

## **The Question of Whether to Remain on Therapy for Chronic Rheumatic Diseases in the Setting of the Covid-19 Pandemic**

Randy Q. Cron, ORCID ID: 0000-0003-2661-3086

W. Winn Chatham

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Name of department(s) and institution(s) to which the work should be attributed:

Randy Q. Cron, MD, PhD, University of Alabama at Birmingham, Department of Pediatrics, Division of Rheumatology

W. Winn Chatham, MD, University of Alabama at Birmingham, Department of Medicine, Division of Clinical Immunology and Rheumatology, Birmingham, Alabama, USA

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Dr. Cron serves as a consultant to SOBI. Dr. Chatham has served as a consultant to SOBI.

Initials, surnames, appointments, and highest academic degrees of all authors (e.g., MD, PhD):

RQ Cron, MD, PhD, Professor of Pediatrics

WW Chatham, MD, Professor of Medicine

Name, address, and e-mail of author responsible for correspondence:

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

Short running head (maximum of 4 words): DMARDs During Covid-19 Pandemic

We appreciate our Italian colleagues' interest in our editorial denoting the rheumatologist's role in helping to diagnose and treat cytokine storm syndrome (CSS) in the setting of the Covid-19 pandemic (1). It is encouraging that none of the 123 pediatric rheumatology patients (primarily juvenile idiopathic arthritis) on background biological disease modifying anti-rheumatic drug (bDMARD) therapies in Milan, Italy surveyed over a 7-week period from February 25 through April 14, 2020 (during which time Covid-19 was hyper-endemic there) had either confirmed or suspected Covid-19 (2). Moreover, 67% of this cohort were concomitantly taking conventional DMARDs (e.g. methotrexate), and 5% were on systemic corticosteroids (2). This lack of symptomatic infection with SARS-CoV-2 (viral etiology of Covid-19) in children treated with immunomodulatory and immunosuppressive treatment is in keeping with the reportedly low rate (3 out of 200) of SARS-CoV-2 infections among a cohort of liver transplant patients on immunosuppressive therapy (3).

Fortunately, even for children who contract SARS-CoV-2, the rate of serious infection, while not absent, appears to be lower in comparison to adults (4). For Covid-19+ individuals who have severe infections requiring hospitalization, there is a significant percentage of patients, under 60 years of age and without apparent pre-existing co-morbidities, suffering a CSS (5). It is unclear why some individuals develop a CSS and others do not, but there may be host genetic risk factors as have been identified in individuals with other CSS (6). Interestingly, many of the therapies that are currently under exploration in clinical trials to treat the CSS associated with Covid-19 are immunomodulatory therapies frequently used to treat a variety of rheumatic disorders (7). Thus, for patients with rheumatic diseases on bDMARD treatment, this therapy may potentially spare them a CSS in the setting of Covid-19.

The question nonetheless lingers as to whether or not pediatric as well as Covid-19 infected or exposed patients should remain on immunomodulatory or immunosuppressive therapy that is controlling their underlying rheumatic condition. It is plausible that keeping pre-existing the autoimmunity or autoinflammation in better balance may make the overall host response more effective despite the immune effects of the therapy (Figure). Some have suggested for patients to remain on their current therapies at this time, but to perhaps withhold immunosuppressant therapy in the setting of confirmed Covid-19 infection [(8), American College of Rheumatology webpost\*]. International registries have been created to collect data on rheumatic patients with Covid-19. Ultimately, time and these registries will tell what the right decision is regarding maintaining current therapy for patients with rheumatic diseases. Outcomes will likely be mixed depending on factors such as underlying disease, comorbidities, individual treatments, and combinations of therapies. Until then, basic approaches applying to everyone, including social distancing, hand washing, etc., will benefit our patients with rheumatologic conditions substantially (9).

\* - <https://imsva91-ctp.trendmicro.com:443/wis/clicktime/v1/query?url=https%3a%2f%2fwww.rheumatology.org%2fPortals%2f0%2fFiles%2fACR%2dCOVID%2d19%2dClinical%2dGuidance%2dSummary%2dPatients%2dwith%2dRheumatic%2dDiseases.pdf&umid=C4384CE2-A398-E605-B916-F5120592E1B9&auth=132a346bd7e3f9923315736765aae83d1a4b5435-5e7b73967b84227acee4e694fb952216b4a33d52>

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**Figure. Immunodeficiency and autoimmunity share a dysregulated immune response.**

The broken teeter-totter more accurately depicts the relationship among these disorders than the traditional thinking of immunodeficiency on the low side of the teeter-totter and autoimmunity up high in terms of immune strength. Immunomodulatory therapies benefit the overall strength/balance of the immune response in those with autoimmunity, and immune replacement (e.g. parenteral immunoglobulin) help to strengthen the immune response in subsets of patients with primary immunodeficiencies. CVID – common variable immunodeficiency

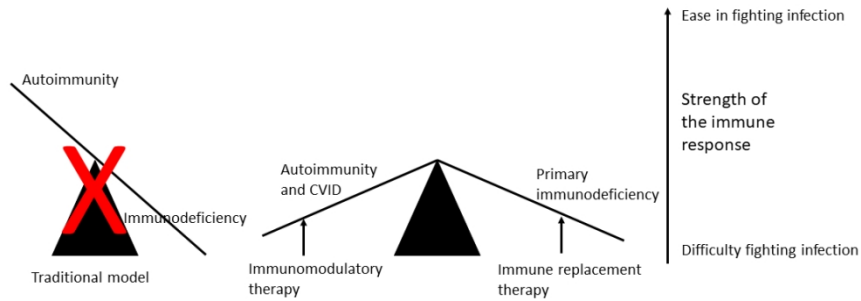


Figure. Immunodeficiency and autoimmunity share a dysregulated immune response. The broken teeter-totter more accurately depicts the relationship among these disorders than the traditional thinking of immunodeficiency on the low side of the teeter-totter and autoimmunity up high in terms of immune strength. Immunomodulatory therapies benefit the overall strength/balance of the immune response in those with autoimmunity, and immune replacement (e.g. parenteral immunoglobulin) help to strengthen the immune response in subsets of patients with primary immunodeficiencies. CVID – common variable immunodeficiency

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