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world is more interconnected now than during any era before; let the rheumatology community reflect that, now and after the COVID-19 pandemic.

We declare no competing interests. LL was funded in part by the Intramural Research Programme of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health. EH was supported by the Fogarty International Center, National Institutes of Health, Bethesda, MD, USA (K01TW009995).

**Laura B Lewandowski, Evelyn Hsieh*
laura.lewandowski@nih.gov

National Institute of Arthritis, Musculoskeletal, and Skin Diseases, National Institutes of Health, Department of Health and Human Services, Bethesda, MD 20892-1102, USA (LBL); Section of Rheumatology, Allergy, and Immunology, Yale School of Medicine, New Haven, CT, USA (EH); and Section of Rheumatology, Veteran Affairs Connecticut Healthcare System, West Haven, CT, USA (EH)

- 1 Fauci AS, Lane HC, Redfield RR. Covid-19 — Navigating the Uncharted. *N Engl J Med* 2020; **382**: 1268–69.
- 2 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; published online Feb 24. DOI:10.1001/jama.2020.2648.
- 3 Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA* 2020; published online March 19. DOI:10.1001/jama.2020.4326.
- 4 McCreary EK, Pogue JM. COVID-19 treatment: a review of early and emerging options. *Open Forum Infect Dis* 2020; published online March 23. DOI:10.1093/ofid/ofaa105.
- 5 Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020; published online March 13. DOI:10.1001/jamainternmed.2020.0994.

Caution and clarity required in the use of chloroquine for COVID-19

As the coronavirus disease 2019 (COVID-19) outbreak continues to spread rapidly, efforts are ongoing in China and around the world to develop effective treatments. Among the drugs being tested for COVID-19 in China is chloroquine, which was reported on Feb 4, 2020, to inhibit severe acute respiratory syndrome coronavirus 2

in vitro. The drug was rapidly pushed to clinical testing as an experimental treatment in China; on Feb 15, 2020, it was included in the sixth version of the COVID-19 treatment guidelines by the National Health Commission of the People's Republic of China. This guideline established the use of chloroquine nationwide for patients with COVID-19, at a recommended adult dose of 500 mg twice per day for no more than 10 days.¹

The lethal dose of chloroquine in adults is about 5 g.² In the human body, chloroquine has a large volume of distribution with an elimination half-life of 20–60 days and a tendency to accumulate in metabolically active tissues at higher levels compared with the plasma concentration.^{3,4} In view of these properties, the recommended dose of 500 mg twice per day can quickly approach danger thresholds with sustained use. At the maximum course of 10 days, this regimen is substantially more aggressive than recommended regimens for the use of chloroquine as an antimalarial. The effects of chloroquine poisoning are well documented and include retinopathy and immunosuppression, with contraindications in several conditions including pregnancy.³ On Feb 26, 2020, the treatment guidelines were revised, shortening the maximum course to 7 days while recommending a lower dose for patients weighing less than 50 kg and highlighting contraindications including pregnancy.⁵ It is encouraging that an appropriate adjustment with improved consideration for the toxicological properties of the drug was made so quickly given the urgency of the situation. However, we advise continued caution in bringing new treatments to clinical use in such a rapid manner. Recommended doses should be established with close reference to pharmacological profiles and side-effects must be closely monitored. The less toxic hydroxychloroquine should also be considered as an alternative. Finally, the potential toxicities of experimental treatments

should be meticulously reported in peer-reviewed publications to avoid potentially misleading accounts and the risk of dangerous self-medication by the public. The rapid identification and development of such novel treatments is encouraging and will be instrumental in the battle against COVID-19, as long as prudence and rigour continue to be practised in both implementation and reporting.

We declare no competing interests.

*Yin Kwan Wong, Jing Yang, *Yingke He*
heyingsk2246@gmail.com

Yong Loo Lin School of Medicine (YKW) and Department of Biological Sciences (JY), National University of Singapore, Singapore; and Division of Anaesthesiology, Singapore General Hospital, 169608 Singapore (YH)

- 1 National Health Commission of the People's Republic of China. Interpretation of COVID-19 treatment guidelines (6th version). Feb 19, 2020. http://www.gov.cn/zhengce/2020-02/19/content_5480958.htm (accessed Feb 26, 2020; in Chinese).
- 2 Riou B, Barriot P, Rimailho A, Baud FJ. Treatment of severe chloroquine poisoning. *N Engl J Med* 1988; **318**: 1–6.
- 3 Tanenbaum L. Antimalarial agents. *Arch Dermatol* 1980; **116**: 587.
- 4 Ducharme J, Farinotti R. Clinical pharmacokinetics and metabolism of chloroquine. *Clin Pharmacokinet* 1996; **31**: 257–74.
- 5 National Health Commission of the People's Republic of China. Regarding dosage adjustments to the experimental use of chloroquine phosphate in the treatment of COVID-19. Feb 26, 2020. <http://www.nhc.gov.cn/xcs/zhengcwj/202002/0293d017621941f6b2a4890035243730.shtml> (accessed Feb 29, 2020; in Chinese).

Preventing COVID-19-induced pneumonia with anticytokine therapy

Immune-mediated disorders are a group of disabling conditions that affect millions of individuals worldwide.¹ These pathologies include, but are not limited to, rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, and inflammatory bowel diseases. Each of these diseases has a unique epidemiology and pathophysiology, despite sharing several pathways of tissue damage,

Published Online
April 2, 2020
[https://doi.org/10.1016/S2665-9913\(20\)30093-X](https://doi.org/10.1016/S2665-9913(20)30093-X)

Published Online
April 6, 2020
[https://doi.org/10.1016/S2665-9913\(20\)30092-8](https://doi.org/10.1016/S2665-9913(20)30092-8)