

Dr. 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) pandemic¹. 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 syndrome³. 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 mortality⁶. 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 University², 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 blockade⁷, IL-6 blockade⁸, and even glucocorticoids⁹. These approaches appear to be particularly useful for hospitalized COVID-19 patients with evidence of CSS but prior to intensive care and invasive mechanical ventilation¹⁰. Temple University personifies this approach with > 92% of its over 1000 hospitalized patients with COVID-19 being discharged to home². 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 survival¹⁰. Teamwork will help us to achieve this goal.

RANDY Q. CRON , MD, PhD, Professor of Pediatrics, University of Alabama at Birmingham, Department of Pediatrics, Division of

Rheumatology; W. WINN CHATHAM, MD, Professor of Medicine, University of Alabama at Birmingham, Department of Medicine, Division of Clinical Immunology and Rheumatology, Birmingham, Alabama, USA. Address correspondence to Dr. R.Q. Cron, Children's of Alabama, Division of Rheumatology, 1600 7th Ave. S., CPPN, suite G10, Birmingham, Alabama 35233-1711, USA. E-mail: rcron@peds.uab.edu. 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.

REFERENCES

1. Cron RQ, Chatham WW. The rheumatologist's role in COVID-19. *J Rheumatol* 2020;47:639-42.
2. Caricchio R, Criner GJ. Rheumatologists and pulmonologists at Temple University weather the COVID-19 storm together. *J Rheumatol* 2020;47:xxxxx.
3. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* 2020;368:m1091.
4. Henderson LA, Canna SW, Schuler G, Volpi S, Lee PY, Kernan KF, et al. On the alert for cytokine storm: immunopathology in COVID-19. *Arthritis Rheumatol* 2020 Apr 15 (E-pub ahead of print).
5. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033-4.
6. Eloseily EM, Weiser P, Crayne CB, Haines H, Mannion ML, Stoll ML, et al. Benefit of anakinra in treating pediatric secondary hemophagocytic lymphohistiocytosis. *Arthritis Rheumatol* 2020;72:326-34.
7. Cavalli G, De Luca G, Campochiaro C, Della-Torre E, Ripa M, Canetti D, et al. Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study. *Lancet Rheumatol* 2020 [Internet. Accessed June 2, 2020.] Available from: [www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(20\)30127-2/fulltext](http://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30127-2/fulltext)
8. Toniati P, Piva S, Cattalini M, Garrafa E, Regola F, Castelli F, et al. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: a single center study of 100 patients in Brescia, Italy. *Autoimmun Rev* 2020;19:102568.
9. Fadel R, Morrison AR, Vahia A, Smith ZR, Chaudhry Z, Bhargava P, et al. Early short course corticosteroids in hospitalized patients with COVID-19. *Clin Infect Dis* 2020 May 19 (E-pub ahead of print).
10. Chatham WW, Cron RQ. Treating Covid-19 at the inflection point. *J Rheumatol* 2020 May 25 (E-pub ahead of print).

First Release July 1 2020; *J Rheumatol* 2020;47:xxxx;
doi:10.3899/jrheum.200744