEST Study Group. Regular vs prn nebulized treatment in wheeze preschool children. Allergy 2009; 64: 1463–1471



Kaplan–Meier estimates of the time to first asthma exacerbation in the intention-to-treat population.



Papi A, BEST Study Group. Regular vs prn nebulized treatment in wheeze preschool children. Allergy 2009: 64: 1463–1471



Regular vs prn nebulized treatment in wheeze preschool children

Results: As compared with prn salbutamol (61.0 ± 24.83 [SD]), the percentage of symptom-free days was higher with regular beclomethasone (69.6%, SD 20.89; $P = 0.034$) but not with prn combination (64.9%, SD 24.74).

Results were no different in children with or without risk factors for developing persistent asthma. The effect of prn combination was no different from that of regular beclomethasone on the primary and on several important secondary outcomes.

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Papi A, BEST Study Group. Regular vs prn nebulized treatment in wheeze preschool children. Allergy 2009; 64: 1463–1471



Gli apparecchi per aerosol vanno bene per qualsiasi farmaco





Drug delivery systems.

Nebulizers, both jet and ultrasonic, were originally designed to convert a liquid solution into an aerosol.

During years suspensions for nebulization have been developed and nebulized with the available devices.

Drug output from jet and ultrasonic nebulizers have shown significant differences between solutions and suspensions.

Ex-vivo comparisons have confirmed the in-vitro results.

Nikander K. Drug delivery systems.
Aerosol Med. 1994;7(Suppl 1):S19-24.

Ability of jet nebulizer and ultrasonic nebulizer to aerosolize a solution of terbutaline versus a suspension of budesonide.

An ex-vivo trial

10 adult healthy volunteers

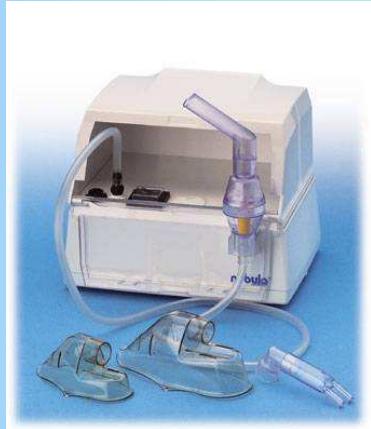
Budesonide suspension vs Terbutaline solution

Inhaled mass of drug measured

Nikander K. Drug delivery systems.
Aerosol Med. 1994;7(Suppl 1):S19-24.



Drug out-put



Nebula Plus



BimboNeb

- FLU 600 µg (*Lunibron A*)
in 2ml di soluzione fisiologica
- BDP 400ug/ml (*Clenil A*)
fiale da 2ml
- BUD 0,25 mg/ml (*Spirocort*)
fiale da 2ml

O'Callaghan Riv Ital Pediatr 2000, J Pharm Pharmacol 2002 , J Pharm Pharmacol 2005



Glass Multistage Liquid Impinger

Methodologies to determine the drug dose

MSLI estimates the percentage of the nominal cumulative dose.

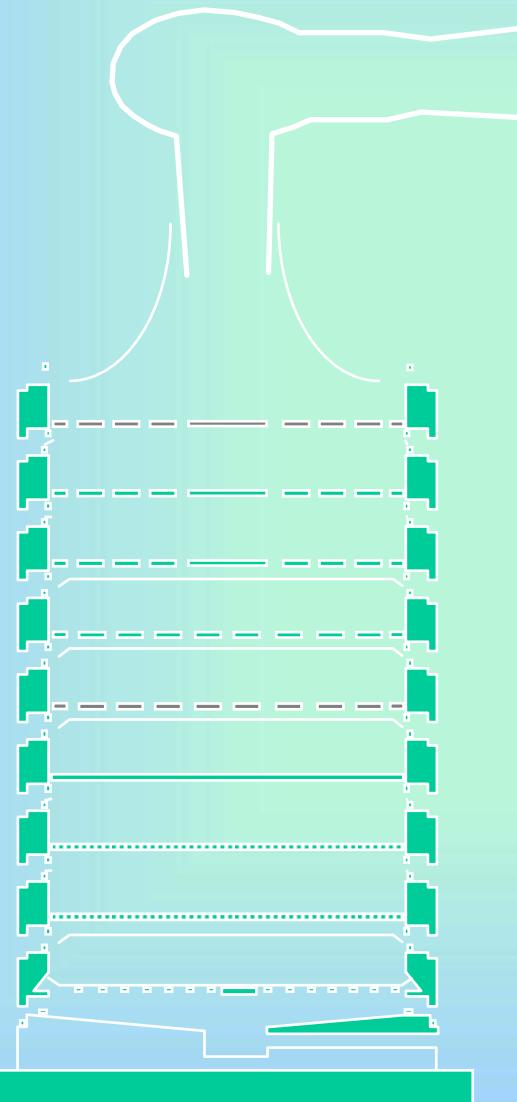
Recommended for submissions to FDA

Evaluation of comparative aerosol deposition data.

Wong W. Pharmacopeial methodologies for determining aerodynamic mass distributions of ultra-high dose inhaler medicines.
Pharm Biomed Anal. 2010; 51:853-7.



Glass Multistage Liquid Impinger



- 4 stages
- Flow 60L/min
- calibrated with aerosol of known particle size distribution
- cut off diameters for stages: 12.6 um, 10.1 um, 6.8 um and 4.3um.
- nebuliser mouthpiece held at 2 cm away from MSLI



| | BUD (500µg) | | FLU (600µg) | | BDP (800µg) | |
|-----------------------------------|----------------|----------------|-------------------|------------------|-----------------|----------------|
| | Nebula | BimboNeb | Nebula | BimboNeb | Nebula | BimboNeb |
| MMAD | 3,38 (0,38) | 4,48 (0,44) | 3,86 (0,21) | 3,87 (0,14) | 5,36 (0,16) | 6,37 (0,36) |
| Erogated mass in part. <6,8 (mcg) | 86,8 (4,0) | 76,7 (3,5) | 208,7 (14,4) | 201 (10,4) | 149,6 (21,4) | 105,2 (6,3) |
| % of nominal dose in part. <6,8 | 17,4% | 15,3% | 34,6% | 33,5% | 18,6% | 13,1% |
| Erogated mass in part. <4,3 (mcg) | 67,0 (5,4) | 53,5 (5,4) | 154,18 (10,85) | 148,53 (7,44) | 91,53 (15,9) | 57,26 (1,7) |
| % of nominal dose in part. <4,3 | 13,4% | 10,7% | 25,7% | 24,7% | 11,5% | 7,2% |

O'Callaghan Riv Ital Pediatr 2000, J Pharm Pharmacol 2002 , J Pharm Pharmacol 2005



Nebulised budesonide (Pulmicort Respules) vs. beclomethasone dipropionate (Clenil Aerosol)

In vitro performance of budesonide 0.5 mg/mL vs. beclomethasone dipropionate 0.4 mg/mL).

Five different nebulisers

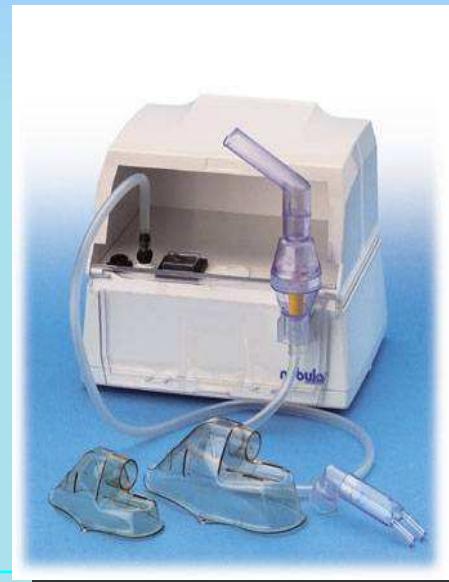
A finer particle dose achieved with Pulmicort Respules versus Clenil Aerosol

estimated dose to the lungs of 8-14 and 3-6% of nominal dose respectively

budesonide particles small, 2-3 microm in diameter

BDP were needle-shaped up to approximately 10 microm long.

Vaghi A. In vitro comparison of nebulised budesonide (Pulmicort Respules) and beclomethasone dipropionate (Clenil per Aerosol). Pulm Pharmacol Ther. 2005;18:151-3



| | | |
|--------------------|----------------------|----------------------------|
| Nebula Plus | Retained dose | Output MMAD 5.36 |
| BDP 800ug | 75% | Filter 5.6% |
| BimboNeb | Retained dose | Output MMAD 6.37 |
| BDP 800ug | 73% | Filter 8.3% |

Vaghi A. In vitro comparison of nebulised budesonide (Pulmicort Respules) and beclomethasone dipropionate (Clenil per Aerosol). Pulm Pharmacol Ther. 2005;18:151-3



| | Cirrus BDP 800ug | Retained dose 75% | Output Filter 10% MMAD 4.8 um | Size distribution Nominal <5um 5-6% <3um 2-3% |
|--|---------------------------------------|--------------------------|---|--|
| | Pari LC Plus BDP 800ug | Retained dose 55% | Output Filter 27% MMAD 7.5 um | Size distribution <5um 6% <3um 2% |
| | Ormon COMP Air Elite BDP 800ug | Retained dose 50% | Output Filter 37% MMAD 10 um | Size distribution <5um 2-3% <3um 1% |

Vaghi A. In vitro comparison of nebulised budesonide (Pulmicort Respules) and beclomethasone dipropionate (Clenil per Aerosol). Pulm Pharmacol Ther. 2005;18:151-3



Tutti i metodi di inalazione vanno bene





Nebulisation of corticosteroid suspensions and solutions with a beta(2) agonist.

BimboNeb and Nebula nebulisers

3.0 mL of salbutamol plus either flunisolide, 600 microg, or BDP, 800 microg

Particle size determined

Total outputs of drugs from both nebulisers

O'Callaghan CL. Nebulisation of corticosteroid suspensions and solutions with a beta(2) agonist. Pharm Pharmacol. 2008;60:601-5.



Nebulisation of corticosteroid suspensions and solutions with a beta(2) agonist.

Drug outputs from both mixtures greater from the BimboNeb than from the Nebula after 5 and 10' nebulisation.

Outputs with the BimboNeb lower with the paediatric breathing pattern than with the adult pattern.

10 min produced significantly greater drug output than after 5 min.

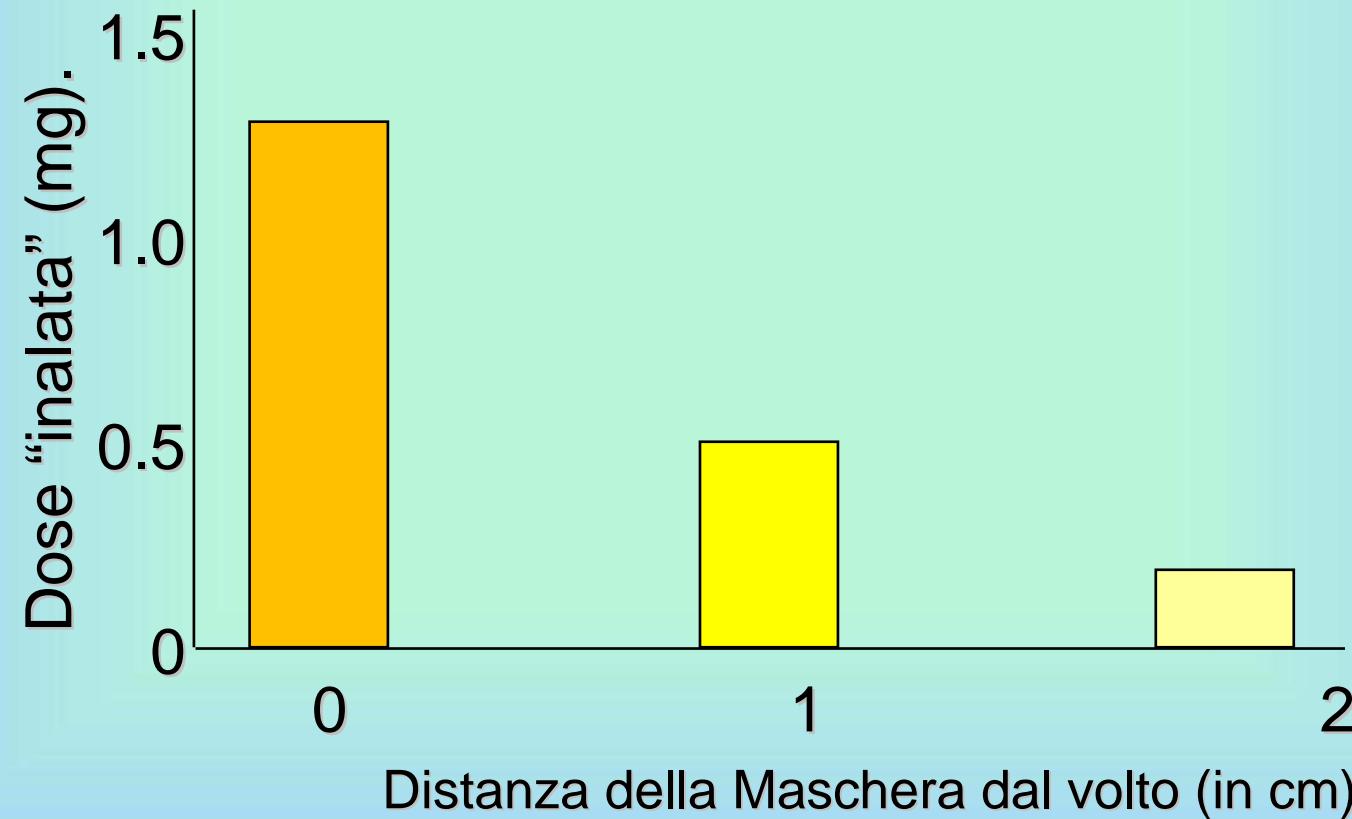
Device matters

Time matters

O'Callaghan CL. Nebulisation of corticosteroid suspensions and solutions with a beta(2) agonist. Pharm Pharmacol. 2008;60:601-5.



Dose di farmaco inalata aumentando la distanza tra mascherina e volto a VC di 50 ml, con un flusso di 8 l/min.



Everard M. Arch Dis Child 1992; 67: 586-91.



Costs for 1-month treatment

Costs for 1-month treatment

- Nebulised fluticasone (2000 μg daily) excluding the cost of nebuliser costs £120.48 (pound sterling)
- Inhaled fluticasone pMDI (250 μg twice daily), excluding cost of spacer, costs £ 19.43 (pound sterling)
- Costs matter



Il distanziatore serve solo per il bambino grande





DISTANZIATORE IDEALE

- Volume adeguato all'età
- Facilmente trasportabile
- Costruito con materiali antistatici
- Fornito di valvole
- Facile da utilizzare
- Durevole e di basso costo
- Adattabile con più tipi di spray

Modificata da *Ausili strumentali per la prevenzione e terapia delle malattie allergiche. RIAP 2000*



Caratteristiche distanziatori

| | <u>vol</u> | <u>forma</u> | <u>lungh</u> | <u>valvole</u> | <u>univers</u> |
|-------------|------------|--------------|--------------|----------------|----------------|
| Aerochamber | 145 ml | cilindrica | 11cm | 2(I-E) | sì |
| Babyhaler | 350 ml | cilindrica | 32 cm | 2(I-E) | no |
| Volumatic | 750 ml | diamante | 23 cm | 1(I) | no |
| Fluspace | 305 ml | cilindrica | 20 cm | 1(I) | sì |
| Jet | 103 ml | circolare | 10 cm | | no |
| Vortex | 105 ml | cilindrica | 9 cm | 2(I-E) | sì |

Effect of delay, inspiratory flow, and spacer washing on the drug output of metered dose inhalers (MDIs)

Amount of drug in particles <5 microm diameter from MDI+spacer, sampling after a delay of up to 20 s, measured using a Multistage Liquid Impinger.

Drug output measured at different flow rates, and after washing the Babyhaler in household detergent.

More fluticasone in small particles recovered from the Babyhaler than the Volumatic or the Aerochamber spacers

More beclomethasone and salmeterol recovered from the Babyhaler and Volumatic spacers than from the Aerochamber.

Washing the Babyhaler reduced the recovery of salmeterol, and did not alter the recovery of the other drugs tested.

Barry PW. The output of budesonide from spacer devices assessed under simulated breathing conditions. J Allergy Clin Immunol. 1999;104:1205-10.



Fluticasone dose to patient (μg)

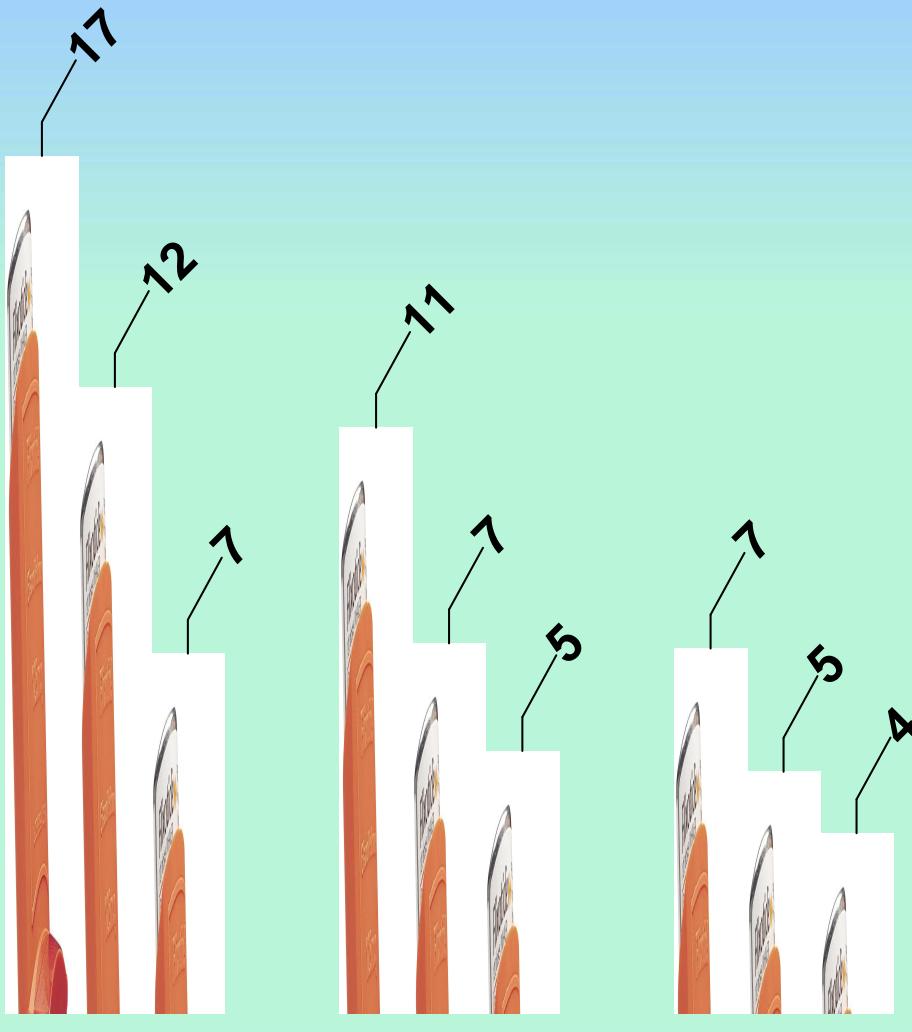
10

0

1s 5s 10s
Babyhaler

1s 5s 10s
Volumatic

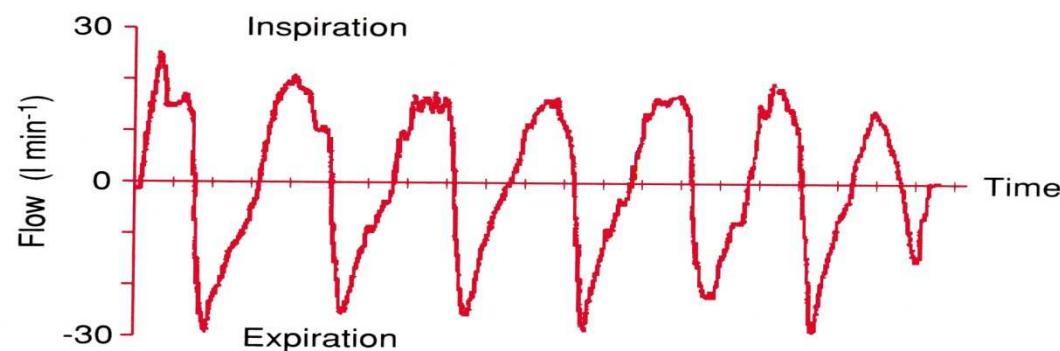
1s 5s 10s
Aerochamer



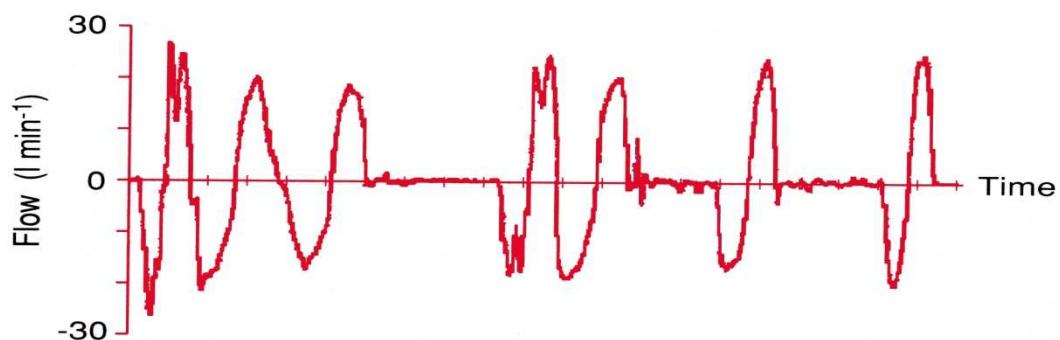
Barry PW. The output of budesonide from spacer devices assessed under simulated breathing conditions. J Allergy Clin Immunol. 1999;104:1205-10.

Periodo di erogazione prolungato

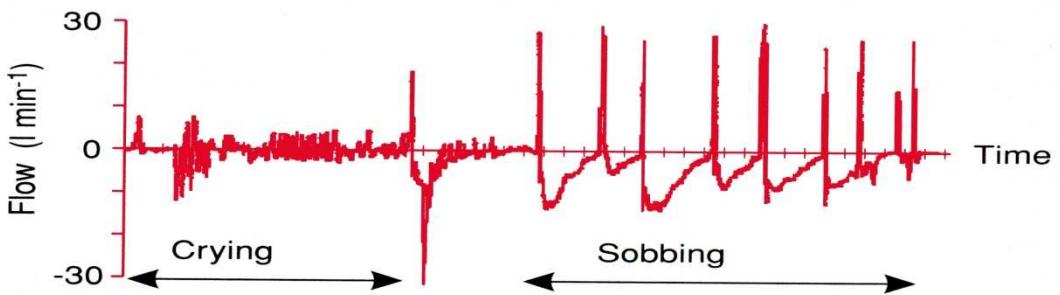
A. 12 year old child



B. Young child



C. Infant



Pattern respiratorio nel bambino



Cosa possiamo concludere





Cosa possiamo concludere

- Non tutti gli apparecchi per aerosol vanno bene
- Posso trattare a lungo il lattante, ma questo non gli modifica la storia naturale
- Non conviene che tratti il bambino al bisogno perché le dosi efficaci non garantiscono sicurezza
- Se è un asma persistente, il trattamento intermittente al bisogno non garantisce una buona crescita polmonare
- La quantità di farmaco e la sua deposizione variano con caratteristiche del farmaco, dell'aerosol e della compliance
- Posso usare il distanziatore anche nel bambino piccolo, ma con attese minori.