

# Management strategies for patients with autoimmune diseases during the COVID-19 pandemic: A perspective from China

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Today is April 4<sup>th</sup>, the Chinese traditional “Tomb-Sweeping Day” when people mourn their dead, and the designated National Mourning Day to grieve over those who perished as a result of the COVID-19 pandemic. China has battled the new COVID-19 pandemic for several months, beginning in December of last year. Many courageous Chinese citizens lost their lives in the battle, some while caring for others who were sick from SARS-CoV-2, especially early on when medical resources were scarce. Although much was done to contain this highly contagious and deadly virus, it has now spread globally through 205 countries with over 1.3 million confirmed cases and over 70,000 deaths so far (1).

Studies have identified patients at risk for severe disease or higher mortality as those of advanced age and those with chronic conditions, particularly chronic cardiovascular disease, diabetes mellitus and chronic pulmonary disease (2-4). In addition, rheumatic patients are of increased risk for infection because immunodeficiency often accompanies autoimmune diseases, and also because many of our patients are treated with corticosteroids and other immunosuppressive agents (5). It is therefore particularly important to protect these patients from exposure to SARS-CoV-2, since there is at present no clear effective treatment.

To block the transmission of 2019-nCoV, one of the most effective measures is to reduce person-to-person contact (6). We recommend that our patients wear masks and wash their hands regularly. For stable patients, we suggest that they reduce in-person follow-up visits and maintain their current medication regimens. Social media apps or teleconsultation systems can be used to manage patients (7). For patients requiring hospitalization, screening of clinical symptoms, epidemiological history and lung CT scan may be necessary. For patients suspected of having COVID-19, a nasopharyngeal or oropharyngeal swab test is obtained. Once confirmed, the patient should be isolated to prevent further transmission. Patients in the hospital should be accompanied by only one fixed caregiver (two for pediatric patients). Temperature monitoring is conducted on each caregiver every day. Patients and caregivers are educated to wear masks during ward rounds and when going out. They are required to inform the nurses and security when go off the ward and perform face and hand hygiene when they return. Visitors are not allowed during the outbreak (8, 9). Patients with clinically suspected disease but negative swabs should be placed in a separate room in the medical ward. Medical staff are at particularly high risk of infection. All medical staff should be trained on the use of personal protective equipment (PPE) and strictly comply with hand washing, donning of masks and gowns and other recommendations. Each staff member is required to report his or her health status and epidemiology history on a daily basis. The entire inpatient facility should be sterilized at least three times each day with chlorine-containing disinfectant. The central air conditioning system should be turned off (Figure 1) (10, 11).

Although rheumatic patients are particularly vulnerable to the virus, they may in some cases be unexpectedly protected, by virtue of the medications that are used to control their disease. One of the major causes of critical illness in COVID-19 patients is cytokine storm, which often leads to death (12, 13). Drugs used in autoimmune diseases have anti-inflammatory properties which may counteract the proinflammatory cytokines released during cytokine storm associated with COVID-19 (14).

Chloroquine and hydroxychloroquine (HCQ) are anti-malaria drugs that have an excellent track record in the treatment of rheumatism for more than seventy years (15). Recently, these old drugs have been reported to be effective as an anti-viral agent (16). Several randomized controlled trials on chloroquine and hydroxychloroquine are currently being conducted in China. The data shows that these two drugs can reduce the transmission and replication of SARS-CoV-2, and ameliorate clinical symptoms and lung CT lesions of

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COVID-19 pneumonia (17). Accordingly, rheumatic patients who are taking chloroquine and hydroxychloroquine should remain on these drugs through the pandemic.

Corticosteroids have been used in the treatment of autoimmune diseases (AIDs) since the 1950s and have shown great efficacy in reducing morbidity and mortality, despite their well-known side effects. Due to their potent immunomodulatory activity, corticosteroids are commonly used in the treatment of cytokine storm that occur in severe infections such as sepsis and septic shock (18). During the epidemic of SARS Coronavirus (SARS-CoV) in 2002, Middle East Respiratory Syndrome (MERS)-CoV in 2012, and influenza, corticosteroids were also widely used as a primary mode of therapy

to regulate inflammatory reactions (14). In the current pandemic, systemic administration of corticosteroid is used to treat severe complications in COVID-19 patients. However, the adverse effects of glucocorticoid sometimes may outweigh its benefits (19, 20).

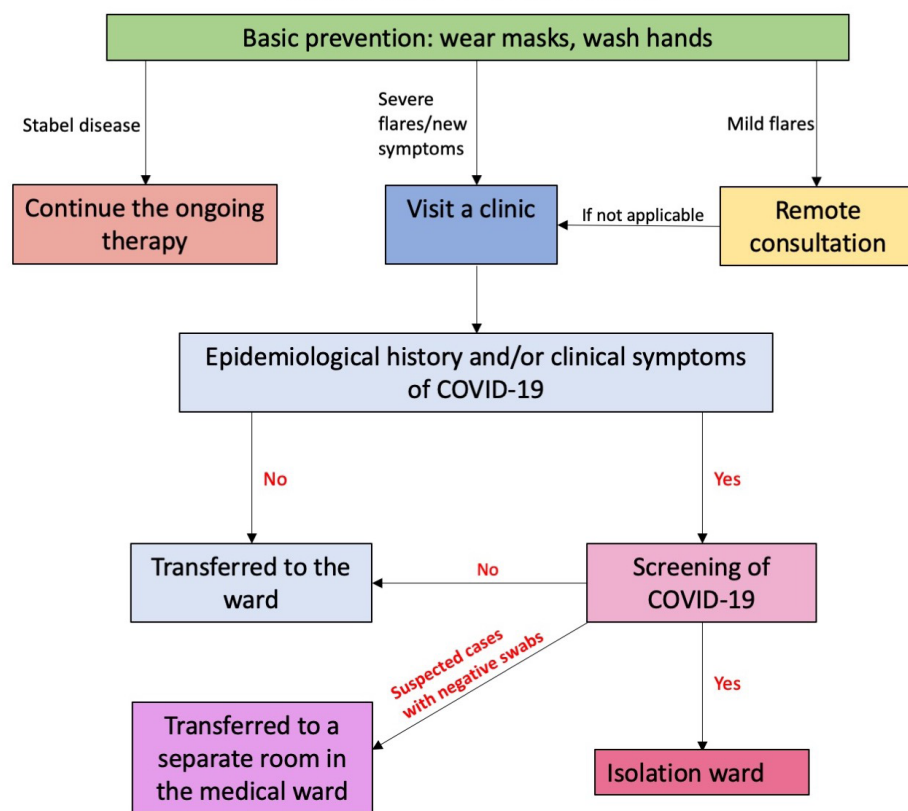
Traditional immunosuppressive agents like mycophenolate mofetil (MMF) and calcineurin inhibitors (CNIs) are also widely used in rheumatic patients. Although there are no case series or reports of COVID-19 in rheumatic patients treated with these immunosuppressive agents, experience from transplantation patients has shown us that traditional immunosuppressive agents can be a predisposing factor for COVID-19 infection. However, the withdrawal of an immunosuppressant in a

rheumatic patient with COVID-19 should be carefully considered only in severe COVID-19 patients (21, 22).

The cytokine profile of COVID-19 patients show increased expression of interleukin (IL)-2, IL-6, IL-7, interferon- $\gamma$  inducible protein 10, granulocyte colony stimulating factor (G-CSF), monocyte chemo-attractant protein 1 (MCP-1), tumor necrosis factor  $\alpha$  (TNF  $\alpha$ ), and macrophage inflammatory protein 1- $\alpha$  (MIP1- $\alpha$ ), and levels are associated with disease severity. Moreover, increased IL-6 is a predictor of fatality (23). To block the inflammatory cascade reactions in COVID-19 patients, several biological agents may be considered (24). The IL-6 receptor antagonist tocilizumab and the IL-6R $\alpha$  receptor inhibitor sarilumab can successfully block the IL-6 pathway and have been shown to be effective in improving the pulmonary complications of COVID-19 in several studies (13, 25). Currently, several clinical trials on tocilizumab use in severe COVID-19 patients are ongoing. When SARS-CoV-2 binds to toll-like receptor, it can induce the release of IL-1 which also contributes to the inflammation of COVID-19. IL-1 blockade (anakinra) showed great survival benefit in sepsis patients with hyperinflammation. Therefore, it is believed that IL-1 blockade will be a potential therapy for COVID-19 (26, 27). Another promising therapy is the Janus Kinase (JAK) blocker baricitinib. It is also an inhibitor of AP2-associated protein kinase 1 (AAK1) which is a key regulator of endocytosis. Baricitinib can prevent virus entry and decrease the risk of severe lung disease (28). Patients are suggested to continue their ongoing biological therapy unless they have confirmed COVID-19 (29).

During this pandemic, rheumatologists should establish a remote consultation system to decrease person-to-person contact with our patients. A well-managed hospitalization policy should be in effect. Patients are required to wear masks and wash hands. We also recommend that rheumatic patients maintain their current maintenance medications unless they have confirmed COVID-19 infection (Table 1). Chloroquine and hydroxychloroquine should be continued even in case of infection. The decision to withdrawal of corticosteroids and immunosuppressive agents should be made after consideration of all benefits and risks. Charles Dickens wrote in 1850, "It was the season of light, it was the season of darkness. It was the spring of hope, it was the winter of despair." The pandemic of 2019-nCoV has dealt a heavy blow to global health and economics since last winter. However, we believe that through working together and helping each other out, we shall walk through the darkness and into the light.

### Management of rheumatic patients



**Figure 1.** Workflow to manage patients with autoimmune diseases during the COVID-19 pandemic.

**Table 1.** Recommendations on drugs used in patients with autoimmune diseases during the COVID-19 pandemic.

Medication	Mild COVID-19	Severe COVID-19
Chloroquine and HCQ	Continue	Continue
Corticosteroids	Continue or decrease the dosage	Should be applied under close monitoring
Immunosuppressive agents	Continue or decrease the dosage	Withdrawal
IL-1/IL-6 inhibitor or baricitinib	Continue	Continue

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