As scientists and humanitarians, we should aspire to a standard that both assures individuals are not being arbitrarily excluded from job opportunities, and simultaneously that they are not put in situations that would compromise their health because they occupy a genuinely elevated risk stratum. The current state of knowledge is not sufficient to address either concern. Therefore, we strongly agree that all possible causes of lung function differences should be vigorously investigated. However, it is helpful in this regard to understand the direction of prior scientific work. Anthropometry as a cause of difference in mean racial lung function has been investigated persistently since the mid-19th century, but has never been found to explain the majority of the difference (2, 3). Helpfully, though, its origins have been shown to be socially influenced, and not solely genetic. Despite moving away from the equator, Mayan immigrants have in contravention of Allen's Rule (4) developed progressively longer limbs and shorter trunks as they've arrived in more affluent nations (5). This suggests a complex, multifactorial relationship that might be predicted from the need for all determinants of lung function to be mediated through some biological mechanism. But skewed trends in scientific investigation are not well-poised to capture these dynamics. Over a decade ago, genetic and genomic-centered projects were among the top ten areas for publicly funded healthcare research funds disbursed in the United States (6). By contrast, proposals that prominently feature ideas like socioeconomic status or psychosocial environment have been less commonly funded (7). Relative to the ability to capture genetic influences, assessing the impact of environmental exposures is still in its infancy (8). So, too, is our understanding of the connection between lung function and clinical outcomes. Perhaps like the study of transplant, deepening our knowledge will reveal that we have over-estimated the importance of lung function relative to other determinants in our inquiries of greatest interest (9).

As for all professions that routinely measure lung function, cotton workers with ethnically normal but globally abnormal lung function may be at unique risk, equivalent risk, or lung function may not be a meaningful determinant of risk at all. In the interval, we agree that omitting race is not an appropriate or reasonable solution. We have advocated the use of composite equations derived from multiple racial and ethnic groups that reflect the rich diversity of our population. This approach naturally accounts for greater variance to address the concerns raised in the case of cotton worker standards, and improves on the current standard's handling of multiracial individuals and those for whom there are not currently appropriate race-specific equations elaborated.

Recognizing that these questions are unresolved is one important step to promoting their continued study. Gathering the data to resolve these unknowns will not only help address health disparities, it will augment our ability to care for all people by advancing our knowledge of physiology and disease. This is an important mission to which all healthcare professionals are called. ■

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Aaron D. Baugh, M.D.*
Neeta Thakur, M.D., M.P.H.
Prescott G. Woodruff, M.D., M.P.H.

University of California San Francisco
San Francisco, California

ORCID ID: 0000-0002-9527-691X (A.D.B.).

*Corresponding author (e-mail: Aaron.baugh@ucsf.edu).

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Genetic Ancestry Has the Same Major Problems as Phenotypic Ancestry

To the Editor:

Using genetic scores to identify ethnic background (1) is more precise but no different in principle from using physical characteristics and carries the same hazards for the misuse of "race" as a variable in medicine. Skin tone is largely inherited, and even among African Americans it is associated with educational level, income, and employment either as a manager or professional (2, 3). Nobody would believe that these indicators of social advantage are genetically determined. Using genotyping to "improve" the determination of what social position an individual ought to aspire to would horrify

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most people; its use to determine what lung function an individual should expect should also raise alarm. Using specific genes that may explain lung function would be useful and doesn't have the same problem, though the information may still be abused. However, where specific genes are known there is no longer any need to know the "% African" inheritance or any other information on ethnicity. This is the logic that supports the screening of neonates for sickle cell genotypes without regard to reported ethnicity. Unfortunately, there has still been relatively little success in identifying the genes that are believed from family studies to explain around 50% of the variation in lung function. Until this situation improves, genes are of limited use in interpreting lung function. ■

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Peter Burney, M.A., M.D.
Imperial College
London, United Kingdom

Corresponding author (e-mail: p.burney@imperial.ac.uk).

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Finite Element Modeling of Pulmonary Mechanics in Severe Acute Respiratory Distress Syndrome: Explaining the Inclination Angle?

To the Editor:

With great interest, we read the research letter by Marazzo and colleagues (1) in which the effect of changing trunk inclination on respiratory function in patients with coronavirus disease (COVID-19)-associated acute respiratory distress syndrome is described. In our clinical practice, we repeatedly observed such rapid improvement of V_{TS} upon change of trunk position from semirecumbent to supine flat. The rapidity of altered respiratory mechanics does not, in our view, favor a major role for alveolar recruitment but rather a varying distention of different lung areas compatible with a patchy pathomorphological manifestation of COVID-19. This clinical observation led us to hypothesize that different configurations of, for example, fibrotic and emphysematous pulmonary parenchyma differentially influence lung aeration depending on the inclination of the individual patient's trunk.

Therefore, we set out to model diseased COVID-19 lungs using a finite element method–based mathematical pulmonary model using Ansys (2020 R2 ANSYS, Inc.), allowing simulation of distinct geometrical configurations of heterogeneously distributed parenchymal pathomorphology and its related local tissue mechanics (Figure 1). The model consists of five rows and three columns of rectangular blocks, representing a single lung, surrounded by a rigid supporting structure representing the thoracic cage. Each of the 15 blocks is composed of homogeneous material with mechanical properties described as elastic moduli, density, and yield strength as derived from the pathoanatomical literature and related to the modeled pathomorphological state of a specific anatomical lung area: fibrotic, emphysematous, or edematous (2, 3). The diaphragm at the caudal lung border is modeled as a plane with an imposed dynamic force simulating the intraabdominal pressure. The intraabdominal pressure depends on the degree of bed inclination: 8.4 mm Hg for 0°, 9.5 mm Hg for 15°, and 11 mm Hg for 30° of inclination (4). The gravitational force is represented by the x- and y-components, adapted accordingly for 15° and 30°. To test a representative set of clinically relevant pathomorphological manifestations as pulmonary COVID-19, more than 30 configurations of mechanical properties of the 15 blocks were tested, starting from homogeneous edema with an increasing number of blocks with fibrosis and emphysema in different and opposite positions (caudal versus cranial and dorsal versus ventral).

The output was defined as aeration of the lung, summed over the 15 individual modeled blocks. After simulating all different configurations in three bed inclination angles, it was particularly the modeled phenotype of an edematous lung configurated with both cranial dorsal emphysema ($\geq$3 blocks) and caudal dorsal fibrosis ($\geq$3 blocks) that appeared to predict an increase in aeration when changing the bed inclination both from 0° to 15° and from 15° to 30° (Figure 1).

Although this straightforward computational finite element method approach is merely hypothesis generating, it is tempting to speculate whether combining these insights with pulmonary imaging techniques (e.g., computational tomography or electrical impedance tomography) would allow us to further validate our findings on a patient-specific basis. Ultimately, such modeling approach of pulmonary pathomorphological heterogenicity may advance our understanding of more patient-specific mechanical ventilation at an individualized degree of bed inclination in severe acute respiratory distress syndrome. ■

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