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R. Alfonso Hernandez Acosta, Zerelda Esquer Garrigos, Jasmine R. Marcelin, and Prakhar Vijayvargiya
In this review, we summarize the current knowledge about the virology, the host-pathogen interactions and pathogenesis of coronavirus disease 2019 in humans. We also describe the various clinical presentations of the disease including respiratory system and extrapulmonary manifestations.

SARS-CoV-2 Virology 251
Yijia Li and Jonathan Z. Li
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in 2020 and has led to an unprecedented global pandemic. Understanding the virology behind SARS-CoV-2 infection has provided key insights into our efforts to develop antiviral agents and control the COVID-19 pandemic. In this review, the authors focus on the genomic features of SARS-CoV-2, its intrahost and interhost evolution, viral dynamics in respiratory tract, and systemic dissemination.

SARS-CoV-2 Transmission and Prevention in the Era of the Delta Variant 267
Eric A. Meyerowitz and Aaron Richterman
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) delta variant transmits much more rapidly than prior SARS-CoV-2 viruses. The primary mode of transmission is via short range aerosols that are emitted from the respiratory tract of an index case. There is marked heterogeneity in the spread of this virus, with 10% to 20% of index cases contributing to 80% of secondary cases, while most index cases have no subsequent transmissions. Vaccination, ventilation, masking, eye protection, and rapid case identification with contact tracing and isolation can all decrease the transmission of this virus.

Awakening: The Unveiling of Historically Unaddressed Social Inequities During the COVID-19 Pandemic in the United States 295
Michele P. Andrasik, Alika K. Maunakea, Linda Oeso, Carlos E. Rodriguez-Diaz, Stephaun Wallace, Karina Walters, and Michi Yukawa
The violence and victimization brought by colonization and slavery and justified for over a century by race-based science have resulted in enduring inequities for black, Indigenous and people of color (BIPOC) across the United States. This is particularly true if BIPOC individuals have other intersecting devalued identities. We highlight how such longstanding inequities paved the way for the disproportionate burdens of COVID-19 Infection

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coronavirus disease 2019 (COVID-19) among the BIPOC populations across the country and provide recommendations on how to improve COVID-19 mitigation strategies with the goal of eliminating disparities.

**Infection Prevention and Control of Severe Acute Respiratory Syndrome Coronavirus 2 in Health Care Settings**

Marisa L. Winkler, David C. Hooper, and Erica S. Shenoy

The authors describe infection prevention and control approaches to severe acute respiratory syndrome coronavirus 2 in the health care setting, including a review of the chain of transmission and the hierarchy of controls, which are cornerstones of infection control and prevention. The authors also discuss lessons learned from nosocomial transmission events.

**Laboratory Diagnosis for SARS-CoV-2 Infection**

Bianca B. Christensen, Marwan M. Azar, and Sarah E. Turbett

The optimal diagnostic test for SARS-CoV-2 infection should be selected based on a patient’s clinical syndrome and presentation in relation to symptom onset. Molecular testing, most often reverse-transcriptase polymerase chain reaction, offers the highest sensitivity and specificity during acute infection, whereas antigen testing can also be useful for acute diagnosis when rapid turnaround of results is necessary or if molecular testing is unavailable. Serologic testing is often reserved for identifying individuals with prior or late COVID-19 infection.

**Pharmacologic Treatment and Management of Coronavirus Disease 2019**

Amy Hirsch Shumaker and Adarsh Bhimraj

Over the last 2 years, there has been gradual and sustained progress toward our understanding of pharmacotherapy for coronavirus disease 2019 (COVID-19) as a result of large- and small-scale randomized controlled trials. Numerous new and repurposed treatments have been evaluated; some have demonstrated benefit in clinically important outcomes like mortality and hospitalization, and optimism for oral antiviral treatments is growing. Given the rapidly evolving landscape of COVID-19 treatments, frontline clinicians should use treatment and management guidelines to guide their approach to each patient, with the individual’s severity and location of illness in mind to appreciate the nuances in clinical evidence.

**COVID-19 in the Critically Ill Patient**

Taison D. Bell

The COVID-19 pandemic has led to significant mortality in the United States with more than 800,000 deaths in 2020 and 2021. The proportion of patients with COVID-19 who develop severe disease varies but is decreasing over time with growing population immunity and improved therapeutic options. Patients who are 65 years and older represent the largest proportion of deaths from COVID-19. Additional risk factors include immunosuppression and chronic medical conditions. Vaccination dramatically reduces the risk of severe COVID-19. Although critical illness from
COVID-19 is mostly driven by respiratory disease, critical illness can manifest in several ways and affect several organ systems.

Postacute Sequelae of Severe Acute Respiratory Syndrome Coronavirus 2 Infection 379
Aluko A. Hope and Teresa H. Evering

Postacute sequelae of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or long coronavirus disease (COVID) is an emerging syndrome characterized by multiple persisting or newly emergent symptoms following the acute phase of SARS-CoV-2 infection. For affected patients, these prolonged symptoms can have a relapsing and remitting course and may be associated with disability and frequent health care utilization. Although many symptom-driven treatments are available, management remains challenging and often requires a multidisciplinary approach. This article summarizes the emerging consensus on definitions, epidemiology, and pathophysiology of long COVID and discusses what is understood about prevention, evaluation, and treatment of this syndrome.

COVID-19 in the Immunocompromised Host, Including People with Human Immunodeficiency Virus 397
Niyati Jakharia, Aruna K. Subramanian, and Adrienne E. Shapiro

This review describes the incidence, epidemiology, and risk factors for mortality of COVID-19 in immunocompromised patients, including persons with human immunodeficiency virus. It describes various preventive measures, including vaccines and their effectiveness and the role of monoclonal antibodies for pre-exposure prophylaxis. It also reviews the different treatment options for immunocompromised individuals, including antivirals, monoclonal antibodies, and immunomodulators. Lastly, it describes the impact of COVID-19 on transplantation and continuity care of this population.

COVID-19 and Pregnancy 423
Sonja A. Rasmussen and Denise J. Jamieson

Pregnancy seems to be a risk factor for severe disease with COVID-19. Although SARS-CoV-2 intrauterine transmission seems to be rare, most studies show COVID-19 during pregnancy increases the risk for pregnancy complications, with higher risk among those with severe disease compared with those mildly affected. Studies suggest that COVID-19 vaccination during pregnancy is safe and effective. Antibodies to SARS-CoV-2 have been found in umbilical cord blood and breast milk following maternal vaccination, which might provide protection to the infant. However, vaccination rates during pregnancy remain low. Studies are needed to understand ways to address SARS-CoV-2 vaccine hesitancy among pregnant persons.

Severe Acute Respiratory Syndrome Coronavirus 2 Infections in Children 435
Eric J. Chow and Janet A. Englund

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections in children generally have milder presentations, but severe disease can
occur in all ages. MIS-C and persistent post-acute COVID-19 symptoms can be experienced by children with previous infection and emphasize the need for infection prevention. Optimal treatment for COVID-19 is not known, and clinical trials should include children to guide therapy. Vaccines are the best tool at preventing infection and severe outcomes of COVID-19. Children suffered disproportionately during the pandemic not only from SARS-CoV-2 infection but because of disruptions to daily life, access to primary care, and worsening income inequalities.

COVID-19 Vaccines

William O. Hahn and Zanthia Wiley

This article is a narrative review of the rapidly moving coronavirus disease 2019 vaccine field with an emphasis on clinical efficacy established in both randomized trials and postmarketing surveillance of clinically available vaccines. We review the major clinical trials that supported authorization for general use of the Janssen (Ad.26.CoV2), Pfizer-BioNTech (BNT162b2), and Moderna (mRNA-1273) vaccines and the publicly available postmarketing information with the goal of providing a broad, clinically relevant comparison of efficacy and safety. This review is primarily focused on the US market.