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Drs. Cron and Chatham reply

To the Editor:

We value Dr. Caricchio's and Dr. Criner's appreciation of our commentary on the role of rheumatologists in the coronavirus disease 2019 (COVID-19) pandemic[1]. We applaud Temple University for collaborating in the care of hospitalized patients with COVID-19, many of whom are experiencing a cytokine storm syndrome (CSS)[2]. COVID-19 infection results in up to 20% of individuals requiring hospitalization for pneumonia, which can progress to acute respiratory distress syndrome, shock, and multiorgan dysfunction syndrome[3]. Many of the clinical and laboratory features of hospitalized patients with COVID-19 are reminiscent of a CSS[1,4,5]. Because CSS is frequently fatal, recognition of the CSS and early initiation of treatment directed specifically at the CSS is critical for reducing mortality[6]. This not only requires infectious disease experts to treat the trigger and intensivists/pulmonologists to support the organs involved, but experts in diagnosing and treating CSS, often rheumatologists and oncologists.

In late April of this year, an informal questionnaire was posed to pediatric and adult rheumatology division directors based at academic institutions in the United States and Canada to survey rheumatology's involvement in the care of hospitalized patients with COVID-19. From 35 respondents, 69% reported "none" (14%) or "some" involvement in the co-management of patients with COVID-19 in their respective university hospitals. As at Temple University[2], fewer than a third (31%) of responding rheumatology division directors stated a "high" degree of rheumatology involvement in the care of patients with COVID-19. This is disturbing, with individual comments ranging from "only treating the virus" to "politics in the intensive care units dictating management." This is particularly worrisome without a vaccine or a "home run" antiviral approach for an infection that has killed over 350,000 individuals globally.

We all await clinical trial results of antiviral or anti-CSS therapies that will substantially save the lives of COVID-19 victims. Until then, many clinicians worldwide in regions overrun by SARS-CoV-2 are, out of desperation from the extreme mortality witnessed, resorting to treating CSS associated with COVID-19 outside of clinical trials. Early case series, often comparing results to historical controls at the same sites prior to the studied intervention, are being published and reporting the benefit of treating the COVID-19 CSS with interleukin (IL)-1 blockade[7], IL-6 blockade[8], and even glucocorticoids[9]. These approaches appear to be particularly useful for hospitalized COVID-19 patients with evidence of CSS but prior to intensive care and invasive mechanical ventilation[10]. Temple University personifies this approach with > 92% of its over 1000 hospitalized patients with COVID-19 being discharged to home[2]. This is particularly impressive given the inner-city patient population treated at Temple University, including many high-risk patients with 2 or more dangerous comorbid conditions as well as ethnic risk factors for poor outcomes.

Kudos to Drs. Caricchio, Criner, and colleagues for working as a team to help save lives in these challenging times. Clinicians of multiple subspecialties have much to offer in connection with their expertise and experience in caring for patients with COVID-19, and it shows. Multiple aspects of COVID-19 need to be recognized and treated. In addition to treating the coronavirus when substantial therapies become available, diagnosing and treating the CSS/host immune response (which is killing the patient in the later inflammatory phase of the disease) is critical to optimizing patient survival[10]. Teamwork will help us to achieve this goal.

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Drs. Cron and Chatham are co-principal investigators on an investigator-initiated clinical trial to study interleukin 1 blockade in treating secondary hemophagocytic lymphohistiocytosis in children and adults. The trial is funded by Swedish Orphan Biovitrum Inc. (SOBI; ClinicalTrials.gov: NCT02780583), which manufactures anakinra. Dr. Cron serves as a consultant to SOBI. Dr. Chatham has served as a consultant to SOBI.

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