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Preface: COVID-19 Lung Disease: Lessons Learned

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Guang-Shing Cheng and Charles Dela Cruz

What Have We Learned About Transmission of Coronavirus Disease-2019: Implications for Pulmonary Function Testing and Pulmonary Procedures

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David A. Kaminsky, Shaikh M. Noor Husnain, and Danaï Khemasuwan

Because of the potential for high aerosol transmission during pulmonary function testing and pulmonary procedures, performing these tests and procedures must be considered carefully during the coronavirus disease-2019 (COVID-19) pandemic. Much has been learned about the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by aerosols and the potential for such transmission through pulmonary function tests and pulmonary procedures, and subsequently preventative practices have been enhanced and developed to reduce the risk of transmission of virus to patients and personnel. This article reviews what is known about the potential for transmission of SARS-CoV-2 during pulmonary function testing and pulmonary procedures and the recommended mitigation steps to prevent the spread of COVID-19.

Coronavirus Disease-2019 Pneumonia: Clinical Manifestations

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Husham Sharifi and Joe Hsu

Coronavirus disease-2019 (COVID-19) pneumonia has diverse clinical manifestations, which have shifted throughout the pandemic. Formal classifications include presymptomatic infection and mild, moderate, severe, and critical illness. Social risk factors are numerous, with Black, Hispanic, and Native American populations in the United States having suffered disproportionately. Biological risk factors such as age, sex, underlying comorbid burden, and certain laboratory metrics can assist the clinician in triage and management. Guidelines for classifying radiographic findings have been proposed and may assist in prognosis. In this article, we review the risk factors, clinical course, complications, and imaging findings of COVID-19 pneumonia.

Pathophysiology of Hypoxemia in COVID-19 Lung Disease

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Kai E. Swenson and Charles C. Hardin

As the pandemic has progressed, our understanding of hypoxemia in coronavirus disease 2019 (COVID-19) lung disease has become more nuanced, although much remains to be understood. In this article, we review ventilation-perfusion mismatching in COVID-19 and the evidence to support various biologic theories offered in explanation. In addition, the relationship between hypoxemia and other features of severe COVID-19 lung disease such as respiratory symptoms, radiographic abnormalities, and pulmonary mechanics is explored. Recognizing and understanding hypoxemia in COVID-19 lung disease remains essential for risk stratification, prognostication, and choice of appropriate treatments in severe COVID-19.

Impact of COVID-19 on Nonpulmonary Critical Illness: Prevalence, Clinical Manifestations, Management, and Outcomes 249

Mina Pirzadeh and Hallie C. Prescott

Although respiratory manifestations are the most common driver of hospitalization, SARS-CoV-2 infection has a wide range of manifestations, including multisystem organ failure in severe cases. This review discusses the prevalence, pathophysiology, clinical manifestations, treatment, and outcomes of nonpulmonary organ dysfunction from SARS-CoV2, including renal, liver, cardiac, neurologic, and coagulation system dysfunction. At this time, management largely focuses on supportive care practices that are applicable regardless of the cause of organ injury.

Post-COVID Interstitial Lung Disease and Other Lung Sequelae 263

Mark Barash and Vijaya Ramalingam

As the world emerges from the COVID-19 pandemic, clinicians and researchers across the world are trying to understand the sequelae in patients recovered from COVID-19 infection. In this article, the authors review post-acute sequelae of SARS-CoV-2, interstitial lung disease, and other lung sequelae in patients recovering from COVID-19 infection.

Antiviral Treatment of Coronavirus Disease-2019 Pneumonia 279

Christopher Radcliffe, Maricar Malinis, and Marwan M. Azar

Direct acting antivirals and monoclonal antibodies reduce morbidity and mortality associated with severe acute respiratory syndrome coronavirus 2 infection. Persons at higher risk for disease progression and hospitalized patients with coronavirus disease-2019 (COVID-19) benefit most from available therapies. Following an emphasis on inpatient treatment of COVID-19 during the early pandemic, several therapeutic options were developed for outpatients with COVID-19. Additional clinical trials and real-world studies are needed to keep pace with the evolving pandemic.

Immunomodulatory Agents for Coronavirus Disease-2019 Pneumonia 299

Dayna McManus, Matthew W. Davis, Alex Ortiz, Clemente Britto-Leon, Charles S. Dela Cruz, and Jeffrey E. Topal

Morbidity and mortality from COVID-19 is due to severe inflammation and end-organ damage caused by a hyperinflammatory response. Multiple immunomodulatory agents to attenuate this response have been studied. Corticosteroids, specifically dexamethasone, have been shown to reduce mortality in hospitalized patients who require supplemental oxygen. Interleukin-6 antagonist, tocilizumab, and Janus kinase inhibitors have also been shown to reduce mortality. However, patients who have severe pulmonary end-organ damage requiring mechanical ventilation or extracorporeal membrane oxygenation appear not to benefit from immunomodulatory therapies. This highlights the importance of appropriate timing to initiate immunomodulatory therapies in the management of severe COVID-19 disease.

Lessons Learned in Mechanical Ventilation/Oxygen Support in Coronavirus Disease 2019 321

Laura Dragoi, Matthew T. Siuba, and Eddy Fan

The clinical spectrum of severe acute respiratory syndrome coronavirus-2 infection ranges from asymptomatic infection or mild respiratory symptoms to pneumonia, with severe cases leading to acute respiratory distress syndrome with multiorgan involvement. The clinical management of patients with coronavirus disease 2019

(COVID-19) acute respiratory distress syndrome (ARDS) changed over the course of the pandemic, being adjusted as more evidence became available. This article will review how the ventilatory management of COVID-19 ARDS evolved and will conclude with current evidence-based recommendations.

The Use of Extracorporeal Membrane Oxygenation for COVID-19: Lessons Learned 335

Madhavi Parekh, Darryl Abrams, Cara Agerstrand, Jenelle Badulak, Amy Dzierba, Peta M.A. Alexander, Susanna Price, Eddy Fan, Dana Mullin, Rodrigo Diaz, Carol Hodgson, and Daniel Brodie

The coronavirus disease 2019 (COVID-19) pandemic has seen an increase in global cases of severe acute respiratory distress syndrome (ARDS), with a concomitant increased demand for extracorporeal membrane oxygenation (ECMO). Outcomes of patients with severe ARDS due to COVID-19 infection receiving ECMO support are evolving. The need for surge capacity, practical and ethical limitations on implementing ECMO, and the prolonged duration of ECMO support in patients with COVID-19-related ARDS has revealed limitations in organization and resource utilization. Coordination of efforts at multiple levels, from research to implementation, resulted in numerous innovations in the delivery of ECMO.

Lung Transplantation in Coronavirus-19 Patients: What We Have Learned So Far 347

Emily Cerier, Kalvin Lung, Chitaru Kurihara, and Ankit Bharat

Coronavirus-19 (COVID-19) can result in irrecoverable acute respiratory distress syndrome (ARDS) or life-limiting fibrosis for which lung transplantation is currently the only viable treatment. COVID-19 lung transplantation has transformed the field of lung transplantation, as before the pandemic, few transplants had been performed in the setting of infectious disease or ARDS. Given the complexities associated with COVID-19 lung transplantation, it requires strict patient selection with an experienced multidisciplinary team in a high-resource hospital setting. Current short-term outcomes of COVID-19 lung transplantation are promising. However, follow-up studies are needed to determine long-term outcomes and whether these patients may be predisposed to unique complications.

SARS-CoV-2 Infection and COVID-19 in Children 359

Alpana Waghmare and Diego R. Hijano

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection is common in children, and clinical manifestations can vary depending on age, underlying disease, and vaccination status. Most children will have asymptomatic or mild infection, but certain baseline characteristics can increase the risk of moderate to severe disease. The following article will provide an overview of the clinical manifestations of coronavirus disease 2019 in children, including the post-infectious phenomenon called multisystem inflammatory syndrome in children. Currently available treatment and prophylaxis strategies will be outlined, with the caveat that new therapeutics and clinical efficacy data are constantly on the horizon.

Coronavirus Disease-2019 in Pregnancy 373

Jose Rojas-Suarez and Jezid Miranda

Coronavirus disease-2019 (COVID-19) infection during pregnancy is associated with severe complications and adverse effects for the mother, the fetus, and the neonate. The frequency of these outcomes varies according to the region, the gestational age, and the presence of comorbidities. Many COVID-19 interventions, including oxygen therapy, high-flow nasal cannula, and invasive mechanical ventilation, are

challenging and require understanding physiologic adaptations of pregnancy. Vaccination is safe during pregnancy and lactation and constitutes the most important intervention to reduce severe disease and complications.

COVID-19 in Patients with Chronic Lung Disease

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Jessica Fae Calver, Laura Fabbri, James May, and R. Gisli Jenkins

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus that causes an acute respiratory tract infection known as coronavirus disease 2019 (COVID-19). SARS-CoV-2 enters cells by binding the ACE2 receptor and coreceptors notably TMPRSS2 or Cathepsin L. Severe COVID-19 infection can lead to acute lung injury. Below we describe the impact of common chronic lung diseases (CLDs) on the development of COVID-19. The impact of treatment of CLD on COVID-19 and any the importance of COVID-19 vaccination in patients with CLD are considered.

Coronavirus Disease-2019 in the Immunocompromised Host

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Christopher D. Bertini Jr., Fareed Khawaja, and Ajay Sheshadri

Immunocompromised hosts, which encompass a diverse population of persons with malignancies, human immunodeficiency virus disease, solid organ, and hematologic transplants, autoimmune diseases, and primary immunodeficiencies, bear a significant burden of the morbidity and mortality due to coronavirus disease-2019 (COVID-19). Immunocompromised patients who develop COVID-19 have a more severe illness, higher hospitalization rates, and higher mortality rates than immunocompetent patients. There are no well-defined treatment strategies that are specific to immunocompromised patients and vaccines, monoclonal antibodies, and convalescent plasma are variably effective. This review focuses on the specific impact of COVID-19 in immunocompromised patients and the gaps in knowledge that require further study.

The Impact of Coronavirus Disease 2019 on Viral, Bacterial, and Fungal Respiratory Infections

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Ashley Losier, Gayatri Gupta, Mario Caldararo, and Charles S. Dela Cruz

Although coronavirus disease 2019 (COVID-19) remains an ongoing threat, concerns regarding other respiratory infections remain. Throughout the COVID-19 pandemic various epidemiologic trends have been observed in other respiratory viruses including a reduction in influenza and respiratory syncytial virus infections following onset of the COVID-19 pandemic. Observations suggest that infections with other respiratory viruses were reduced with social distancing, mask wearing, eye protection, and hand hygiene practices. Coinfections with COVID-19 exist not only with other respiratory viruses but also with bacterial pneumonias and other nosocomial and opportunistic infections. Coinfections have been associated with increased severity of illness and other adverse outcomes.

Lessons Learned from Health Disparities in Coronavirus Disease-2019 in the United States

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Alejandro A. Diaz, Neeta Thakur, and Juan C. Celedón

In the United States, the coronavirus disease-2019 (COVID-19) pandemic has disproportionately affected Black, Latinx, and Indigenous populations, immigrants, and economically disadvantaged individuals. Such historically marginalized groups are more often employed in low-wage jobs without health insurance and have higher rates of infection, hospitalization, and death from COVID-19 than non-Latinx White individuals. Mistrust in the health care system, language barriers, and limited health

literacy have hindered vaccination rates in minorities, further exacerbating health disparities rooted in structural, institutional, and socioeconomic inequities. In this article, we discuss the lessons learned over the last 2 years and how to mitigate health disparities moving forward.

Lessons Learned from a Global Perspective of Coronavirus Disease-2019

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Viren Kaul, Japjot Chahal, Isaac N. Schrastzhaupt, Heike Geduld, Yinzhong Shen, Maurizio H. Cecconi, Andre M. Siqueira, Melissa M. Markoski, and Leticia Kawano-Dourado

Coronavirus disease-2019 has impacted the world globally. Countries and health care organizations across the globe responded to this unprecedented public health crisis in a varied manner in terms of public health and social measures, vaccination development and rollout, the conduct of research, developments of therapeutics, sharing of information, and in how they continue to deal with the widespread aftermath. This article reviews the various elements of the global response to the pandemic, focusing on the lessons learned and strategies to consider during future pandemics.