

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).

Author disclosures are available with the text of this article at www.atsjournals.org.

(Received in original form June 19, 2017; accepted in final form July 13, 2017)

Supported by AllerGenNCE, WorkSafeBC, British Columbia Lung Association, Canadian Institutes of Health Research (CIHR), CIHR Integrated and Mentored Pulmonary and Cardiovascular Training Program, Sumitomo Life Social Welfare Services Foundation, and Mochida Memorial Foundation for Medical and Pharmaceutical Research.

Correspondence and requests for reprints should be addressed to Christopher Carlsten, M.D., M.P.H., The Lung Centre, 7th Floor, 2775 Laurel Street, Vancouver, BC V5Z1M9, Canada. E-mail: carlsten@mail.ubc.ca.

The data presented in this talk were published in Rider CF, Yamamoto M, Günther OP, Hirota JA, Singh A, Tebbutt SJ, Carlsten C. Controlled diesel exhaust and allergen coexposure modulates microRNA and gene expression in humans: effects on inflammatory lung markers. *J Allergy Clin Immunol* 2016;138:1690–1700.

Ann Am Thorac Soc Vol 15, Supplement 2, pp S130–S131, Apr 2018
Copyright © 2018 by the American Thoracic Society
Internet address: www.atsjournals.org

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

Cullen M. Dutmer^{1,2}, Allison M. Schiltz^{1,2}, Kristy L. Freeman^{1,2}, Matthew J. Christie^{1,2}, Juana A. Cerna^{1,2}, Seung-Hyun Cho³, Ryan T. Chartier³, Jonathan W. Thornburg³, Katharine L. Hamlington⁴, James L. Crooks^{2,5}, Tasha E. Fingerlin^{2,5}, David A. Schwartz², and Andrew H. Liu^{1,2,5}

¹Children's Hospital Colorado, Aurora, Colorado; ²University of Colorado School of Medicine, Aurora, Colorado; ³Research Triangle Institute International, Research Triangle Park, North Carolina; ⁴University of Vermont, Burlington, Vermont; and ⁵National Jewish Health, Denver, Colorado

ORCID ID: 0000-0001-9806-4739 (C.M.D.).

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.

Author disclosures are available with the text of this article at www.atsjournals.org.

(Received in original form July 22, 2017; accepted in final form September 25, 2017)

Supported by Environmental Protection Agency grant RD834515010, NIH/National Institute of Environmental Health Sciences grant P01-ES018181, and NIH grant T32-HL076122.

Correspondence and requests for reprints should be addressed to Cullen M. Dutmer, M.D., 13123 East 16th Avenue, Box 518, Aurora, CO 80045. E-mail: cullen.dutmer@childrenscolorado.org.

Ann Am Thorac Soc Vol 15, Supplement 2, pp S131–S132, Apr 2018
Copyright © 2018 by the American Thoracic Society
Internet address: www.atsjournals.org

Chronic Obstructive Pulmonary Disease and Herbicide Exposure in Vietnam-Era U.S. Army Chemical Corps Veterans

Yasmin Cypel¹, Stella E. Hines², Victoria J. Davey³,
Stephanie M. Eber¹, and Aaron I. Schneiderman¹

¹Epidemiology Program, Post-Deployment Health Services (10P4Q), Office of Patient Care Services, and ³Office of Research and Development, Department of Veterans Affairs, Washington, District of Columbia; and ²University of Maryland–Baltimore School of Medicine, Baltimore, Maryland

Rationale: Past research demonstrates a possible association between herbicide exposure and respiratory health. Biologic plausibility and inhalation as a mode of exposure further support the contention that herbicides may act as adverse contributors to respiratory status, especially in military personnel who were responsible for chemical maintenance and distribution during the Vietnam War.

Objectives: This study examines the association between chronic obstructive pulmonary disease and herbicide exposure among Vietnam-era U.S. Army Chemical Corps veterans.

Methods: A 2013 three-phase health study was conducted that included a survey (mail or telephone), in-home physical examinations, and medical record reviews/abstractions. Living, eligible veterans ($n = 4,027$) were identified using an existing cohort of men ($n = 5,609$) who either served in Vietnam ($n = 2,872$) or never served in Southeast Asia ($n = 2,737$). The health survey collected self-reported data on physician-diagnosed pulmonary conditions (chronic obstructive pulmonary disease, emphysema, and chronic bronchitis), service-related herbicide spraying history, cigarette smoking status, alcohol use, and demographics. Data from service personnel files confirmed chemical operations involvement and service status, whereas serum samples analyzed for 2,3,7,8-tetrachlorodibenzo-p-dioxin supported self-reported herbicide exposure. National Institute for Occupational Safety and Health quality-assured spirometry was performed during the physical examinations on a subset of survey respondents ($n = 468$ of 733 selected for participation and who provided consent) to determine mainly spirometric obstructive respiratory disease (forced expiratory volume in 1 second [FEV₁]/forced vital capacity [FVC] < lower limit of normal [LLN], FVC ≥ LLN, and FEV₁ < LLN; and FEV₁/FVC < LLN and FEV₁ ≥ LLN). Associations between chronic obstructive pulmonary disease and veteran characteristics were examined ($n = 403$) using multivariable models.

Results: Reporting here specifically on spirometrically diagnosed disease, prevalence of obstructive disease was 8.4%. No significant differences in mean values of FEV₁/FVC or mean percentage of predicted for FEV₁ and FVC between herbicide sprayers and nonsprayers were found. The odds of spirometric obstructive disease among sprayers were 0.65 times the odds among nonsprayers (adjusted odds ratio, 0.65; 95% confidence interval, 0.28–1.47), although elevated odds for spirometric restrictive disease were observed for sprayers versus nonsprayers (adjusted odds ratio, 1.61; 95% confidence interval, 0.85–3.06). Race/ethnicity, anthropometric measures, and cigarette smoking status accounted for differences among veterans' respiratory patterns.

Conclusions: No significant association between herbicide exposure and spirometry-determined chronic obstructive pulmonary disease was found. Greater focus is required on confirming diagnoses of respiratory disease through spirometry in epidemiological research.

Keywords: herbicides; chronic obstructive pulmonary disease; Vietnam War

Author disclosures are available with the text of this article at www.atsjournals.org.

(Received in original form June 21, 2017; accepted in final form July 20, 2017)

Supported by the Epidemiology Program, Post-Deployment Health Services (10P4Q), Office of Patient Care Services, Department of Veterans Affairs.

Correspondence and requests for reprints should be addressed to Yasmin Cypel, Ph.D., M.S., Epidemiology Program, Post-Deployment Health Services (10P4Q), Office of Patient Care Services, 810 Vermont Avenue, NW, U.S. Department of Veterans Affairs, Washington, DC 20420. E-mail: yasmin.cypel@va.gov.

Ann Am Thorac Soc Vol 15, Supplement 2, p S132, Apr 2018
Copyright © 2018 by the American Thoracic Society
Internet address: www.atsjournals.org

Effects of Household Air Pollution in Malawi and Human Immunodeficiency Virus Status on Respiratory Symptoms and Inflammation, Injury, and Repair Markers

Charles Kim¹, Hannah Jary^{2,3}, Kevin Mortimer³,
Kelly S. Schweitzer⁴, Doug Curran-Everett^{1,4}, Stephen Gordon⁵,
and Irina Petrache^{1,4}

¹University of Colorado Denver, Anschutz Medical Campus, Aurora, Colorado; ²Wellcome Trust Tropical Centre, University of Liverpool, Liverpool, United Kingdom; ³Malawi Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi; ⁴National Jewish Health, Denver, Colorado; and ⁵Liverpool School of Tropical Medicine, University of Liverpool, Liverpool, United Kingdom

Rationale: Household air pollution (HAP) and human immunodeficiency virus (HIV) are associated with increased risk for chronic obstructive pulmonary disease. Both HAP and HIV are widespread in Sub-Saharan Africa, including Malawi, where HIV has 10.6% prevalence in patients 15–49 years old.