Author disclosures are available with the text of this letter at www.atsjournals.org.

Joshua D. Lee, M.D.
University of Washington
Seattle, Washington

Charles D. Burger, M.D.
Mayo Clinic Florida
Jacksonville, Florida

Sam G. Rayner, M.D.
University of Washington
Seattle, Washington

John J. Ryan, M.D.
University of Utah
Salt Lake City, Utah

Peter J. Leary, M.D., Ph.D.*
University of Washington
Seattle, Washington

ORCID IDs: 0000-0001-7715-2107 (J.D.L.); 0000-0001-5716-248X (P.J.L.)

*Corresponding author (e-mail: learyp@uw.edu).

References

1 Lee JD, Burger CD, Delossantos GB, Grinnan D, Ralph DD, Rayner SG, *et al*. A survey-based estimate of COVID-19 incidence and outcomes among patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension and impact on the process of care. *Ann Am Thorac Soc* 2020;17: 1576–1582.
2 Rajgor DD, Lee MH, Archuleta S, Bagdasarian N, Quek SC. The many estimates of the COVID-19 case fatality rate. *Lancet Infect Dis* 2020;20:776–777.
3 Yang W, Kandula S, Huynh M, Greene SK, Van Wye G, Li W, *et al*. Estimating the infection-fatality risk of SARS-CoV-2 in New York City during the spring 2020 pandemic wave: a model-based analysis. *Lancet Infect Dis* 2021;21:203–212.
4 Belge C, Quarck R, Godinas L, Montani D, Escribano Subias P, Vachiéry JL, *et al*. COVID-19 in pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: a reference centre survey. *ERJ Open Res* 2020;6:00520-2020.
5 Farha S, Heresi GA. COVID-19 and pulmonary arterial hypertension: early data and many questions. *Ann Am Thorac Soc* 2020;17: 1528–1530.

A Role for Steroids in COVID-19–associated Pneumonitis at Six-Week Follow-Up?

To the Editor:

We read with interest the recent paper by West and colleagues (1) regarding the use of corticosteroids in persistent inflammatory interstitial lung disease (ILD) after a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. In their timely and well-implemented observational treatment study, 3.6% of patients with coronavirus disease (COVID-19) discharged from the hospital were diagnosed with persisting organizing pneumonia at 6 weeks and deemed eligible for corticosteroid treatment. Cases were assessed in a multidisciplinary team meeting, and lung function was performed before and after treatment.

As ILD physicians in a tertiary referral center, we have extensive experience in treating organizing pneumonia with corticosteroids in the context of autoimmune disease, adverse drug reactions, and infection. We agree that, intuitively, corticosteroids should have a role in the treatment of patients with significant parenchymal disease secondary to COVID-19. From our own large cohort captured during a similar time frame, before acute corticosteroid treatment was the standard of care (2, 3), the incidence of interstitial changes at 6-week follow up is comparable to these data. However, in our cohort without targeted outpatient corticosteroid administration, there was a significant spontaneous recovery in the majority of patients by 12 weeks. This raises the question as to whether there would have been some spontaneous recovery in these patients without any intervention, especially as there is no matched comparator group. Treatment was only offered if patients were not getting better on a weekly basis, but it is not clear how this assessment was made. It is also important to note that, although treatment was for a short duration, these patients had obesity (25.7%), hypertension (31.4%), and diabetes (22.9%) and were therefore a population in which steroids would ideally be avoided if possible.

We applaud the speed and completeness of this work, particularly in the current climate when access to aerosol-generating respiratory physiology testing to robustly quantify changes is challenging. However, there is clearly equipoise about the use and timing of corticosteroid administration and how they affect the natural history of COVID-19 associated with organizing pneumonia. The RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial (2) showed that dexamethasone resulted in reduced 28-day mortality in those patients requiring oxygen and is now standard of care in this cohort of patients for 10 days. In a second much smaller randomized control trial of just 68 patients with hypoxia (oxygen saturation as measured by pulse oximetry $< 90\%$) who were not intubated and ventilated, methylprednisolone was administered at 250 mg/d for 3 days and showed a significant reduction in mortality (4). We also know from this observational treatment study (1), albeit in a small number of patients, that steroids have a beneficial effect when administered at 6 weeks postdischarge. Two large systematic reviews have further identified acute corticosteroid administration has a mortality benefit in patients with severe disease but does not seem to have a significant impact at lower doses (5, 6). What is less clear is if corticosteroids should be prolonged or augmented after

Supported by University College London Hospital (UCLH) Biomedical Centre grant BRC775 (E.K.D.). This work was undertaken at UCLH/UCL, which received a proportion of funding from the Department of Health's National Institute of Health Research Biomedical Research Centre's funding scheme.

completion of dexamethasone and in what patient cohort and using what objective parameters.

To further address this unmet need, we propose ILD physicians, respiratory and general physicians, intensivists, and interested others collaborate to generate clinically valid research questions that can be answered by a randomized control trial.

Author disclosures are available with the text of this letter at www.atsjournals.org.

Emma K. Denneny, M.B. B.S., M.R.C.P.
University College London Hospitals National Health Service (NHS) Foundation Trust
London, United Kingdom
and
University College London
London, United Kingdom

Helen S. Garthwaite, M.B. B.S., B.Sc., M.R.C.P.*
University College London Hospitals NHS Foundation Trust
London, United Kingdom
and
Royal Free Hospital NHS Foundation Trust
London, United Kingdom

Melissa J. Heightman, M.B. B.Ch., M.A., M.R.C.P.
University College London Hospitals NHS Foundation Trust
London, United Kingdom

Joanna C. Porter, M.B. B.Ch., M.A., Ph.D., F.R.C.P.
University College London Hospitals NHS Foundation Trust
London, United Kingdom
and
University College London
London, United Kingdom

ORCID ID: 0000-0002-7695-325X (E.K.D.).

*Corresponding author (e-mail: helen.garthwaite1@nhs.net).

References

1 Myall KJ, Mukherjee B, Castanheira AM, Lam JL, Benedetti G, Mak SM, *et al*. Persistent post–COVID-19 interstitial lung disease: an observational study of corticosteroid treatment. *Ann Am Thorac Soc* 2021;18:799–806.
2 Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, *et al*.; RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 2021;384:693–704.
3 Angus DC, Derde L, Al-Beidh F, Annane D, Arabi Y, Beane A, *et al*.; Writing Committee for the REMAP-CAP Investigators. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19: the REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. *JAMA* 2020;324:1317–1329.
4 Edalatifard M, Akhtari M, Salehi M, Naderi Z, Jamshidi A, Mostafaei S, *et al*. Intravenous methylprednisolone pulse as a treatment for hospitalised severe COVID-19 patients: results from a randomised controlled clinical trial. *Eur Respir J* 2020;56:2002808.
5 Cano EJ, Fuentes XF, Campioli CC, O'Horo JC, Saleh OA, Odeyemi Y, *et al*. Impact of corticosteroids in coronavirus disease 2019 outcomes: systematic review and meta-analysis. *Chest* 2021;159:1019–1040.
6 Sterne JAC, Murthy S, Diaz JV, Slutsky AS, Villar J, Angus DC, *et al*.; WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA* 2020;324:1330–1341.

Reply: A Role for Steroids in COVID-19–associated Pneumonitis at Six-Week Follow-Up?

From the Authors:

We thank Denneny and colleagues for their insightful comments and would like to take this opportunity to clarify some of the points raised in their letter.

Early on in the first wave, we began to realize it would be important to understand the natural recovery and the incidence of pulmonary sequelae after coronavirus disease (COVID-19) infection (1). We carefully evaluated 837 recovering patients, first by telephone at 3–4 weeks after discharge, when 316 (38%) reported they were already back to their physical functional baseline. After face-to-face structured assessment and COVID-19 multidisciplinary team meeting discussion, only 59/837 (7%) had persistent post–COVID-19 interstitial changes with associated symptoms and physiological impairment and were therefore referred to the interstitial lung disease (ILD) service. At this stage, 24 patients had either minimal inflammatory infiltrates (<15%) on computed tomography (CT) or an absence of persistent symptoms or physiological impairment, similar to the self-resolving cohort Denneny and colleagues describe. However, this left 35 patients with persistent symptoms causing significant distress at a median of 61 days (9 wk) after discharge from the hospital. This represents only 4.2% of the surviving population, and although almost all our patients were recovering over time, this group of patients demonstrated a large ongoing symptom burden that was directly attributable to the ongoing inflammatory changes seen on CT, predominately organizing pneumonia. This left a clinical decision: to observe or to treat.

Given the risk factors for severe COVID-19 pneumonitis, we agree that steroid therapy is not without risk in this group. Individual patient discussion was key, and hence, five patients did not commence steroid treatment after review. It is therefore worth noting that the quoted proportions of patients with comorbidity refers to the whole cohort referred to the ILD service and not to the treatment group, who had lower rates of comorbidity. All patients had weekly telephone support and diabetes team input as appropriate. As a result, we saw no major complications of treatment.

This is observational work, and in keeping with Denneny and colleagues' observations, we also saw an improvement in the small number of patients who did not receive treatment and completed 12-week follow-up. However, this improvement was of lower magnitude than the improvement we saw in our patients at 3 weeks after treatment.

This study was commenced before the RECOVERY data were published, and only 19% of patients we treated had received any