

STAT1 deficiency, highlighting the importance of tube rigidity and genetic susceptibility. The mechanism of STAT1 susceptibility to MWCNTs-induced fibrosis appears to be through dysregulated transforming growth factor- β 1 production and signaling.

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Deployment-related Lung Disease Is Associated with Abnormal Ventilation on Cardiopulmonary Exercise Testing and with Increased Lung Clearance Index Score

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Rationale: An unknown number of post-9/11 military deployers to Iraq and Afghanistan have returned with respiratory symptoms and may be at risk for deployment-related distal lung disease, detected only on surgical lung biopsy. We hypothesized that cardiopulmonary exercise testing and lung clearance index scores would differ significantly between deployers with and without biopsy-proven deployment-related distal lung disease.

Objectives: To assess if there are differences in cardiopulmonary exercise testing and lung clearance index scores between deployers with and without biopsy-proven deployment-related distal lung disease.

Methods: We compared 36 deployers with definite deployment-related distal lung disease (based on surgical lung biopsy findings of bronchiolitis, granulomatous pneumonitis, and/or emphysema)

with 26 deployers without definite deployment-related distal lung disease. We used a two-sample *t* test assuming unequal variances to compare ventilatory and gas exchange cardiopulmonary exercise testing variables at submaximal and maximal workloads. We then conducted lung clearance index testing in 24 healthy nondeployed control subjects and 28 symptomatic deployers (17 with definite deployment-related distal lung disease), and compared mean lung clearance index scores using adjusted *t* tests.

Results: At maximum workload, those with definite deployment-related distal lung disease had higher respiratory rates and mean measured ratio of minute ventilation to maximal voluntary ventilation greater than 80%, compared with a mean ratio of 69.5% in those without deployment-related distal lung disease. There were no significant differences in cardiopulmonary exercise testing gas exchange parameters. Adjusting for smoking and age, there were differences ($P = 0.001$) in lung clearance index between deployers (7.76; 95% confidence interval, 7.34–8.17) and control subjects (6.95; 95% confidence interval, 6.73–7.17); but after adjusting for body mass index, differences became insignificant ($P = 0.10$) between deployers (7.42; 95% confidence interval, 7.13–7.71) and control subjects (7.06; 95% confidence interval, 6.74–7.39).

Conclusions: Increased lung clearance index scores and abnormal exercise ventilatory parameters consistent with small-airway disease show promise as noninvasive diagnostic markers that may help identify symptomatic deployers with deployment-related distal lung disease.

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Effects of Controlled Diesel Exhaust and Allergen Exposure on microRNA and Gene Expression in Humans Modulation of Lung Inflammatory Markers Associated with Asthma

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Rationale: Air pollution may contribute to the development of allergic diseases, including asthma, by enhancing immune responses to allergen, but the effects on microRNA, messenger RNA, and inflammatory markers remain unexplored.

Objectives: To determine if acute exposure to diesel exhaust and/or allergen alters expression of microRNA and genes with effects on inflammatory markers associated with asthma.

Methods: Fifteen atopic participants were exposed in a crossover trial to inhaled filtered air or diesel exhaust (DE; 300 μg particulate matter with aerodynamic diameter less than or equal to $2.5 \mu\text{m}/\text{m}^3$), followed by saline-controlled, segmental allergen challenge. Lung inflammatory markers, gene expression, and microRNAs were measured in bronchial brushings, bronchial wash, or bronchoalveolar lavage 48 hours after exposure.

Results: DE + saline and DE + allergen significantly modulated the highest number of microRNAs and messenger RNAs. Allergen exposure significantly modulated microRNAs, including miR-324-5p, miR-132-3p, and miR-183-5p, and genes, including cyclin-dependent kinase inhibitor 1C (*CDKN1A*) and nuclear factor κB inhibitor α (*NFKBIA*), but DE did not significantly modify this effect. Inflammatory markers, including bronchoalveolar lavage eosinophil cell percentages and eosinophil cationic protein, were significantly increased, whereas bronchoalveolar lavage epithelial cell percentages were reduced after allergen exposure.

Conclusions: Expression of genes and microRNAs associated with bronchial immune responses were significantly modulated by allergen and DE.

Clinical trial registered with www.clinicaltrials.gov (NCT01699204).

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Observed Home Dampness and Mold Are Associated with Sustained Spikes in Personal Exposure to Particulate Matter Less than $10 \mu\text{m}$ in Diameter in Exacerbation-Prone Children with Asthma

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Rationale: Home dampness and mold are associated with asthma severity and exacerbations, but little is known about the nature of these exposures in at-risk children.

Objectives: To test the hypothesis that observed dampness, water damage, and mold in the home are associated with higher exposure to particulate matter less than $10 \mu\text{m}$ in diameter in a cohort of at-risk children with asthma.

Methods: We performed a pilot study in 8- to 16-year-old children with exacerbation-prone asthma ($n = 29$; Denver Asthma Panel Study). Exposure to particulate matter less than $10 \mu\text{m}$ in diameter was measured over ~ 72 hours with personal wearable monitors (MicroPEM [RTI International] and iTrack Micro GPS tracker) and stationary bedroom-located monitors (PEM, MSP Corporation). Mean percentage personal monitored time was 93% (95% confidence interval, 90–96%). Mean and spikes of real-time exposure to particulate matter less than $10 \mu\text{m}$ in diameter were calculated and, for personal monitored samples, partitioned into exposure while at home, school, or other locations. We defined a sustained spike exposure as a continuous period of 20 minutes or longer during which levels were greater than $50 \mu\text{g}/\mu\text{L}$ over the participant's minimum levels, using a 2-minute moving average of the particulate matter measurements. Mold and dampness were assessed by detailed home inspection.

Results: Visible water damage/moisture/mold and mold/mildew were common in the homes of exacerbation-prone children: bathroom, 60% and 46%; basement, 30% and 34%; kitchen, 22% and 39%; living room, 20% and 2%; bedroom, 12% and 2%; and other rooms, 21% and 7%, respectively. Personal and bedroom filter-based levels of particulate matter less than $10 \mu\text{m}$ in diameter were associated with home cumulative measures of water damage/moisture/mold (personal $r^2 = 0.13$, $P = 0.02$; bedroom $r^2 = 0.19$, $P = 0.006$; analysis of variance) and mold/mildew (personal $r^2 = 0.11$, $P = 0.04$; bedroom $r^2 = 0.18$, $P = 0.008$). Real-time integrated particulate matter less than $10 \mu\text{m}$ in diameter during sustained spike exposures that occurred when participants were home (normalized by total duration of sustained spike exposures) was associated with cumulative drips/leaks/wet areas ($r^2 = 0.27$; $P = 0.004$), mold/mildew ($r^2 = 0.15$; $P = 0.04$), and water damage/moisture/mold ($r^2 = 0.14$; $P = 0.04$). Other measures of exposure to particulate matter less than $10 \mu\text{m}$ in diameter from personal or stationary monitors were not associated with home dampness or mold indicators.

Conclusions: Although mold exposure was not directly quantified in the respirable aerosol in this study, observations of home dampness and mold were associated with sustained spikes in respirable particulate matter less than $10 \mu\text{m}$ in diameter that was measured by wearable real-time monitors. In our cohort of at-risk children, this finding could imply that mold may exert respiratory health effects via sustained spikes in exposure and help to guide future studies and interventions to reduce these spikes and improve asthma outcomes.

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