Preface

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Editors

We are pleased to introduce this issue of *Critical Care Clinics*, focused on acute respiratory distress syndrome (ARDS). Although planned before the COVID-19 pandemic, this issue is particularly timely given the world events of the past 18 months. The articles in this issue address several key topics in the field of ARDS with both a clinical and a research focus, as well as define some of the important questions that need to be answered for our understanding of the pathogenesis and treatment of ARDS to advance. Some of the articles include studies on COVID-19 ARDS, noting that this field is changing rapidly. This preface provides a brief overview of each of the articles and then our brief perspective on some of the opportunities for progress in ARDS.

The articles cover much that we have learned in the last few years. The issue starts with an article on epidemiology that identifies patients who are at higher risk and discusses the recent COVID-19 pandemic. This is followed by an article on environmental factors that emphasizes the impact of inhaled factors, including cigarette smoke, air pollution, and vaping, and an article that reviews the clinical diagnosis, including how to exclude mimics such as heart failure and volume overload. Next, there is a detailed article on the physiology of ARDS, including up-to-date information (at the time of publication) on how COVID-19 is similar to and different from classical ARDS. This is followed by two complementary articles on pathogenesis, one focused on clinically relevant experimental studies and one focused on recent advances in our understanding of the biologic and clinical heterogeneity of ARDS in critically ill patients, including those with COVID-19. The field of genetics and ARDS is just beginning to provide important insights into disease risk and pathogenesis, which is covered in the next article. Nonpulmonary organ failure is an important risk factor for adverse outcomes in ARDS, and there has been significant interest in organ cross-talk in the pathogenesis of ARDS and multiorgan failure. One of the organs of particular interest in clinical and experimental studies is the kidney, and our current understanding is well covered in an article on acute kidney injury and ARDS. The next three articles cover important aspects of the treatment of ARDS. At present, our most important management strategies for ARDS are supportive care therapies, including lung protective ventilation and a fluid conservative management strategy. Beyond

lung protective ventilation, a number of ventilator strategies have been tested in randomized clinical trials, and these are reviewed, along with potential indications for extracorporeal membrane oxygenation. Fluid therapy, including fluid selection, is a critical part of ARDS management, and current management based on clinical trials is discussed in detail. With regards to pharmacologic therapies for ARDS, numerous agents have been tested yet been unsuccessful. However, some of these agents might be reconsidered for testing with the use of both predictive and prognostic enrichment strategies. Last, but not least, studying the long-term outcomes of ARDS is a rapidly growing field; this is an area that was recognized as important and now in the COVID-19 era is even more appreciated for its importance clinically and for future research studies.

In addition to all these topics, we would like to emphasize how ARDS has clearly become even more recognized since COVID-19 as a major cause of morbidity and mortality that needs new strategies for testing novel therapeutics. The importance of novel approaches has been emphasized in several recent articles.^{1,2} A number of platform trials have rapidly tested therapies in the setting of COVID-19. Specifically, I-SPY COVID has tested a number of novel and repurposed agents that could rapidly be manufactured/supplied at large scale using a phase 2 design to rapidly identify candidate agents with the potential for large therapeutic benefit in the setting of severe COVID-19. The open-label RECOVERY and REMAP-CAP platform trials have identified pharmacologic therapies with significant benefit in subpopulations of COVID-19, including dexamethasone and tocilizumab.^{3,4} In addition, there is a good rationale for expanding the current Berlin definition of ARDS to include high-flow nasal cannula oxygen,⁵ as well as developing additional criteria that would allow the definition to be adapted to resource-limited areas so the recognition of ARDS can be global, facilitating early recognition and early treatments for both classical ARDS and COVID-19-related ARDS.

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