Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Microbiology and Infection 28 (2022) 1319–1320

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Editorial

Acute and latent viral infections in immunocompromised patients: a tale of brave battles and menacing foes

Although some infections have been with us for many millennia, others, like SARS-CoV-2, are new enemies who silently emerged, upended our way of life, and entrenched us in a perpetual struggle to control its spread. Nevertheless, all inflict damage in unique ways, with the highest costs being paid by those with weakened defenses. We refer to the devastation inflicted by viruses on our most vulnerable populations, such as those with chronic conditions, the elderly, the critically ill, patients with hematologic malignancies and other cancers, hematopoietic cell transplant (HCT) recipients, and patients receiving cellular therapy.

Tactically, herpes simplex virus I/II (HSV), varicella-zoster virus (VZV), human herpesvirus 6 (HHV-6), and cytomegalovirus (CMV), among others, act like sleeping giants, infecting most humans early in life before retreating into latency. Subsequently, these viruses sit and wait for a kink in the immunological armor to emerge. On the other hand, the respiratory viral pathogens, like influenza, SARS-CoV-2 (the etiological agent of COVID-19), and respiratory syncytial virus (RSV), act like lurking predators seeking out new hosts to infect.

Herpes simplex virus I/II, VZV, and HHV-6 can cause severe infections in immunocompromised hosts with impaired cellular immunity. Antiviral agents are currently being used to prevent HSV I/II and VZV flare-ups; however, this approach may have limitations, including breakthrough and resistant infections and negative effects on the T cell immune reconstitution. Heldman et al. explore the literature on novel and alternative methods for preventing and managing herpesvirus reactivations. The strategies discussed in their review include using virus-specific cellular immunity assays, such as enzyme-linked immunospot (ELISPOT) assays [1], as a precise correlate of risks and guide for therapeutic decision making. Likewise, the authors discuss using highly immunogenic vaccines and novel approaches for restoring humoral immunity in solid organ transplant and HCT recipients.

Critically ill patients are a unique population that is not typically considered immunocompromised. Ong et al. discuss CMV infections in this population and compare their clinical presentation to more characterized immunocompromised patients (i.e. HCT recipients). The authors stress that although clinical studies demonstrating definite proof of CMV-induced pathogenicity are lacking in critically ill patients, many studies suggest an independently attributable morbidity and mortality in these patients due to CMV reactivation. The authors underscored the importance of steroid use as a risk factor for CMV reactivation, as demonstrated in a recent publication in critically ill COVID-19 patients [2], and the need for further studies to determine viral load thresholds to distinguish clinically significant CMV infection from inconsequential reactivation. Furthermore, the benefit of viral therapy is still to be determined.

Unintended viral reactivations can occur in patients receiving novel systemic anticancer agents, like immune checkpoint inhibitors, Bruton tyrosine kinase inhibitors, and T-cell-directed therapies (i.e. chimeric antigen receptor T-cell). Subsequently, viral reactivations become the by-product of the direct impact of these anticancer drugs on the immune system or indirectly because of the treatment of the immune therapy-related hyperimmune reactions. In their review, Mustafayev and Torres summarize the data on the risk of chronic hepatitis B and C virus reactivation in the setting of these novel anticancer therapies while also outlining preventative strategies and knowledge gaps on this topic. Importantly, the authors conclude that awareness of the risk for infection and close monitoring of patients with chronic and past hepatitis B infection can help safely guide therapy and prevent unintended outcomes [3].

Although those with intact immune systems may never battle their sleeping giants, most will fight and recover from several respiratory viral infections (RVI) throughout their lives with little-to-no sequelae. However, the consequences of RVI in immunocompromised patients can be severe. In their article on respiratory viral pathogens, Paraskevi et al. review the literature on what is known and not known about alterations of innate and adaptive immune pathways caused by Immunosenescence and low-level, chronic inflammation that occurs in patients with comorbid conditions (e.g. obesity, diabetes mellitus, cardiovascular disease, among others) and altered physiological states (e.g. pregnancy, aging). Although these patient populations, like critically ill patients, are not considered classically immunocompromised, the implication of their immune dysregulation may increase their susceptibility to RVI with subsequent poor outcomes. The authors also discuss potential therapeutic targets that may be identified through further investigations of the affected immune pathways.

The disease burden in vulnerable patient populations caused by the viruses discussed here is vast and cannot be understated. In this

DOIs of original article: https://doi.org/10.1016/j.cmi.2022.02.001, https://doi.org/10.1016/j.cmi.2022.02.042, https://doi.org/10.1016/j.cmi.2022.03.010, https://doi.org/10.1016/j.cmi.2022.05.034.

https://doi.org/10.1016/j.cmi.2022.06.010

issue of *Clinical Microbiology and Infection*, the authors have constructed comprehensive reviews of the common herpesviruses, hepatitis viruses, and respiratory viral pathogens and the special patient populations they impact, while emphasizing current knowledge in viral diagnostics, preventative measures, management, and the interplay of immune mechanisms, responses, and infection. Although advances have been made to better manage many of the viruses discussed, the unmet medical needs for more effective and safer therapies and improved diagnostics remain large. Likewise, further unraveling the immune system's adaptation and its role in viral reactivation and containment is crucial.

Transparency declaration

The authors have no conflicts of interest or financial support/sponsorship to declare.

References

[1] El Haddad L, Ariza-Heredia E, Shah DP, Jiang Y, Blanchard T, Ghantoji SS, et al. The ability of a cytomegalovirus ELISPOT assay to predict outcome of low-level CMV reactivation in hematopoietic cell transplant recipients. J Infect Dis 2019;219(23):898–907.

[2] Yamamoto Y, Shiroyama T, Hirata H, Kuge T, Matsumoto K, Yoneda M, et al. Prolonged corticosteroid therapy and cytomegalovirus infection in patients with severe COVID-19. J Med Virol 2022;94:1067–73.

[3] Hwang JP, Feld JJ, Hammond SP, Wang SH, Alston-Johnson DE, Cryer DR, et al. Hepatitis B virus screening and management for patients with cancer prior to therapy: ASCO provisional clinical opinion update. J Clin Oncol 2020;38:3698–715.

Amy Spallone, Ella J. Ariza-Heredia, Roy F. Chemaly*
University of Texas MD Anderson, Department of Infectious Diseases, Infection Control and Employee Health, Houston, TX, USA

* Corresponding author: Roy F. Chemaly.
E-mail address: rfchemaly@mdanderson.org (R.F. Chemaly).

7 June 2022
Available online 17 June 2022

Editor: L. Leibovici