



COPD in the COVID-19 era, challenging concepts and developments in COPD, and occupational exposures and susceptibilities

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The COVID-19 pandemic may have passed its peak, but the virus (SARS-CoV-2 or a variant) is likely to remain with us in spurts and in an endemic form. Three articles in this issue discuss obstructive lung diseases and COVID-19. Singh and associates [1] review the published experience with COVID-19 and chronic obstructive pulmonary disease (COPD) in 3 areas- susceptibility, outcomes and inhaled corticosteroids. Aggarwal and associates [2], in a commendable effort, searched a large data base and have reported on the impact and relationships of the two in developing (based on per capita gross national income) countries. They suggest that a higher prevalence of COPD may be associated with higher COVID-19 related mortality but overall the adverse outcomes appeared to be similar to those for developed countries. The review by Sculley, Musick, and Krishnan [3] covers telehealth in COPD before, during, and after the pandemic and its incorporation into future management strategies. Although randomized controlled studies prior to the pandemic that compared telehealth to in-person usual care on clinical outcomes were inconclusive, in the pandemic times telehealth as an add-on improved both patient access and satisfaction with care. While easier access, time efficiency and cost savings in transportation are clear pluses for telehealth, socioeconomic barriers involving vulnerable populations need to be recognized and overcome. In the next article, Wang and associates [4] revisit and update the various risk assessment tools applicable to COPD. This area will continue to evolve given the heterogeneous nature of COPD.

Though the definition of COPD has gone through several iterations over the years, one common and required element in all of them is the demonstration of airflow limitation by spirometry currently defined as postbronchodilator forced expiratory volume in one second/forced vital capacity < 0.7. The concept was easy to understand and teach and a master pulmonologist, Thomas Petty, advocated the use of a spirometer for detection of airflow limitation as an essential part of medical practice analogous to a sphygmomanometer for detection of

hypertension. The relative ease of an inexpensive spirometry test and its high specificity for detecting obstructive diseases overrode its limitations (e.g., primarily detect airway pathology, less than ideal sensitivity). Exposure to cigarette smoke or pollutants can cause pathological changes in the lungs and symptoms even without spirometrically defined obstruction. In 2019, COPDGene study researchers expanded the spirometric definition of COPD to include those with restriction (or preserved ratio impaired spirometry) and took into account imaging changes in computed tomography of chest [5]. The objective was to detect COPD early (pre-COPD) with the intent to target treatments that would halt or change the course of the disease. Two substantive and thought-provoking articles in this issue relate to pre-COPD. Mkorombindo and Dransfield [6] define pre-COPD, along the lines of previous referenced article and present it in a tabular form. Khan, Cole and Mannino [7] expand on the rationale for inclusion of radiographic imaging changes and symptoms with focus on 'treatable traits.' The features of 'early' COPD included young age (<50 years) and modest smoking history (≥ 10 pack-years). However, it should be noted that a sizable minority of COPD patients are nonsmokers and many early life factors (maternal smoking, low birth weight, nutritional deficiency, and respiratory infections) affect airway and lung development. Mkorombindo and Dransfield pose the question of whether pre-COPD is a pathophysiologic process or an opinion term? [6] Though this may be a rhetorical question, the answer is that it is a

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pathological process similar to clinically unapparent early stage in other chronic diseases. However, the important question is 'How does the expanded definition of COPD that includes pre-COPD translate to the diagnosis and care of patients' particularly when we do not have any effective tools to alter the progression of COPD apart from smoking cessation.

Physicians, often primary care practitioners, use smoking history and symptoms for a provisional diagnosis of COPD and use spirometry for confirmation. The expanded definition introduces a contradictory element: COPD without obstruction (by spirometric criteria), whereas the term obstruction is already embedded. The addition of computed tomographic features to the diagnosis makes it expensive and impractical to use. These comments are not to question or diminish the efforts to expand our knowledge but to point out the chasm that exists between researchers and care providers (physicians and others) who work in the trenches.

In definitions and descriptions of COPD 'heterogeneous' and 'spectrum' are commonly encountered terms and no one can contest their veracity. This writer (BV) has long viewed COPD not as a single disease but multiple diseases conveniently tied together with the common feature of airflow obstruction [8]. Harking back to a time long ago, Bright's disease encompassed all types of glomerulonephritis, and progress in research led to liberation from that all-inclusive name and identification of specific subtypes and targeted treatments. COPD is in need of such liberation.

The next two articles [9,10] invite the readers to the world of Lung microbiome. The human body hosts a vast microbial population comprised of bacteria, archaea, viruses, and eukaryotes [11]. Trillions of microbes, similar in numbers in comparison to human cells, inhabit just about every part of the human body [12]. We often consider microorganisms as sickness-causing, but most of the time, they live in harmony with their human hosts not just as commensals but providing vital functions essential for human survival. The 'microbiome' of a given organ or system is defined as the microbial population of an organ or system and its interactions with host tissue(s) [13]. Our understanding of the lung microbiome is immature but is expanding rapidly given newer tools such as next-generation sequencing which allows us to study microbiomes with a precision not possible from cultures alone. However, there are many unsolved questions as to whether an altered microbial community is the cause or the consequence of a respiratory disease, how adaptive immunity influences the microbiota composition and vice versa, or what environmental factors might impact the respiratory microbiome.

Tiew, Aogáin, and Chotirmall [9] summarize the recent advances to our understanding of the bacteriome, virome and mycobiome in COPD reviewing studies employing sputum as an airway surrogate. The authors' findings suggest that although diverse microbiome profiles are reported in COPD, the neutrophilic *Haemophilus* predominant bacteriome remains a prominent COPD phenotype, relatively stable over time and during exacerbations. Gokulan, Joshi, Khare, and Bartter [10] queried data on the microbiome of the lungs and how it changes with the evolution of COPD and also to explore initial data with respect to COPD and the gut-lung axis. They concluded that Lung injury/inflammation alters the milieu of the lung and favors an evolving microbiome which reflects and probably participates in the processes of inflammation and injury; some evidence also suggests that the gastrointestinal tract participates in that inflammatory processes.

The application of artificial intelligence in diagnosis of diseases ushers in a new world of great possibilities. Tran, Kwo, and Ngyuen [14] discuss the potential application of artificial intelligence in occupational respiratory medicine. Authors suggest that artificial intelligence can match trained clinicians in specific applications, but artificial intelligence has limitations that require clearly defined questions and a high quality of data.

Sarcoidosis is an enigmatic multisystem granulomatous disease of unknown etiology. The history of sarcoidosis is fascinating that stretches over all the continents and covers the last one and a half century. There has been multitude of studies suggesting occupational exposures and sarcoidosis [15]. Maier and Lin [16] in their review article summarize recent studies associating occupational exposure and sarcoidosis phenotypes and concludes that evidence at best is preliminary and require more research to establish a causal relationship. However, the authors opine that World Trade Center dust has a causative relationship with sarcoidosis using the Bradford Hill criteria for causation.

Pulmonary rehabilitation is a standard of care for management of COPD [17,18]. However, COVID-19 pandemic forced many traditional (in-person) pulmonary rehabilitation programs to shift to remote home-based programs in the form of telerehabilitation (tele-pulmonary rehabilitation). Wen, Milne, and Sin [19] summarize the recent evidence for the feasibility and effectiveness of remote pulmonary rehabilitation programs, and their implications for the delivery of pulmonary rehabilitation in a postpandemic world. The authors conclude that a 'hybrid' model (with some components held in person and others via telehealth) may be more desirable in the post-COVID-19 world.

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There are no conflicts of interest.

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