cannot afford out-of-pocket costs to purchase a POC ($2,000–$4,000), or live alone and cannot manage equipment without assistance.

Dakkak and colleagues present a notable and novel finding about the trade patients may make to preserve their mobility. Nearly half (47%) of respondents used a POC despite knowing that the device did not produce sufficient oxygen to meet their needs. This finding should raise alarms, given the known survival benefits of LTOT in patients with severe resting hypoxemia (9, 10).

Whereas respondents frequently listed duration of all three portable devices as a problem, when they were asked to prioritize device design needs, portability was ranked as a higher priority than device duration. Notwithstanding limitations in study methodology in the report by Dakkak and colleagues (unclear psychometric properties of the questionnaire, uncertain flow rates, missing data about sex in a substantial number of respondents, lack of objective data about weight of oxygen equipment), the verdict from the study by Dakkak and colleagues is clear—patients are likely to choose hypoxemia over social isolation when considering home oxygen equipment.

Clinicians frequently prescribe pulmonary rehabilitation and exercise to their patients with chronic pulmonary problems, yet the technology for portable oxygen devices continues to impede mobility. We hope that oxygen equipment manufacturers, researchers, the healthcare provider community, and policymakers take notice of the need for lightweight, long-lasting portable equipment that can consistently deliver high-flow continuous oxygen. ■

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

References

1 Jacobs SS, Lindell KO, Collins EG, Garvey CM, Hernandez C, McLaughlin S, *et al.* Patient perceptions of the adequacy of supplemental oxygen therapy: Results of the American Thoracic Society Nursing Assembly Oxygen Working Group Survey. *Ann Am Thorac Soc* 2018;15:24–32.

2 Jacobs SS, Lederer DJ, Garvey CM, Hernandez C, Lindell KO, McLaughlin S, *et al.* Optimizing home oxygen therapy: An official American Thoracic Society workshop report. *Ann Am Thorac Soc* 2018; 15:1369–1381.

3 Dobson A, Heath S, Kilby D, Hu J, DaVanzo J. Access to home medical equipment: Survey of beneficiary, case manager and supplier experiences [serial online]. Vienna, VA: Dobson DaVanzo & Associates; 2017 [accessed 2017 Oct 10]. Available from: https://s3.amazonaws.com/aafh/downloads/1287/Dobson_DaVanzo_Patient_Access_Survey_Final_Report_10.11.17_FINAL.pdf?1507750324.

4 Lindell KO, Collins EG, Catanzarite L, Garvey CM, Hernandez C, Mclaughlin S, *et al.* Equipment, access and worry about running short of oxygen: Key concerns in the ATS patient supplemental oxygen survey. *Heart Lung* 2019;48:245–249.

5 Jacobs SS, Krishnan JA, Lederer DJ, Ghazipura M, Hossain T, Tan AM, *et al.* Home oxygen therapy for adults with chronic lung disease: An official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med* 2020;202: e121–e141.

6 Branson RD. Oxygen therapy in COPD. *Respir Care* 2018;63: 734–748.

7 Dakkak J, Tang W, Smith JT, Balasubramanian A, Mattson M, Ainechi A, *et al.* Burden and unmet needs with portable oxygen in patients on long-term oxygen therapy. *Ann Am Thorac Soc* 2021; 18:1498–1505.

8 Arnold E, Bruton A, Donovan-Hall M, Fenwick A, Dibb B, Walker E. Ambulatory oxygen: Why do COPD patients not use their portable systems as prescribed? A qualitative study. *BMC Pulm Med* 2011; 11:9.

9 Stuart-Harris C. Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema: report of the Medical Research Council Working Party. *Lancet* 1981;1: 681–686.

10 Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: A clinical trial. *Ann Intern Med* 1980;93:391–398.

Just as the Twig Is Bent, the Tree's Inclined

Kenneth R. Chapman, M.D., M.Sc.[1,2]

[1]Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; and [2]Asthma and Airway Centre, University Health Network, Toronto, Ontario, Canada

ORCID ID: 0000-0002-2498-9859 (K.R.C.).

A time-honored remedy for respiratory symptoms has been to expose the cough sufferer to increased airborne moisture. A simple homemade approach has been the readily available hot shower, an option when one's child begins to cough and wheeze unexpectedly in the middle of the night. But concerned and conscientious parents of children with chronic or recurrent cough will often invest in small commercial humidifiers meant to be run at a child's bedside through the night. By the late 20th century, epidemiologists expressed concern when they identified strong associations between bedroom

DOI: 10.1513/AnnalsATS.202106-743ED

humidifier use and the presence of childhood asthma. Could such an association imply a cause-and-effect relationship? Other associations reported by epidemiologists were almost certainly causative; exposure to secondhand tobacco smoke or the use of household natural gas for cooking have plausible mechanistic roles in producing airway inflammation and injury. Those who espoused a cause-and-effect relationship between humidifier use and childhood asthma observed that dust mites thrive in conditions of high relative humidity as do a variety of molds (1). Indeed, at least one epidemiologic study has reported an association between humidifier use and subsequent new asthma diagnoses (2). However, a precise causal pathway between humidifier use and asthma has been difficult to confirm. Although the theory that humidifier use increases asthma risk by encouraging dust mite exposure remains controversial, all parents and physicians agree that if humidifiers are used in a child's bedroom, the humidifier must be kept clean. And so once again, we are reminded that "the road to hell is paved with good intentions."

Between 1994 and 2011, when the products were withdrawn from the market, up to 20 humidifier disinfectants were available in South Korea, and it is believed that up to 8 million people were exposed to these agents, the chief culprit among them being polyhexamethylene guanidine hydrochloride (PHMG) (3). Various pulmonary injuries have been reported with the official death toll set at 130 people as of 2016. It has since been suggested that the actual death toll may be far higher.

In this issue of *AnnalsATS*, Lee and colleagues (pp. 1523–1532) report their careful examination of children exposed to these toxic humidifier cleaners and subsequently treated for asthma (4). As compared with children treated for asthma without a history of exposure to PHMG, children with a history of low-dose exposure had asthma that was different in terms of airway physiology and inflammatory markers. Children with asthma unrelated to such toxic exposures had typical responses to methacholine, greater airflow limitation on spirometry, and a familiar pattern of type 2 inflammatory markers such as elevated serum periostin levels. Children receiving asthma therapy after prolonged low-dose exposure to PHMG were less likely to exhibit these features. The study by Lee and colleagues takes advantage of an unfortunate but discrete and readily defined childhood exposure to examine the genesis of a distinct asthma phenotype. Their study has broad implications for asthma care and research.

Although the phrase "personalized medicine" is often spoken, it is still uncommon to find evidence of a personalized approach to common respiratory diseases in clinical settings. In the case of asthma, we have begun to characterize phenotypes of severe asthma, an approach driven by highly specific monoclonal interventions (5). But this approach seems limited to the 5 or 10% of asthma sufferers considered to have severe disease; the majority receive a "one-size-fits-all" approach. Post-PHMG asthma may be rare and seldom seen outside South Korea but a more general phenotype of postinjury asthma without type 2 inflammatory biomarkers is likely to be readily identifiable in clinics. A history of early life pulmonary injury and less variable airflow limitation might be the first clue that a patient suffers from such an asthma variant. Could exhaled nitric oxide be used to distinguish postinjury asthma from more commonplace type 2 inflammatory airway disease (6)? This seems plausible but this clinically available measurement was not part of the post-PHMG study.

The authors remind us that early childhood can influence adult lung health. Indeed, prenatal exposure to tobacco smoke, low birth weight, and childhood asthma are well known risk factors for chronic obstructive pulmonary disease in adulthood, a fact largely unknown to the general public and overlooked by most clinicians (7). The lungs have little or no ability to regenerate or return to normal after significant injury whether acute or chronic, yet pulmonologists tackling adult dyspnea seldom look beyond the current and obvious factors to explain the abnormalities they see. Although none of us would minimize the impact of current smoking or pet dander exposure, we are unwise to ignore a lifetime of potentially significant events. The bronchopulmonary dysplasia of prematurity looks like emphysema in the young and breathless adult (8). An episode of respiratory syncytial virus bronchiolitis may make it seem that adult asthma has been accompanied by surprisingly premature "remodeling" (9). Lee and colleagues have described a phenotype of asthma present in a relatively small number of children exposed carelessly to a substance now withdrawn from the marketplace and widespread household use. But the children they describe will almost certainly have different responses to therapy and different outcomes as compared with children with more commonplace asthma phenotypes. Sadly, we have done little to develop this notion of preserving lung health throughout a lifetime. Dentists have been more successful preserving adult dentition than pulmonary doctors have in ensuring adults can continue to breathe comfortably into old age. Except for cystic fibrosis, few pulmonary diseases cross the artificial pediatric/adult divide in terms of our awareness and shared approaches to care.

As thought-provoking as we may find the study by Lee and colleagues, it is not without its limitations. Some might argue with the term asthma as applied to the PHMG-exposed group given that they were less likely to be hyperresponsive to methacholine, had less pronounced obstruction, and had little or no inflammation of the sort associated with early onset allergic asthma in children. In this regard, the investigators were pragmatic and used a working definition of physician-diagnosed and treated asthma. A more important limitation was the small number of subjects studied and the limited number of patient characteristics measured. The conclusions of the study rest heavily on the examination of just 10 PHMG-exposed children. As the authors note, the different and refractory nature of their PHMG-exposed cohort may reflect a self-referral bias by concerned parents. In addition, the physiologic studies were limited to spirometry, there were no reported radiologic studies, and there was no assessment of airway inflammation by quantification of exhaled nitric oxide or sputum eosinophil counts. As an opportunistic study aiming to be minimally intrusive in the pediatric setting, these limitations are understandable. One hopes that these intriguing data will be followed by larger and more detailed studies and that eventually the adult long-term consequences of the finding will be reported. ■

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

References

1 Liccardi G, Cazzola M, Russo M, Gilder JA, D'Amato M, D'Amato G. Mechanisms and characteristics of airway sensitization to indoor allergens. *Monaldi Arch Chest Dis* 2001;56:55–63.
2 McConnell R, Berhane K, Gilliland F, Islam T, Gauderman WJ, London SJ, *et al.* Indoor risk factors for asthma in a prospective study of adolescents. *Epidemiology* 2002;13:288–295.
3 The humidifier disinfectant scandal: the need for vigorous government oversight of chemicals and household products to secure public safety. *Environ Health Toxicol* 2016;31:e2016012.
4 Lee SY, Ahn HS, Kim EM, Kim KK, Kang MJ, Park MJ, *et al.* Different characteristics of childhood asthma related to polyhexamethylene guanidine exposure. *Ann Am Thorac Soc* 2021;18: 1523–1532.
5 Kim H, Ellis AK, Fischer D, Noseworthy M, Olivenstein R, Chapman KR, *et al.* Asthma biomarkers in the age of biologics. *Allergy Asthma Clin Immunol* 2017;13:48.
6 Baraldi E, Bonetto G, Zacchello F, Filippone M. Low exhaled nitric oxide in school-age children with bronchopulmonary dysplasia and airflow limitation. *Am J Respir Crit Care Med* 2005; 171:68–72.
7 Chapman KR, Mannino DM, Soriano JB, Vermeire PA, Buist AS, Thun MJ, *et al.* Epidemiology and costs of chronic obstructive pulmonary disease. *Eur Respir J* 2006;27:188–207.
8 Pérez-Tarazona S, Rueda Esteban S, García-García ML, Arroyas Sanchez M, de Mir Messa I, Acevedo Valarezo T, *et al.*; Working Group of Perinatal Respiratory Diseases of the Spanish Society of Pediatric Pulmonology. Respiratory outcomes of "new" bronchopulmonary dysplasia in adolescents: A multicenter study. *Pediatr Pulmonol* 2021;56: 1205–1214.
9 Tuffaha A, Gern JE, Lemanske RF Jr. The role of respiratory viruses in acute and chronic asthma. *Clin Chest Med* 2000;21:289–300.