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.

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Letter to the Editor Regarding "Diagnostic Considerations for COVID-19 in Recipients of Allogeneic Hematopoietic Cell Transplantation"

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In immunocompromised HCT recipients, diagnosis of infections is extremely time-sensitive owing to the need to rapidly institute therapy. This assumes even greater relevance during the current pandemic of coronavirus disease-2019 (COVID-19) [1,2], in which allogeneic HCT recipients on therapeutic immune suppression are at increased risk for mortality, and the sole approved treatment (remdesivir) appears to be more effective in earlier stages of COVID-19 [3-6]. Similarly, published studies in COVID-19 and other viral illnesses have shown that convalescent plasma therapy is more effective earlier in the course of disease, with recovery either less likely or taking much longer in COVID-19 patients who develop acute respiratory distress syndrome (ARDS) [7-9].

Ardura et al [6] have provided a framework for guidelines for the diagnosis and management of COVID-19 and special considerations in the vulnerable population of allogeneic HCT recipients. They emphasize that a high index of suspicion is required to perform rRT-PCR analysis of NP swabs in patients who present with fever and/or symptoms of lower respiratory tract infection (LRTI) and have been in an area of high community SARS-CoV-2 prevalence or have been exposed to a confirmed or suspected COVID-19 case in the previous 14 days. In addition, in patients with a productive cough, sputum may be tested, but aerosol-generating procedures, including bronchoscopy, are discouraged and not recommended in patients known to be positive for SARS-CoV-2, unless a coinfection is suspected. The American Association of Bronchology and Interventional Pulmonology also advocate for a limited role for bronchoscopy in COVID-19 diagnosis, with consideration in intubated patients if NP swab samples are negative and alternative diagnoses are considered that would require a change in management [10].

In general, the management of LRTI in allogeneic HCT recipients requires consideration of multiple differential diagnoses in parallel. Because such patients can progress rapidly without early effective treatment, a delay in diagnosis leads to much worse outcomes. In hospitalized patients, COVID-19 is mostly diagnosed by NP rRT-PCR, and bronchoscopy is rarely required. We argue that allogeneic HCT recipients with LRTI symptoms and a negative NP swab for COVID-19 should be considered for early bronchoscopy when the index of clinical suspicion is high. Based on our clinical experience, allogeneic HCT recipients with clinical LRTI may have a high false-negative rate on NP swab testing. Wang et al [11] reported positive nasal and pharyngeal swabs in 63% and 32% of actual cases, respectively, whereas BAL fluid was positive in 93%. Wölfel et al [12] demonstrated that NP shedding predominates in the first week of COVID-19, whereas rRT-PCR-positivity persists in sputum as long as 3 weeks after the onset of respiratory symptoms and may remain positive even after NP testing becomes negative.

Assuming that a negative NP swab rRT-PCR misses 27% to 50% of cases of true COVID-19 with symptoms in the second week [12,13], we recommend early bronchoscopy when the clinical stakes are high. Time is of the essence in the immunocompromised host, and if ARDS has set in by the time the diagnosis of pulmonary COVID-19 is made, the window for effective treatment may have closed. The decision of whether to perform bronchoscopy for BAL sampling in allogeneic HCT patients may involve examining the trade-off between the probability of diagnosing COVID-19 and the risk to staff from aerosolization during the procedure. A multidisciplinary discussion involving transplantation, infectious diseases, critical care, and/or pulmonary specialists to estimate the pretest probability of COVID-19 and to ascertain the urgency of performing bronchoscopy is crucial.

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Bronchoscopy has an established role in the evaluation of respiratory pathologies in allogeneic HCT recipients [14] and should be considered in the event that NP rRT-PCR is negative for COVID-19 and also when a possible coinfection (eg, influenza [15]) is suspected. In such cases, early bronchoscopy will likely save time by facilitating early diagnosis of pulmonary COVID-19 and also may improve survival with the use of effective therapies [14]. Furthermore, early diagnosis can potentially decrease the risk of SARS-CoV-2 exposure to other hospital patients and healthcare workers caring for such patients.

In conclusion, COVID-19 should remain an important differential in patients with LRTI symptoms in the setting of community spread. Such patients need early bronchoscopic evaluation even when NP rRT-PCR is negative; an expectant stepwise approach is not advised in this population.

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