

Isocyanate Sensitization: A Cross Sectional Study of MDI Exposure and Effects in the Production of Polyurethane Coated Fabrics

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Rationale: Isocyanates are the most commonly identified cause of occupational asthma, but risk factors, including the role of skin exposure in sensitization, remain poorly defined. Markers of exposure and early disease are greatly needed. **Methods:** To characterize the effects and potential markers of methylene diphenyl diisocyanate (MDI) skin and respiratory exposures, we conducted a cross sectional evaluation of a corporate workforce manufacturing polyurethane coated fabrics. Questionnaire, immunologic and pulmonary physiologic assessments were performed on all 90 employees. Air, skin and surface MDI measurements were also collected. **Results:** Eight percent of employees had an established asthma diagnosis. MDI-specific IgG was present in 35 of 90 employees (39%) and was strongly associated with MDI exposure, as determined by job title ($p < 0.01$). Among 35 workers with MDI-specific IgG, 30 (86%) worked on production lines, while 0 of 12 office workers had MDI-specific IgG. Those with MDI-IgG did not differ from colleagues in regards to age, race, smoking status, spirometry, asthma or atopy. However, MDI-specific IgG was associated with positive methacholine challenge testing ($p = 0.03$) and with symptoms of cough ($p = 0.03$) and chest tightness ($p < 0.01$). Air sampling for MDI monomer ranged from 0 to 8 ppb, well under OSHA exposure limits. Qualitative dermal MDI exposure was detected on 14 (23%) of the 61 skin wipes collected. **Conclusions:** MDI-IgG was seen in a substantial proportion of workers and associated strongly with exposure, assessed by job title, and with increased prevalence of airways hyper-responsiveness and asthma symptoms. Low MDI air levels and documented dermal exposures suggest dermal exposure may play a significant role in immune sensitization to MDI.

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Cross-Sectional Study of Auto Body Workers Exposed to Isocyanates: Immunologic Responses

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Rationale: Isocyanates are a common cause of immune-mediated occupational asthma. However, the health and immunologic effects of isocyanates under current working conditions and risk factors remain poorly defined. **Methods:** A cross-sectional epidemiologic study of 262 body shop workers from 36 shops, Survey of Painters and Repairers of Autobodies by Yale (SPRAY), was performed to characterize isocyanate exposures and their effects on body shop workers, using questionnaires, physiologic and immunologic assessment of the workers. Individual isocyanate exposures were estimated based upon total reactive isocyanate concentration determined from air and personal sampling and personal worker activity diaries. **Results:** A low prevalence of asthma (2.3%) using spirometry, methacholine challenge, symptoms, and peak flows was noted, but isocyanate-specific immunologic responses were present in 26% workers. Hexamethylene diisocyanate (HDI)-specific IgG was present in 21% of HDI-exposed workers. The presence of HDI-specific IgG was strongly associated with current total isocyanate exposure (total NCO 24.1 vs 8.8 $\mu\text{g NCO}/\text{m}^3$; $p = .0004$), but did not correlate with race, total IgE, asthma symptoms or smoking. However, work-related asthma-like symptoms and methacholine responsiveness were more prevalent in those with higher HDI-specific IgG ($> 1:160$). HDI-specific IgE was present in 6 workers (3%), 5 of whom also had HDI-specific IgG, only one of whom had work-related asthma symptoms. **Conclusions:** These findings demonstrate that HDI-IgG is present in a substantial proportion of HDI-exposed workers and correlates with current isocyanate exposure. High HDI-IgG titres may suggest isocyanate asthma.

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Pleural Plaques in Workers Exposed to Asbestiform Contaminated Vermiculite Ore: A Twenty Year Follow-Up

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Rationale: Vermiculite mined in Libby Montana was shown to be contaminated with asbestiform fibers. This study is a follow up investigation of a 1980 cross sectional study of 513 workers exposed predominantly to Libby vermiculite ore. The rationale is to determine the long term pulmonary effects of exposure to this vermiculite.

Methods: Of the original 513 workers, 293 have participated, 82 are deceased, 54 refused and 84 remain to be contacted. The majority of participants, as representative of the original cohort, are male (94%) and Caucasian (98%).

Primary outcomes are pleural and interstitial changes as determined from chest radiograph. Exposure to vermiculite ore will be defined categorically (control, low, high) and cumulatively (fiber/cc/year). Chest radiographs are interpreted by three board certified radiologists (B readers). For a radiograph to be classified as abnormal, two of the three B readers must agree.

Results: Preliminary data indicate an increase in the number of workers with pleural changes. Among the first 194 participants, prevalence of pleural plaques is 25% compared to 4% among the overall cohort in 1980. Results will be presented examining the association of pleural and interstitial findings with exposure indices.

Conclusion: Vermiculite contaminated with asbestiform fibers has the propensity to cause an increase in pleural changes at low exposure levels. The public health implications of these preliminary findings are important in view of the national distribution of the Libby vermiculite ore for home and industrial uses.

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Incident Respiratory Symptoms in Older California Farmers

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Rationale: California's generally arid climate and land cultivation practices combine to generate agricultural dusts which present challenges to the respiratory health of farmers. **Methods:** 620 (72%) of current UC Davis Farmer Health Study cohort members who were still working in 2004, were questioned about symptoms of asthma, persistent wheeze, chronic cough and bronchitis using a CATI. Exposures to a range of animal and crop tending tasks, previously associated with dust generation, were recorded in four ways; ever performed, number of years, performed last year, and number of days. From Chi-sq analyses, significant associations ($p < 0.05$) between incident symptoms and exposures were assessed in multivariable logistic regression models adjusted for age and smoking status. **Results:** Mean age of farmers in 2004 was 62.4 (sd 11.6) years, range 36-94. 124 farmers reported current respiratory symptoms, who were symptom free in 1993 (when first contacted), 94 of these reported one, 20 reported two and 10 reported three symptoms. 7.7% (48) were evaluated to have incident persistent wheeze, 6.8% (42) with chronic bronchitis, 6.6% (41) with chronic cough, and 5.3% (33) with asthma. New CC was associated with last year dust intensity, OR = 1.19 (95%CI 1.05-1.35) and with time working in dust OR = 1.02 (95% CI 1.003-1.028). More specifically, new PW was significantly associated with years performing mechanical harvesting and number of days last year driving a tractor. Incident asthma was associated with days hand harvesting last year, CB with any hand harvesting last year, and CC with number of days performing maintenance shop work. **Conclusions:** In this population of older working farmers, incident respiratory symptoms were associated with tasks which generated agricultural dusts, including tractor driving, mechanical and hand harvesting and general shop/repair work.

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Coal Workers' Pneumoconiosis: Geographic Clustering of Rapidly Progressive Disease in the U.S.

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The overall prevalence of coal workers' pneumoconiosis (CWP) has been declining over the last 30 years; nevertheless, short tenure workers continue to develop severe forms of the disease, including progressive massive fibrosis (PMF). Using consensus International Labor Office classifications of films from the NIOSH Coal Workers' X-ray Surveillance Program, we sought to identify and investigate rapidly progressive cases of CWP. Rapid progression was defined as the development or progression of PMF, and/or an increase in small opacity profusion greater than one minor category over five years, after 1985 (allowing >10 years latency following reduction in the permissible dust exposure level in 1973). County-based statistics were derived by dividing the number of rapidly progressive cases by the number of miners evaluated. Of 29,521 coal miners examined between 1996 and 2002, 886 had radiographic changes consistent with CWP, and 783 miners also had a previous film permitting assessment of progression (total 2214 earlier films). A total of 277 (35.4%) miners showed rapid progression on sequential radiographs. PMF was seen on 41 (14.8%) of those cases. Miners with rapidly progressive CWP were younger (mean age \pm SD = 48 \pm 6 vs. 51 \pm 6 years; $p < 0.01$) and reported greater mean tenure in jobs at the coal face (19 \pm 10 vs. 17 \pm 10 years; $p < 0.01$), than the other miners with CWP. Rapidly progressive cases were more likely to have worked in small mines (<50 employees) than in larger mines (OR = 1.55 [95% CI = 1.2-2.0]; $p < 0.01$). A higher proportion of rapidly progressive cases appeared to cluster in eastern Kentucky and western Virginia counties. Despite regulations directed at controlling coal mine dust levels, severe CWP continues to occur. Surveillance for rapid progression of CWP may enhance prevention efforts by identifying specific locations for intervention.

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Chronic Beryllium Disease and Sensitization at a Beryllium Processing Facility

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Rationale: Factors involved in the development of cellular immunity to beryllium (Be) still need to be determined. **Methods:** A medical screening for Be disease of 574 former Be production workers, which included: a medical and work history, a chest x-ray and blood lymphocyte proliferation testing for Be. A task and job exposure matrix was constructed to examine the association between exposure to Be and the development of Be disease. **Results:** Over 90% of the cohort completed the questionnaire and 74% completed the blood and x-ray component of the screening. Forty three (7.5%) had definite or probable chronic Be disease (CBD) and another 40 (7.0%) were sensitized to Be (BeS). The prevalence of CBD and BeS in our cohort was greater than that reported in other Be exposed cohorts. Various exposure measures evaluated included duration, first decade worked, last decade worked, cumulative, mean and peak exposure (both soluble and non-soluble forms) of Be. Soluble cumulative and mean exposure levels were lower in individuals with CBD. BeS individuals had shorter duration of exposure, began work later, last worked earlier, and had lower cumulative and peak exposures and lower non-soluble cumulative and mean exposures. **Conclusion:** A possible explanation for the exposure-response findings of our study relating to an interaction between genetic predisposition and the less permanence of soluble Be in the body is discussed. Both CBD and BeS occurred in former workers at daily working lifetime average mean exposures less than the current allowable Occupational Safety and Health Administration workplace air level standard of 2 $\mu\text{g}/\text{m}^3$ and the Department of Energy standard of 0.2 $\mu\text{g}/\text{m}^3$.

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