

**Incidence of Probable Occupational Asthma and of Changes in Airway Caliber and Responsiveness in Apprentice Welders**

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To our knowledge, no prospective study of the incidence of airway obstruction and hyperresponsiveness as well as of probable OA has been performed in welders. The aim of the study was to determine the incidence of occupational asthma (OA), bronchial obstruction and hyperresponsiveness brought about by early exposure to welding fumes and gases among apprentice welders.

This prospective cohort study consisted of a baseline and two follow-up assessments in 286 apprentices starting vocational training in the welding profession. A respiratory symptoms questionnaire, spirometry and methacholine bronchial challenge tests were conducted at baseline and 15 months later on average. The incidence of probable OA was close to 3% (6/194 or 5/194). OA was defined as the presence of at least one welding-related symptom of cough, wheezing, and/or chest-tightness at first follow-up that persisted throughout the second follow-up or presence of at least one of the above symptoms as of the second follow-up with a 2-fold or a 3.2-fold or greater decrease in PC20 by the end of study. The incidence of BHR was 11.9% defined as a 3.2-fold or greater decrease in PC20 from baseline to end of study and 14.9% when defined as a 2-fold decrease or greater in PC20. A statistically significant difference was found among the lung function test results between the baseline and end of study. In particular, FEV<sub>1</sub>, % predicted has significantly dropped by 8.4% on average.

This study has shown that pulmonary function changes can occur early following exposure to welding fumes. Their significance in relation to possible chronic effects remains to be explored.

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**Pulmonary Function Decrease in Popcorn Production Workers: One-Year Follow-Up**

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Rationale: Following the report of a cluster of clinical bronchiolitis obliterans in former workers of a microwave popcorn production plant, a cross-sectional survey of current workers showed a 3.3-fold excess of airways obstruction. The purpose of this study was to investigate the lung function changes over time in this group and possible influences of occupational factors.

Method: We conducted four cross-sectional surveys in which we administered questionnaires, spirometry, and calculated job-specific exposure levels to diacetyl (as a marker of butter flavoring volatile organic compounds (VOCs) exposure). We tested percent-predicted FEV<sub>1</sub> (%FEV<sub>1</sub>) and airways obstruction against three measures of exposure: job category, date of starting before or after industrial hygiene controls, and an estimate of cumulative exposure based on job history and measured exposure levels.

Results: We found 30 workers (12.3%) with airways obstruction. There was a significant negative correlation between VOCs exposure and %FEV<sub>1</sub> levels (p=0.003) and airways obstruction was significantly higher among those exposed to high-level VOCs (p=0.025). %FEV<sub>1</sub> was significantly higher among workers started after implementing preventive industrial hygiene controls (p<0.001). %FEV<sub>1</sub> levels among quality control workers were also significantly lower than other workers (p=0.002).

Conclusion: We observed a significant level of airways obstruction and decrease in pulmonary functions in the current workers related to high-level VOCs exposure.

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**Repeated Measures of FEV<sub>1</sub> over 6 to 12 Months: What Change Is Abnormal?**

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Longitudinal change in FEV<sub>1</sub> ( $\Delta$ FEV<sub>1</sub>) is useful for assessing adverse respiratory effects, but high variability impedes reliable recognition of accelerated decline in an individual. ATS (1991) recommends that a  $\geq 15\%$  decline in FEV<sub>1</sub> from year-to-year be the criterion for clinically significant abnormality. We examined the mean, lower 5<sup>th</sup> percentile, and lower 5% cutoff value (mean minus 1.64\*SD) of  $\Delta$ FEV<sub>1</sub> in both percentage (%) and milliliter (ML) for 6- and 12-mo. intervals from actual data obtained using ATS recommended equipment and procedures in 389 white male coal miners and working nonminers (initial age 39, range 19-65 yrs) with 3 to 11 spirometry tests over 5 years.  $\Delta$ FEV<sub>1</sub> was "normal" by the ATS criterion in 99.4% of tests separated by 12 mo. Results are shown for ALL participants, those with stable FEV<sub>1</sub> (5 year slope < -90ml/yr by linear regression)(STB), and nonsmokers without airway hyperresponsiveness who had no new symptoms over 5 years (NSØ). The STB and NSØ results suggest that one-year declines of greater than 8% or 330ml are unlikely when healthy working males perform spirometry according to ATS standards.

Group, N	Interval (months)	# Obs.	$\Delta$ FEV <sub>1</sub> Mean (SD) % , ML	Lower 5% cutoff % , ML	5th %-ile % , ML
ALL, 389	6	2843	-0.78 (4.55), -34 (175)	-8.2, -321	-7.8, -320
	12	2511	-1.47 (4.77), -61 (184)	-9.3, -363	-9.0, -350
STB, 292	6	2157	-0.53 (4.42), -24 (169)	-7.8, -301	-7.1, -300
	12	1911	-1.03 (4.57), -44 (175)	-8.5, -331	-8.1, -330
NSØ, 71	6	555	-0.57 (3.92), -28 (167)	-7.0, -302	-6.5, -280

declines in individuals, and suggest that the 15% ATS criterion may be too large.

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**Isocyanate-Based Spray-Paint Exposure and Change in Lung Function**

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RATIONALE: A cross-sectional study of spray-painters was conducted to quantify adverse respiratory effects of exposure to polyurethane enamels using HDI-based isocyanates. METHODS: The population consisted of 287 spray-painters at 4 facilities. Each subject was administered a spirometric test and a medical, smoking, and occupational questionnaire (including spray-painting history and respirator usage). Total and respirable personal samples (n=152) were collected during spray-painting. For each subject, cumulative exposures were computed for total and respirable paint aerosol (TPA & RPA) and isocyanate in total and respirable aerosol (TIA & RIA) as arithmetic mean facility exposure, times years painting. Multiple linear regression was used to relate percent predicted (PP) FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC, and FEF<sub>25-75</sub> to cumulative exposure, after adjusting for age, cigarette smoking, asthma and respiratory protection. RESULTS: Cumulative exposures in (mg/m<sup>3</sup>)-years ranged up to 578.0 TPA, 57.6 RPA, 69.4 TIA and 6.9 RIA. For all exposure indices, after adjusting for smoking, asthma and respiratory protection, higher exposure was significantly associated with reduced PPFEV<sub>1</sub>, PPFEV<sub>1</sub>/FVC, and PPFEF<sub>25-75</sub>. Significant Smoking-related reductions were observed for PPFEV<sub>1</sub>, PPFEV<sub>1</sub>/FVC, and PPFEF<sub>25-75</sub>. Respirator usage was associated with significantly higher PPFEV<sub>1</sub> and PPFVC. No significant smoking and exposure interactions were noted. Adjusting for asthma resulted in a significant reduction in PPFVC only, with no effect on the significance of exposure. CONCLUSION: Exposure levels were within total and respirable "nuisance dust" standards, but were significantly associated with adverse effects. Respiratory protection was beneficial, but more stringent exposure controls are required for spray-painting with polyurethane enamels.

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**Exposure to Isocyanates Increases Neutrophils in Sputum of Subjects with Occupational Asthma**

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Exposure to isocyanates (Is) can induce both eosinophilic and neutrophilic inflammation in subjects with occupational asthma. Isocyanates are known to be a source of leukotrienes (LT) released by their respective receptors. Aim: To determine if exposure to Is is associated with an increased expression of LTC<sub>4</sub>/LTD<sub>4</sub> (CysLT<sub>2</sub>) in sputum due to Is and in healthy controls. Methods: Specific inhalation challenges to Is were performed in subjects with OA and healthy controls. Sputum induction was performed before and 7h after exposure to Is. Flow cytometry was performed on sputum samples to measure receptor expression. Results: 14 subjects with OA and 4 controls were enrolled. After exposure to Is, subjects with OA experienced an asthmatic reaction with increased significantly ( $\Delta$  42.3%) eosinophils and 13.1% (14.7%) neutrophils. There was a significant increase in expression of CysLT<sub>1</sub> (4-fold, p=0.01), CysLT<sub>2</sub> (15-fold, p=0.02) and BLT1 (5-fold, p=0.003), whereas their macrophages only showed a significant (2-fold, p<0.05) increase in BLT1 expression. No significant changes were seen in cells from controls. Conclusion Exposure of isocyanate-sensitive OA subjects to Is induces a neutrophilic lung inflammation with an increased expression of leukotriene receptors (CysLT<sub>1</sub>, CysLT<sub>2</sub> and BLT1) mainly on neutrophils.

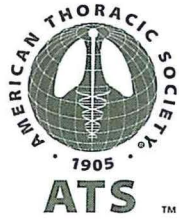
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**Isocyanate (MDI) Exposure Causes an eNO Increase in Workers with Asthma and/or Bronchial Hyperreactivity (BHR)**

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The time course of eNO during asthmatic responses after exposure to isocyanates has not been closely investigated yet. Methods: We determined eNO before, during and after workplace-related inhalative exposure to MDI (3 and 5 ppb; 120 min) for 22 workers examined due to suspected isocyanate asthma. Each patient also underwent a methacholine provocation test. Results: 14 of the 22 investigated MDI workers showed BHR. 10 out of these 14 showed an eNO increase of > 30% at 22h after MDI challenge (range 31 - 502%). Only one of the eight subjects without BHR exhibited an eNO increase of > 30%. Differences between both groups are significant ( $\Delta$ eNO: 12.4  $\pm$  5 ppb vs. -1  $\pm$  1.2 ppb; p = 0.02). Five of the 22 MDI-challenged subjects (23%; all with BHR) developed an asthmatic response after MDI challenge (three had a dual response, two a late one). Four of the five asthmatic responders showed an eNO increase of > 30% at 22 h ( $\Delta$ eNO: 16.2  $\pm$  5 ppb). The highest eNO increase was found in the three patients with MDI-HSA specific IgE antibodies ( $\Delta$ eNO: 27.7  $\pm$  13.7 ppb). There is a significant association between the presence of BHR and eNO increase of > 30% at 22 h after MDI challenge (Odd ratio 17.5 (95%: 1.6, 191.1)). Conclusions: The significant eNO increase after occupational-type challenge test with MDI in most symptomatic workers with BHR - which rarely occurs in the absence of BHR - is remarkable. The eNO increase is more pronounced when MDI concentrations of < the TLV elicit an asthmatic response and especially when IgE mediated isocyanate asthma is present. eNO measurement obviously is a new suitable method for monitoring isocyanate workers under respiratory risk.

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