



同济医院



UNIVERSITÉ DE STRASBOURG



Polluants intérieurs et asthme allergique

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Pôle de pathologie thoracique

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Université de Huazhong, Wuhan, Chine

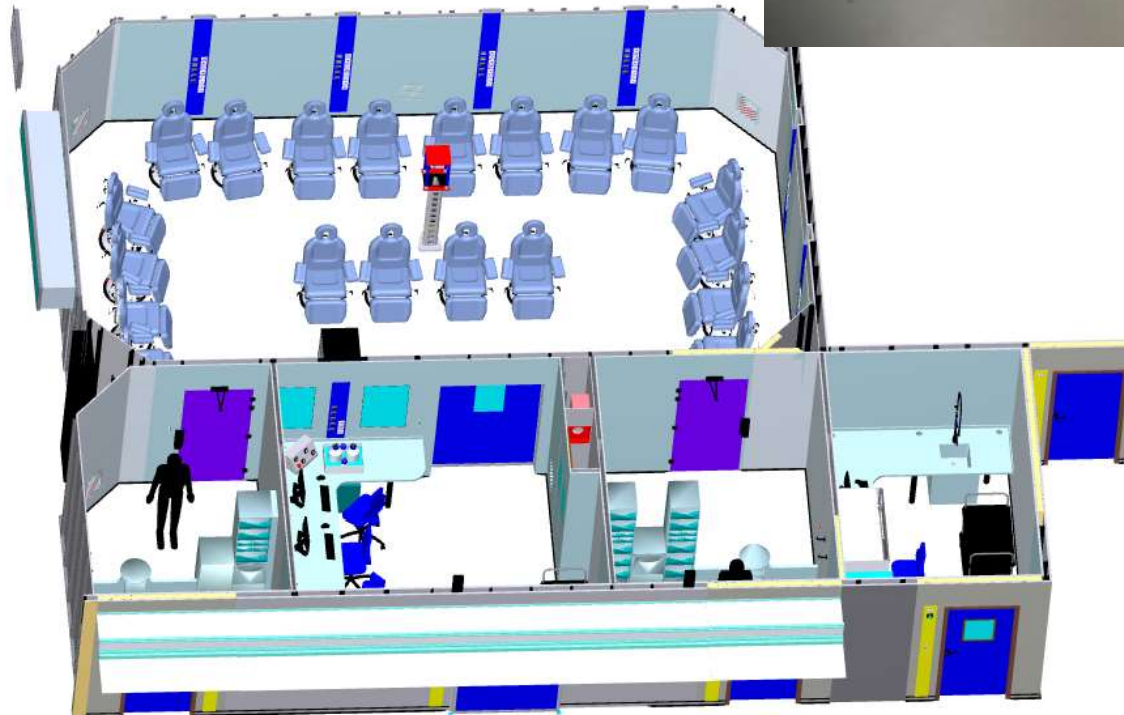
Liens d'intérêt

- ◆ **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)**

Les allergènes

Exposure chamber

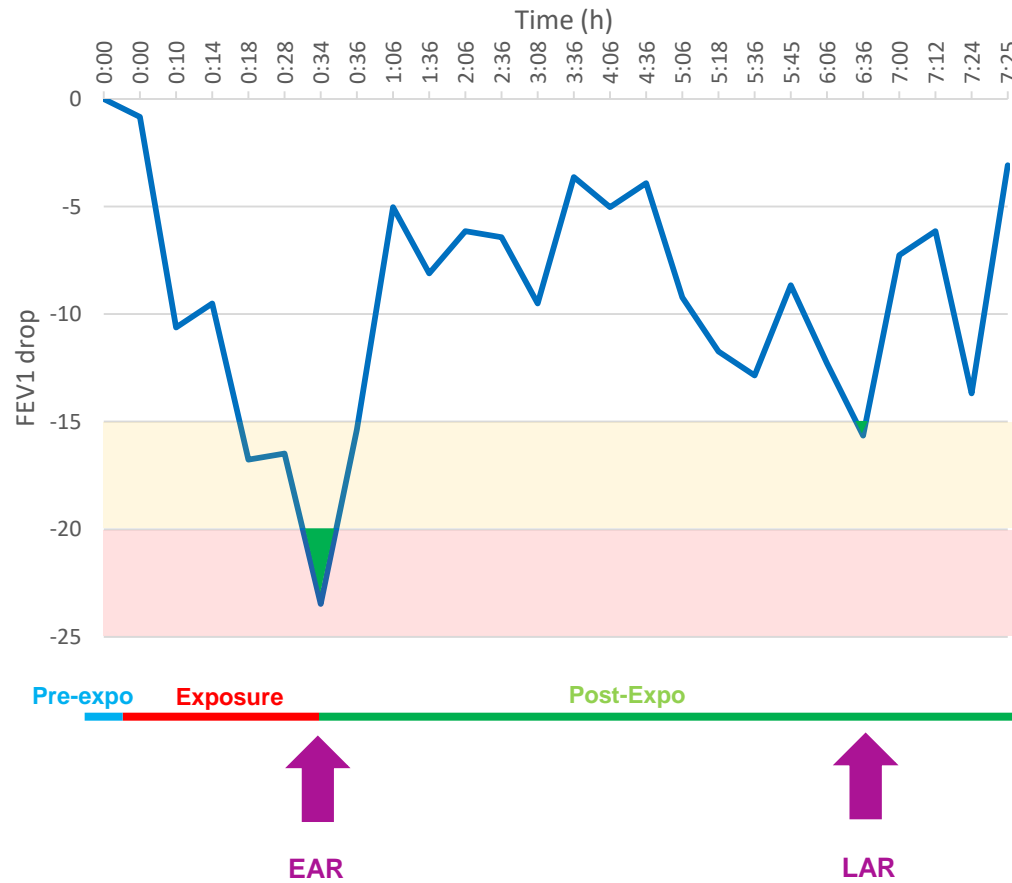
- 65 m², 147 m³
- 20 seats



EXPOSURE Chamber Spirometry and questionnaires on the tablets



VO-16-K-0168



Group 2 patients

- Exposed to airborne mite allergen concentrations which induced more than 60% of EAR or LAR in mite allergic patients:
 - No change in bronchial symptoms
 - No significant bronchial response (Early or late phase)
 - No rhinoconjunctivitis symptoms:
 - TNSS/ RTSS/ EVA: no significant change
 - TOSS/EVA: no significant change

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
Dodécane, pentane, nhexane...

Terpènes
Limonène, α -pinène

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

Hydrocarbures aliphatiques cycliques
Hexane, méthylhexane...

Phtalates
Diméthylphtalate, dibutylphtalate...

Cétones
2 butanone, cyclopentanone...

Aldéhydes
Formaldéhyde, acétaldéhyde, propanal...

Acides
Acide butyrique, acide
propanoïque...

Ethers de glycol
Éthylèneglycol...

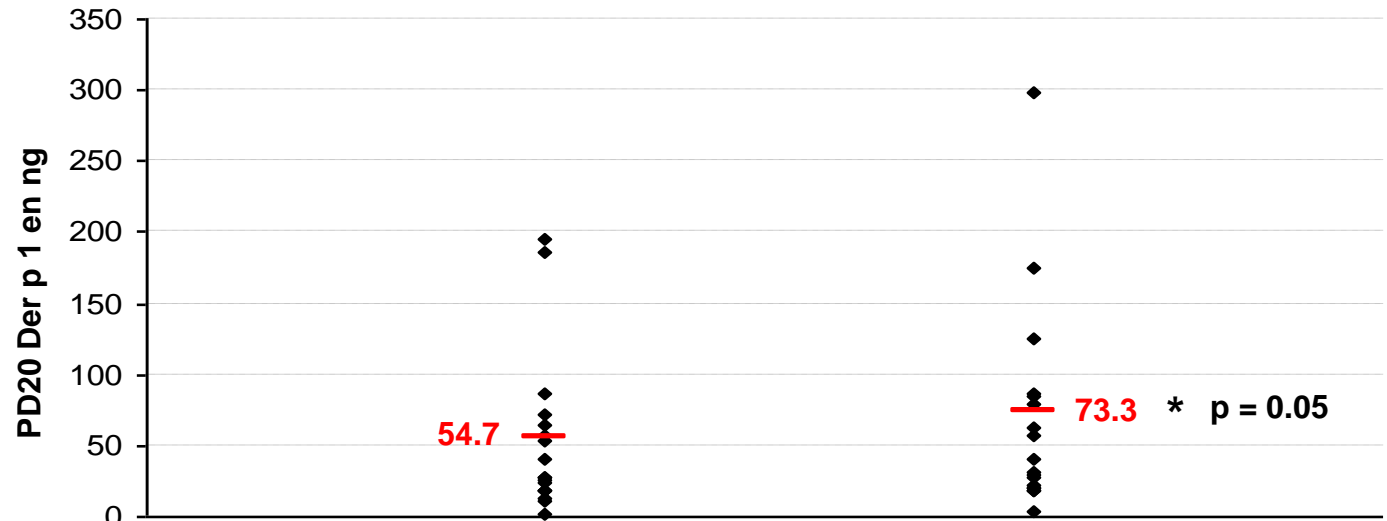
Modification de la réponse bronchique allergique

-Etude expérimentale :



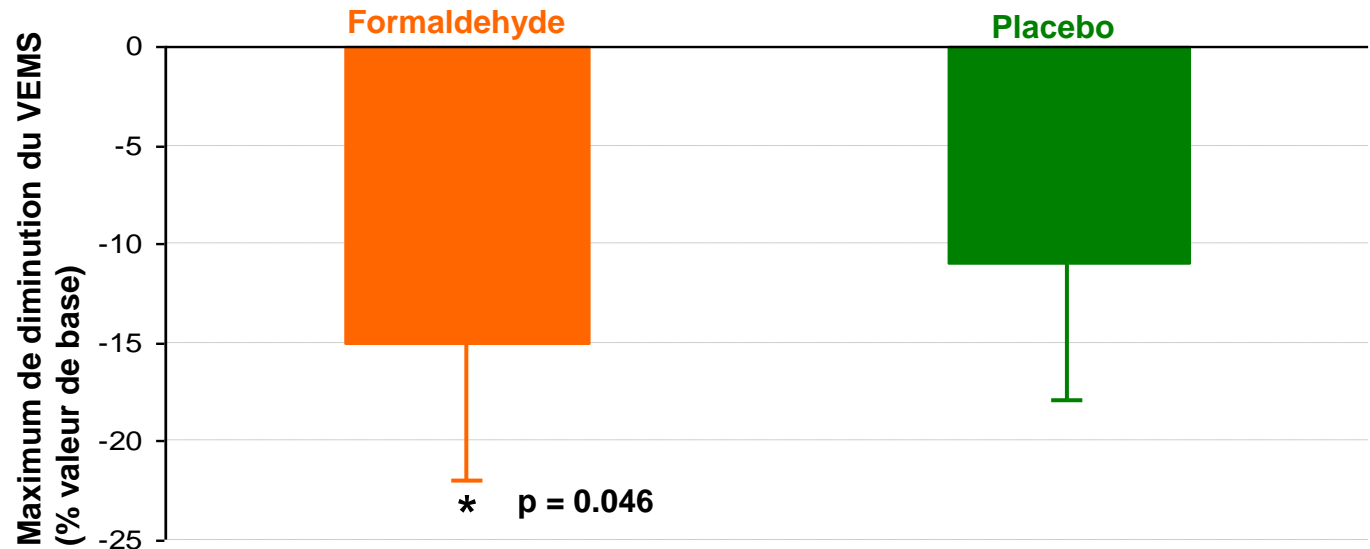
- 19 sujets : asthme intermittent aux allergènes d'acariens
- Exposition : $100\mu\text{g.m}^{-3}$ de FA pendant 30 min
- TPB à Dpt consécutif à l'exposition

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

- ◆ **Particles < 2.5 μm (PM 2.5)**
- ◆ **NO₂**
- ◆ **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

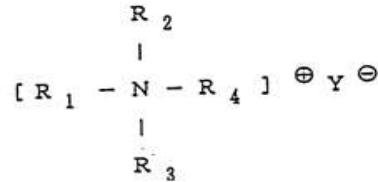
Type of surface	Products	Purposes of use	Typical frequency of application
Hard floors (stone, tiles, marble, synthetic)	Multi-use cleaners, floor cleaners, bleach	Remove accumulated dust and dirt, surface care, disinfection, give shine	Weekly
Wooden floors	Floor cleaners suitable for wood, floor waxes	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

- ◆ **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 + O₃ → Formaldehyde)**

Les ammoniums quaternaires (AQ)

◆ Formule générale :



◆ Largement utilisés :

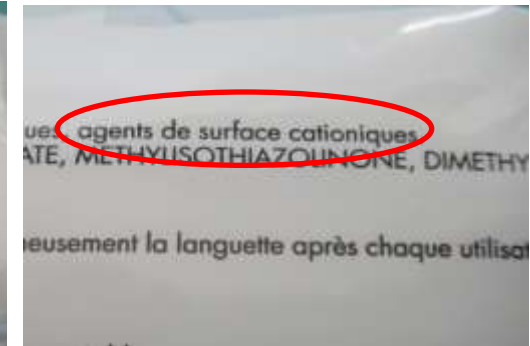
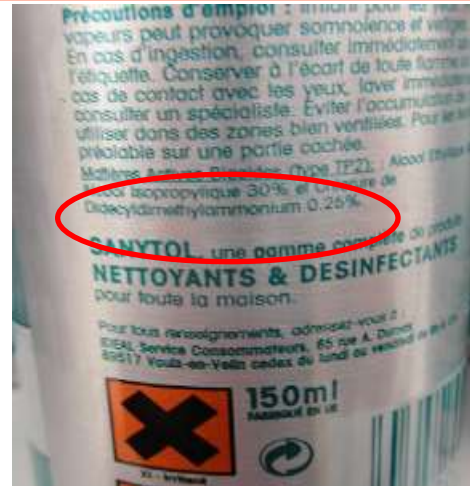
- désinfectants, détergents (milieu hospitalier : nettoyage des instruments, des sols et surfaces)
- antiseptiques, conservateurs (cosmétiques, savon, lotion corporelle, shampooing, collyre, solution de nettoyage des lentilles de contact...)

Les plus utilisés : le chlorure de benzalkonium, le bromure de cetrimonium, 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 sels d’ammonium.

Quelques exemples de produits ménagers courants contenant de AQ



Cif Easy Clean Sols Citron
Ingrédients
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



Mesure de l'exposition: Ammonium quaternaire

Results of DDAC sampling in the indoor Lyautey Hospital atmosphere

No. support	XAD-2 resin			Volume of air sampling	Sampling time	Working station	[DDAC]
	DDAC						C ($\mu\text{g}/\text{ml}$)
	C_x ($\mu\text{g}/\text{ml}$)	v (ml)	m (μg)	V (l)	Δt (min)	Description of working station	C ($\mu\text{g}/\text{m}^3$)
110505-01	–	5	<2.80	275.17	272	Floor disinfection Surfanios® 0.25%	<10.18
120505-01	–	5	<2.80	1,121.12	1,165	Disinfection container Surfanios® 0.25%	<2.50
120505-02	–	5	<2.80	282.21	276	Floor disinfection Surfanios® 0.50%	<9.92
130505-01	–	5	<2.80	1,089.50	1,083	Disinfection container Surfanios® 0.5%	<2.57
160505-01	–	5	<2.80	250.33	251	Floor disinfection Surfanios® 0.75%	<11.19
170505-01	–	5	<2.80	999.98	995	Dinsinfection container Surfanios® 0.75%	<2.80
170505-02	–	5	<2.80	1,300.00	1,250	Dinsinfection container Ampholysine +® 0.50%	<2.15
180505-01	–	5	<2.80	1300.00	1250	Dinsinfection container Ampholysine +® 0.50%	<2.15
200505-01	–	5	<2.80	14.94	15	Spray disinfection Amphospray 41®	<187.42

It was not possible to measure airborne QAT.

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
<i>Ammoniums quaternaires</i>	48	15,3
<i>Persulfates alcalins</i>	27	8,6
<i>Isocyanates</i>	26	8,3
<i>Autres produits de nettoyage</i>	21	6,7
<i>Aldéhydes</i>	9	2,9
<i>Colles et résines</i>	9	2,9
<i>Chloramines</i>	7	2,2
<i>Matières plastiques</i>	5	1,6
<i>Acides</i>	4	1,3
<i>Huiles de coupe</i>	4	1,3
<i>Solvants</i>	4	1,3
<i>Autres</i>	3	1,0
<i>Autres produits de coiffure</i>	3	1,0
<i>Chlore</i>	3	1,0
<i>Amines</i>	2	0,6
<i>Anhydrides d'acide</i>	2	0,6
<i>Soude</i>	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
Tasks and occupational exposures				
<i>Quaternary ammonium compounds *</i>				
Not exposed	1		1	
Exposed	5.67 [1.58-20.36]	0.008	11.88 [1.26-111.92]	0.030
<i>Chlorinated/bleach *</i>				
Not exposed	1		1	
Exposed	0.91 [0.48-1.72]	0.793	2.00 [0.69-5.78]	0.200
<i>Latex glove *</i>				
Not exposed	1		1	
Exposed	0.81 [0.42-1.55]	0.530	0.60 [0.22-1.64]	0.323
<i>Glutaraldehyde *</i>				
Not exposed	1		1	
Exposed				
<i>Spray use at work **</i>				
Not exposed	1		1	
Exposed	0.91 [0.50-1.66]	0.773	1.27 [0.50-3.21]	0.614
<i>Disinfection tasks **</i>				
Not exposed	1		1	
Exposed	2.84 [1.15-7.04]	0.024	5.54 [1.19-25.65]	0.028
<i>Cleaning tasks **</i>				
Not exposed	1		1	
Exposed	2.17 [1.00-4.70]	0.048	4.55 [1.19-17.26]	0.026
<i>Dilution of disinfection products**</i>				
Not exposed	1		1	
Exposed	3.27 [1.24-8.62]	0.017	6.63 [1.24-35.40]	0.027
<i>Soaking solutions preparation **</i>				
Not exposed	1		1	
Exposed	1.53 [0.83-2.84]	0.168	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

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)

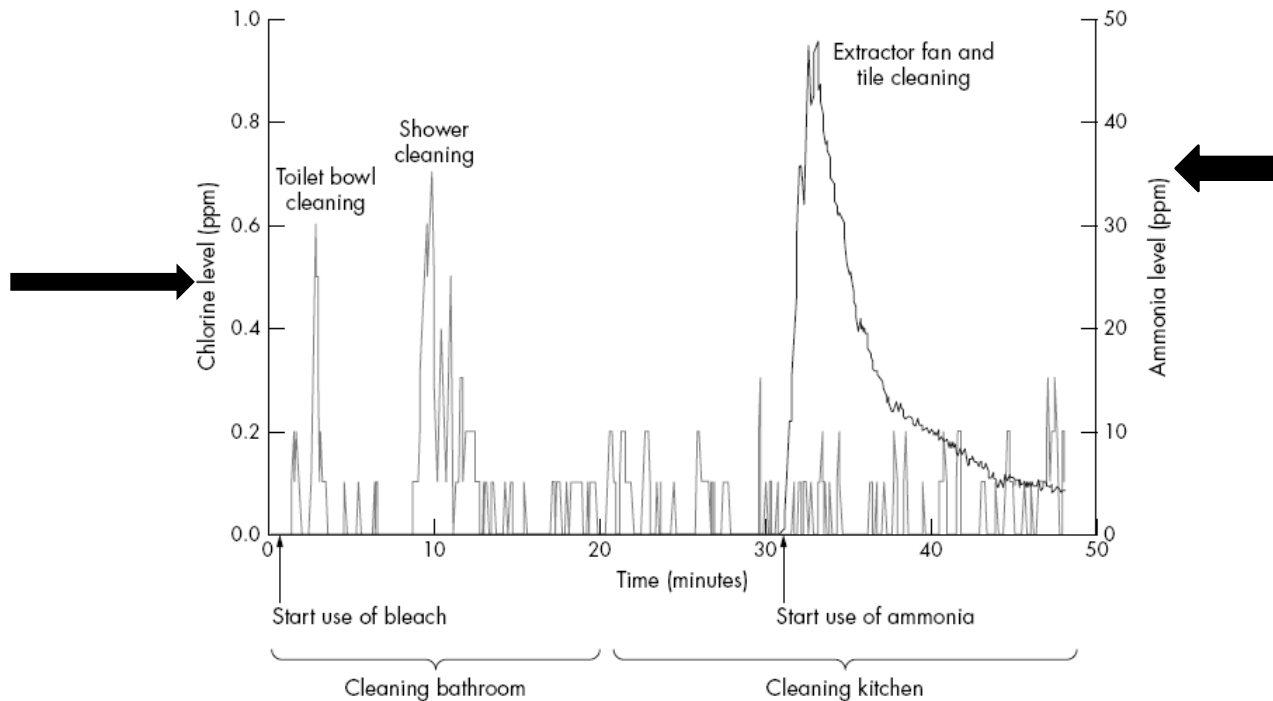
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*Variables in the model for product exposures: gender, age, atopy, BMI, tobacco consumption status, quaternary ammonium compounds, latex gloves, chlorinated/bleach use, glutaraldehyde

** 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 55 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

	OR [IC]
✓ Exposure to bleach	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

◆ 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 m³ : 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 m³.
 - mesure de la concentration de limonène dans l'air de la cabine toutes les 30 secondes pendant 30 minutes.



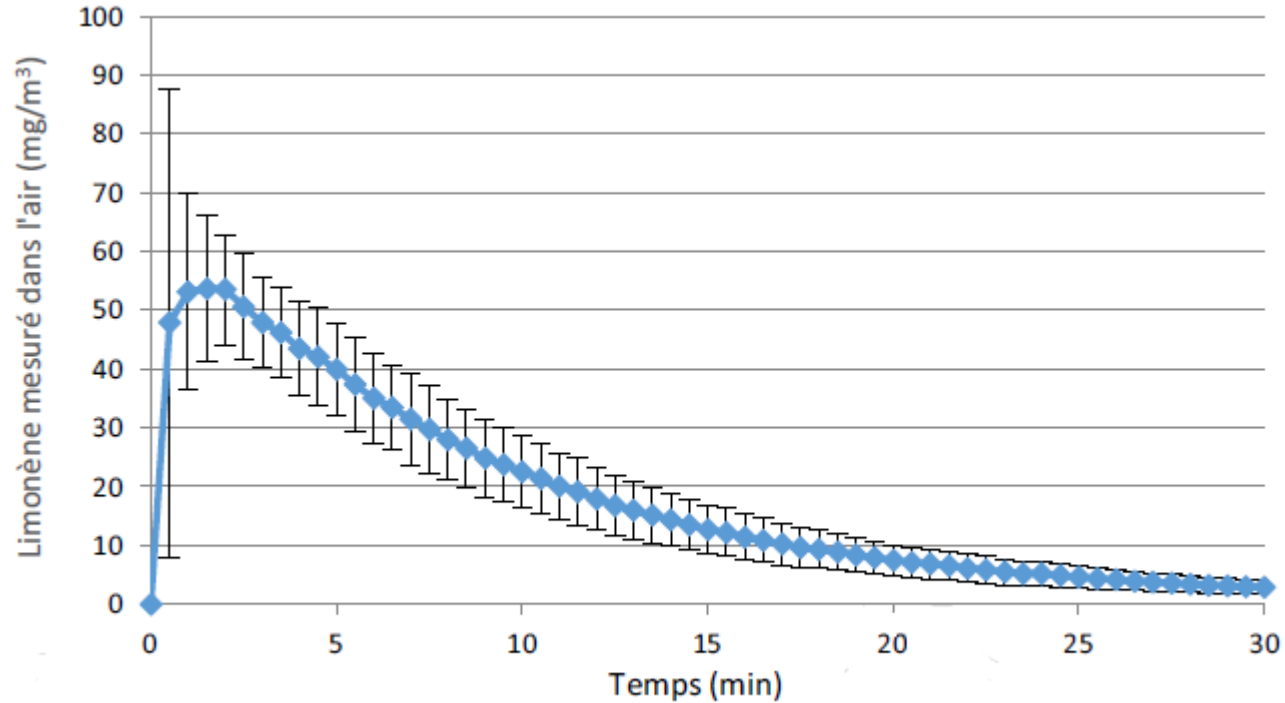
pulvérisation



Appareil de photo-ionisation
ppbRAE3000® Katrem® France

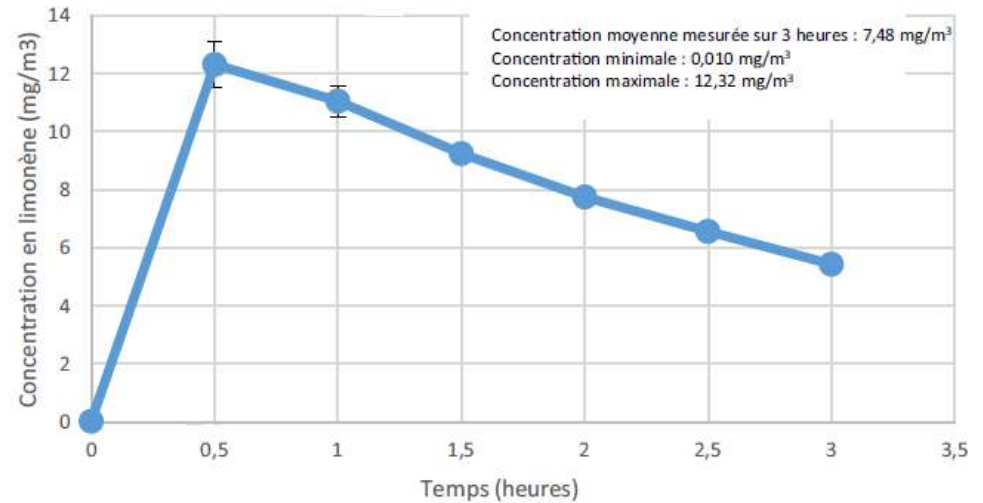
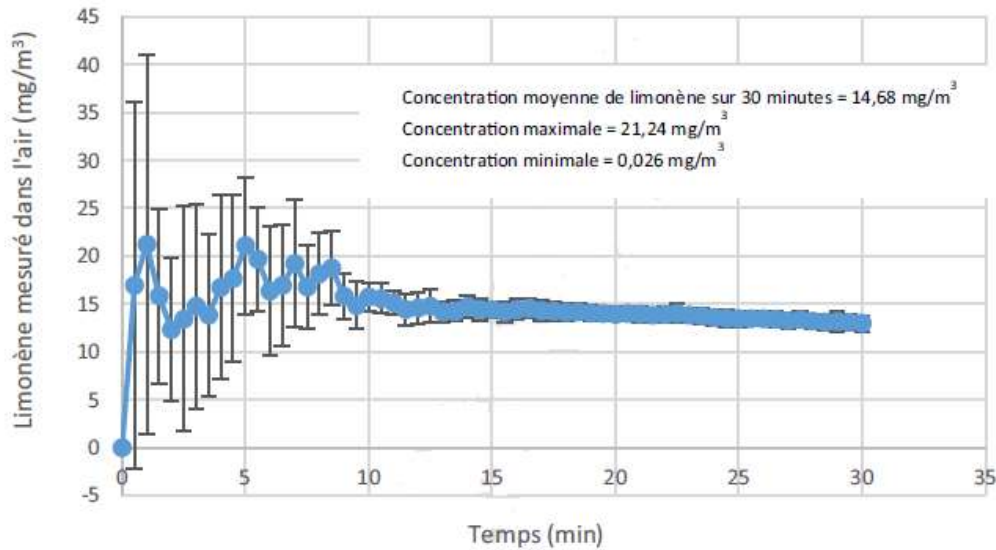


Concentration of limonene in a room of 9 m³ after 4 sprays



Average concentration of 15 mg / m³

Concentration of limonene in a room of 42 m³



- ANSES (french) norm : 450 µg/m³
- European Norm: 200-300 µg/m³

DISCUSSION (2)

◆ Dans la littérature :

→ les TCOV a une concentration de 25 mg/m³ provoquent des réactions bronchospastiques chez les asthmatiques (1), dans notre étude les valeurs de TCOV dépassaient 38 mg/m³.

→ les COV dont le limonène irritant non-spécifique des voies respiratoires(2)

→ corrélation directe entre sa concentration dans l'air intérieur et l'hyper-réactivité bronchique (2)

→ formation de polluants secondaires, réaction du limonène avec l'ozone (3)

(1) HARVING H, AM REV RESPIR DIS 1991; 143:751-754

(2) NORBACK D, Occup Environ Med 1995;52:388-395

(3) ANDERSON SE Toxicology in vitro 2013; 721-730

DISCUSSION (3)

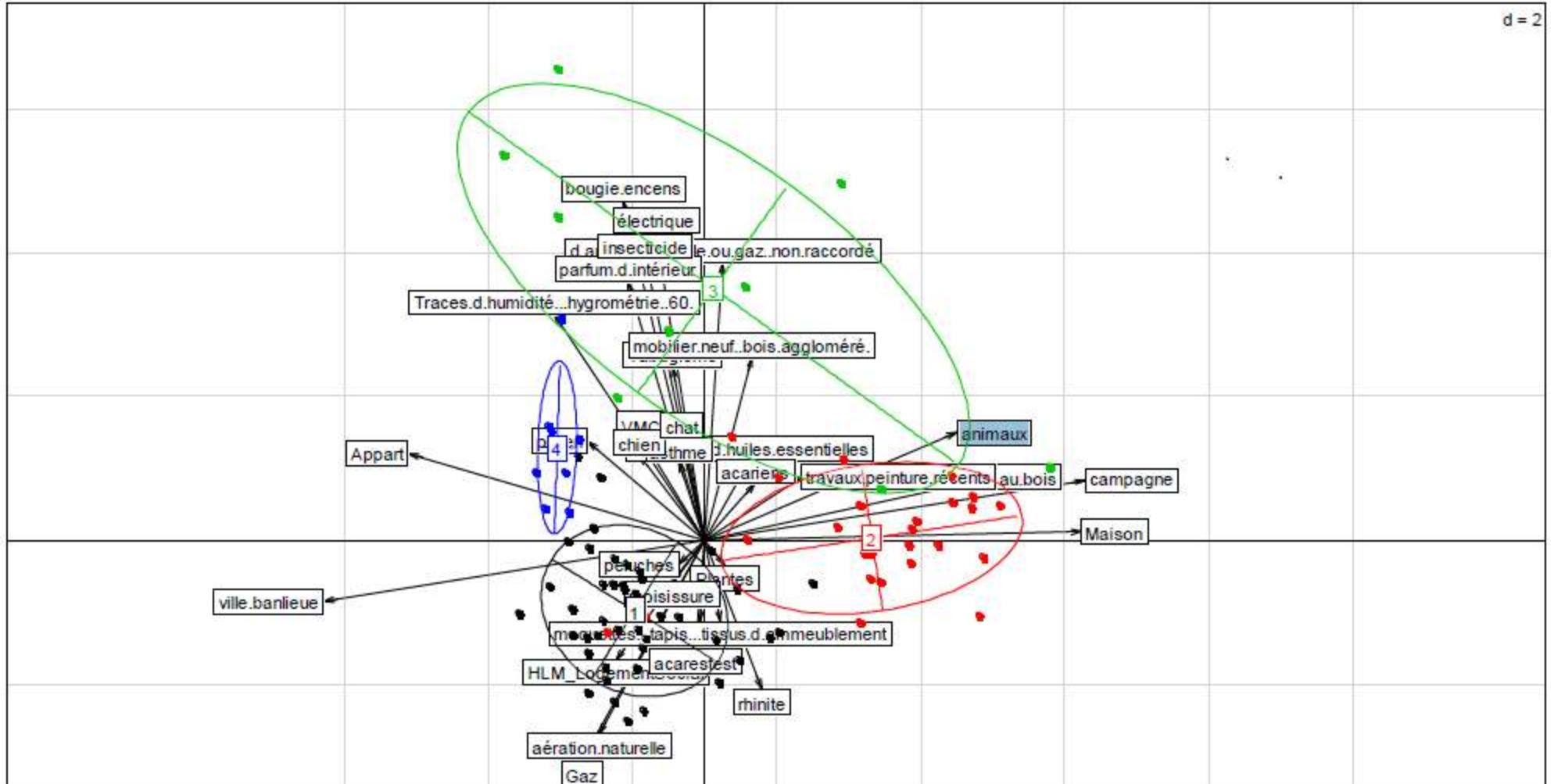
◆ D'après l'ANSES :

- la limite d'exposition à courte durée du limonène est de $450 \mu\text{g}/\text{m}^3$. (limite européenne d'exposition à courte durée issues de l'INDEX 2005).

◆ Dans notre étude :

- La limite d'exposition proposée par l'ANSES est très largement dépassée (10 x).

Home visit : types of housing



Housing types

◆ Different housing types :

- **Group 1 : (55)**

- ✓ Patients in urban or suburban area
- ✓ Apartment
- ✓ Polysensitized (cat, dog, birch pollens)
- ✓ Rug, carpet and green plant
- ✓ Good ventilation and Mechanical ventilation
- ✓ Positive Acares-tests
- ✓ Rhinitis: 100%, Asthma: 42%

Housing types

◆ Différents housing types :

- **Groupe 3 : 174**

- ✓ Patients in urban or suburban area
- ✓ Public housing
- ✓ Central heating with gas
- ✓ Use of insecticides or perfumes
- ✓ Visibles molds
- ✓ Active or passive smoking
- ✓ Recent paintings
- ✓ Less exposed to mite
- ✓ **Asthma: 82%, Rhinitis: 41%**

Types of housing in mite allergic patients

	C1 (rhinitis) N: 55 (%)	C3 (asthma) N: 174 (%)	p
Rural	0 (0)	22 (12,6)	0,0005
Urban or suburban	55 (100)	152 (87,4)	0,0005
Active tobacco	3 (5,4)	20 (11,5)	0,0015
Passive tobacco	8 (14,6)	58 (33,3)	0,001
Insecticides	0 (0)	14 (8,1)	0,008

Indoor chemical were more frequent in the asthmatic group

Conclusion

- ◆ **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 NO₂ et le formaldéhyde apparaissent comme des facteurs de potentialisation des symptômes chez les asthmatiques allergiques**

CONCLUSION

- ◆ **Tous ces éléments semblent plus importants lorsque l'on prend en compte l'exposition dans son ensemble : les enfants, la sensibilisation aux allergènes de l'intérieur, l'humidité, l'ozone, les désodorisants, les peintures, les produits de nettoyage**
- ◆ **La prise en compte de tous ces éléments doivent faire partie de l'interrogatoire d'un asthmatique ou d'un allergique.**

remerciements

Pneumologie, allergologie et pathologie respiratoire de l'environnement

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CONCLUSION

DOCTEUR [REDACTED]
DIPLOMÉ DE LA FACULTÉ DE MÉDECINE DE STRASBOURG
ANCIEN INTERNE EN MÉDECINE GÉNÉRALE
MÉDECIN AÉRONAUTIQUE ET SPATIALE
ANCIEN ATTACHÉ DES HÔPITAUX

N° RPPS



10-04-2013
CONSULTATIONS :
TOUS LES JOURS DE 10 H A 12 H 30 SAUF SAMEDI
ET SUR RENDEZ-VOUS

① Ventoline Ce1

à la demande.

1.

② Pone Ementil spray au 41 bulles enrobées 1.