

3. Jakkula M, Le Cras TD, Gebb S, Hirth KP, Tuder RM, Voelkel NF, *et al.* Inhibition of angiogenesis decreases alveolarization in the developing rat lung. *Am J Physiol Lung Cell Mol Physiol* 2000;279:L600–L607.
4. Kasahara Y, Tuder RM, Taraseviciene-Stewart L, Le Cras TD, Abman S, Hirth PK, *et al.* Inhibition of VEGF receptors causes lung cell apoptosis and emphysema. *J Clin Invest* 2000;106:1311–1319.
5. Bilan VP, Schneider F, Novelli EM, Kelley EE, Shiva S, Gladwin MT, *et al.* Experimental intravascular hemolysis induces hemodynamic and pathological pulmonary hypertension: association with accelerated purine metabolism. *Pulm Circ* 2018;8:2045894018791557.
6. Tuder RM, Zhen L, Cho CY, Taraseviciene-Stewart L, Kasahara Y, Salvemini D, *et al.* Oxidative stress and apoptosis interact and cause emphysema due to vascular endothelial growth factor receptor blockade. *Am J Respir Cell Mol Biol* 2003;29:88–97.
7. Taraseviciene-Stewart L, Kasahara Y, Alger L, Hirth P, Mc Mahon G, Waltenberger J, *et al.* Inhibition of the VEGF receptor 2 combined with chronic hypoxia causes cell death-dependent pulmonary endothelial cell proliferation and severe pulmonary hypertension. *FASEB J* 2001;15:427–438.
8. Abe K, Toba M, Alzoubi A, Ito M, Fagan KA, Cool CD, *et al.* Formation of plexiform lesions in experimental severe pulmonary arterial hypertension. *Circulation* 2010;121:2747–2754.
9. Bonnet S, Provencher S, Guignabert C, Perros F, Boucherat O, Schermuly RT, *et al.* Translating research into improved patient care in pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2017;195:583–595.

Copyright © 2019 by the American Thoracic Society

Ⓔ Hypersensitivity Pneumonitis Mortality by Industry and Occupation

To the Editor:

We read with interest the research letter by Fernández Pérez and colleagues (1) and agree that population-level mortality from hypersensitivity pneumonitis (HP) has not been well characterized in the United States. However, the role of occupation in the development and severity of HP is well established (2–4). Occupational exposures are responsible for a substantial portion of HP cases, and it is important to monitor trends in morbidity and mortality so that prevention activities can be prioritized. To that end, we conducted a similar analysis of HP mortality data from 2003 to 2017 (ICD-10 code J67.x) while also taking available employment history into account.

We identified a similar demographic risk profile: 58% of decedents were male, 93% were white, and a high proportion lived in the Midwest or Northeast. Using data obtained from 21 states during 2003, 2004, and 2007–2013, we calculated proportionate mortality ratios (PMRs) by usual industry and occupation while adjusting for age, sex, and race. Among industries, the PMR was highest for animal production (PMR, 9.9; 95% confidence interval [CI], 5.1–17.3) and crop production (PMR, 5.2; 95% CI, 2.9–8.7), and among occupations, it was highest among farmers and ranchers (PMR, 7.9; 95% CI, 5.0–11.8).

Fernández Pérez and colleagues acknowledge that exposure information was not available in these data; however, because HP is often caused by workplace exposures, a decedent's work history is a

significant factor that should be considered. The authors suggest that genetic differences among racial groups could play a role in determining susceptibility to HP. We think it is unlikely that the racial differences observed are the result of genetic factors. It is far more likely that this observation is confounded by associations with geographical clustering of agricultural industries and occupations that are associated with race, which are in turn associated with exposure to antigens primarily found in organic substances.

We applaud the authors for highlighting the public health importance of HP, especially because mortality has been increasing and the root cause of this increase is unknown. Collecting a thorough clinical and occupational history is key to diagnosing HP and identifying an inciting antigen. If an occupational cause is identified, the individual worker might benefit from exposure reduction or avoidance, and a workplace evaluation could be conducted to identify additional cases and assess exposure controls. ■

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

Noemi B. Hall, Ph.D.*
John M. Wood, M.S.
A. Scott Laney, Ph.D.
David J. Blackley, Dr.P.H.
National Institute for Occupational Safety and Health
Morgantown, West Virginia

ORCID ID: 0000-0002-6710-2015 (N.B.H.).

*Corresponding author (e-mail: nhall@cdc.gov).

References

1. Fernández Pérez ER, Sprunger D, Ratanawatkul P, Maier LA, Huie TJ, Swigris JJ, *et al.* Increasing hypersensitivity pneumonitis-related mortality in the United States from 1988 to 2016 [letter]. *Am J Respir Crit Care Med* 2019;199:1284–1287.
2. Bang KM, Weissman DN, Pinheiro GA, Antao VC, Wood JM, Syamlal G. Twenty-three years of hypersensitivity pneumonitis mortality surveillance in the United States. *Am J Ind Med* 2006;49:997–1004.
3. Quirce S, Vandenplas O, Campo P, Cruz MJ, de Blay F, Koschel D, *et al.* Occupational hypersensitivity pneumonitis: an EAACI position paper. *Allergy* 2016;71:765–779.
4. Feary JR, Szram J. Occupational hypersensitivity pneumonitis: what is the evidence, when to think of it, and what to do. *Clin Pulm Med* 2016;23:23–29.

Copyright © 2019 by the American Thoracic Society

Reply to Hall *et al.*

From the Authors:

We welcome the comments by Dr. Hall and colleagues on our identified long-term trends in hypersensitivity pneumonitis (HP)

ⒺThis article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0 (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). For commercial usage and reprints, please contact Diane Gern (dgern@thoracic.org).

Originally Published in Press as DOI: 10.1164/rccm.201904-0810LE on May 3, 2019

ⒺThis article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0 (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). For commercial usage and reprints, please contact Diane Gern (dgern@thoracic.org).

Originally Published in Press as DOI: 10.1164/rccm.201904-0876LE on May 3, 2019