

## Biologics, spondylitis and COVID-19

The COVID-19 pandemic has been especially challenging for patients with rheumatic diseases because immune-mediated diseases as well as their treatment could adversely impact susceptibility to or severity of a viral infection.<sup>1,2</sup> A recent study from New York City on 86 patients with COVID-19 infection and a history of immune-mediated disease seemed to show that the use of methotrexate, oral glucocorticoids or hydroxychloroquine increased the risk for hospitalisation,<sup>3</sup> although the authors still concluded that the overall risk for hospitalisation is comparable to that described in the community. Since data to advise patients on these issues are scant and inconclusive, the Spondylitis Association of America (SAA) is conducting a survey to gather information from patient experience.

The SAA contacted by email nearly 40 000 individuals who had previous interaction with the SAA. Between 10 April 2020

and 7 May 2020, 2992 patients completed an online survey and reported a history of spondylitis confirmed by a physician. The survey had been approved by the Institutional Review Board of the Oregon Health & Science University. The respondents included 85.0% with ankylosing spondylitis and others with additional forms of spondyloarthritis such as psoriatic spondyloarthritis. Of those patients who knew results of human leukocyte antigen (HLA) typing, 76.1% were HLA B27+. The respondents included 1104 men, 1838 women and 8 whose gender was non-binary and 42 not providing gender information. The median age was 53 for women and 54 for men. Eighty per cent were from the USA, while other respondents were from 64 other countries. Two hundred twenty-three (7.6%) of 2950 respondents believed that they had been exposed to COVID-19. Thirty-nine (1.3%) believed that they had been infected with COVID-19 of whom 14 (35.9% of those with presumed COVID-19) had confirmation by laboratory testing. As not everyone has access to testing for confirmation, we based our analysis on either confirmed or presumed infection<sup>4</sup> as is the current practice of the Oregon Health Authority.

Table 1 and figure 1 analyse patients according to class of medication taken for spondylitis with some individuals taking more than one class. The figure indicates that roughly one in four patients on a biologic (25% for antitumour necrosis factor (TNF) or 23% for anti-interleukin 17 (IL-17)) reduced their medication (either eliminated, reduced the dosage or reduced the frequency) because of concerns about COVID-19. The changes are prior to acquiring the actual infection. The table shows that several of the same medications that are feared to increase susceptibility to COVID-19 (antimetabolites, corticosteroids, anti-TNF, anti-IL-17) are actually associated with a rate of COVID-19 lower than or equal to 1.3% for the group as a whole. The reduced likelihood for developing COVID-19 for those taking anti-TNF or an antimetabolite is not statistically significant ( $p>0.05$ ). Ironically, one class of medication that was associated with risk above 1.3% is antimalarials, but too few patients took this class to provide definitive results.

Surveys are not reliable instruments to determine if the disease itself predisposes to infection since there is inherent bias as to who responds to the survey. However, we did obtain a modified Bath Ankylosing Spondylitis Disease Activity Index from

**Table 1** Impact of medications on C19

Medication class	Number taking	% with C19
Aminosalicylates	283	0.7
Antimalarials	103	3.9
Antimetabolites	366	0.5
Biologic (anti-TNF)	1442	0.8
Biologic (IL-17)	298	1.3
Corticosteroid	237	0.4
JAK inhibitor	52	1.9
NSAID	1594	1.3
No medication	230	3.5

Number taking includes those who altered the dosage or discontinued the medicine as a result of COVID-19. C19=COVID-19. Per cents are based on those with either definite or presumed COVID-19.

IL-17, interleukin 17; JAK, janus kinase; NSAID, non-steroidal anti-inflammatory drug; TNF, tumour necrosis factor.

respondents and found little correlation between spondylitic disease activity and severity of COVID-19 as graded by days of disease, probability of hospitalisation or subjective scoring of severity (data not shown).

Although our numbers of subjects infected by COVID-19 are small, the trend showing reduced infection for those on anti-TNF or antimetabolites provides reassurance to patients and providers regarding the safety of several classes of medication frequently prescribed to treat spondylitis, psoriasis and other immune-mediated diseases. Our survey is designed to capture longitudinal patient data and data from household contacts. This prospective approach should provide additional, future insight as to how spondylitis and the medications taken for this illness potentially affect susceptibility and severity of COVID-19.

James Todd Rosenbaum<sup>1</sup>,<sup>\*</sup> Hedley Hamilton,<sup>2</sup> Dongseok Choi,<sup>3</sup> Michael H Weisman,<sup>4</sup> John D Reveille,<sup>5</sup> Kevin L Winthrop<sup>6</sup>

<sup>1</sup>Casey Eye Institute, Oregon Health and Science University, Portland, Oregon, USA

<sup>2</sup>Any-3, London, UK

<sup>3</sup>Public Health, Oregon Health and Science University, Portland, Oregon, USA

<sup>4</sup>Cedars-Sinai Medical Center, Los Angeles, California, USA

<sup>5</sup>Rheumatology, University Texas, Houston, Texas, USA

<sup>6</sup>Oregon Health Sciences University, Portland, Oregon, USA

**Correspondence to** Dr James Todd Rosenbaum, Casey Eye Institute, Oregon Health and Science University, Portland, OR 97239, USA; [rosenbaj@ohsu.edu](mailto:rosenbaj@ohsu.edu)

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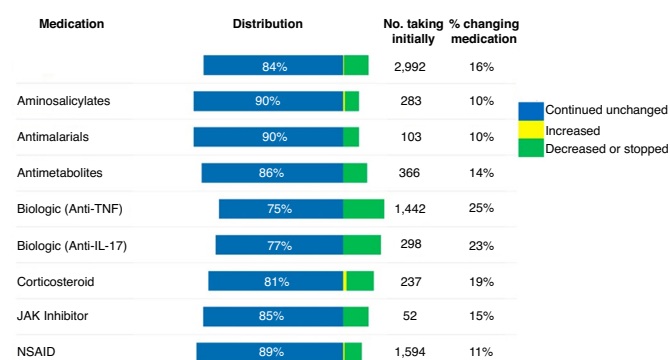
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**Patient consent for publication** Not required.

**Ethics approval** This study was approved by the IRB of the Oregon Health & Science University, Study00021375.



**Figure 1** Reduction in medication taking across all patients, 16% have changed their medication, primarily reducing or stopping entirely. This is the highest with biologics for which 25% of 1442 patients on antitumour necrosis factor (TNF) and 23% of 298 on anti-interleukin 17 (IL-17) made changes. NSAID, non-steroidal anti-inflammatory drug; aminosaliclates include sulfasalazine and mesalamine; antimetabolites include azathioprine, methotrexate and mycophenolate. Note that per cent changing medication includes those who increased the dosage, but increasing dosage was rare.

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**Data availability statement** The data on which this study are based are available by contacting Hedley Hamilton at Any-3.com.

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#### ORCID iDs

James Todd Rosenbaum <http://orcid.org/0000-0002-8452-2441>

Kevin L Winthrop <http://orcid.org/0000-0002-3892-6947>

#### REFERENCES

- 1 Curtis JR, Xie F, Yang S, *et al.* Risk for herpes zoster in Tofacitinib-Treated rheumatoid arthritis patients with and without concomitant methotrexate and glucocorticoids. *Arthritis Care Res* 2019;**71**:1249–54.
- 2 Winthrop KL, Baddley JW, Chen L, *et al.* Association between the initiation of anti-tumor necrosis factor therapy and the risk of herpes zoster. *JAMA* 2013;**309**:887–95.
- 3 Haberman R, Axelrad J, Chen A, *et al.* Covid-19 in Immune-Mediated Inflammatory Diseases - Case Series from New York. *N Engl J Med* 2020. doi:10.1056/NEJMc2009567. [Epub ahead of print: 29 Apr 2020].
- 4 Lipsitch M, Swerdlow DL, Finelli L. Defining the Epidemiology of Covid-19 - Studies Needed. *N Engl J Med* 2020;**382**:1194–6.