



Introduction to a review series on COVID-19 and the hematologist

The first reports describing severe pneumonia resulting from a novel coronavirus identified in Wuhan, China, appeared in the medical literature in early January 2020.^{1,2} Within a month, the World Health Organization (WHO) had announced COVID-19 to be the name of this new disease. One month later, with new infections rapidly appearing in many areas around the world, the WHO declared the outbreak to be a pandemic. Currently, 2.5 years after the initial reports, >520 million confirmed infections and 6 million deaths globally have been reported, including >1 million deaths in the United States alone.³ Multiple treatment strategies, new therapies, and vaccines have been developed, and the world is learning to live with COVID-19 as it evolves into an endemic disorder rather than an explosively spreading pandemic.

The hematology community has been closely involved from the beginning in the study of this novel disease and how to prevent and treat it. This review series includes 5 articles, listed below, that address key hematologic aspects related to this coronavirus and the pandemic it has caused.

- Thomas and Scully, "Clinical features of thrombosis and bleeding in COVID-19"
- Tobian et al, "COVID-19 convalescent plasma"
- Conway et al, "Cellular therapies for the treatment and prevention of SARS-CoV-2 infection"
- Flaumenhaft et al, "Vasculopathy in COVID-19"
- Langerbeins and Hallek, "COVID-19 in patients with hematologic malignancy"

Early reports describing hospitalized patients with COVID-19 reported that thromboembolic events were extremely common and raised the concern that standard doses of anticoagulation used for thromboprophylaxis in hospitalized patients were inadequate.^{4,5} Thomas and Scully address the laboratory features of the coagulopathy observed with COVID-19, review the venous and arterial thrombotic manifestations encountered, and cover the latest clinical trials investigating optimal strategies for anticoagulant therapy. Bleeding manifestations are also addressed, including the contribution of anticoagulation to hemorrhagic complications.

Convalescent plasma, obtained from individuals who had been infected with COVID-19 and recovered, was an intervention applied early in the pandemic in selected high-risk individuals.⁶ Tobian et al discuss the rapid evolution of the use of this therapy, addressing the changes in regulatory requirements and the response of collection programs in the context of accumulating data from ongoing clinical studies and changes in the clinical

standard of care. They conclude that, based on current data, high-titer convalescent plasma should be prioritized for patients with early disease, particularly those who are immunosuppressed.

Conway et al describe cellular therapies and how these might be used in the prevention and treatment of COVID-19, particularly for the immunocompromised population. They discuss how COVID-19-specific T cells and natural killer cells can be used as adaptive immunotherapies to enhance viral clearance, describing recent and ongoing phase 1/2 clinical trials investigating these approaches. They also address how regulatory T cells and mesenchymal stromal cells can be used as immune modulatory strategies, applied to correct dysregulated immune response in patients with severe COVID-19 infections.

As with thrombotic complications, evidence for endothelial cell injury was described early in the pandemic, particularly in association with severe clinical manifestations.⁷ Flaumenhaft et al review the contribution of the endothelium to the inflammatory response, the transformation of endothelial cell surfaces to provide a prothrombotic environment, and the impact on barrier function and vascular tone of the endothelium in the setting of infection with COVID-19. They reference ongoing clinical trials targeting different steps contributing to endotheliopathy and summarize the clinical manifestations associated with the disease and how they relate to the injured endothelium.

Patients with hematologic malignancies represent a group at high risk of adverse outcomes associated with COVID-19. Langerbeins and Hallek review this topic, beginning with immune response in patients with hematologic malignancies after infection with COVID-19 and vaccination. Recent chemoimmunotherapy, particularly anti-CD20 therapy, has a significant impact on immune response in these patients. The authors next address the different therapies used for the prevention and treatment of COVID-19, including antiviral therapies, convalescent plasma, dexamethasone, and monoclonal antibody therapies, and their role in patients with hematologic malignancies.

The articles in this review series will provide the reader with the latest updates on key hematologic topics related to the COVID-19 pandemic.

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