ULB UNIVERSITÉ LIBRE DE BRUXELLES

Asthme, rhino-conjonctivite et dermatite professionnelle du boulanger (16)

- Clinique d'Immuno-Allergologie du CHU-Brugmann / Fedris

- Dr Joël Thimpont

Conférence postuniversitaire : 25.10.2021

Plan

- Cas clinique
- Ecartement
- Discussion
- Allergènes
- Farine de blé
- IgE spécifiques
- Physiopathologie
- Tests allergiques
- Conclusion
- Urticaire et dermatite de contact professionnel

Cas Clinique : D.L. 30 ans

- Antécédents :
  - « bronchites » avec sifflements respiratoires dans l'enfance
  - Tabac : 10 cigarettes/j (arrêt à 22 ans)
- Histoire clinique
  - 2004 : apprenti boulanger
  - 2007 : boulanger
  - En fin d'apprentissage : symptômes de rhinite (PREO), tous les jours, au travail!
  - 2017 : oppression thoracique – sifflements respiratoires : non pas au travail, mais au réveil. ≥ 1x/sem. Pas de plainte cutanée (UE) ni oculaire (PRL)

Traitement et bilan allergologique (26.03.2018)

- R/ Rupatall® : 1 co/j - Avamys®
- Ventolin® si nécessaire (« très rarement »)
- TCA :
  - Témoin - / histamine positive : 9 mm
  - + : farine de blé (ALK) : 4 mm , + DPT
  - - : alpha-amylase, seigle, sésame, lupin, farine d'avoine, d'orge, soja, latex

Biologie

- DPT : 2.43 kU/l
- Froment (f4) : 3.03 kU/l (N < 0,35)
- Seigle (f5) : 3.01 kU/L
- Orge (f6) : 1.45 kU/L
- Sésame (f10) : 1.51 kU/L
- Sarrasin (f11) : 0.60 kU/L
- Alpha-amylase (k87) : <0.1 kU/L
- Dactyle pelotonné (g3) : 0.63 kU/L
- IgE totales : 160 kU/L (N ?)
- Taux d'éosinophiles sanguins : 440 éléments / mm^3 (N < 300)

TPS

- J1 : journée de contrôle (poudre de lactose): 30 min
  - EFR
  - CP20 (à la 6ème h)
  - Eo expectoration

- J2 : exposé à la farine utilisée au travail
  - Périodes de longueurs croissantes
  - Exposition cumulée de 35 minutes
  - EFR+ (pas de réaction retardée)
  - CP20
  - Eo expectoration

Tableau : Résultats des tests fonctionnels respiratoires

Dates	30/10/2017	17/09/2018 Pré-TPS (J1)	18/09/2018 J2	19/09/2018 Post-TPS	13/05/2019
CVF (% prédite)	4.39 L (98%)	4.30 L (95%)			3.88 L (86%)
VEMS (% prédite)	3.77 L (99%)	3.56L (93%)	- 34%	3.47L (90%)	3.27 L (86%)
VEMS/CVF (%)	85%	83%			84%
FeNO (ppb)	32	67		116	49
Eo Expectoration (%)		1.75	12,7	12.5	
CP_{20} Histamine		4.0 mg/ml	1 mg/ml	1.43 mg/ml	

TPS : Test de provocation bronchique spécifique ; CP_{20} Histamine : concentration d'histamine provocant une diminution de 20% du VEMS

Examen de suivi (13,05,2019)

- Toujours exposé
- R/ 2 doses d'Inuvair®/j et Rupatall*
- Symptômes identiques, ainsi qu'en pratiquant du sport
- Formation en pédagogie (enseignant en boulangerie)

Conclusions

- TPS : +
- Inflammation de type éosinophilique (Th2 ou T2)
- Rhinite a précédé l'asthme de plusieurs années
- Changement dans le traitement
- Ecartement !?

SERIES "CONTROVERSIES IN OCCUPATIONAL ASTHMA"
Edited by O. Vandenplas and J-L. Malo
Number 6 in this Series

Health and socioeconomic impact of work-related asthma

O. Vandenplas*, K. Toren#, P.D. Blanc¶

Health and socioeconomic impact of work-related asthma. O. Vandenplas, K. Toren, P.D. Blanc. ©ERS Journals Ltd 2003.
ABSTRACT: There is accumulating evidence that the workplace environment contributes significantly to the general burden of asthma. The purpose of this review is to explore the respiratory health and socioeconomic consequences of work-related asthma by addressing a series of controversial issues: 1) what is the natural history of occupational asthma and in what ways does ongoing exposure to the causal agent impact clinical outcomes?; 2) how does the natural history of irritant-induced asthma differ in its health outcomes from immunologically-mediated occupational asthma?; 3) do working conditions have a significant impact on asthma regardless of the aetiology of the disease?; 4) what is the scope of work disability from work-related-asthma in social and economic terms?; 5) what is the clinician's role in reducing the respiratory health consequences of work-related asthma? 6) to what extent do existing compensation and other social insurance schemes successfully address occupational asthma and work-aggravated asthma?
Eur Respir J 2003; 22: 689–697.

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Keywords: Asthma, disability, occupational disease

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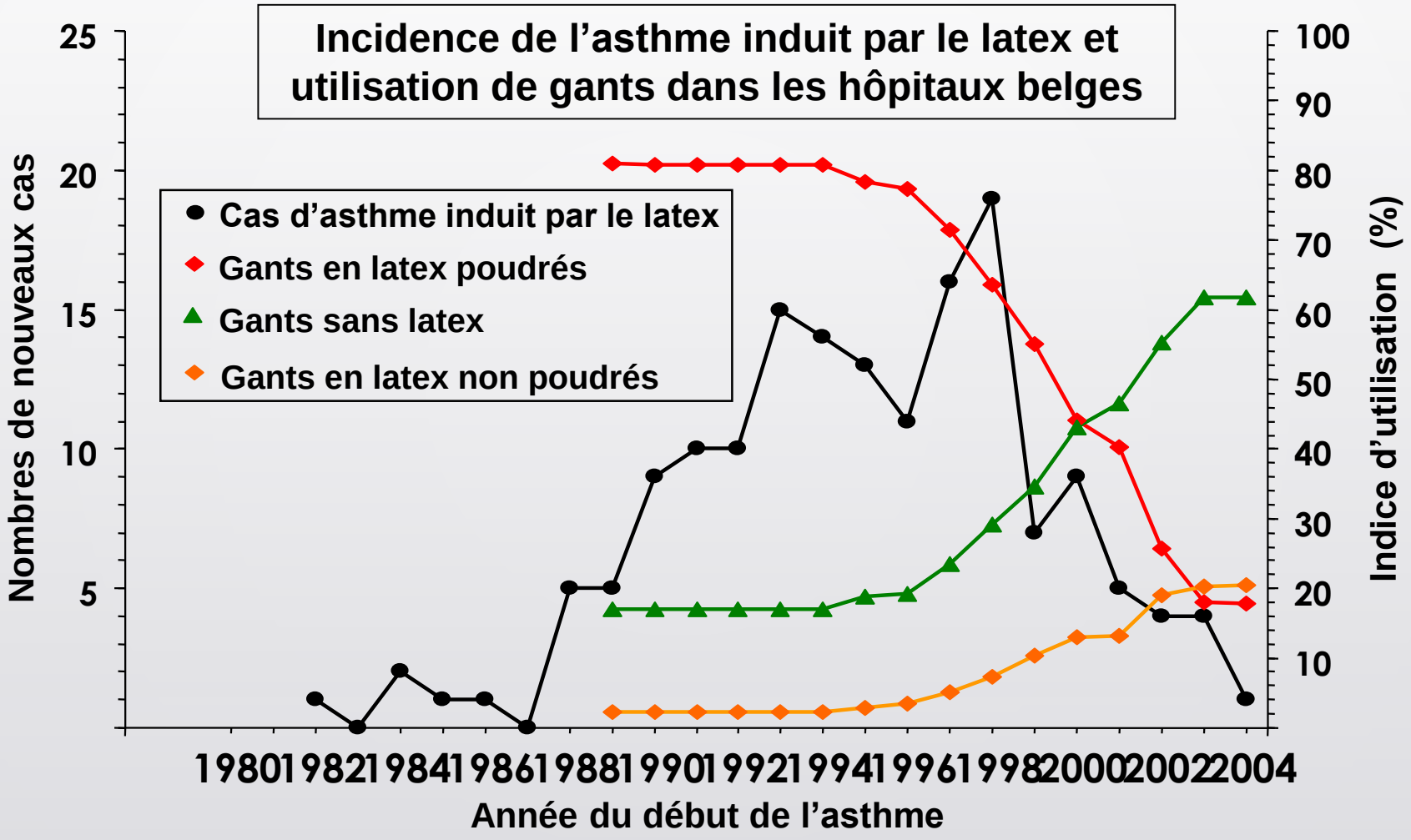
Table 1. – Comparison of asthma severity after cessation or reduction of exposure to the causative agent

Causative agent	Persistence of symptoms	Persistence of NSBH	Improvement of asthma#	Worsening of asthma#	1st author [ref no.]	Year of study
Cessation of exposure						
Colophony	16/20	3/7	5/7	0/7	BURGE [7]	1982
Isocyanates	10/20	9/12	10/20	6/20	ROSENBERG [9]	1987
Isocyanates	31/43	31/43	22/43	5/43	PISATI [11]	1993
Isocyanates	NA	6/9	3/9	0/9	PAGGIARO [12]	1993
Red cedar	37/75	25/33	20/33	4/33	CHAN-YEUNG [14]	1982
Latex	13/16	16/16	8/16	1/16	VANDENPLAS [15]	2002
Total	107/174 (61)	90/120 (75)	68/128 (53)	16/128 (12)		
Reduction of exposure						
Colophony	5/8	4/4	1/4	0/4	BURGE [7]	1982
Isocyanates	7/7	7/7	4/7	0/7	ROSENBERG [9]	1987
Isocyanates	17/17	17/17	0/17	13/17	PISATI [11]	1993
Isocyanates	NA	4/7	3/7	0/7	PAGGIARO [12]	1993
Red cedar	50/50	22/22	0/22	9/22	CHAN-YEUNG [14]	1982
Latex	16/20	19/20	15/20	0/20	VANDENPLAS [15]	2002
Total	95/102 (93)	73/77 (95)	23/77 (30)	22/77 (28)		

Data are presented as number of subjects with outcome variable/number of subjects studied, data in the totals rows are presented as number of subjects with outcome variable/number of subjects studied (% with outcome variable). NA: data not available; NSBH: nonspecific bronchial hyperresponsiveness; #: improvement and worsening of asthma assessed on changes in symptoms and/or medication [9], NSBH [7, 12, 14, 15], or a combination of symptoms, spirometry, and NSBH [11].

Asthme induit par le latex



Vandenplas, Allergy 2009: 64: 415–420

Discussion

- AP : 10 à 15% des asthmes de l'adulte

Toren K, BMC Pulm. Med 2009

- AP : co-facteurs importants, modifiables de risque d'exacerbation (GINA)
- 16% des AP présentent un asthme sévère

Vandenplas , JACI Pract 2019

- AP provoqué par les allergènes de boulangerie est un des asthmes professionnels les plus fréquents : 1350 cas / 10^6 de travailleurs en Belgique (1993-2002) (et tableau final)

Vandenplas, Respiratory Medecine 2011

- Autres professions touchées : pâtissiers, meuniers, céréaliers, …

Allergènes impliqués (volatiles)

	Nom scientifique / origine
Farines de céréales	
Blé	Triticum aestivum
Seigle	Secale cereale
Orge	Hordeum vulgare
Farines de légumineuse	
Soja	Glycine max
Lupin	Lupinus albus
Enzymes fongiques	
Alpha-amylase	Aspergillus orizae
Glycoamylase	Aspergillus niger
Hémicellulase/cellulase	Aspergillus niger
Betaxylloxidase	Aspergillus niger
Xylanase/cellulase	Aspergillus niger

	Nom scientifique / origine
Insectes	
Charençons du blé	Sitophillus granarius
Mites de la farine	Ephestia spp. And Eurigaster
Levure de boulanger	Saccharomyces cerevisiae
moisissures	Aspergillus fumigatus
	Alternaria alternata
Protéines de l'œuf (poudre)	
Ovumucoïdes	Gal d 1
Ovalbumines	Gal d 2
Conalbumines	Gal d 3
Lysozymes	Gal d 4

	Nom scientifique / origine
Autres ingrédients	
Farine de sarrasin	Fagopyrum echulentum (polygonaceae)
Lécithine de soja	Glycine max
Graines de tournesol	Helianthus annuus (compositae)
Acariens de stockage	Lepidoglyphus destructor
	Acarus siro
	Tyrophagus putrescentiae

Farines de blé

- Groupes des protéines de HPM (HMW)
  - Augmentation du FeNO
  - Eo sanguine
  - IgE médiée
  - R(C) , asthme, DC

Vandenplas, Allergy 2019

- Fréquence de sensibilisation par TCA (SPT) : 5-15%
  - Réactivité cutanée dépend de :
    - Qualité de la concentration
    - Qualité de la standardisation des extraits allergéniques

Sander, Allergy 2004 ; 59 :95-8.

- Blé et seigle
  - Se des TCA : 40-67%
  - Sp des TCA : 86-100%

IgE spécifiques par immunocap®

- Sensibilité des dosages IgE spécifiques : plus grande que les SPT (extraits commerciaux)
  - Se 83% : blé
  - 72% : seigle
  - Sp : 59 à 81%
- En présence de taux augmenté IgE sp. pour la farine
  - ≥ 2.32 kU/l pour le blé
  - SPT > 5mm pour des boulangers symptomatiques
  - Positivité des TPS avec une VPP de 74 à 100%

Van Kampen, Allergy, 2008

Physiopathologie

Allergènes de céréales (Blé)

- Protéines: 10 – 15% du poids sec des grains de blé
  - H^20 : albumines
  - Diluants salins pour les globulines

    } 20%
  - Alcool et H^20 : gliadines
  - Acide dilué : gluténines

    } 80%
  - Gluten : 50% de gliadines – 50% gluténines
- <u>Inhibiteurs</u> de l'α-amylase et de la trypsine = principaux allergènes responsables de l'APB
- Péroxydase, incriminée dans la DCA et AA au blé
- Thiorédoxine (75% d'homologie avec le maïs)

Physiopathologie (Suite)

LTP

- Par voie orale
- Allergènes respiratoires (CRX) : pollens et végétaux
- Allergène majeur (?) de l'APB

Palacin, J Allergy Clin Immunol. 2007

- Grande homologie de structure avec Pru p3 de la pèche (SOAC)
- r Tri a 14 (f 433)

BLE

- ImmunoCap® de blé (**f4**)
  - Majoritairement des protéines solubles (APB)
  - Comporte **tous** les extraits de farine de blé (Se++)
- ImmunoCap® Ω-5 gliadine (rTri a 19, f416)
  - WDEIA
  - FA
- Recombinants : non pertinents
- BAT : en cours d'évaluation (pas en clinique)
- **Améliorant (additifs) :**
  - α-amylase (aspergillus orizae) : 20-30% des boulangers S+

Conclusions

- Intensité de l'exposition
- Atopie

} Facteurs de risques principaux de l'APB

- Farines de céréales
  - HPM : caractéristiques propres

Vandenplas, Allergy 2019

- Anamnèse (rythmicité avec le travail)
- Sensibilisation IgE : TCA-Immunocap® : limites
- TPS : gold standard
- R/idem que l'asthme et la rhinite, l'urticaire non professionnels

Conclusions (suite)

- Rhinite(Conjonctivite) précède l'apparition de l'asthme
- Diagnostic précoce – correct
- Ecartement du risque professionnel (ORL- Pneumologue - Dermatologue - Médecin du travail)
- **Orientation professionnelle** des jeunes asthmatiques, atopiques, apprentis
  - « Quel métier souhaites - tu exercer plus tard ? » (Pédiatres - pneumologues - médecins traitants , médecine scolaire, écoles professionnelles)

Moscato, Allergy 2011

POSITION PAPER

EAACI Position Paper: Prevention of work-related respiratory allergies among pre-apprentices or apprentices and young workers

G. Moscato[1], G. Pala[1], M. A. Boillat[2], I. Folletti[3], R. Gerth van Wijk[4], D. Olgiati-Des Gouttes[5], L. Perfetti[1], S. Quirce[6,7], A. Siracusa[3], J. Walusiak-Skorupa[8] & S. M. Tarlo[9,10]

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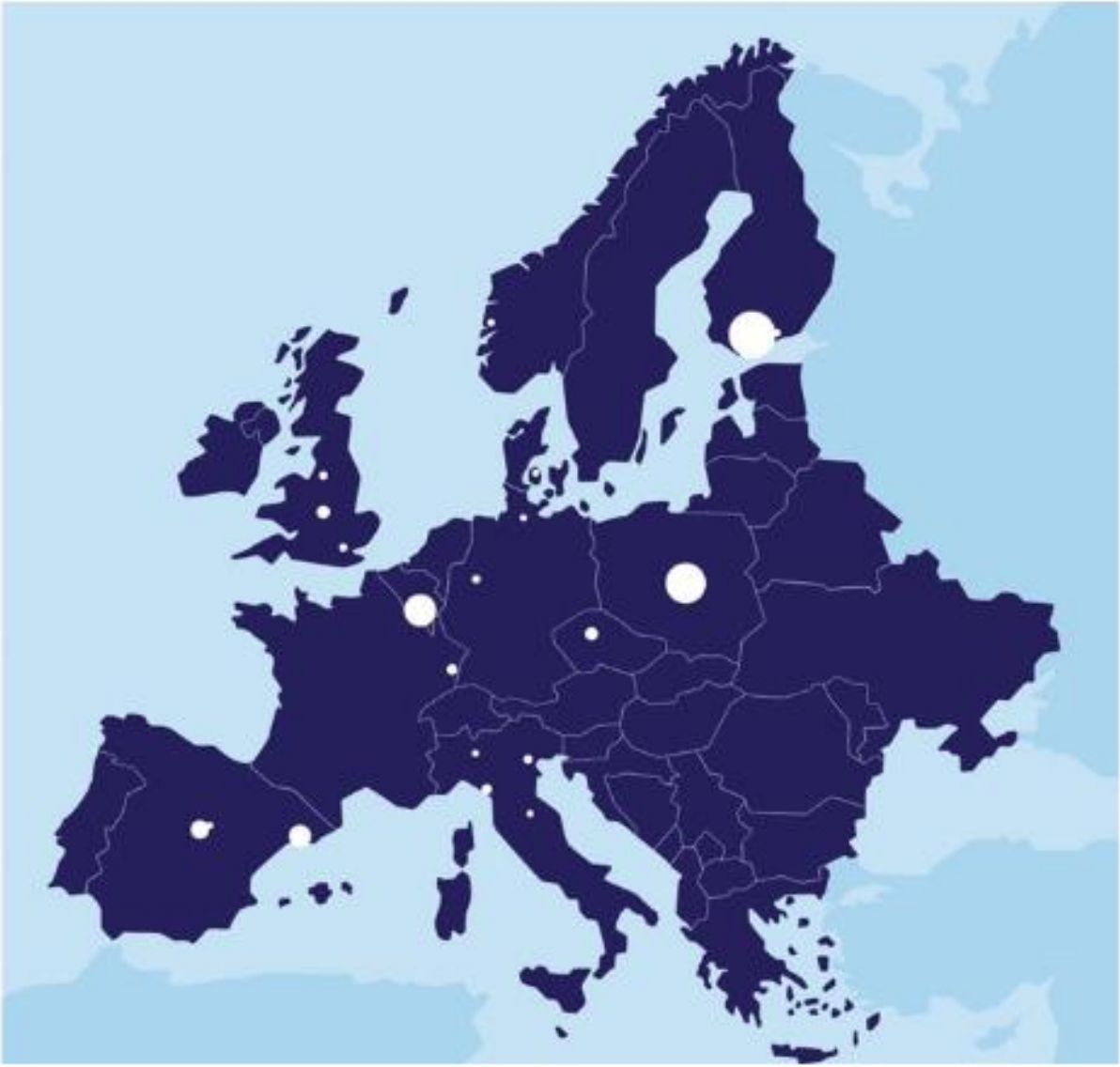

Retrospective multicenter study (2006-2015)
20 tertiary centers from 11 European countries
1.180 subjects with positive specific inhalation challenge

LOW-MOLECULAR-WEIGHT AGENTS
(n=544)

- ↑ Chest tightness at work
- ↑ Daily sputum at work
- ↑ Late asthmatic reaction
- ↑ Severe exacerbations

HIGH-MOLECULAR-WEIGHT AGENTS
(n=635)

- ↑ Work-related conjunctivitis
- ↑ Work-related rhinitis
- ↑ Atopy
- ↑ Early asthmatic reaction
- ↑ Airflow limitation
- ↑ FeNO
- ↑ Blood eosinophils

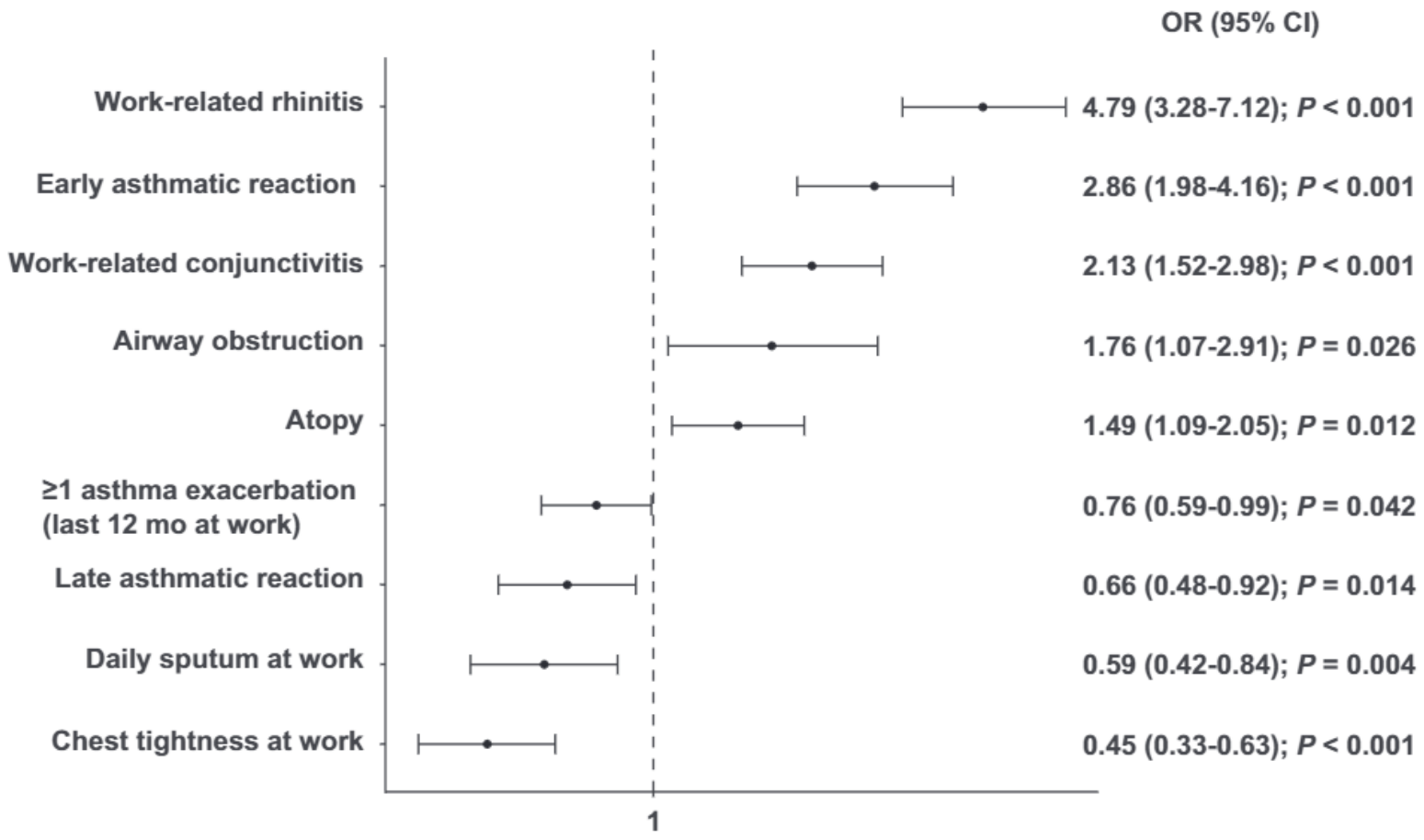

FIGURE 1 The figure illustrates the main results of the multivariate logistic regression analysis for the clinical and functional characteristics that are associated with occupational asthma caused by high-molecular-weight agents as the outcome (odds ratio > 1) and low-molecular-weight agents as the reference (odds ratio < 1). Work-related rhinitis and conjunctivitis were physician-based diagnoses. Airway obstruction was defined by a FEV_1 < 80% predicted value and a FEV_1/FVC ratio <70%. The presence of atopy was documented by at least one positive skin-prick test response to a battery of locally relevant inhalant allergens. Asthma exacerbations were defined by the need for oral corticosteroids for at least 3 consecutive days or emergency room visit or hospitalization during the last 12 mo at work[16]

European network on PHenotyping of OCcupational Asthma (E-PHOCAS)

High-molecular-weight agents	n (%)*	Low-molecular-weight agents	n (%)*
Flour/grains	341 (34.6)	Isocyanates	139 (14.1)
Latex	35 (3.6)	Persulfate salts	57 (5.8)
Enzymes	23 (2.3)	Quaternary ammonium compounds	38 (3.9)
Storage mites	10 (1.0)	Metals	30 (3.0)
Cow dander	9 (0.9)	Welding	30 (3.0)
Rodents	9 (0.9)	Wood dusts	28 (2.8)
Fish/seafood	8 (0.8)	Acrylate compounds	28 (2.8)
Ornemental plants	6 (0.6)	Cleaning products/disinfectant (NOS)	26 (2.6)
Insects and derived products	5 (0.5)	Aldehydes	15 (1.5)
Vegetal gums	3 (0.3)	Metal working fluids	15 (1.5)
Soybean flour	3 (0.3)	Resins/glues/paints (NOS)	15 (1.5)
Spices	3 (0.3)	Epoxy resins	14 (1.4)
Moulds	2 (0.2)	Amines	10 (1.0)
Various plant-derived products	22 (2.2)	Acid anhydrides	10 (1.0)
Various animals and derived products	14 (1.4)	Drugs	9 (0.9)
		Colophony	4 (0.4)
		Reactive dyes	2 (0.2)
		Styrene	2 (0.2)
		Triglycidylisocyanurate	1 (0.1)
		Various low-molecular-weight agents	17 (1.7)
Total:	493 (50.1)	Total:	492 (49.9)

Contact Dermatitis • **Original Article**

COD
Contact Dermatitis

Occupational contact urticaria and protein contact dermatitis: causes and concomitant airway diseases

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Summary

Background. Contact urticaria (CU) and protein contact dermatitis (PCD) are mainly induced by an immediate, IgE-mediated immunological mechanism. Immediate sensitization is also linked to asthma and/or allergic rhinitis.

Objectives. To report causes of work-induced CU and PCD, and to evaluate the occurrence of concomitant airway diseases.

Methods. We retrospectively reviewed the patient files of cases diagnosed with CU or PCD at the Finnish Institute of Occupational Health during 1995–2011. We obtained data on occupation, exposures, clinical and immunological test results, and diagnosed occupational skin and respiratory diseases.

Results. Altogether, 291 cases of occupational CU or PCD were diagnosed during the study period. The most common causes were flour, cow dander, natural rubber latex and acid anhydrides. Concomitant occupational asthma caused by the same agent as the skin disease was detected in 60 patients (21%), and occupational rhinitis was detected in 111 patients (38%).

Conclusions. Almost half of the patients (46%) with occupational CU and PCD had concomitant occupational airway disease. Patients with CU/PCD should always be asked about respiratory symptoms, and preventive measures at the workplace should include protection of both the skin and the airways.

Key words: acid anhydrides; chemicals; cow dander; enzymes; flour; grain; natural rubber latex; occupational asthma; occupational rhinitis; plants.

2017

Table 2. The most common occupations of patients with immunological contact urticaria and protein contact dermatitis at the Finnish Institute of Occupational Health, 1995–2011 and the most common causes according to occupation

Occupation	Number of cases	Most common causes
Food service (chefs, bakers)	93	Flour (n = 43), vegetables (n = 18), fish and shrimps (n = 10), meat (n = 6), NRL (n = 4), egg (n = 3)
Farmers	60	Cow dander (n = 46), grains and animal feed (n = 12)
Healthcare (nurses, dentistry)	32	NRL (n = 27), chloramine-T (n = 4), chlorhexidine (n = 1)
Gardeners, florists	25	Ornamental plants (n = 19), vegetables (n = 3)
Electrical equipment assemblers	17	Organic acid anhydrides (n = 17)
Researchers, laboratory workers	15	Rats and mice (n = 8)
Hairdressers	8	Persulfates (n = 5), permanent (oxidative) hair dyes (n = 3)
Other	37	NRL (n = 12), animal dander (n = 8), chemicals (n = 6), enzymes (n = 5)
Total	291	–

NRL, natural rubber latex

- Avec mes remerciements au Pr Olivier Vandenplas

Je vous remercie de votre attention