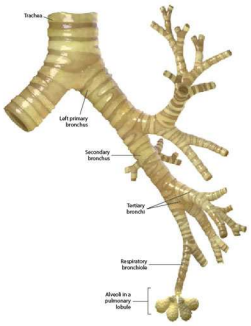
Aérosolthérapie

Quelle spécificité dans l'asthme ?

Gregory Reychler
Cliniques universitaires Saint-Luc

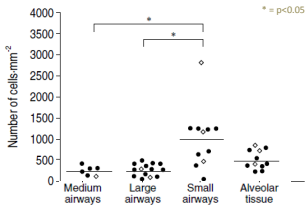


Atteintes des petites voies aériennes

⇩

Traitement des petites voies aériennes

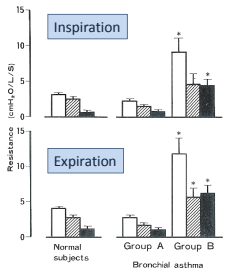
Inflammation et petites voies aériennes



Densité de cellules inflammatoires dans les biopsies chez des patients asthmatiques sévères

Balzar et al, Eur Respir J, 2002

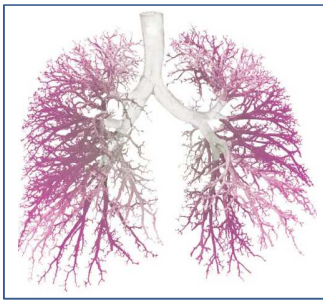
Petites voies aériennes et résistance



Group A: FEV>80% pred
Group B: FEV<70% pred

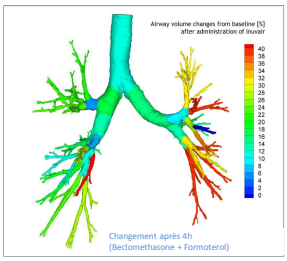
Yanai M et al. J Appl Physiol 1992; 72:1016–1023

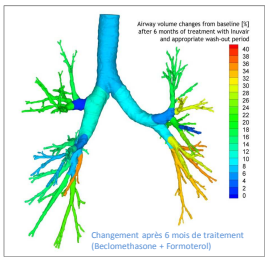
Voies aériennes



Airways		
	Large	Small
Internal Diameter	>2 – 18mm	≤2mm
Surface Area	290 cm^2	140 m^2
Volume	50 ml	4500 ml
Corticosteroid receptors density	High	High
$ß_2$-adrenoceptors density	Low	High

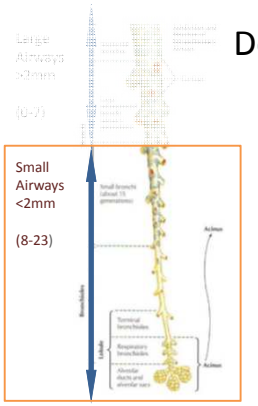
Effet sur les petites voies aériennes

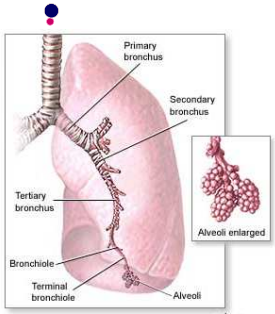




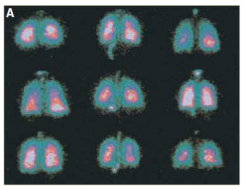
Vos, ERS congress 2009

Déposition et particule

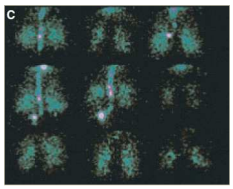




Influence de la taille des particules



Small-particle HFA-beclomethasone



CFC-beclomethasone

Scintigraphic images showing the deposition of a large-particle aerosol *vs* a small-particle aerosol in 9 healthy volunteers. A brighter image represents a better deposition.

Leach et al. CHEST. 2002; 122:510-516

Des particules extra-fines?

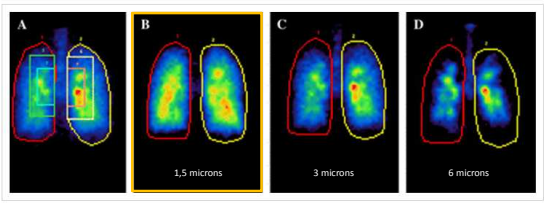
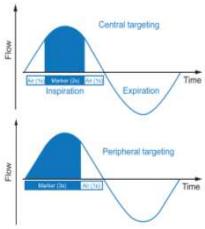


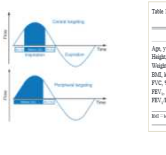
Figure 2. (*A*) Regions of interest, where a 5 × 8 matrix was closely fitted to the krypton ventilation-scan lung boundary and superimposed on the posterior thorax aerosol deposition images, which was partitioned into a central zone, 2 × 3 matrix centered on the lung hilum; an intermediate zone, 3 × 5 matrix excluding the central zone; and a peripheral zone defined as the remaining lung field within the lung outline. (*B*) 1.5 μm, (*C*) 3 μm, and (*D*) 6 μm MMAD posterior thorax images of technetium-99m–labeled albuterol aerosol deposition in the lungs. *Red areas* indicate regio of highest radioactivity, and *black* of least radioactivity.

Usmani., AJRCCM.172.12 (2005), pp. 1497-1504.

AKITA (Activaero)

- Contrôle complet du débit médicamenteux et pas de perte durant l'expiration
- Adapté à chaque patient et à la cible
- Contrôle de compliance





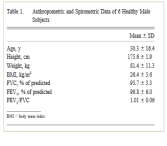


Table 1. Anthropometric and Spirometric Data of 6 Healthy Male Subjects

	Mean ± SD
Age, y	30.3 ± 10.4
Height, cm	175.6 ± 1.9
Weight, kg	81.4 ± 11.3
BMI, kg·m^2	26.4 ± 3.6
FVC, % of predicted	95.7 ± 3.3
FEV_1, % of predicted	90.5 ± 6.0
FEV_1/FVC	1.01 ± 0.08

BMI = body mass index

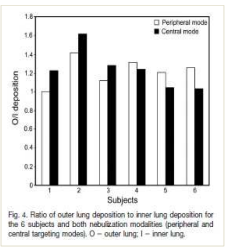


Fig. 4. Ratio of outer lung deposition to inner lung deposition for the 6 subjects and both nebulization modalities (peripheral and central targeting modes). O = outer lung; I = inner lung.

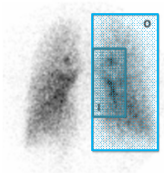
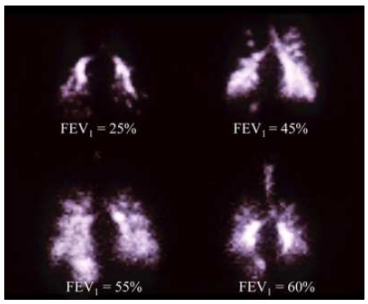


Table 2. Radioactivity Deposition Parameters for Central and Peripheral Drug Targeting Nebulization

Parameter	SDD (% VBD)		EnD (% VBD)		O/I Ratio		PI	
	C	P	C	P	C	P	C	P
Mean ± SD	83.3 ± 6.5	82.8 ± 7.3	16.7 ± 6.5	17.2 ± 7.3	1.24 ± 0.21	1.22 ± 0.14	85.6 ± 13.5	92.8 ± 16.1
Coefficient of variation (%)	8	9	39	42	17	12	16	17
P	.86		.86		.79		.77	

Reychler, Respir Care 2014

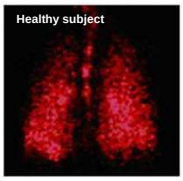
Influence de la sévérité de la maladie sur la déposition

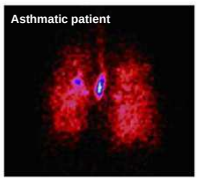


Gamma camera images of four adult patients with cystic fibrosis and different FEV_1 values showing distribution of an aerosol containing the radioisotope ^{99m} technetium. Uniform deposition of aerosolized radioisotope is reduced in patients with low FEV_1 and severe obstruction

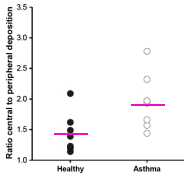
Laube, Transl Respir Med. 2014

Déposition et asthme





Lower C/P = deeper deposition



Déposition pulmonaire : 34% (Sujets sains) et 31% (Asthmatiques) de la DN

De Backer W, Devolder A, Poli G et al. J Aerosol Med Pulm Drug Deliv, Vol 23 2010

Technique compliquée

Table 1 Step-by-step MDI checklist of proper inhalation technique and errors recorded in our population.[a]

Correct step of inhalation technique	Checklist of inhalation technique errors	Errors, % of users
Remove mouthpiece cap	Failure to remove cap*	0.15
Shake inhaler (suspensions only)	Not shaking the inhaler	37
Breathe out before firing	No exhalation before actuation	50
Inhaler upright during firing	Not holding the inhaler in the upright position	9
One inhalation for actuation	More actuations for a single inhalation	19
Place mouthpiece between lips and over tongue	Actuation against teeth, lips, or tongue*,[b]	0.7
Actuation in the first half of inhalation	Actuation in the second half of inspiration	18
	Activation after end of inhalation*	5
Fire while breathing in deeply and slowly and continue until total lung capacity	Stopping inhalation immediately after firing*	10
	Forceful inhalation	52
Inhalation by mouth	Inhalation through nose whilst and after actuation*	2
Hold breath for 10 s	No or short (less than 2–3 s) breath-holding after inhalation	53

* = critical errors.
[a] All data are presented as the percentage of patients performing the uncorrected step compared to the total number of observations.
[b] Hold the mouthpiece inhaler between open lips (19% of total) or even a few centimeters from the open mouth is an acceptable alternative to place the mouthpiece between closed lips.

N=1664 (COPD and asthma)

Melani AS et al., Resp Medicine,2011

TABLE 4. PERCENTAGE OF MISTAKES PER STEP, TOTAL PERCENTAGE OF PATIENTS MAKING AT LEAST ONE MISTAKE PER DEVICE, AND MULTIVARIATE ANALYSIS PER DEVICE

	Diskus n = 41	Turbuhaler n = 51	Diskhaler n = 24	Single-dose dry powder inhaler n = 20	pMDI with spacer n = 36	pMDI n = 32
Shake inhaler thoroughly					25[a]	16[a]
Remove duster cap						0[a]
Keep inhaler in upright position		77				3[a]
Activate inhaler	5[a]					
Twist the grip to the right and twist back until the "click"sound		14[a]				
Place inhaler in horizontal position		26	0			
Open and close device			21[a]			
Place canister correctly in spacer					3[a]	
Open device in vertically position with body below				11[a]		
Place capsule in the device				19[a]		
Turn back mouthpiece				11[a]		
Push the buttons once				35[a]		
Sit upright or stand	17	16	17	25	22	22
Breathe out to residual volume	61	75	63	70		59
Tilt head back (hyperextend)	63	61	75	55		63
Close lips on inhaler	0	0	8	15	0	3
Activate canister in beginning of Slow inhalation						72[a]
Continue to inhale slowly and deeply						31[a]
Inhale forcefully and deeply	10[a]	6[a]	0[a]	0[a]		
Activate inhaler once					25[a]	
Breath in and out through mouthpiece at least three times					33	
Hold breath for at least 5 sec	51	38	58	80		50
Brath out away from mouthpiece	10	2	8	10		13
Patients performing at least one essential step incorrectly	15%	18%	21%	45%	47%	81%
Odds ratio	1.0	1.1	1.5	5.2	4.4	25.7
95% confidence interval		0.4–3.6	0.4–5.8	1.5–18.3	1.5–13.3	7.3–90.7

[a]Essential step.
Percentage of patients performing at least one step incorrectly does not have to be sum of the essential steps separately since per demonstration multiple essential steps can be performed incorrectly. Odds ratio from Diskus is reference value for other devices.Odds ratios were adjusted for whether or not receiving inhalation instruction.pMDI, pressurized meter dose inhaler.

Rootmensen et al. Journal of Aerosol Medicine and Pulmonary Drug Delivery. 2010; 23(5): 323-328

J Asthma. 2009 Nov;46(9):944-50.

Inappropriate techniques used by internal medicine residents with three kinds of inhalers (a metered dose inhaler, Diskus, and Turbuhaler): changes after a single teaching session.

Kim SH, Kwak HJ, Kim TB, Chang YS, Jeong JW, Kim CW, Yoon HJ, Jee YK.
Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea.

Abstract

BACKGROUND: While initial education and regular evaluation of inhaler technique in patients are emphasized in the management of asthma and chronic obstructive pulmonary disease, health care professionals are not experienced in using inhalers. This study assessed whether internal medicine residents used common inhalers correctly and whether a single teaching session successfully improved their performance.

METHODS: We evaluated 142 internal medicine residents from six university hospitals in Korea for their techniques with three different inhaler devices: a metered dose inhaler (MDI), Diskus, and Turbuhaler. We assessed whether participants completed each step in using the three inhalers and classified overall performance as good, adequate, or inadequate for each inhaler type. To estimate the effect of a single teaching session, reassessment was performed 2 months after education.

RESULTS: Performance grade was inadequate for 58.7% of participants with a MDI, 43.0% for Diskus, and 51.4% for Turbuhaler. An early year of residency was associated significantly with inappropriate technique for Diskus (p = 0.003), but not for MDI and Turbuhaler. After a single teaching session, overall skills improved significantly for all three inhalers. The proportion of subjects with good or adequate skill changed notably from 39.7% to 83.8% for MDI (p = 0.001), from 50.0% to 86.8% for Diskus (p = 0.001), and from 44.1% to 88.2% for Turbuhaler (p = 0.001).

CONCLUSIONS: These findings demonstrate that a high proportion of internal medicine residents cannot use inhalers correctly and just a single teaching can effectively enhance their inhaler technique.

Modes de déposition

IMPACTION

SEDIMENTATION

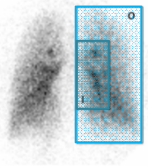
DIFFUSION

Impaction
- Déposition par inertie
- Particules de grande taille
- Débit élevé

Sédimentation
- Déposition par la pesanteur
- Faible débit
- Modalité optimale pour la nébulisation

Diffusion
- Déposition par mouvements Browniens
- Particules de petite taille

Influence du débit inspiratoire



Penetration index
O/I

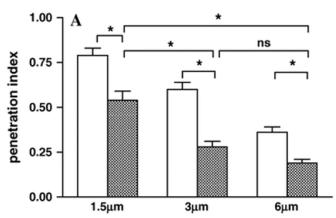
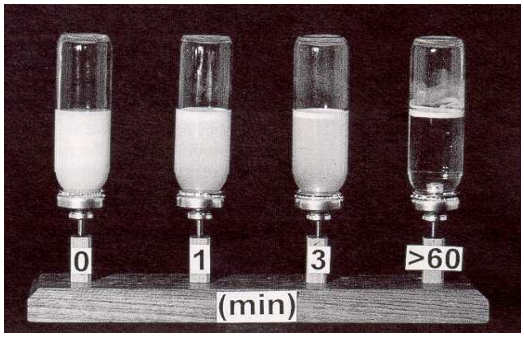


Figure 6. Effect of fast inhalation (*shaded bars*) compared with slow inhalation (*white bars*) on (*A*) aerosol penetration into the lung and (*B*) FEV_1. *$p < 0.001$; †$p < 0.05$. ns = not significant.

Usmani., AJRCCM, 172, 12 (2005), pp. 1497-1504.

Influence de l'agitation



Lung Deposition of ^{99m}Tc-Radiolabeled Albuterol Delivered through a Pressurized Metered Dose Inhaler and Spacer with Facemask or Mouthpiece in Children with Asthma

William Ditcham, PhD,[1] Jasminka Murdzoska, PhD,[1] Guicheng Zhang, PhD,[2] Christina Roller, PhD,[1] Dirk von Hollen, BSc,[3] Kurt Nikander, BA,[4] and Sunalene G Devadason, PhD[1]

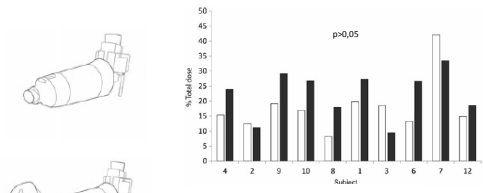
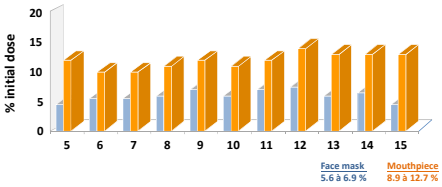


FIG. 5. Percent of total dose deposition; lung dose. Facemask (□) and mouthpiece (■). Sorted by age; youngest first.

Children aged 3-5 years

J Aerosol Med Pulm Drug Deliv. 2014 Aug;27 Suppl 1:S63-75

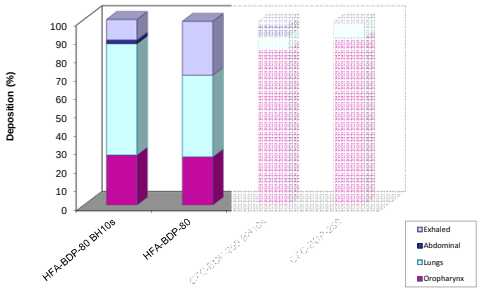
Interface



323 asthmatics (5-15y)
budesonide 0.5mg/ml in 2 ml
Compressor: 7,5 L/min
Time : 5 minutes

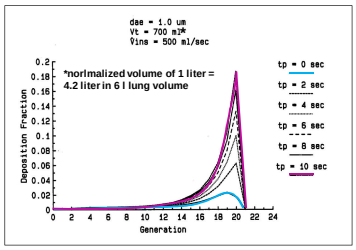
Nikander, J Aerosol Med 1994, 7(S1):S19-S24

Influence de la pause inspiratoire



Leach CL, J Aerosol Med Pulm Drug Deliv. 2010;23(6):355-61

Effect of breathhold



Particle deposition in the different airway generations with different time of breath-hold

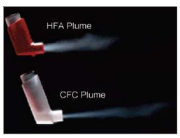
Longer breath-hold will generate more particle deposition

Reference:
Byron et al., Respiratory Drug Delivery ,1990

Influence du gaz propulseur

Inhaled Steroid	MMAD (μm)	Lung Deposition (%)
Fluticasone Rotadisk	> 4	15
Triamcinolone	4.5	14
CFC flunisolide	3.8	15–20
CFC beclomethasone	3.5	10–15
CFC fluticasone	2.5	20
HFA flunisolide	1.2	40
HFA beclomethasone	1.1	40
HFA ciclesonide	1.0	42

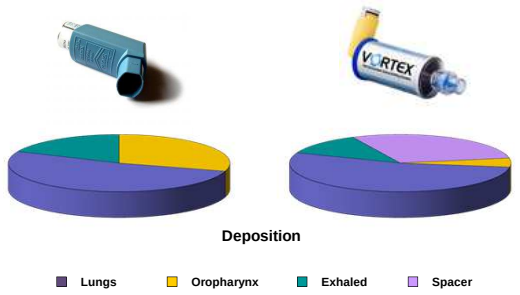
MMAD = mass median aerodynamic diameter
CFC = chlorofluorocarbon
HFA = hydrofluoroalkane



Meilleure taille des particules et meilleure déposition (surtout pour les corticoïdes)

Leach CL., Respir Care 2005;50(9):1201–1206

Intérêt de la chambre



Leach CL, J Aerosol Med Pulm Drug Deliv. 2010;23(6):355-61

Influence du nettoyage

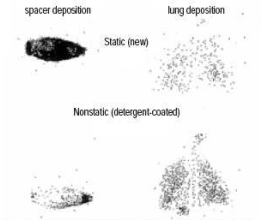


Fig. 5. – Typical deposition patterns of radioaerosol in the same subject after inhalation through a new and a detergent-coated spacer (posteroanterior view).

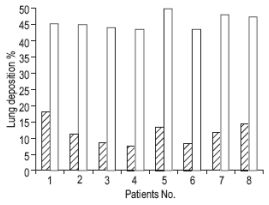


Fig. 3. – Comparison of salbutamol lung deposition, expressed as percentage of total actuated dose, after inhalation of salbutamol through electrostatically charged (new; ▩) and non-electrostatically charged (detergent-coated; □) Volumatic spacers in eight healthy adults.

Nettoyage augmente la déposition pulmonaire!

Pierart F, Eur Respir J 1999; 13: 673-678

Influence de l'éducation

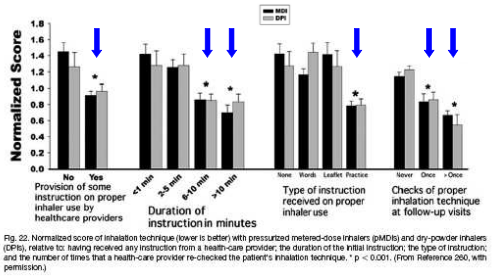


Fig. 22. Normalized score of inhalation technique (lower is better) with pressurized metered-dose inhalers (pMDIs) and dry-powder inhalers (DPIs), relative to: having received any instruction from a health-care provider; the duration of the initial instruction; the type of instruction; and the number of times that a health-care provider re-checked the patient's inhalation technique. * $p < 0.001$. (From Reference 260, with permission.)

Rau JL, Respir Care 2008;53(6):699-723

An Innovative Childhood Asthma Score Predicts the Need for Bronchodilator Nebulization in Children With Acute Asthma Independent of Auscultative Findings

Arvid WA Kamps MD PhD, Nic JGM Veeger PhD, and Sigrid M Heijsman MD

"… In daily practice, a physician is not always readily available to perform the assessment… it has been demonstrated that the use of an asthma score in a clinical pathway for acute asthma reduced the hospital stay without increased morbidity… the currently available pediatric asthma scores require auscultation… requires adequate training to minimize subjectivity"

Table 1. Items of Childhood Asthma Score Per Age Group

	0 Point	1 Point	2 Points	3 Points
Breathing frequency, breaths/min				
2–3 y old		< 35	35–39	> 39
4–5 y old		< 31	31–35	> 35
6–12 y old		< 27	27–30	> 30
> 12 y old		< 24	24–27	> 27
S_{pO_2}, %		> 95 in room air	90–95 in room air	< 90 in room air or > 90 with extra O_2
Accessory muscle use	Absent	Absent or intercostal	Intercostal and subcostal	Intercostal, subcostal, and supraclavicular
Dyspnea				
2–5 y old	Asleep or normal feeding, vocalizations, and activity	One of the following: decreased appetite, increased coughing after play, hyperactivity	Two of the following: decreased appetite, increased coughing after play, hyperactivity	Stops eating or drinking, no vocalizations, drowsy or confused
> 5 y old	Asleep or counts to > 10 in one breath	Counts to 7–9 in one breath	Counts to 4–6 in one breath	Counts to < 4 in one breath

Using a cutoff value of 4, the newly developed CAS accurately predicts the requirement for bronchodilator nebulization in children with acute asthma without use of auscultative findings

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