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## Global rheumatology in the time of COVID-19

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At the 2019 American College of Rheumatology (ACR) annual meeting, we chaired a session entitled “Frontiers and Opportunities in Global Rheumatology Research”, which was a call to action for the rheumatology community to think globally about the burden of rheumatic and musculoskeletal diseases. The current outbreak of a novel coronavirus has caught the attention of the medical community and the world at large. A local outbreak of a respiratory illness was first reported to WHO on Dec 31, 2019, in Wuhan, China. The causative agent was identified as a novel coronavirus now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the resulting disease is now known as coronavirus disease 2019 (COVID-19).<sup>1</sup> The virus spread quickly throughout China, and subsequently the world. At the time of the ACR session in November, 2019, no-one could have imagined the global pandemic that is now unfolding.

For the COVID-19 Global Rheumatology Alliance see <https://rheum-covid.org>

### Panel: Scientific and clinical challenges facing the rheumatology community during the COVID-19 pandemic

- Elucidating the host response to viral infection and risk factors for progression to severe or critical disease and mortality, particularly in the context of the aging immune system
- Identifying potential genetic susceptibility factors that influence the risk of acquisition of SARS-CoV-2 and mortality from COVID-19
- Identifying optimal management strategies for patients on immunosuppressant medications with consideration of SARS-CoV-2
- Understanding the short-term and long-term multisystem effects of COVID-19
- Measuring the outcomes of patients with specific rheumatological conditions who are infected with SARS-CoV-2
- Addressing anticipated drug shortages for hydroxychloroquine, tocilizumab, anakinra, and other medications commonly in use in rheumatology
- Working through unprecedented logistical and ethical challenges (eg, rapidly setting up global registries and en masse transitions to telehealth)

COVID-19=coronavirus disease 2019. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

The rheumatology community has responded rapidly to SARS-CoV-2, a highly contagious virus with a case fatality rate ranging from 0.9% overall to 5.0–10.0% in patients older than 70 years in the Chinese population.<sup>2</sup> There is substantial concern among rheumatologists regarding a potentially increased risk of infection and death among patients who are immunosuppressed, including those with rheumatic disease. Few data on this possible risk exist to date; at the time of this Correspondence being published, there is a registered retrospective study in China for patients with rheumatic disease and a case series from the USA listing rheumatic disease as a pre-admission comorbidity.<sup>3</sup> As studies regarding treatments for and outcomes of COVID-19 emerge, it seems possible that immunomodulation could alter the disease course of COVID-19. Many reports have cited the use of medications commonly found in the rheumatology armamentarium for the management of COVID-19, including hydroxychloroquine, glucocorticoids, intravenous immunoglobulin, anti-interleukin (IL)-1 and anti-IL-6 therapies, and Janus kinase inhibitors.<sup>4</sup> The world is watching with great interest to see if those drugs can save lives during this pandemic. In addition to the rapid progression of respiratory failure, COVID-19 seems to be most fatal when it triggers a cytokine storm.<sup>5</sup> However, there are currently no tools to identify patients at greatest risk of developing this complication, and the mechanisms by which this reaction occurs in the setting of COVID-19 are not fully understood.

In the rheumatology community, an international coalition, the COVID-19 Global Rheumatology Alliance, has come together to launch a global registry of patients with rheumatic and musculoskeletal diseases with COVID-19, for physicians worldwide to report these cases of COVID-19 and support the collection of patient-reported cases. The alliance was developed and publicised through social

media, email listservs, and personal and professional networks. Within 48 h of inception, the COVID-19 Global Rheumatology Alliance had engaged rheumatologists across six continents; support from non-profit organisations promoting the health of patients with rheumatic diseases and major rheumatology journals followed soon after, with approximately 100 organisations endorsing the alliance at the time of this Correspondence. The COVID-19 Alliance will obtain data on any patient with rheumatic disease who tests positive for SARS-CoV-2, capturing the range from mild to severe cases, with the goal of informing risk and best practice during the outbreak. With this novel pathogenic threat, there is much that is not yet known, and many ways this virus could impact the rheumatology community (panel).

The global coordinated and rapid response to this devastating outbreak shows the tenets of global health: that humans are all connected, and that the health of a person in one part of the world is relevant to the health of humans everywhere. Rheumatology professionals care for patients with diseases that have a high risk of morbidity and mortality and manage rare diseases; a global collaboration enables these professionals to collect enough data to inform clinical decisions. The sharing and dissemination of information about the diagnosis and management of rheumatic diseases worldwide is important at all times, but is especially crucial during these uniquely uncharted times. Rheumatologists are managing a new threat, but the development of tools, such as telehealth platforms and open-source algorithms, can help inform strategies for global education and communication within the rheumatology community beyond the COVID-19 threat. We believe that the global community created in this dire time has the power and commitment to remain unified when the pandemic has passed. Our modern

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

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\**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)

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## 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.<sup>1</sup>

The lethal dose of chloroquine in adults is about 5 g.<sup>2</sup> 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.<sup>3,4</sup> 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.<sup>3</sup> 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.<sup>5</sup> 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.

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*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)

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## Preventing COVID-19-induced pneumonia with anticytokine therapy

Immune-mediated disorders are a group of disabling conditions that affect millions of individuals worldwide.<sup>1</sup> 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,

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