Published in final edited form as:

Ann Am Thorac Soc. 2017 May; 14(5): 810-811. doi:10.1513/AnnalsATS.201612-1026LE.

Deaths from Nonmalignant Respiratory Disease in Styrene-Exposed Workers: Does Obliterative Bronchiolitis Contribute to Mortality?

Randall J. Nett, M.D., M.P.H.,

National Institute for Occupational Safety and Health Morgantown, West Virginia

Nicole T. Edwards, M.S.,

National Institute for Occupational Safety and Health Morgantown, West Virginia

Avima M. Ruder, Ph.D.,

National Institute for Occupational Safety and Health Cincinnati, Ohio

Stephen J. Bertke, Ph.D.,

National Institute for Occupational Safety and Health Cincinnati, Ohio

Isna Keumala, M.S.,

National Institute for Occupational Safety and Health Morgantown, West Virginia

Jean Cox-Ganser, Ph.D., and

National Institute for Occupational Safety and Health Morgantown, West Virginia

Kristin J. Cummings, M.D., M.P.H.

National Institute for Occupational Safety and Health Morgantown, West Virginia

To the Editor:

Since the 1970s, the U.S. National Institute for Occupational Safety and Health has monitored a cohort of 5,204 workers from two reinforced plastic boat–building facilities where exposures to styrene were characterized (1–3). Styrene is a volatile organic compound used during fiberglass production (4). An analysis of this cohort demonstrated that short-tenured workers with high styrene exposures had elevated standardized mortality ratios for nonmalignant respiratory disease (1.99; 95% confidence interval [CI], 1.38–2.79) and chronic obstructive pulmonary disease (COPD) (2.60; 95% CI, 1.70–3.81) (2).

These findings are noteworthy considering that nine cases of obliterative bronchiolitis have been reported after employment in similar industries that use styrene to make reinforced plastics (5). Nontransplantation-associated obliterative bronchiolitis occurs rarely after occupational exposure to inhalational toxins (6). In addition, rodent models have demonstrated damage to the respiratory epithelium after inhalational exposure to high

Author Contributions: R.J.N. and K.J.C. had the idea for the letter. A.M.R. and S.J.B. contributed to record and exposure data acquisition. N.T.E. and I.K. contributed to data management and analysis. R.J.N., K.J.C., and J.C.-G. contributed to writing the letter. All authors accept responsibility for the letter.

Nett et al. Page 2

concentrations of styrene (7–10). We hypothesized that styrene-related obliterative bronchiolitis contributed to the excess burden of nonmalignant respiratory disease mortality in this cohort but went unrecognized and was incorrectly categorized on death certificates as COPD (11). We therefore aimed to describe any decedents from this cohort who died of nonmalignant respiratory disease and who had possible underlying obliterative bronchiolitis.

Methods

From the cohort, 157 decedents were identified who had a known cause of death as COPD, pneumonia, or other respiratory disease as of December 31, 2011. Medical records were requested from the hospital listed on the death certificate and additional health care facilities identified in the medical records, as needed. Available death certificates and medical records were reviewed and abstracted.

We examined decedents who died at less than 55 years of age, as these deaths were unlikely to be attributable only to tobacco use (12). For example, U.S. death rates from COPD during 1968–2011 were low among persons aged less than 55 years (ranging from fewer than 0.10–0.35, 1–2, and 6–10 deaths per 100,000 population among persons aged 25–34, 35–44, and 45–54 yr, respectively) (13). Industrial hygiene data were used to categorize workers as ever having worked in departments with high styrene exposures (42.5 or 71.7 ppm, 8-h time-weighted averages, depending on company).

Results and Discussion

We obtained 142 death certificates and medical records for 31 decedents. For those with a death certificate, 125 (88%) were male, and the median age at death was 69 years (range, 32–97 yr). One death was attributed to bronchiolitis. Fifteen decedents died at less than 55 years of age, only one of whom had available medical records. Of these younger decedents, median tenure was 0.5 years (range, 0.1–6.8 yr) and respiratory causes of death included COPD (n = 9), pneumonia (2), bronchiolitis (1), bronchiectasis (1), pneumonitis (1), and lung abscesses (1). Eight (53%) younger decedents had high styrene exposures compared with 40% of the entire cohort (3).

Four of the nine younger decedents from COPD had known tobacco exposure and five had unknown tobacco exposure as tobacco use was not assessed on their death certificates; five had high styrene exposures; and seven had known COPD onset (early 30s [n=1], early 40s [n=3], and 40s not further specified [n=3]). Two of these younger decedents had prior tobacco use and exposure to high styrene concentrations, tenure for less than 1 and 1-5 years, and COPD for 10 and 20+ years at the time of death. The only younger decedent with available medical records had high styrene exposure with tenure less than 1 year, unknown tobacco use, pulmonary function testing that demonstrated severe airway obstruction and air trapping, and a cause of death listed as COPD that had been present for "years."

Limitations of this analysis included difficulty in obtaining medical records as many were destroyed, potentially resulting in an underestimation of possible cases of obliterative bronchiolitis. In addition, this analysis did not assess other occupational and nonoccupational exposures that might have contributed to respiratory mortality.

Nett et al. Page 3

Multiple boat builders were characterized as having died of COPD before age 55 years and had disease onset in their early 30s to 40s. These findings suggest some of the excess burden of nonmalignant respiratory disease in this cohort could be associated with obliterative bronchiolitis. An estimated 90,000 U.S. workers are likely exposed to styrene (14) and many others are exposed globally. Our data, although preliminary, add to the growing body of literature that suggests respiratory health risks among workers exposed to styrene and support further research in this area (5).

Acknowledgments

The findings and conclusions in this letter are those of the author(s) and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

References

- Okun AH, Beaumont JJ, Meinhardt TJ, Crandall MS. Mortality patterns among styrene-exposed boatbuilders. Am J Ind Med 1985;8:193–205. [PubMed: 4050802]
- 2. Ruder AM, Meyers AR, Bertke SJ. Mortality among styrene-exposed workers in the reinforced plastic boatbuilding industry. Occup Environ Med 2016;73:97–102. [PubMed: 26574575]
- 3. Ruder AM, Ward EM, Dong M, Okun AH, Davis-King K. Mortality patterns among workers exposed to styrene in the reinforced plastic boatbuilding industry: an update. Am J Ind Med 2004;45:165–176. [PubMed: 14748047]
- 4. International Agency for Research on Cancer, World Health Organization. IARC monographs on the evaluation of carcinogenic risks to humans, Vol. 82: Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. Lyon, France: IARC Press; 2002.
- Nett RJ, Cox-Ganser JM, Hubbs AF, Ruder AM, Cummings KJ, Huang YT, Kreiss K. Non-malignant respiratory disease among workers in industries using styrene: a review of the evidence. Am J Ind Med 2017;60:163–180. [PubMed: 28079275]
- Barker AF, Bergeron A, Rom WN, Hertz MI. Obliterative bronchiolitis. N Engl J Med 2014;370:1820–1828. [PubMed: 24806161]
- 7. Cruzan G1, Cushman JR, Andrews LS, Granville GC, Miller RR, Hardy CJ, Coombs DW, Mullins PA. Subchronic inhalation studies of styrene in CD rats and CD-1 mice. Fundam Appl Toxicol 1997;35:152–165. [PubMed: 9038236]
- 8. Coccini T, Fenoglio C, Nano R, De Piceis Polver P, Moscato G, Manzo L. Styrene-induced alterations in the respiratory tract of rats treated by inhalation or intraperitoneally. J Toxicol Environ Health 1997;52:63–77. [PubMed: 9269323]
- 9. Cruzan G, Bus J, Hotchkiss J, Sura R, Moore C, Yost G, Banton M, Sarang S. Studies of styrene, styrene oxide and 4-hydroxystyrene toxicity in CYP2F2 knockout and CYP2F1 humanized mice support lack of human relevance for mouse lung tumors. Regul Toxicol Pharmacol 2013;66:24–29. [PubMed: 23454103]
- Ohashi Y, Nakai Y, Ikeoka H, Koshimo H, Nakata J, Esaki Y, Horiguchi S, Teramoto K.
 Degeneration and regeneration of respiratory mucosa of rats after exposure to styrene. J Appl Toxicol 1986;6:405–412. [PubMed: 3805568]
- 11. Centers for Disease Control and Prevention (CDC). Obliterative bronchiolitis in workers in a coffee-processing facility: Texas, 2008–2012. MMWR Morb Mortal Wkly Rep 2013;62:305–307. [PubMed: 23615673]
- Shavelle RM, Paculdo DR, Kush SJ, Mannino DM, Strauss DJ. Life expectancy and years of life lost in chronic obstructive pulmonary disease: findings from the NHANES III Follow-up Study. Int J Chron Obstruct Pulmon Dis 2009;4:137–148. [PubMed: 19436692]
- 13. Ford ES. Trends in mortality from COPD among adults in the United States. Chest 2015;148:962–970. [PubMed: 25411775]

Nett et al. Page 4

14. Occupational Safety and Health Administration, U.S. Department of Labor. Safety and health topics: styrene. 2016 [accessed 2015 Nov 13]. Available from: https://www.osha.gov/SLTC/styrene/