Executive Summary: NHLBI Workshop on the Primary Prevention of Chronic Lung Diseases

William W. Busse¹, Serpil C. Erzurum², Carol J. Blaisdell³, and Patricia Noel³

¹Division of Allergy, Pulmonary, and Critical Care Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin; ²Department of Pathobiology, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio; and ³Division of Lung Diseases, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland

Lung function is essential for good health, and compromises in this capacity have a large and broad effect on the ability to lead a full and satisfying life. Given the impact that diseases of the lung have on overall health, the National Institutes of Health (NIH) support a substantial portfolio of research to define mechanisms of lung diseases, and to translate discoveries into effective patient care. This approach has led to revolutionary advances in the management of lung diseases, but nearly all strategies aim to treat diseases that are fully established in symptomatic patients.

In July 2012, the Division of Lung Diseases, National Heart, Lung, and Blood Institute convened a working group to develop a research strategy for the next significant step toward lung health, that is, the primary prevention of lung diseases. It was apparent that the implementation of a disease prevention program was more mature in some areas than others, but the principles of how to approach this major new effort would likely be similar across lung disease categories. With this in mind, the Division of Lung Diseases convened a workshop in September 2013, at which pulmonary experts provided state-of-the-art status of prevention for several specific lung diseases, identified key questions, and considered approaches to facilitate prevention. The results of the workshop are presented in this issue of the *Journal* (1–7).

Overall, the 2013 workshop distinguished two major concepts as uniquely important to primary prevention

of lung disease: the promotion of lung health and the prevention of lung disease. The lung continues to develop in postnatal, early childhood, and young adult life, after which time lung function declines with aging. This offers intriguing opportunities, not only for promotion of healthy lungs, but also for interventions for development of healthier lungs by accelerating growth and/or slowing decline. Likewise, successful prevention of lung diseases requires clear demarcation of the predisease state from the onset of disease. In this context, a major barrier to health promotion and disease prevention is the current lack of biomarkers or proxy measures of lung health or disease. Lung function tests, defined in terms of an absolute value relative to a population, were noted to be limiting for detection of the predisease state, which may manifest with a range of variation still within the “normal” range. There was consensus that to achieve prevention, it is essential to more fully and comprehensively define what lung health is across the life course (Figure 1). This topic became the cornerstone of discussions and framed the approaches for metrics of prevention outcomes. The life course approaches take into consideration exposures (i.e., biological, behavioral, and psychosocial) that operate across an individual’s life as well as across generations.

In addition to lung health, specific diseases under review and discussion included asthma, bronchopulmonary dysplasia, chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease, and pulmonary hypertension,

which follow in this supplement with specific recommendations. In general, recommendations from the workshop describe an approach to identify both the at-risk patient (e.g., genotype and/or exposure) and the response that marks a shift from health to disease, as well as providing general strategies to begin to implement primary prevention interventions. A number of key points emerged during the workshop, which were common across disease areas, and had broad directive influence to establish programs of prevention.

- **Standardization:** There is a need for standardization across definitions, methodologies, and technologies such that data can be compared and/or integrated across studies.
- **Lung health and disease:** These are dynamic states and need to be defined using biologic phenomena as a foundation. Health is not merely the absence of disease. Symptoms, clinical outcomes, and/or response to treatments may provide context to refine phenotypes and/or endotypes but should not be used as the basis for definition.
- **Metrics of health:** Population measures of lung physiology and defense across the life stages should be developed that identify relevant, specific markers for comparison with early disease.
- **Existing cohorts:** Data from existing studies should be leveraged to increase sample size and to identify commonalities to aid description of new phenotypes and endotypes.

(Received in original form December 3, 2013; accepted in final form December 13, 2013)

NHLBI wishes to acknowledge the generous support of ATS through its shared contribution to the publication of this special issue.

Correspondence and requests for reprints should be addressed to Carol J. Blaisdell, M.D., Division of Lung Diseases, National Heart, Lung, and Blood Institute, National Institutes of Health, 6701 Rockledge Drive, 10-042, Bethesda, MD 20892-7952. E-mail: blaisdellcj@nhlbi.nih.gov

Ann Am Thorac Soc Vol 11, Supplement 3, pp S123–S124, Apr 2014

Published 2014 by the American Thoracic Society

DOI: 10.1513/AnnalsATS.201312-421LD

Internet address: www.atsjournals.org

Figure 1. Integration of birth cohort and longitudinal, population-based studies reveal heterogeneity of lung disease in all aspects: onset, severity, etiology, and burden. These findings point to the need to identify target populations at risk (phenotypes and endotypes) in a focused and restrictive manner because preventive strategies are likely to have varying success across pivotal time points in the life course. The goals are promotion of lung health and primary prevention of asthma, bronchopulmonary dysplasia, chronic obstructive lung disease, cystic fibrosis, interstitial lung disease, and pulmonary hypertension.

- **Biomarkers:** Biomarkers need to be identified and validated to distinguish health and the predisease state. These measures will be used to predict health status and risk, and should be quantifiable and modifiable.
- **Prematurity:** To the extent possible, sampling and longitudinal assessment of premature infants need to be performed to determine trajectory of pulmonary and immune system development and abnormalities.
- **Concomitant studies:** A dual approach is needed to mechanistic and interventional studies to test approaches with preventive potential, within reasonable timeframes, while continuing to understand pulmonary and immune development and homeostasis.
- **Novel technologies:** Technologies need to be developed that can identify regional perturbations of lung biology and “at risk” individuals.

- **Environmental modifications:** Broad, low-risk interventions (e.g., nutrition, smoking cessation, prenatal care) need to be implemented at the population level to promote lung health and to reduce risk.

These broad recommendations, along with the specific recommendations in the workshop summaries, provide actionable next steps, which include identification of health, predisease, and disease phenotypes and endotypes; development of proxy measures such as genomic and proteomic biomarkers and imaging; determination of risk factors for disease in the general and high-risk populations; and strategies for the development of clinical trials that will provide the basis for a paradigm-changing approach to promote and enhance lung health and prevent chronic lung disease. We have already begun to see significant benefits of early identification of at-risk individuals with cystic fibrosis. The overall goal is to detect at-risk individuals, using quantitative modifiable biomarkers, that will allow effective prevention of a wide variety of lung diseases and ensure optimal lung health over the entire life of an individual. ■

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

Acknowledgment: The authors thank Drs. Veronica Gunn and Daniel Levy for thoughtful presentations that helped to frame discussions at the meetings. The authors also thank Drs. Jeffrey Galvin, Teri Franks, Tim Le Cras, Robert Lemanske, Lisa Miller, Michael O'Reilly, and Lawrence Prince for valuable insights and discussion.

References

- 1 Camargo CA Jr, Budinger GRS, Escobar GJ, Hansel NN, Hanson CK, Huffnagle GB, Buist AS. NHLBI workshop on the primary prevention of chronic lung diseases: promotion of lung health. *Ann Am Thorac Soc* 2014;11:S125–S138.
- 2 Jackson DJ, Hartert TV, Martinez FD, Weiss ST, Fahy JV. NHLBI workshop on the primary prevention of chronic lung diseases: asthma. *Ann Am Thorac Soc* 2014;11:S139–S145.
- 3 McEvoy CT, Jain L, Schmidt B, Abman S, Bancalari E, Aschner JL. NHLBI workshop on the primary prevention of chronic lung diseases: bronchopulmonary dysplasia. *Ann Am Thorac Soc* 2014;11:S146–S153.
- 4 Drummond MB, Buist AS, Crapo JD, Wise RA, Rennard SI. NHLBI workshop on the primary prevention of chronic lung diseases: chronic obstructive pulmonary disease. *Ann Am Thorac Soc* 2014;11:S154–S160.
- 5 Pittman J, Cutting G, Davis SD, Ferkol T, Boucher R. NHLBI workshop on the primary prevention of chronic lung diseases: cystic fibrosis. *Ann Am Thorac Soc* 2014;11:S161–S168.
- 6 Rosas IO, Dellaripa PF, Lederer DJ, Khanna D, Young LR, Martinez FJ. NHLBI workshop on the primary prevention of chronic lung diseases: interstitial lung diseases. *Ann Am Thorac Soc* 2014;11:S169–S177.
- 7 Austin ED, Kawut SM, Gladwin MT, Abman SH. NHLBI workshop on the primary prevention of chronic lung diseases: pulmonary hypertension. *Ann Am Thorac Soc* 2014;11:S178–S185.