Popcorn Worker's Lung: *In Vitro* Exposure to Diacetyl (D), an Ingredient in Microwave Popcorn Butter Flavoring, Damages Guinea-Pig Tracheal Epithelium (E) and Increases Reactivity to Methacholine (MCh)

J.S. Fedan[1], J.A. Dowdy[1], A.F. Hubbs[1], K.B. Fedan[1]. [1]HELD & DRDS, NIOSH, Morgantown, WV. Email: jsf2@cdc.gov

Workers exposed by inhalation to volatile microwave popcorn butter flavorings experience decrements in lung function and develop bronchiolitis obliterans, i.e., "popcorn worker's lung." D, a major flavoring ingredient, is implicated in causing workers' symptoms. After inhalation exposure of rats, D caused necrosis of E in upper and lower airways. We investigated the hypothesis that D-induced damage to E alters airway reactivity by examining in the guinea-pig isolated, perfused trachea, its direct effects, and its effect on reactivity to MCh and terbutaline (T). Cumulative additions of D to the intraluminal (IL) bath resulted in responses that began with contraction and ended with relaxation, with a threshold of ca. 3 mM. After a 4-h incubation with IL-applied D (3 mM), contractions to cumulative concentrations of MCh added to the extraluminal (EL) bath were increased; the EC50 was unaffected. However, sensitivity to IL-applied MCh was increased (EC50s [M] were, control: $3.4x10^{-4}$, D-treated: $3.0x10^{-5}$; $p<0.05$). D had no effect on maximum responses to MCh. Reactivity to EL-applied T in MCh($3x10^{-7}$ M)-contracted tracheas was unaffected by D. These findings indicated that the increase in reactivity to IL MCh after D-treatment resulted from an alteration in E, e.g., a compromise in its barrier function and/or a decrease in the release of epithelium-derived relaxing factor. H&E sections of tracheas perfused (4 h) with D and not challenged with MCh or T demonstrated E degeneration or necrosis in 2 of 5 preparations; no changes were seen in vehicle controls or in the smooth muscle. These findings suggest that functional changes in reactivity may precede light microscopic evidence of pathologic changes after D-treatment.

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Enzyme-Linked Immunosorbent Assay Specific for (1→6) Branched, (1→3)-β-D-Glucan Detection in Environmental Samples

N. Metwali[1], P.S. Thorne[1], K. Kolegraf[1], M.E. O'Neill[1]. [1]The University of Iowa, College of Public Health, Iowa City, IA. Email: nervana-metwali@uiowa.edu

Rationale: (1→3)-β-D-Glucans have been recognized as potential causative agents responsible for induced respiratory symptoms observed in both indoor and outdoor occupational environments. A specific enzyme immunoassay was developed to quantify (1→6) branched, (1→3)-β-D-glucans in environmental samples in order to assess exposures and investigate glucans as risk factors for asthma.

Methods: The assay was based on the use of a monoclonal antibody specific for fungal cell wall-β-D-glucans as a capture reagent and polyclonal anti-(1→6) branched, (1→3)-β-D-glucans (schleroglucan) as a detector reagent.

Results: This assay showed high sensitivity and specificity for schleroglucan with a detection level below 10ng/ml. The assay had low reactivity with pustulan, laminarin, and yeast with detection levels of 5µg/ml, 250ng/ml and 1mg, respectively. The assay was not responsive to endotoxins, curdlan, phosphate glucan, carboxymethyl cellulose, dextran, barley glucan, mannan, alternaria, or aspergillus fumigatus. Mass Spectroscopy and nuclear magnetic resonance were used to evaluate all tested glucan compounds. This effort demonstrated that our glucan ELISA is specific to high molecular weight (1→6) branched, (1→3)-β-D-glucans. In order to optimize the ELISA, we evaluated three methods for extraction and quantification of glucans. The best method involved elution of samples into PBS-Tween 20 with shaking followed by autoclaving, vigorous mixing and centrifugation.

Conclusions: The sensitivity and specificity of this new sandwich ELISA demonstrate the suitability of this protocol for investigation of the role of glucan exposure in asthma.

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Glutathione Protects Human Airway Proteins and Epithelial Cells from Isocyanates

A.V. Wisnewski[1], Q. Liu[1], J. Liu[1], C.A. Redlich[1]. [1]Yale University School of Medicine, New Haven, CT. Email: adam.wisnewski@yale.edu

Rationale: Glutathione has been linked to the human response to isocyanate exposure. However, the ability of glutathione to modulate key chemical reactions, thought to be central to the development of human isocyanate allergy, has not been directly analyzed. To better understand the potential role of glutathione in the response to occupational isocyanate exposure, we evaluated its effects on two processes thought to be involved in the development of isocyanate allergy, isocyanate-protein conjugation and epithelial cell toxicity.

Methods: The effects of glutathione on (1) isocyanate conjugation with albumin, its major target in the airway fluid and (2) isocyanate-induced toxicity to human airway epithelial cell lines, A549 and NCI-H292, were tested using two different in vitro models. For protein conjugation studies, a newly described vapor exposure system was used to model the air/liquid interface at the surface of the epithelial fluid in the airways. Epithelial cell exposures were performed in fluid phase to mimic the in vivo exposure of airway cells covered by epithelial lining fluid.

Results: GSH levels equivalent to those found in normal human airway fluid (100 uM) provided >90% protection against HDI-protein conjugation at HDI exposure levels 10-fold above permissible occupational limits. Physiologic levels of GSH, but not GSSG, also reduced HDI toxicity to human airway epithelial cells in a dose-dependent manner, when present extra-cellularly, however drugs that modulate intracellular GSH levels did not significantly alter isocyanate toxicity.

Conclusions: Together with previously reported genetic and toxicity studies, the data suggest that airway GSH plays an important role in protection against HDI exposure and may help prevent the development of allergic sensitization and asthma.

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Adolescents Jobs and Course of Rhinitis over Puberty – 1st Follow ISAAC Study in Germany

K. Radon[1], E. Riu[1,2], H. Dressel[1,3], D. Windstetter[1,4], G. Weinmayr[3], S. V Vogelberg[5], W. Leupold[5], E. von Mutius[4], D. Nowak[1]. [1]Institute for Occup Environmental Medicine, Munich, Germany; [2]Hospital Germans Trias i Pujo Spain; [3]Department of Epidemiology, Ulm, Germany; [4]Dr. von Haune Hospital, Munich, Germany; [5]University Childrens Hospital, Dresden, Germ

Rationale: Rhinitis might be caused by workplace allergens and irritants. tive study on occupational rhinitis starting in childhood has been conducted aim of the Study on Occupational Allergy Risks (SOLAR) was to investig dence of rhinitis over puberty taking into account the role of the life-tim holiday and vocational jobs in a population based study. **Methods:** Participa II of the ISAAC study in Munich and Dresden enrolled in 1995 and 19 contacted by a postal questionnaire in 2002 (age at follow-up 16 to 18 years tionnaire included items on atopic diseases, jobs including holiday jobs and training, and potential confounders. The most recent of the adolescents' jobs least eight hours per week and for at least one month was coded according t 88 system. Occupational exposure was assessed by use of a job-expos **Results:** Of the 3785 adolescents included in the study, 951 reported an e history. The median duration of employment was 10 (25th; 75th percen months. After adjusting for potential confounders, subjects working with lo weight antigens were at increased risk for new onset of rhinitis (OR 1.8; 95% In health care workers (OR 1.8; 95% CI 0.8-4.4), construction workers (1.9; 0 metal workers (1.7; 0.8-3.8) there was a trend for a higher incidence of rhinit **sion:** Even early occupational exposures in holiday jobs and during vocatio seem to be relevant in the development of occupational rhinitis.

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Occupational Rhinitis and Asthma Due to Inhaled Lupin Protein

C.P. Campbell[1], A. Jackson[1], A. Johnson[2], P. Thomas[3], D.H. Yates[1]. [1]St. Vincen Sydney, New South Wales, Australia; [2]Dust Diseases Board, Sydney, New S Australia; [3]University of New South Wales, Sydney, New South Wales, Austr jimandcharlotte@talk21.com

INTRODUCTION: Lupin is increasingly used as a flour substitute in food. cross-sectional study of allergy to inhaled lupin in a food processing company. M Workers were screened by: questionnaire; skin prick tests (SPTs) to aeroallergen legumes; spirometry and exhaled nitric oxide (eNO). Methacholine challenge was p symptomatic workers with lupin positive SPTs; one underwent single blinded, sp chial provocation challenge with lupin flour. **RESULTS:** 53 workers: 11 (21%) SPT to lupin: 7/11 had current symptoms of allergy (conjunctivitis, rhinitis, or wh had occupational rhinitis, 3 had conjunctivitis. 2 had bronchial hyperresponsivene choline, one with longstanding asthma. The other had positive specific bronchial challenge with lupin flour: $PD_{20}FEV1$ 1:5000 dilution, early asthmatic response 41% drop FEV1, late asthmatic response 28% drop FEV1. **CONCLUSIONS:** A high rate of lupin sensitisation occurred (21%), with one case of occupational asthma and one case of work-aggravated asthma. Allergic symptoms were positively correlated with lupin sensitisation ($p=0.003$). Positive SPT to legumes were infrequent but commoner in Group 2 ($p=0.001$), suggesting crossreactivity. Atopy may be a risk factor for sensitisation ($p=0.058$).

Table 1. Characteristics of nonsensitised (Group 1), and workers sensitised to lupin

	Group 1 (42)	
Age yrs (Mean ± SE)	36 ± 1.7	4
Sex M:F (%F)	11:31 (74%)	4
SPT atopy (1 or more aeroallergens)	22 (52.4%)	9
Presence of allergic symptoms	9 (21.4%)	7
SPT positive to other legumes	1 (2.3%)	4
eNO av ± SE ppb	5.9 ± 0.3	6

* p= 0.058, ** p= 0.003,# p= 0.001.

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Occupational Asthma – Where Do We Need To Go?

L.M. Bradshaw[1], M.R. Henson[1], J. Elms[1], A.D. Curran[1], D. Fishwick[1]. Saftey Laboratory, Buxton, Derbyshire, England. Email: lisa.bradshaw@hs

Introduction In the United Kingdom (UK), a challenging target has b Government to reduce incident cases of occupational asthma (OA) by 30% We report an integrated approach to identify opportunities to develop interv key stakeholders to deliver this target, particularly in relation to knowle **Method** Data were collected to assess stakeholders knowledge and unders OA. In particular, community nurses and physicians (GPs) (n=366), wo work-related respiratory symptoms (WRRS) (n=97), occupational lun specialists (n=12) and a local occupational health (OH) network (n=159 approaches were used to collect data including questionnaires, intervie groups and audit of diagnostic practice. **Results** GPs take an occupational relevant to the medical complaint, whereas practice nurses routinely docum pation. Both groups received little formal OH training. Workers compl WRRS were not referred immediately to hospital, with a mean referral ti years between onset of symptoms and assessment by a specialist (range 0- Agreement between the 12 physicians for 19 audit cases of possible OA was low, with a median kappa value of 0.26, (range −0.2 to +0.76). Only 7 p agreed significantly ($p<0.05$) with 5 or more of their colleagues. 49% o network stated they would pay for training courses in OH, 68% would a courses, 76% would use of OH fact sheets and 45.6% a free telephone help-l line support. **Conclusion** There appears to be significant gaps in knowledge recognition and referral of workers with potential OA in the UK. In order t the set targets for the reduction of OA, education and support needs to be towards community healthcare professionals and the development and imp tion of a national standard of care for this condition should be a priority.

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