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COVID-19 and Coagulopathy

To the Editor:

We read with interest the recent review article by Rodriguez and colleagues regarding endothelial dysfunction and consequent thrombotic complication in patients with coronavirus disease (COVID-19) (1). Here, we would like to add a point. We will provide supplementary explanation on a molecular group (e.g., IL-1, IL-6, and TNF-α) that has been implicated in coagulation activation in the paper.

We wish to explain the complex role of IL-6 in coagulopathy accompanied by severe inflammation. Using IL-6 knockout (IL-$6^{-/-}$) mice, we have previously demonstrated that IL-6 serves as a protector in coagulatory disturbance and thrombocytopenia during devastating systemic inflammation induced by intraperitoneal administration of bacterial endotoxins (LPS) (2), which was evidenced by prothrombin time and activated partial thromboplastin time. Furthermore, we have confirmed that in the presence of LPS, α_2-plasmin inhibitor activity was significantly lower in IL-$6^{-/-}$ mice than in wild-type mice, indicating that IL-6 can partially inhibit LPS-provocated fibrinolysis by enhancing α_2-plasmin inhibitor activity (3). Interestingly, fibrin degradation product was significantly lower in the IL-$6^{-/-}$ mice administered with LPS than in the wild-type mice, whereas D-dimer was comparable in both groups (unpublished observation; these complicated results require future research for further clarification). Regardless, IL-6 may not be introduced in the same way as other proinflammatory cytokines, such as IL-1 and TNF-α, in coagulatory disturbance with persistent inflammation.

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Reply to: COVID-19 and Coagulopathy

From the Authors:

We read the letter from Dr. Inoue and colleagues with interest and recognize the importance of pointing out that IL-6