



同济医院



alvatec



# **Polluants professionnels intérieurs et allergie respiratoire**

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**Pôle de pathologie thoracique**

**Fédération de médecine translationnelle , EA 3071**

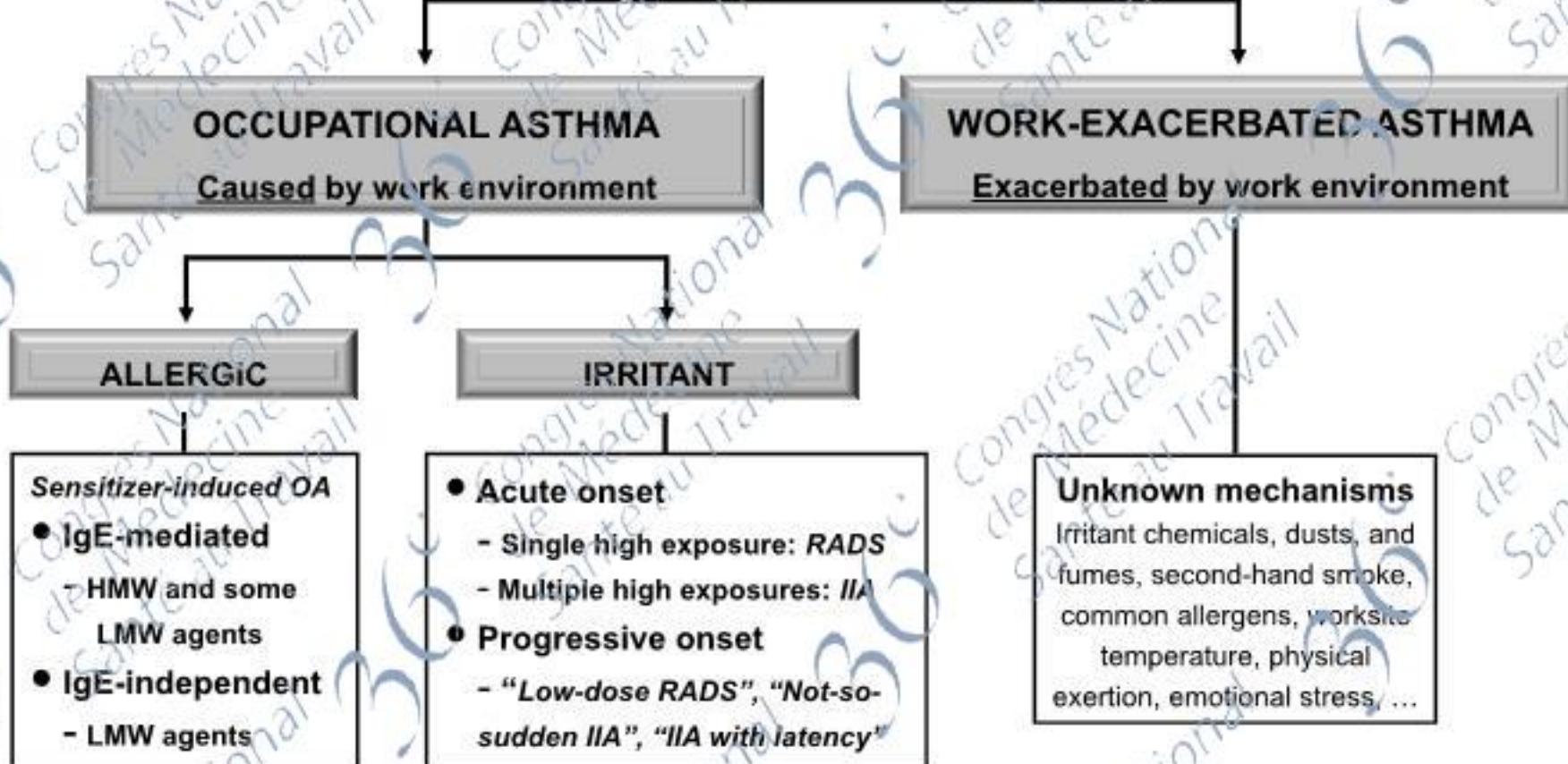
**Université de Strasbourg**

## **Liens d'intérêt**

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- ◆ **ALK, Anergis, Boehringer, GSK, MEDA pharma, Novartis, Stallergènes Labs (board d'expert)**
- ◆ **ALK, Amgen, Anergis, Astra-Zeneca, Circassia, GSK, Novartis, Roche, Sanofi, Stallergènes Labs (études cliniques)**
- ◆ **ALYATEC ( participation financière)**

# Work-related asthma



Malo JL, Vandenplas O. Definitions and classification of work-related asthma.  
*Immunol Allergy Clin North Am* 2011;31:645-62

## **WRA phenotypes**

### **WORK-RELATED ASTHMA (WRA)**

**80%**

Asthma caused by work

=OCCUPATIONAL ASTHMA (OA)

Allergic :

- IgE-dependent
- Non-IgE dependent

Irritant-induced (IIOA) :

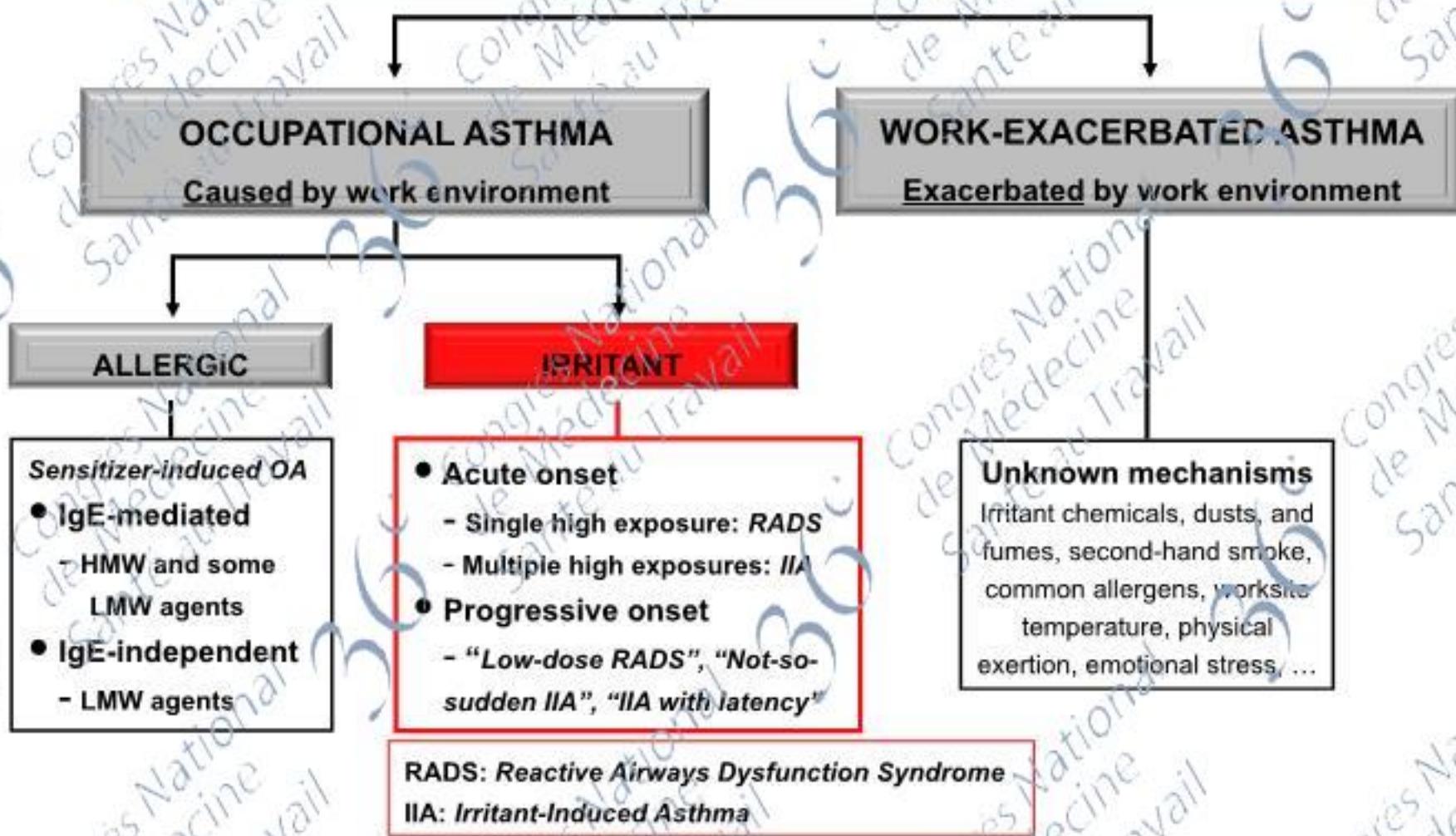
- Acute-Single exposure : RADS\*
- Non acute-Multiple exposures

**20%**

Asthma exacerbated by work

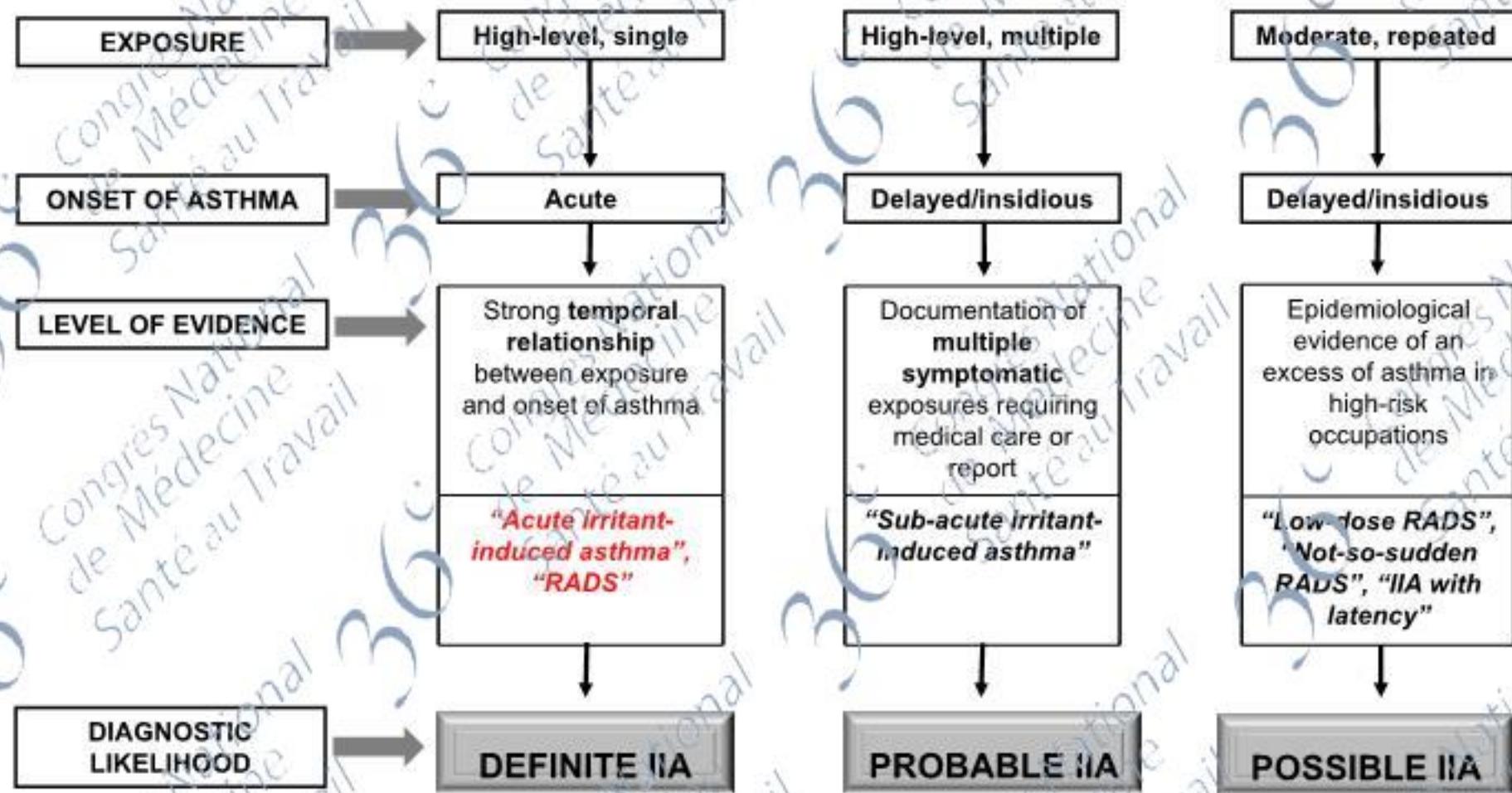
=WORK-EXACERBATED ASTHMA (WEA)

# Work-related asthma



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# Phenotypes of irritant-induced asthma (IIA)



Vandenplas et al. EAACI position paper: irritant-induced asthma. Allergy 2014

## Acute-onset IIA - RADS

**Table 1** Diagnostic criteria for acute-onset irritant-induced asthma<sup>x</sup>

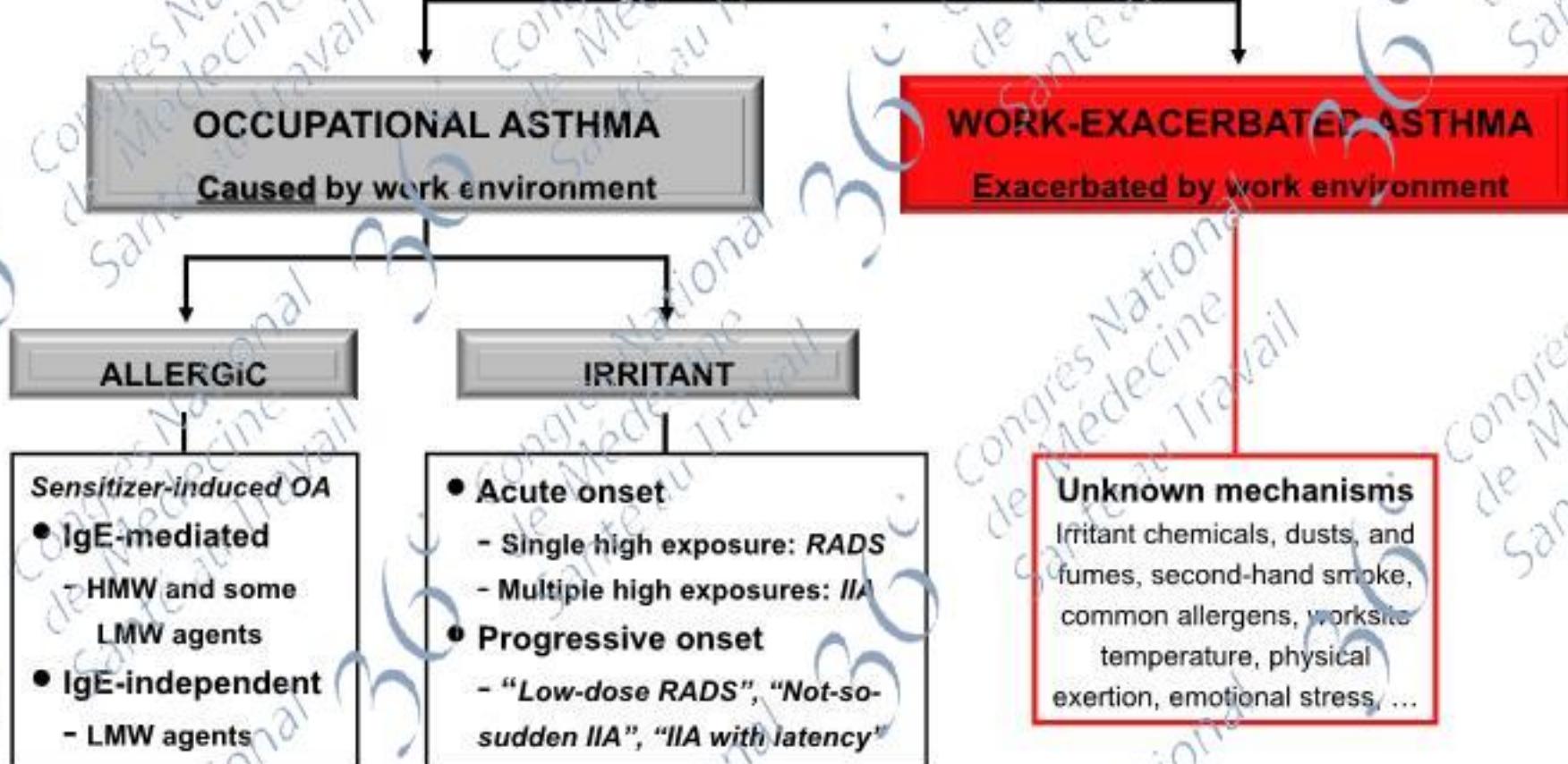
- 1 Absence of preexisting asthma symptomatology
- 2 Onset of asthma symptoms after a single specific inhalational exposure or accident
- 3 Exposure to an irritant vapor, gas, fume, or smoke in very high concentration
- 4 Onset of asthma symptoms within minutes to hours and <24 h after the exposure
- 5 Presence of airflow limitation with a significant bronchodilator response or nonspecific bronchial hyperresponsiveness to histamine/methacholine
- 6 Exclusion of other pulmonary disorders that can explain the symptoms or simulate asthma

\*The diagnostic criteria for Reactive Airways Dysfunction Syndrome have been adapted from Brooks et al (9, 21) and the American College of Chest Physicians guidelines (4).

### Acute- and subacute-onset IIA vs. allergic OA:

- ➔ **No latency period before onset of asthma**
- ➔ **Do not develop work-related asthma symptoms on re-exposure**

# Work-related asthma



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# Work-related asthma

## OCCUPATIONAL ASTHMA

Caused by work environment

### IMMUNOLOGIC

Sensitizer-induced OA

- IgE-mediated
  - HMW and some LMW agents
- IgE-independent
  - LMW agents

### IRRITANT

- Acute onset

- Single high exposure: RADS
- Multiple high exposures: IIA

- Progressive onset

- "Low-dose RADS", "Not-so-sudden IIA", "IIA with latency"

## WORK-EXACERBATED ASTHMA

Exacerbated by work environment

- Pre-existing or concurrent asthma
- Asthma-work temporal relationship
- Conditions exist at work that can exacerbate asthma
- Asthma caused by work is unlikely

Henneberger et al. An official ATS statement: work-exacerbated asthma.  
Am J Respir Crit Care Med 2011;184:368-78

## Clinical characteristics of WEA vs. OA (1)

Outcome	Reference	Study setting	Work-exacerbated asthma		Occupational asthma
<b>Asthma severity</b>	Larbanois, ERJ 2002	Specialized clinic	Median severity score: 7 (n=71)	=	Median severity score: 8 (n=86)
	Lemiere, JOEM 2006	Specialized clinic	Symptoms score: $15\pm9$ (mean $\pm$ SD) (n=10)	=	Symptoms score: $17\pm13$ (mean $\pm$ SD) (n=18)
<b>ICS treatment</b>	Lemiere, JOEM 2006	Specialized clinic	$400\pm394$ $\mu$ g (mean dose $\pm$ SD) (n=10)	=	$430\pm282$ $\mu$ g (mean daily dose $\pm$ SD) (n=18)
<b>Emergency room visit</b>	Goe, OEM 2004	Gases from SENSOR	59% (n=210)	=	52% (n=891)
<b>Hospitalization</b>	Goe, OEM 2004	Cases from SENSOR	23% (n=210)	=	25% (n=891)
<b>Nonspecific bronchial hyperresponsiveness</b>	Larbanois, ERJ 2002	Specialized clinic	$1.46$ ( $0.13$ - $5.27$ ) mg/ml (median [IQR] PC <sub>20</sub> )	>	$0.72$ ( $0.09$ - $2.57$ ) (median [IQR] PC <sub>20</sub> )
	Lemiere, JACI 2007	Specialized clinic	$3.7\pm4.8$ mg/ml (mean $\pm$ SD) (n=129)	=	$3.0\pm6.4$ mg/ml (mean $\pm$ SD) (n=169)

## **Clinical characteristics of WEA vs. OA (2)**

➤ Prospective observational study (Lemiere, JACI 2013) :

- 53 subjects with WEA and 68 subjects with OA (based on SIC result)
- ➔ WEA associated with:
  - more frequent use of ICS (OR: 4.4; 95% CI: 1.4-13.6; p=0 .009)
  - noneosinophilic phenotype (OR: 0.3; 95% CI: 0.1-0.9; p=0.04)
  - lower FEV<sub>1</sub> (OR: 0.9; 95% CI: 0.9-1.0; p=0.06)
  - higher proportion of smokers (OR: 2.5; 95% CI: 0.96-9.7; p=0.06)

# Work-related asthma

## OCCUPATIONAL ASTHMA

**Caused by work environment**

### ALLERGIC

#### Sensitizer-induced OA

- IgE-mediated
  - HMW and some LMW agents
- IgE-independent
  - LMW agents

### IRRITANT

- Acute onset

- Single high exposure: *RADS*
- Multiple high exposures: *IIA*

- Progressive onset

- “*Low-dose RADS*”, “*Not-so-sudden IIA*”, “*IIA with latency*”

## WORK-EXACERBATED ASTHMA

**Exacerbated by work environment**

### Unknown mechanisms

Irritant chemicals, dusts, and fumes, second-hand smoke, common allergens, worksite temperature, physical exertion, emotional stress, ...

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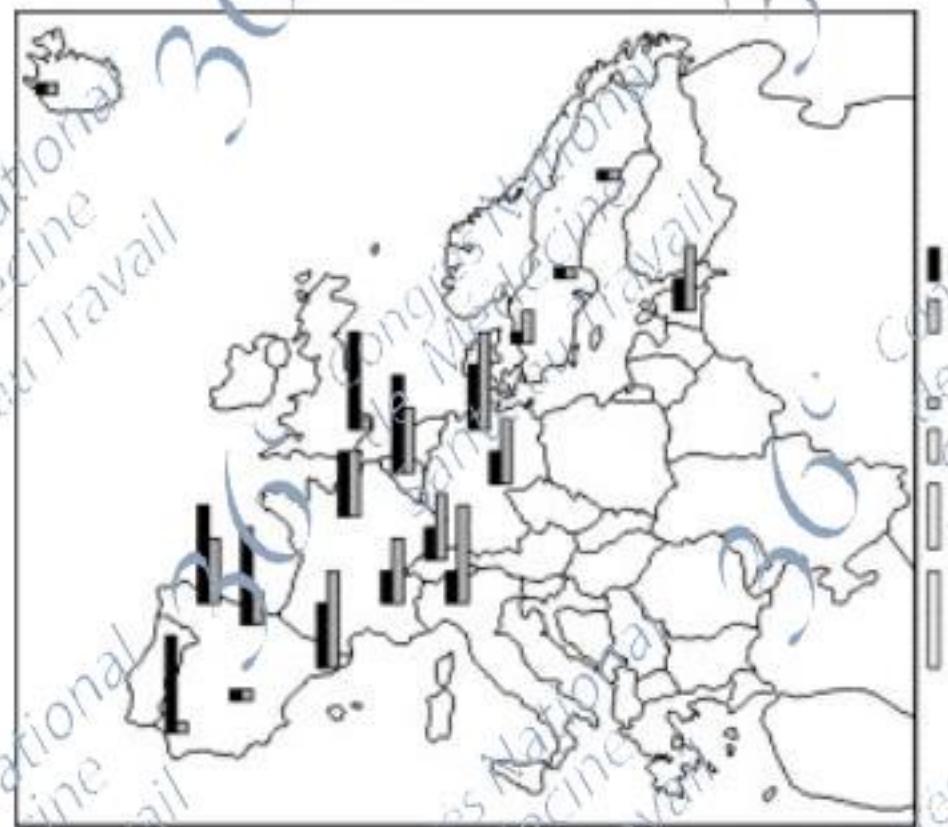
# **Les allergènes**

# Mite exposure in Europe

Distribution of Der p 1 and Der f 1 allergens in Europe (based on 3414 measurements in 22 study centers from 10 countries).

Percentages of dust samples with detectable mite allergen levels (ie,  $\geq 0.1 \mu\text{g}$  per gram of dust) are shown.

Results for adjacent centers within the same country with similar results were combined (Ipswich and Norwich in East Anglia, United Kingdom; Pavia, Turin, and Verona in Northern Italy; Antwerp Center and Antwerp South in Belgium)



# **ALLERGIE CHAT-CHIEN: Exposition**

## ◆ **CHAT**

- **Aux États-Unis 99,9% des logements ont des taux mesurables de Feld d1**
- **Moyenne géométrique: 4,73 µg/g**
- **13,4% ont un chat et pas de chien à la maison**
- **Taux plus élevés:**
  - ✓ **Régions ouest des États-Unis**
  - ✓ **Blancs, population plus favorisée**
  - ✓ **Niveau d'éducation plus haut**
- **Europe: 0,94 à 3,76 µg/g**
- **Présents sur les fauteuils de voiture**

# **ALLERGIE CHAT-CHIEN: Exposition**

◆ **CHIEN**

• **Aux États-Unis**

✓ **100% des logements ont des taux mesurables**

✓ **Les allergènes de chat et de chien sont ubiquitaires**

✓ **Présents sur les fauteuils de voiture**

## Asthme sévère et moisissures

**Table 5.** Allergen-specific relative risks (95% confidence limits), adjusted for the effects of sensitivity to any of the other 10 allergens, for development of asthma symptoms at any age, airway hyperresponsiveness at any age, and concurrent symptoms and hyperresponsiveness at any age, compared with non-sensitivity to that particular allergen

Allergen	Asthma symptoms at any age Risk (95% CL)	Airway hyperresponsiveness (AHR) at any age Risk (95% CL)	Concurrent symptoms and AIIR at same age Risk (95% CL)
Rye grass pollen	1.29 (0.86, 1.92)	0.96 (0.57, 1.62)	1.33 (0.69, 2.58)
House dust mite	1.94 (1.29, 2.92)*	4.45 (2.69, 7.36)*	6.71 (1.21, 13.38)*
Cat fur	2.27 (1.20, 4.30)*	2.66 (1.42, 4.98)*	4.19 (2.11, 8.31)*
Alternaria	0.67 (0.31, 1.46)	0.55 (0.22, 1.36)	0.78 (0.29, 2.13)
Dog fur	1.49 (0.59, 3.77)	2.51 (1.04, 6.06)	3.68 (1.43, 9.49)*
Horse hair	2.25 (0.87, 5.81)	1.16 (0.47, 2.84)	1.03 (0.38, 2.76)
Cladosporium	1.21 (0.37, 3.98)	1.11 (0.38, 3.21)	0.71 (0.22, 2.34)
Kapok	0.86 (0.24, 3.07)	0.88 (0.22, 3.44)	0.31 (0.06, 1.47)
<i>Aspergillus fumigatus</i>	7.15 (1.40, 36.44)*	6.63 (1.79, 24.49)*	13.76 (3.19, 59.45)*
Wool	3.28 (0.74, 14.52)	1.07 (0.28, 4.09)	1.28 (0.29, 5.68)
Penicillium	0.24 (0.05, 1.12)	0.27 (0.04, 1.73)	0.55 (0.07, 4.21)

\*  $P < 0.05$ ; all others not significant.

# Moisissures et asthme sévère

## ◆ Epidémiologie

- Enfant : 5 – 11 ans
- n = 467
- 36 % sensibilisé à **Alternaria**
- Augmentation des exacerbations sévères et des concentrations aériennes extérieures et intérieures

Penicillium: OR : 1.5 IC : 1.01 – 1.27

✓ 3 espèces combinées :

***Cladosporium***

***Aspergillus***

***Alternaria***

OR : 1.13 IC : 1.01 – 1.26

# Moisissures et asthme sévère

Health effects associated with 10-fold increase in concentration of fungi among children with negative skin test to a particular fungal allergen extract

Fungus	Number non-allergic [I]	UV in past 2 months associated with increase in indoor fungi, controlling for outdoor	95% CI	OR
<i>Alternaria</i>	133		1.07	0.89, 1.29
<i>Aspergillus</i>	216		1.05	0.94, 1.17
<i>Cladosporium</i>	300		1.01	0.91, 1.11
<i>Penicillium</i>	347		1.12*	1.03, 1.22

UV=Unscheduled visits to emergency department or clinic for asthma.

## Moisissures et asthme sévère

- ◆ **62 enfants**
- ◆ **2 – 17 ans**
- ◆ **Asthme non contrôlé**

Eviction des moisissures  
Pas d'éviction des moisissures

→ de 90% des taux de consultations ( $p < 0.03$ )

Fréquence de Sensibilisation aux moisissures dans les 2 groupes : 30 %

**Liens de causalité entre exposition et asthme sévère ?**

# **Les composés organiques volatils**

# Composés organiques volatils

- composés organiques : C, H, N, O
- volatils: classement OMS T° ébullition (1989)  
VVOC, VOC, SVOC, POM
- concept de COV totaux – contesté Molhave and Damgaard Nielsen, Indoor air 1992
- composés très différents

Hydrocarbures aliphatiques saturés  
Dodecane, pentane, hexane...

Benzène, toluène, xylène, styrène, éthylbenzène...  
Hydrocarbures aromatiques  
isopropylbenzène...

Terpènes  
Limonène,  $\alpha$ -pinène

Hydrocarbures aliphatiques cycliques  
Hexane, méthylhexane...

Phtalates  
Diméthylphtalate, dibutylphtalate...

Aldéhydes  
Formaldéhyde, acétaldéhyde, propanal...

Cétones  
2-butanone, cyclopentanone...

Acides  
Acide butyrique, acide propanoïque...

Ethers de glycol  
Éthylèneglycol...

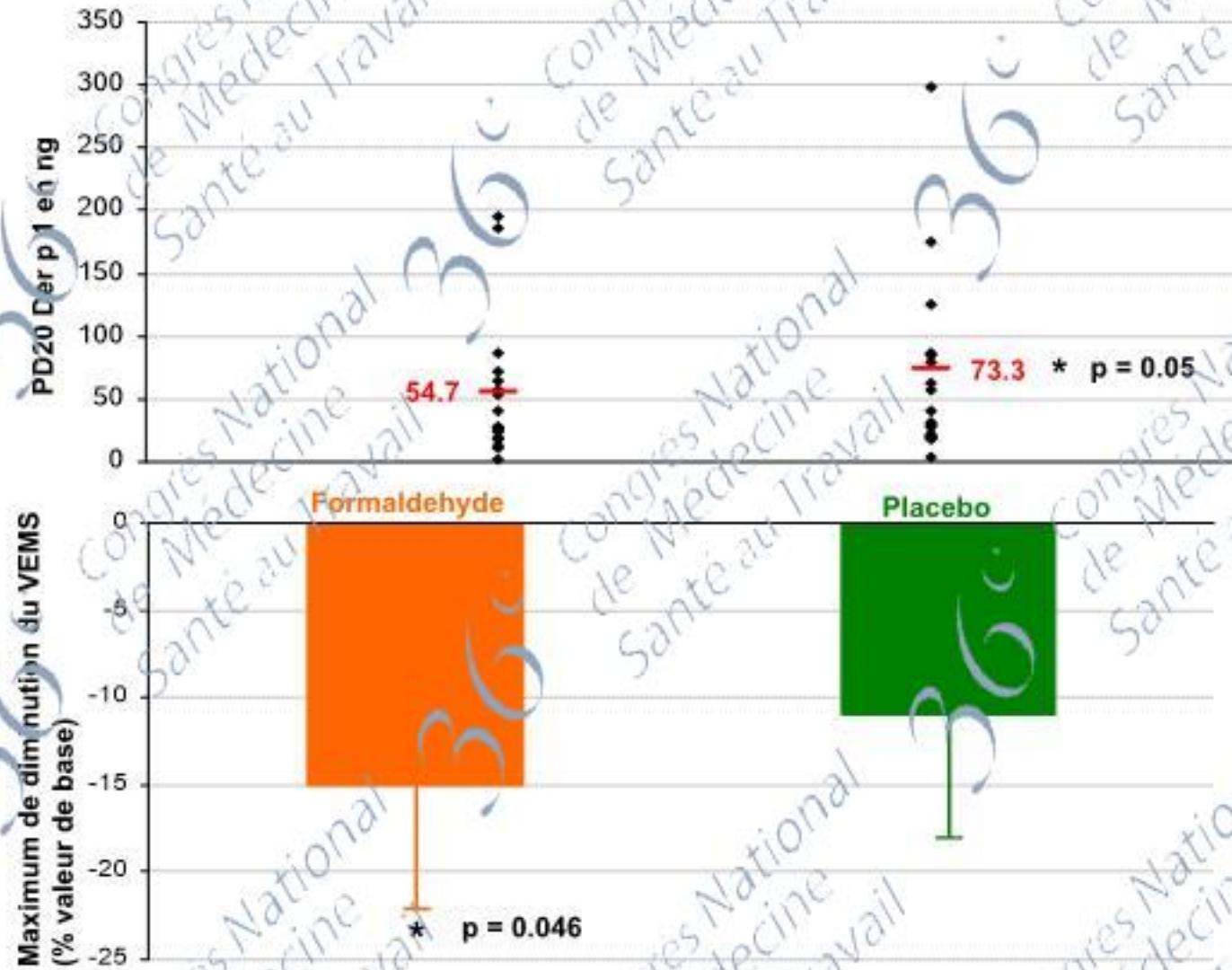
# Modification de la réponse bronchique allergique

## -Etude expérimentale :



- 19 sujets : asthme intermittent aux allergènes d'acariens**
- Exposition :  $100\mu\text{g} \cdot \text{m}^{-3}$  de FA pendant 30 min**
- TPB à Dpt consécutif à l'exposition**

## Immediate bronchial response



## Late bronchial response

formaldéhyde  
placebo  
Mean ± DS

→ Inhalation of low doses of formaldehyde would be an aggravating factor of the immediate and late bronchial response to mite allergens in sensitized asthmatics.

# VOC, school and respiratory allergy

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- ◆ Particles < 2.5 µm (PM 2.5)
- ◆ NO<sub>2</sub>
- ◆ 3 aldehydes (formaldehyde, acetaldehyde et acroleine)
- ◆ 108 school classes in France (Créteil, Strasbourg, Reims, Marseille, Clermont-Ferrand)

# VOC, school and respiratory allergy

◆ Children : 10.4 years on average

◆ Relation :

- Rhino-conjunctivitis the previous year  
Formaldehyde : OR : 1.19 [IC 1.04 – 1.36]
- Asthma previous year :
  - ✓ PM 2.5 µm : OR : 1.21 [1.05 - 1.39]
  - ✓ Acroleine : OR : 1.22 [1.09 – 1.38]
  - NO2 : OR : 1.16 [0.95 – 1.41]

# VOC and respiratory symptoms

- ◆ **Out of 7 epidemiological studies :**

- **3 → relation between VOCs and asthma**

- **Link between aromatic VOCs :**

- OR : 1.63, CI : 1.17 – 2.27 and

- Asthma diagnosed by the doctor**

- VOC measured 3X per personal sampler**

## **Les produits de nettoyage**

# Cleaning agents : Diagnosis and treatment

Overview of the most common surface cleaning products

Type of surface	Products	Purposes of use	Typical frequency of application
Hard floors (stone, tiles, marble, synthetic)	Multi-use cleaners, floor cleaners, bleach	Remove accumulated dust and dirt, surface care, disinfection, give shine	Weekly
Wooden floors	Floor cleaners suitable for wood, floor waxes	Remove accumulated dust and dirt, surface care, give shine	Weekly (waxing less often)
Carpeted (textile) floors	Foams, shampoos, sprays (solvent-based dry-cleaning agents)	Remove accumulated dust and dirt (stains), surface care	Less than once per month
Glass (windows, mirrors, furniture)	Ammonia, alcohol (methylated spirits), glass cleaners (often sprays), multi-use cleaners	Remove accumulated dust, fat and dirt, give shine	Less than once per week
Furniture (wood, metal, plastic)	Furniture cleaners (often sprays), multi-use cleaners	Remove accumulated dust, fat and dirt, give shine	Weekly
Upholstered furniture	Foams, shampoos, sprays (solvent-based dry-cleaning agents)	Remove accumulated dust and dirt (stains), surface care	Less than once per month
Kitchen sink unit, extractor hood	Scouring cream or powder, multi-use cleaners	Remove accumulated fat and dirt, give shine	Weekly
Gas hob, electric cooker, oven, microwave oven	Degreasing sprays, multi-use cleaners	Remove accumulated fat and dirt, give shine	Depends; from daily to monthly
Wash basin, bathtub, taps	Scouring cream or powder, bleach, multi-use cleaners	Remove dirt spots and calcium stains	Weekly
Toilet bowl	Multi-use cleaners, bleach, acids	Remove dirt spots and calcium stains, disinfection	Weekly

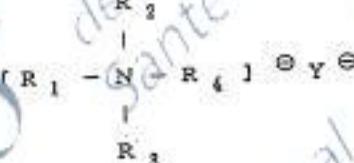
# Cleaning agents : Diagnosis and treatment

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- ◆ Determinant of respiratory exposure depends
  - Evaporation of volatile components (particularly on large surface “floor”)
  - Amount of cleaning product and concentration used
  - T°, humidity
  - The use of products in spray form
  - The possibility of release of secondary pollutants (exp humidity + α Pinene + O<sub>3</sub> → Formaldehyde)

# Les ammoniums quaternaires (AQ)

- ◆ Formule générale :



- ◆ Largement utilisés .

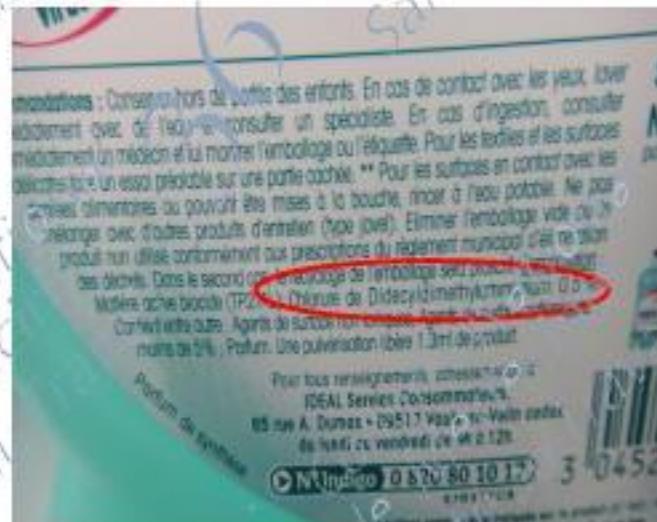
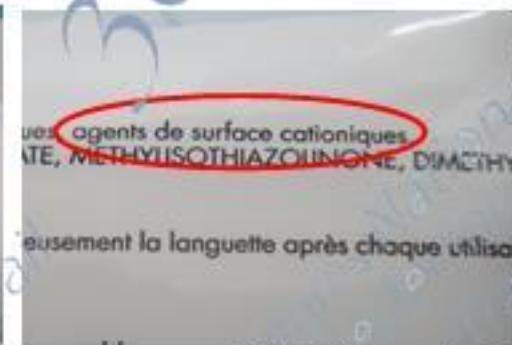
- désinfectants, détergents (milieu hospitalier : nettoyage des instruments, des sols et surfaces)
- antiseptiques, conservateurs (cosmétiques, savon, lotion corporelle, shampooing, collyre, solution de nettoyage des lentilles de contact...)

Les plus utilisés : le chlorure de benzalkonium, le bromure de cetylpyridinium, le benzododecinium, le cetylpyridinium, le quaternium 15.

Ce sont tous des tensioactifs cationiques, appelés aussi « agents de surface cationiques », appellations fréquemment utilisée sur l'emballages des différents produits.

MAIS les tensioactifs cationiques comprennent aussi les amines protonés, cependant, les plus courants sont les seis d'ammonium.

## Quelques exemples de produits ménagers courants contenant de AQ



### Cif Easy Clean Sols Citron

#### Ingédients

Désinfectant: **Chlorure de Benzalkonium 0,75g pour 100 g.**

<5% : **Agents de surface cationiques, Agents de surface non-ioniques, Phosphates, Parfum, Limonene.**

# Quelques exemples de produits cosmétiques couramment utilisés contenant des AQ

## ◆ Les après-shampoings :



Shampooing professionnel – expert nutrition de Franck Provost®

→ hydroxypropyltrimonium chloride

## ◆ Les shampoings :



L'huile merveilleuse – Ultra doux de Garnier®

→ cetrimonium bromide

## ◆ Les produits pour le visage :



TriAcnéal – Avène®

→ cetrimonium bromide



BB Cream – Nude magique de L'Oréal®

→ cetrimonium bromide

## **Ammonium quaternaire : différents produits**



## **ONAP, 2008-2011**

	n	%
Produits chimiques	178	56,9
Substances végétales	94	30,0
Animaux	23	7,3
Métaux et sels métalliques	9	2,9
Médicaments	5	1,6
Autres	4	1,3

*Aminoniums quaternaires* 48 15,3

*Persulfates alcalins* 27 8,6

*Isocyanates* 26 8,3

*Autres produits de nettoyage* 21 6,7

*Aldéhydes* 9 2,9

*Colles et résines* 9 2,9

*Chloramines* 7 2,2

*Matières plastiques* 5 1,6

*Acides* 4 1,3

*Huiles de coupe* 4 1,3

*Solvants* 4 1,3

*Autres* 3 1,0

*Autres produits de coiffure* 3 1,0

*Chlore* 3 1,0

*Amines* 2 0,6

*Anhydrides d'acide* 2 0,6

*Soude* 1 0,3

# Ammonium quaternaire : épidémiologie

- ◆ Physician diagnosed asthma and new onset asthma according to occupational data after adjustment (multivariate analysis) (n = 543) (Poisson regression analysis)

	Physician diagnosed asthma Adjusted RR [95% CI]	p value	New-onset asthma Adjusted RR [95% CI]	p value
<b>Tasks and occupational exposures</b>				
Quaternary ammonium compounds *				
Not exposed	1			
Exposed	5.67 [1.58-20.36]	0.008	11.88 [1.26-111.92]	0.030
Chlorinated/bleach **				
Not exposed	1			
Exposed	0.91 [0.48-1.72]	0.793	2.00 [0.60-5.78]	0.200
Latex glove *				
Not exposed	1			
Exposed	0.81 [0.42-1.55]	0.530	0.60 [0.22-1.64]	0.323
Glutaraldehyde *				
Not exposed	1			
Exposed	0.91 [0.50-1.65]	0.773	1.27 [0.50-2.21]	0.614
Spray use at work ***				
Not exposed	1			
Exposed	0.91 [0.50-1.65]	0.024	0.54 [1.19-25.65]	0.028
Disinfection tasks ***				
Not exposed	1			
Exposed	2.5 [1.15-7.04]	0.048	4.55 [1.19-17.26]	0.026
Cleaning tasks **				
Not exposed	1			
Exposed	2.17 [1.00-4.70]	0.017	6.63 [1.24-35.40]	0.027
Dilution of disinfection products **				
Not exposed	1			
Exposed	3.27 [1.24-8.62]	0.018	1.23 [0.47-3.21]	0.670
Soaking solutions preparation **				
Not exposed	1			
Exposed	1.53 [0.83-2.84]	0.158		

\* Variables in the model for product exposures: gender, age, atopy, BMI, tobacco consumption status, quaternary ammonium compounds, latex gloves, chlorinated/bleach use, glutaraldehyde

\*\* Variables in the model for tasks: gender, age, atopy, BMI, tobacco consumption, latex gloves, task

# AQ: épidémiologie

## ◆ Symptôme en fonction de la tâche:

Physician diagnosed asthma and new onset asthma according to occupational data after adjustment (multivariate analysis) (n = 543) (Poisson regression analysis)

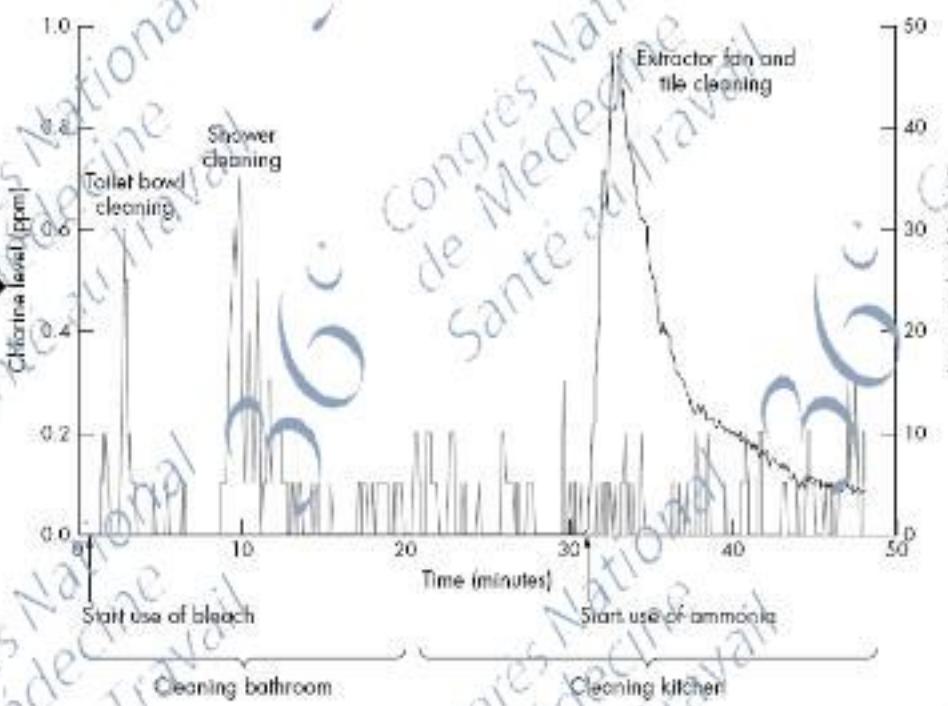
	Physician diagnosed asthma Adjusted RR [95% CI]	p-value	New-onset asthma Adjusted RR [95% CI]	p value
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Exposed	5.67 [1.58-20.36]	0.008		
Chlorinated/bleach *	1			
Not exposed				
Exposed	0.91 [0.48-1.72]	0.793		
Latex glove *	1			
Not exposed				
Exposed	0.81 [0.42-1.55]	0.530		
Glutaraldehyde *	1			
Not exposed				
Exposed			0.60 [0.22-1.64]	0.323
Spray use at work **	1			
Not exposed				
Exposed	1.91 [0.50-1.66]	0.773		
Disinfection tasks **	1			
Not exposed				
Exposed	2.94 [1.15-7.04]	0.024		
Cleaning tasks **	1			
Not exposed				
Exposed	2.17 [1.00-4.70]	0.048		
Dilution of disinfection products	1			
Not exposed				
Exposed	3.27 [1.24-8.62]	0.017		
Soaking solutions preparation **	1			
Not exposed				
Exposed	1.53 [0.83-2.84]	0.163		
			1.23 [0.47-3.21]	0.670

\*Variables in the model for product exposures: gender, age, atopy, BMI, tobacco consumption status, quaternary ammonium compounds, latex gloves, chlorinated/bleach use, glutaraldehyde

\*\*Variables in the model for tasks: gender, age, atopy, BMI, tobacco consumption, latex gloves, task

# Cleaning agents : Diagnosis and treatment

## ◆ Airborne measurement :



Pattern of personal airborne chlorine and ammonia exposure (5-second time weighted average) during domestic cleaning work. The graph corresponds to a 35 year old woman with a history of 26 years in domestic cleaning work, currently employed in one home for cleaning eight hours weekly. Chlorine and ammonia concentrations in ppm are indicated by the grey line and the black line, respectively. Recommended occupational exposure limits (15-minute time weighted average) amount to 0.5 ppm and 35 ppm for chlorine and ammonia, respectively.

## Cleaning agents :

### ◆ **Symptoms : New onset of asthma**

✓ 43 female domestic cleaners (aged 49)

✓ Recent history of asthma :

Asthma attack

Shortness of breath

Chronic bronchitis

✓ Daily change in symptoms and PEF

✓ Diagnostic based

- on computerised diagnosis system  
- on expert occupational asthma

2 weeks study

## Cleaning agents :

- ◆ **Symptoms :**

- **Lower respiratory symptoms related with working day**

**Exposure to bleach**

**OR [IC]**

**2.5 [1.1-5.8]**

**Degreasing spray**

**2.6 [1.1-6.6]**

**Air fresheners spray**

**6.5 [2.1-20]**

**Only 30% scored positively for occupational asthma**

# Cleaning agents : Diagnosis and treatment

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## ◆ RADS:

- (Nested) case-control study of female cleaners (30-65 y)
- 40 cases (asthma or chronic bronchitis) – 155 controls
  - ✓ Higher risk of asthma if use of bleach (dose-related)
  - ✓ Higher risk of asthma if reported inhalation incident (frequent !)
- RADS
- Inadequate mixture of bleach with ammonia or hypochloria acid → free chlorine or chloramine

# Cleaning agents : Diagnosis and treatment

## ◆ Symptoms : Work exacerbated asthma at work

- 25 women with asthma vs 19 without asthma
- 12 weeks study
- No effect on PEF:
  - ✓ After cleaning, in the 2 groups
- Change in number of lower respiratory symptoms
  - ✓ Significant in the asthma groups

Cleaning activities → increased lower respiratory symptoms in asthmatic (independently of the chemical, severity of exposure, duration of cleaning).

# Diagnostic

- ◆ Symptoms : **Work associated irritable larynx syndrome (WILS)**
  - 304 patients (2002-2006) for respiratory symptoms at work
    - ✓ 50 : Occupational asthma
    - ✓ 40 : Work exacerbated asthma
    - ✓ 30 : WILS
    - ✓ 31: respiratory tract irritation

## **WILS:**

**Dysphonia: 86%**

✓ **Cough: 76%**

✓ **Laryngeal stridor: 1%**

✓ **Female**

**GERD**

# **Les huiles essentielles**

# Mesure de la concentration dans l'air de limonène lors de l'utilisation du spray.

- ◆ **Deuxième méthode** : mesure directe dans l'air par un appareil de photo-ionisation ppbRAE3000® Katrem®. 10 mesures ont été réalisées.
- ◆ **Bruit de fond** : réalisé au préalable
  - dans une cabine de 9 m<sup>3</sup> : une pulvérisation est réalisée dans chaque angle de la pièce, bras tendu à environ 1m80 du sol, soit 4 pulvérisations
  - d'après les recommandations du fabricant, 6-8 pulvérisations pour une pièce de 25 m<sup>3</sup>.
  - mesure de la concentration de limonène dans l'air de la cabine toutes les 30 secondes pendant 30 minutes.

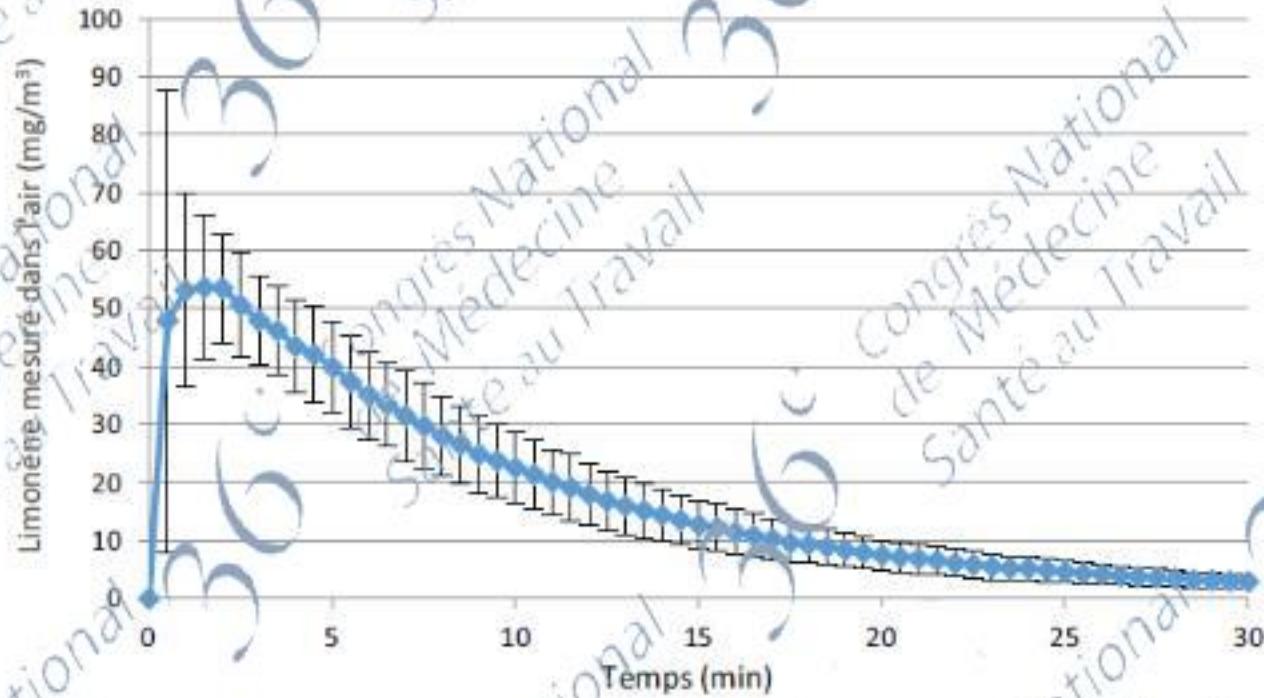


pulvérisation

Appareil de photo-ionisation  
ppbRAE3000® Katrem® France

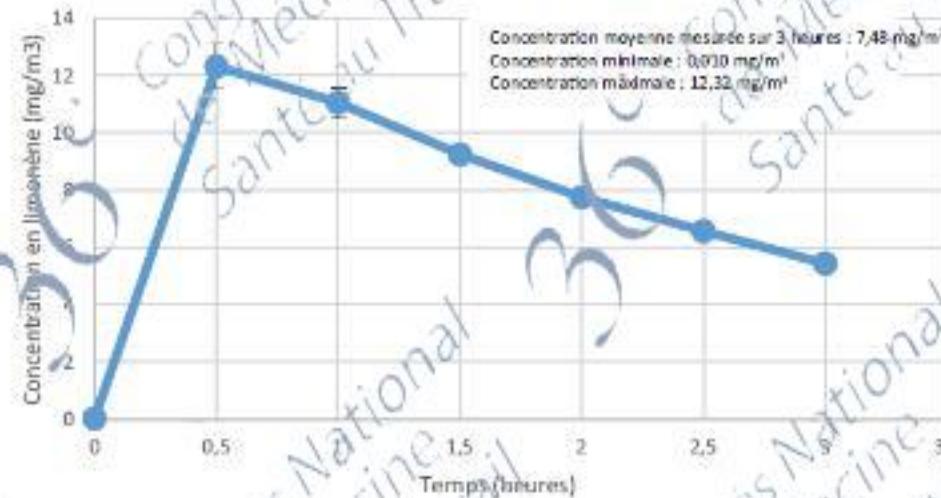
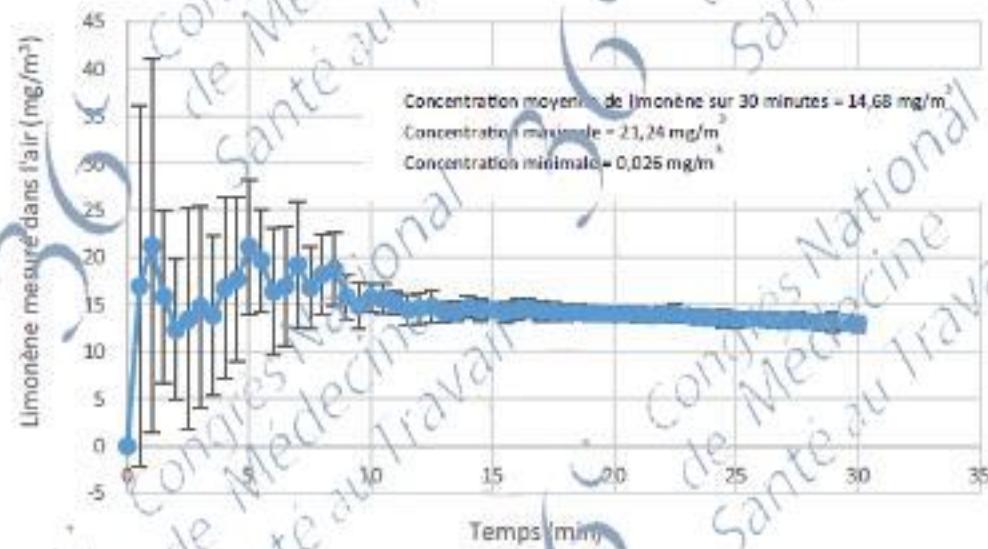


# Concentration of limonene in a room of 9 m<sup>3</sup> after 4 sprays



Average concentration of 15 mg / m<sup>3</sup>

# Concentration of limonene in a room of 42 m<sup>3</sup>



- ANSES ( french) norm : 450 µg/m<sup>3</sup>
- European Norm: 200-300 µg/m<sup>3</sup>

# L'EVICTION



# **Recommendations**

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Although allergens may contribute to asthma symptoms in sensitized patients, allergen avoidance is not recommended as a general strategy for asthma.

These strategies are often complex and expensive, and there are no validated methods for identifying those who are likely to benefit.

**Gina 2014**

## **Tertiary environmental control**

- The majority of single preventive measures of indoor allergen control fail to achieve clinically relevant improvement of asthma and rhinitis.
- Standard procedures for control of indoor allergens in tertiary prevention of rhinitis or asthma are not advisable for public health
- In patients allergic to furred animals who have symptoms on contact with the allergen, animal avoidance is recommended
- In low-income settings with a high load of pollutants (and allergens), a multifaceted intervention may be useful
- Total avoidance of occupational agents is recommended in sensitized subjects
- Occupational agent control may be useful when total avoidance is not possible

## **Eviction : les questions ?**

- ◆ **Les métanalyses avec les études d'éviction sont très difficiles en raison de leur hétérogénéité**

Platts-Mills, JACI 2008

Mac Donald C. et al, Envir Health Perspect 2007

- ◆ **Certaines études ne sont pas intégrées dans la dernière métanalyse**

- **Etudes d'éviction globale : « Multifaced Intervention study »**

de Blay F, Barnig C., Allergy 2008

Platts-Mills T, JACI 2008

## Eviction : les questions ?

### ◆ Pourquoi les études sont négatives ?

1. Celles où il n'y a pas de réduction des allergènes
2. Les méthodes de mesure de l'exposition sont imprécises
3. On pense que les allergènes sont uniquement dans le matelas → ce qui n'est pas le cas
4. **Les méthodes d'éviction doivent être globales**
5. **Les conseils doivent être individualisés**
6. **Il existe des polluants non allergénique : « biotope »**
7. **La réponse à l'allergène varie d'un individu à l'autre**

# **Eviction globale: Conseiller Médicaux en Environnement intérieur**

- ◆ N: 378 patients, Marseille, Montpellier, Paris, Strasbourg.
- ◆ Fréquence de suivi des conseils

	Groupe A	Groupe B	p
Housse de matelas	79,6	99,4	0,06
Laver des oreillers	62,0	94,2	10-4
Laver du duvet	63,1	94,1	10-4
Changer les oreillers	3,2	9,0	0,01
Changer le sommier	18,7	30,8	0,007
Retirer les tapis	26,2	30,3	0,37
Traiter les tapis	40,6	48,1	0,14

de Blay F et al, Allergy 2003

# Éviction globale:

## Conseiller Médicaux en Environnement Intérieur

- ◆ Efficacité sur les concentration d'allergènes

	Groupe A		Groupe B	
	Initial	Final	Initial	Final
Matelas	67,7	46,3*	44,9	20,5*
Sommier	107,0	106,5	83,8	22,9*
Sol	14,5	12,2	15,8	6,3*

\* Différence significative

# Prévention tertiaire aux USA

- ◆ **4 études:**

- **Proof of concept:**

- ✓ **Carter M. et al, JACI 2001**

- **Pivot:**

- ✓ **Morgan W. et al, NEJM 2004**

- **confirmatoires:**

- Krieger J. et al, Am J. Public Health, 2005**

- ✓ **Eggelston P. et al, Ann Allergy Asth Imm, 2005**

➔ **Toutes portent sur les enfants astmatiques**

# Éviction Globale

- ◆ **n = 937, age : 5 - 11 ans**
- ◆ **7 villes américaines, population défavorisée, 2 ans de suivi**
- ◆ **Éducation, tabac, éviction des allergènes**
- ◆ **Asthme allergique tests cutanés positifs( > 2mm du témoin) avec au moins 2 visites aux urgences ou 1 hospitalisation pour asthme dans les 6 mois précédents**

***Morgan et al, NEJM, 2004***

## Eviction globale

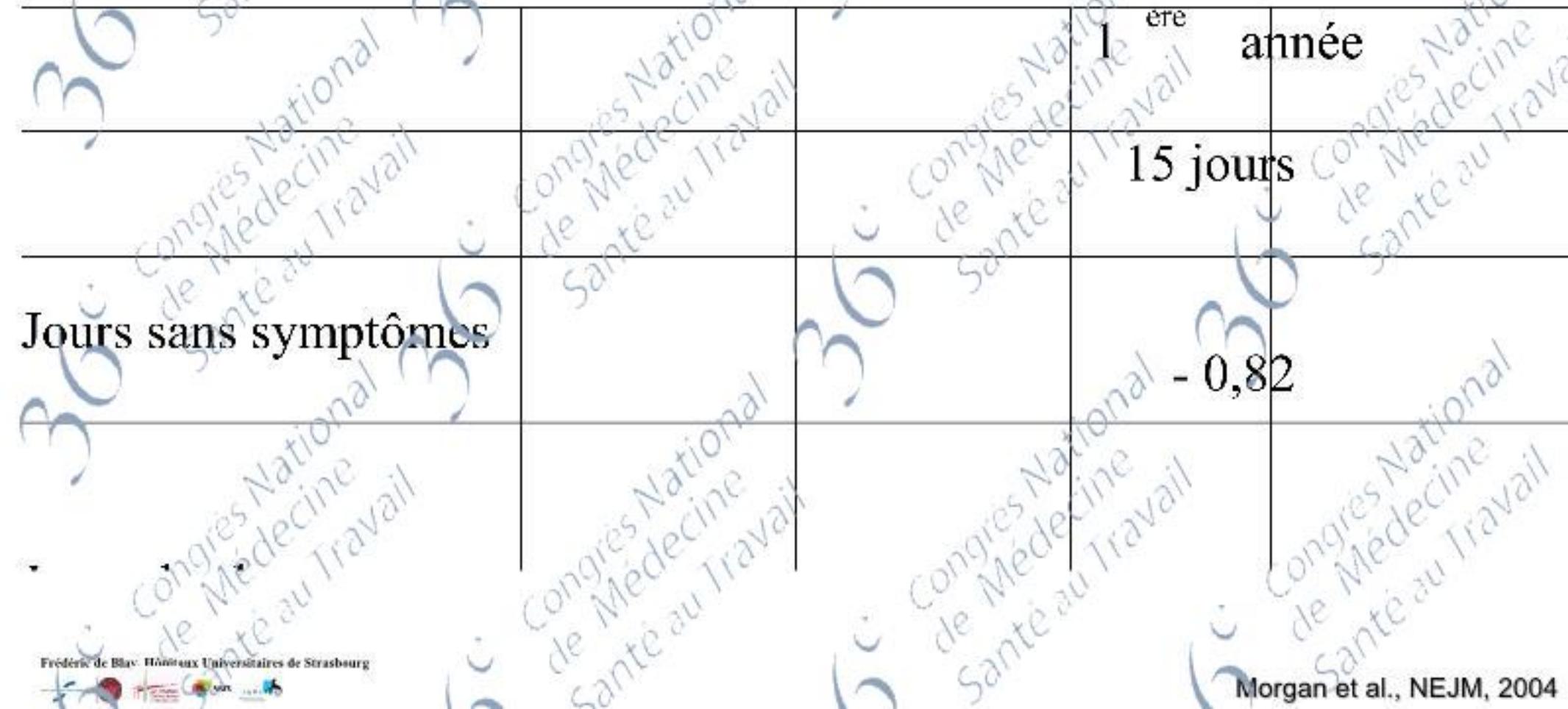
### ◆ Effet de l'intervention sur l'exposition aux allergènes

Allergènes	Année 1		Année 2	
	gr éviction (n=444)	gr contrôle (n=425)	gr éviction (n=407)	gr contrôle (n=414)
Bla g 1 matelas	-44	-34	-51	-46
Der f 1 matelas	-59*	-14	-49*	-25
Der p 1 matelas	-37*	-18	-37	-25
Fel d 1 matelas	-28*	+15	-14*	+30
Bla g 1 sol	-53*	-19	-64*	-47

% par rapport à concentration basale

\* Différence significative

# Éviction globale des allergènes



# Éviction globale

Table 4. Relationship between Reductions in Allergens and Changes in Asthma-Related Morbidity among Children in the Intervention Group

Variable	Year 1 (n=444)		Year 2 (n=407)	
	Change $\pm$	P Value	Change $\pm$	P Value
<b>Maximal no. of days with symptoms per 2-wk period</b>				
Bla g1, floor	-0.25 $\pm$ 0.063	< 0.001	-0.41 $\pm$ 0.066	< 0.001
Der f1, floor	-0.29 $\pm$ 0.071	< 0.001	-0.15 $\pm$ 0.066	0.02
Der f1, bed	-0.23 $\pm$ 0.080	0.004	0.15 $\pm$ 0.076	0.04
Der p1, bed	-0.21 $\pm$ 0.098	0.03	-0.18 $\pm$ 0.089	0.04
<b>No. of unscheduled ED or clinic visits</b>				
Bla g1, floor	-0.051 $\pm$ 0.014	< 0.001	0.093 $\pm$ 0.014	< 0.001
Der f1, floor	-0.059 $\pm$ 0.016	< 0.001	-0.044 $\pm$ 0.015	0.003

## **Eviction globale**

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- ◆ **Enfin pris en charge aux USA**
- ◆ **Dans le guide NAEPP (National Asthma Education and Prevention Program) :**
  - **« to reduce exposure to allergens and pollutants or irritants to which they are sensitive »**
  - **« endorse an individually-tailored, multi-faceted approach to reducing relevant exposures »**

# **CMEI – Validation – Bourgogne MFA**

- Evaluation prospective du CMEI en Bourgogne auprès de 546 patients, neuf mois après la visite : réduction significative de la consommation de médicaments.

L. Blanchon<sup>1</sup>, M. Bochaton<sup>1</sup>, P. Scherer<sup>2</sup>, I. Sullerot<sup>3</sup>, G. Reboux<sup>4</sup>, P. Bonniaud<sup>5</sup>, G. Gardin<sup>1</sup>,

*1 Mutualité Française Bourgogne - Dijon (France) 2 Allergologue - Chalon (France) 3 Allergologue – Sens(France) 4 CHU - Besançon (France) 5 CHU - Dijon(France)*

# CMEI - Validation Bourgogne

- ◆ **Changement de comportement des patients par :**
  - une mise en œuvre durable des conseils
  - une diminution significative de la consommation médicamenteuse à neuf mois.
- ◆ **44% des patients expriment spontanément un changement positif de leur état de santé.**
  - Pour les anti-histaminiques : Arrêt du traitement = 25% des patients
  - Diminution du traitement = 19% des patients
  - Pour la rhinite :
    - Arrêt du traitement = 42% des patients
    - Diminution du traitement = 19% des patients
- ◆ **63% expriment une amélioration de l'état de santé.**
- ◆ **15% affirment mieux respirer (nez moins pris).**

## **EVICTION GLOBALE**

- ◆ **Parmi 20 études:**

- **Réduction de 21 jours avec symptômes par an**
- **Réduction de jours de classe manquée de 12,3/an**  
[ext: 3.4 à 31.2]
- **Réduction des visites aux urgences pour asthme 0,57/an**  
[extr: 0.33 à 1.71]

# COMMENT PROGRESSER ?

## ◆ Chez l'enfant

- **6 – 12 ans**
- **3 groupes**

### Groupe 1 : (103)

Asthme avec exacerbations sévères et des allergies multiples

- Sensibilisation aux pneumallergènes
- Allergies alimentaires
- Eosinophiles

### Groupe 2 : (72)

Asthme et obstruction bronchique

- Plus gros
- VEMS
- Plus de neutrophiles

### Groupe 3 : (140)

Asthme léger

- Moins de sensibilisation
- Asthme contrôlé par des corticoïdes inhalés

# Eviction

	C1 n (%)	C3 n (%)	p
Rural	0 (0)	22 (12,6)	0,0005
Ville ou Banlieue	55 (100)	152 (87,4)	0,0005
Maison	2 (3,6)	31 (17,8)	0,0005
Appartement	37 (67,3)	102 (58,6)	0,0005
Logement social	17 (30,9)	41 (23,6)	0,0005
VMC	33 (60)	92 (52,9)	0,0085
Ventilation naturelle	22 (40)	81 (46,5)	0,006
Plantes	23 (41,8)	71 (40,8)	0,0005
Tabagisme actif	3 (5,4)	20 (11,5)	0,0015
Tabagisme passif	8 (14,6)	58 (33,3)	0,001
Insecticides	0 (0)	14 (8,1)	0,008
Rhinite	55 (100)	72 (41)	0,0005
Asthme	18 (32)	150 (86)	0,0005
Asthma Step 4/5*	1 (1,8)	71 (40,8)	0,0005

\* According to GINA guideline 2016

## **CONCLUSION**

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- ◆ **La prévention tertiaire globale a fait la preuve de son efficacité**
- ◆ **L'utilité des CMEI est de plus en plus reconnu**
- ◆ **Cependant des études sur des populations plus ciblées permettraient sûrement d'augmenter l'efficacité**
  - **Les enfants et les adultes jeunes où le rôle des allergènes dans l'apparition des symptômes seraient les patients de choix**
  - **Importance de déterminer le phénotype du patient et les caractéristiques de l'habitat**

## **Conclusion**

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- ◆ **Les COV ne semblent pas être des allergènes ou des haptènes**
- ◆ **Certains polluants chimiques sont plus présents à l'intérieur qu'à l'extérieur**
- ◆ **Le NO<sub>2</sub> et le formaldéhyde apparaissent comme des facteurs de potentialisation des symptômes chez les asthmatiques allergiques**

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