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Defining Resilience: A Critical Step to Promote Respiratory Health

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Smoking-related chronic respiratory disease is a significant source of morbidity and mortality. The respiratory community has traditionally defined chronic obstructive pulmonary disease (COPD) by the presence of abnormal obstructive lung physiology on spirometry. Yet respiratory symptoms are present in a large number of smokers and nonsmokers and are associated with a variety of adverse health consequences even in the setting of normal lung function (1–3). In addition, many individuals who do not meet criteria for COPD by spirometry demonstrate abnormal radiographic findings consistent with lung parenchymal or airways injury (4, 5). The presence of respiratory symptoms, abnormal imaging, and healthcare use in the absence of spirometric impairment reflect intermediate phenotypes of impaired respiratory health (6). The concept of impaired respiratory health implies that it functions on a continuum between "ideal" respiratory health and chronic lung disease. The specific features of ideal

versus impaired respiratory health, however, remain ill-defined (7).

In this issue of AnnalsATS, Oh and colleagues (pp. 1822-1831) present important work that seeks to define resilience to the development of lung disease in cigarette smokers (8). The authors used a modified Delphi method with a panel of chronic lung disease experts to determine a consensus definition of a resilient smoker. The threeround Delphi process resulted in resilience being defined by a lack of reports of cough and sputum production, the absence of dyspnea, no documentation of healthcare use requiring antibiotics and/or steroid use, the absence of emphysema or functional airway small disease on computed tomographic scan, and a normal rate of decline of forced expiratory volume in 1 second. When this consensus definition of resilience was applied to participants in the SPIROMICS (SubPopulations and InteRmediate Outcome Measures In COPD Study) cohort, 16.7% of cigarette smokers met the definition. In addition to the clinical features, the authors also identified that resilient smokers had biologic differences in levels of systemic inflammation. CRP (Creactive protein) levels in resilient smokers were similar to those in nonsmokers, whereas the nonresilient smokers had 56.6% higher levels of CRP. sTNFRSF1a (TNF receptor α) levels were lower in resilient smokers than in nonresilient smokers (8).

There are a number of reasons to define resilience among smokers. Among these are obtaining an understanding of mechanisms and pathways that protect individuals from injury, identifying targets for preventive therapies based on these pathways, and, when applied to clinical practice, acknowledging that features such as frequent cough and phlegm or shortness of breath, even if absent impaired lung physiology, are not, in fact, normal. However, could defining resilience as the absence of several unfavorable features help advance the concept of ideal lung health and

result in greater promotion of respiratory health? The precedent of the cardiovascular community's success in defining ideal cardiovascular health indicates that it could. The American Heart Association has advanced the concept of ideal cardiovascular health according to seven health factors and behaviors and is defined by the presence of ideal health behaviors (nonsmoking, optimal physical activity levels, healthy diet) and health factors (the absence of high blood cholesterol, absence of hypertension, and absence of high blood glucose) (9). Indeed, targeting these modifiable risk factors has resulted in improved cardiovascular mortality in the United States (10).

Undoubtedly, there is more work to do in defining resilience and ideal respiratory health to replicate the advances made in cardiovascular disease. It is worth noting that Oh and colleagues only studied cigarette smokers, which is obviously a modifiable behavior that confers impaired respiratory health (8). In addition, some factors presented by Oh and colleagues are not easily applied to clinical practice. For example, the assessment of percent emphysema and functional small airways disease remains largely a research tool, and serial measurements of spirometry to evaluate for decline in lung function are not easy to implement clinically (11).

Despite these limitations, the current work represents a significant advance for the respiratory community to achieve a consensus definition of ideal versus impaired respiratory health. Such a definition will allow for further investigation into the biologic mechanisms of resilience as well as biomarkers that are associated with impaired versus ideal respiratory health. Many in the respiratory community lament that we do not have a readily obtained biomarker that helps us understand risk of future disease; we lack the "lung's cholesterol." The discovery that cholesterol is not only a biomarker but a

Ann Am Thorac Soc Vol 18, No 11, pp 1780–1785, Nov 2021 Internet address: www.atsjournals.org

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Supported by the National Heart, Lung, and Blood Institute of the U.S. National Institutes of Health (grants U01-HL146408 and R01-HL122477).

DOI: 10.1513/AnnalsATS.202106-758ED

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causative agent on the pathway from health to atherosclerosis to coronary artery disease to cardiovascular death required remarkable discovery science (12). However, without concurrent foundational epidemiologic work that defined the clinical features of intermediate phenotypes (some of which we now consider true risk factors) and the risks they confer for future disease, the clinical application of testing cholesterol would not be achieved (13, 14). The work by Oh and colleagues to begin to establish a clinical definition of resilience to cigarette smoking–induced lung impairment represent a key step as we consider how to shift our focus toward respiratory health promotion as well as disease prevention.

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

References

- 1 Kalhan R, Dransfield MT, Colangelo LA, Cuttica MJ, Jacobs DR Jr, Thyagarajan B, et al. Respiratory symptoms in young adults and future lung disease. The CARDIA Lung Study. Am J Respir Crit Care Med 2018;197:1616–1624.
- 2 Woodruff PG, Barr RG, Bleecker E, Christenson SA, Couper D, Curtis JL, et al.; SPIROMICS Research Group. Clinical significance of symptoms in smokers with preserved pulmonary function. N Engl J Med 2016;374: 1811–1821.
- 3 Wheaton AG, Ford ES, Thompson WW, Greenlund KJ, Presley-Cantrell LR, Croft JB. Pulmonary function, chronic respiratory symptoms, and health-related quality of life among adults in the United States–National Health and Nutrition Examination Survey 2007-2010. *BMC Public Health* 2013;13:854.
- 4 Harmouche R, Ash SY, Putman RK, Hunninghake GM, San Jose Estepar R, Martinez FJ, et al.; COPDGene Investigators. Objectively measured chronic lung injury on chest CT. Chest 2019;156:1149– 1159.
- 5 Labaki WW, Gu T, Murray S, Hatt CR, Galbán CJ, Ross BD, et al. Voxelwise longitudinal parametric response mapping analysis of chest computed tomography in smokers. Acad Radiol 2019;26:217–223.
- 6 Liu GY, Kalhan R. Impaired respiratory health and life course transitions from health to chronic lung disease. *Chest* 2021;S0012-3692(21)00695-4 [online ahead of print].
- 7 Reyfman PA, Washko GR, Dransfield MT, Spira A, Han MK, Kalhan R. Defining impaired respiratory health. A paradigm shift for pulmonary medicine. *Am J Respir Crit Care Med* 2018;198:440–446.

- 8 Oh AL, Mularski RA, Barjaktarevic I, Barr RG, Bowler RP, Comellas AP, et al.; SPIROMICS Investigators. Defining resilience to smoking-related lung disease: a modified Delphi approach from SPIROMICS. Am Am Thorac Soc 2021;18:1822–1831.
- 9 Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al.; American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation* 2010;121:586–613.
- 10 Michos ED, Khan SS. Modest gains confer large impact: Achievement of optimal cardiovascular health in the US population. J Am Heart Assoc 2021;10:e021142.
- 11 Heffler E, Crimi C, Mancuso S, Campisi R, Puggioni F, Brussino L, et al. Misdiagnosis of asthma and COPD and underuse of spirometry in primary care unselected patients. *Respir Med* 2018;142:48–52.
- 12 Goldstein JL, Brown MS. A century of cholesterol and coronaries: from plaques to genes to statins. *Cell* 2015;161:161–172.
- 13 Terry DF, Pencina MJ, Vasan RS, Murabito JM, Wolf PA, Hayes MK, et al. Cardiovascular risk factors predictive for survival and morbidity-free survival in the oldest-old Framingham Heart Study participants. J Am Geriatr Soc 2005;53:1944–1950.
- 14 Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PW, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006; 113:791–798.

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Physician Mistrust and Discrimination in Sarcoidosis: It's Real and It's Prevalent

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Sarcoidosis is heterogeneous in presentation (1). However, the risk for developing the disease, severity of disease, and outcomes for

patients have been strongly tied to socioeconomic status and income (2–4). In addition, Black individuals in the United States experience worse sarcoidosis outcomes than other groups (2, 3, 5, 6). ACCESS (A Case-Control Etiologic Study of Sarcoidosis) was the first study to demonstrate that low-income (total household income <\$20,000) cases were more likely to be Black and female and encounter barriers to medical care. Individuals



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