The Journal of Infectious Diseases
CORRESPONDENCE

## Response to Malkovsky

To the Editor—Convalescent plasma has been regarded as a promising treatment option for coronavirus disease 2019 (COVID-19) [1–3]. However, its effect on survival rate in critically ill patients is controversial. To date, several studies have reported beneficial effects of convalescent plasma therapy on the survival rate in patients with severe COVID-19 or critically ill with COVID-19 [4–9]; on the contrary, 5 of 6 critically ill patients died in our group's previous study [10].

We thank Dr Malkovsky for his concern regarding our study of convalescent plasma therapy for COVID-19. However, we do not agree that the high mortality rates may be associated with unknown levels of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–neutralizing antibodies. We do agree that neutralizing antibody titers should be tested in convalescent plasma before treatment in future clinical studies or practice, if possible. We also agree that therapeutic plasma exchange with convalescent plasma may be a potential option for the treatment of critically ill patients with COVID-19.

Although we did not have the ability to test the amounts of antibody at the time of convalescent plasma therapy in mid- and late February 2020, we were certain that there were antibodies from donors who had recovered from COVID-19, because all donors have been tested by the Henan Provincial Red Cross Blood Center, the leading official Blood Center in Henan Province, China. Most importantly, all 6 patients had SARS-CoV-2 clearance within 3 days after the first convalescent plasma infusion, which strongly suggests the presence of neutralizing antibodies in the convalescent plasma.

However, it is worthwhile to consider why there was the huge disparity in survival rates between the 2 studies [6, 10] that Malkovsky mentions. We present the clinical characteristics of our 11 patients in Table 1. The interval between symptom onset and plasma transfusion was 21.5 (range, 13.8–23.3) days in survivors and 30 (25–31.5) days in nonsurvivors ($P = .009$). Nearly 10 days of delay in convalescent plasma therapy means more than the time itself alone, and as time goes by, the cytokine storm may be more severe. Therefore, relatively late initiation of the convalescent plasma therapy at the end stage of COVID-19 may be the main reason for the high mortality rate in our study.

Currently, many patients are receiving a one-time dose of convalescent plasma, while some receive 2 doses and larger volumes of convalescent plasma. In our view, convalescent plasma given earlier in the course of the disease may be more beneficial, and more important than either the dosing schedule or the antibody titers. The most effective regimen with respect to timing, titer, and dosing needs further clarification.

### Notes

***Acknowledgments.*** We thank Yingxia Liu, MD and Zheng Zhang, MD, from Shenzhen Third People's Hospital, Shenzhen, China, for their kind responses concerning the details of their published article [6] .

***Disclaimer.*** The funders had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; the preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication.

***Financial support.*** This work was supported by the National Natural Science Foundation of China (grant 81970517), Zhongyuan (Henan) Thousand Outstanding Talents Plan (grant ZYQR201912179), the Foundation for Distinguished Young Talents of Zhengzhou University Medical School (grant 2020ZQLMS), and the Key Scientific Research Project of Henan Higher Education Institutions of China (grant 20B320028).

***Potential conflicts of interest.*** All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

**Qing-Lei Zeng,[1,a] Fanpu Ji,[2,a] and Ji-Yuan Zhang,[3,a]**

[1]Department of Infectious Diseases, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan Province, China, [2]Department of Infectious Diseases, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China, and [3]Treatment and Research Center for Infectious Diseases, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, China.

### References

1. Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. Lancet Infect Dis **2020**; 20:398–400.
2. Rubin R. Testing an old therapy against a new disease: convalescent plasma for COVID-19. JAMA **2020**; 323:2114–7.
3. Bloch EM, Shoham S, Casadevall A, et al. Deployment of convalescent plasma for the prevention and treatment of COVID-19. J Clin Invest **2020**; 130:2757–65.

**Table 1. Clinical Characteristics of 11 Patients Treated with Convalescent Plasma in 2 Studies**

| Study and Patient No. | Sex | Age, y | Time From Symptom Onset to Plasma Transfusion, d | Respiratory Failure | Convalescent Plasma Treatments, No. | Convalescent Plasma Dosage, mL | Survival |
|---|---|---|---|---|---|---|---|
| Shen et al [6] | | | | | | | |
| 1 | Male | 73 | 24 | Yes | 1 | 400 | Yes |
| 2 | Male | 60 | 14 | Yes | 1 | 400 | Yes |
| 3 | Female | 50 | 22 | Yes | 1 | 400 | Yes |
| 4 | Female | 36 | 21 | Yes | 1 | 400 | Yes |
| 5 | Male | 60 | 23 | Yes | 1 | 400 | Yes |
| 1 | Male | 32 | 13 | Yes | 1 | 200 | Yes |
| Zeng et al [10] | | | | | | | |
| 2 | Female | 30 | 26 | Yes | 2 | 600 | No |
| 3 | Male | 76 | 33 | Yes | 2 | 400 | No |
| 4 | Male | 61 | 30 | Yes | 2 | 600 | No |
| 5 | Male | 62 | 23 | Yes | 1 | 200 | No |
| 6 | Male | 83 | 30 | Yes | 1 | 200 | No |


4. Ahn JY, Sohn Y, Lee SH, et al. Use of convalescent plasma therapy in two COVID-19 patients with acute respiratory distress syndrome in Korea. J Korean Med Sci **2020**; 35:e149.
5. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci U S A **2020**; 117:9490–6.
6. Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA **2020**; 323:1582–9.
7. Zhang B, Liu S, Tan T, et al. Treatment with convalescent plasma for critically ill patients with SARS-CoV-2 infection. Chest doi:10.1016/j.chest.2020.03.039.
8. Zhang L, Pang R, Xue X, et al. Anti-SARS-CoV-2 virus antibody levels in convalescent plasma of six donors who have recovered from COVID-19. Aging (Albany NY) **2020**; 12:6536–42.
9. Ye M, Fu D, Ren Y, et al. Treatment with convalescent plasma for COVID-19 patients in Wuhan, China. J Med Virol doi:10.1002/jmv.25882.
10. Zeng QL, Yu ZJ, Gou JJ, et al. Effect of convalescent plasma therapy on viral shedding and survival in COVID-19 patients. J Infect Dis doi:10.1093/infdis/jiaa228.



Received 22 May 2020; editorial decision 27 May 2020; accepted 29 May 2020; published online May 30, 2020.


[a]Q. L. Z., F. J., and J. Y. Z. contributed equally to this work.


Correspondence: Qing-Lei Zeng, Department of Infectious Diseases, The First Affiliated Hospital of Zhengzhou University, No.1, Eastern Jianshe Rd, Zhengzhou 450052, Henan Province, China (zengqinglei2009@163.com).



**The Journal of Infectious Diseases® 2020;XX:1–2**





DOI: 10.1093/infdis/jiaa313