

---

## Commentary: The good vaccine, the bad virus, and the ugly inflammation

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has wreaked havoc worldwide. At this juncture, anti-SARS-CoV-2 vaccines have appeared to be a boon for humankind, substantially reducing the risk of severe disease and death because of SARS-CoV-2 infection. Vaccination is known to bring a cascade of events in our immune system. A host immune response to antigens and

achieving memory T-cell response over a period of time are the goals of vaccination.<sup>[1]</sup> The production of specific auto-antibodies and molecular mimicry by vaccines can thus contribute substantially to auto-immune phenomena.<sup>[1]</sup> Adjuvants that are used to increase the immunogenicity of the vaccine can further add to this reactogenicity. There are reports of flaring up of auto-immune diseases and several new-onset immune-mediated inflammatory episodes following anti-SARS-CoV-2 vaccines in a small fraction of the vaccine recipients.<sup>[2]</sup> Similarly, there has been a tremendous increase in reports of intra-ocular inflammation following

anti-SARS-CoV-2 vaccination.<sup>[3]</sup> The majority of intra-ocular inflammations ranged from mild to moderate in severity and responded to corticosteroids. Uveitis following vaccination is not new and has been reported following Bacille Calmette Guérin, varicella, hepatitis B, human papillomavirus, influenza human papillomavirus (HPV), pneumococcus, and measles-mumps-rubella (MMR) vaccines.<sup>[4]</sup> Along with vaccine- and adjuvant-induced auto-immunity, reports of the re-activation of numerous infectious agents, especially herpes viruses, have been reported.<sup>[5]</sup>

In this issue of the Indian Journal of Ophthalmology, Cam *et al.* have reported a case of granulomatous anterior uveitis in a 23-year-old lady who developed ocular symptoms 15 days after receiving the third dose of anti-SARS-CoV-2 vaccine. An extensive battery of investigations failed to find a relevant cause for her eye inflammation, which made the authors correlate uveitis with the vaccination. There are plenty of reports of new onset as well as re-activation of anterior uveitis following anti-SARS-CoV-2 vaccinations.<sup>[6]</sup> The close temporal relationship between vaccination and uveitis makes it often difficult to elucidate whether the association is coincidental or causal. For example, it is difficult to ascertain such association when the third (booster) dose of anti-SARS-CoV-2 vaccine causes an intra-ocular inflammation, whereas the first two doses of the vaccination remain uneventful.<sup>[7]</sup> Use of standardized assessment systems or tools such as Naranjo Adverse Drug Reaction Probability Scale (Naranjo Scale)<sup>[4]</sup> and/or World Health Organization-Uppsala Monitoring Centre (WHO-UMC) system for standardized case causality assessment in adverse drug reactions<sup>[8]</sup> may provide a better insight. Naranjo Scale is a widely used tool which assesses the likelihood of whether an adverse drug reaction is actually because of the drug or not. Based on the answers to 10 questions, this scale allows categorical classification of adverse drug reactions as 'definite', 'probable', 'possible', or 'doubtful'. WHO-UMC system is another similar tool for classifying adverse drug reactions into 'certain', 'probable/likely', 'possible', and 'unlikely'. In a retrospective cohort of 431 patients in a tertiary hospital from Singapore who received anti-SARS-CoV-2 vaccinations, six patients (1.39%) developed uveitis.<sup>[5]</sup> Three of these six patients presented with granulomatous anterior uveitis, and three had non-granulomatous anterior uveitis. Three patients had a previous history of uveitis, and all these patients were quiescent for more than 3 years. The authors applied Naranjo scale WHO-UMC system to grade the adverse drug reactions. Two patients with recurrence of uveitis with two separate vaccine doses (both second and third boosters) received a Naranjo score of +6, suggesting a 'probable' association with anti-SARS-CoV-2 vaccination. The remaining four patients showed a score of only +4, suggesting a 'possible' association. The authors also used the WHO-UMC system, and patients with a +6 Naranjo score could be classified as "certain". Patients with a +4 Naranjo score were classified as "likely/possible." Thus, the use of Naranjo and/or the WHO-UMC system can help to standardize the assessment and help to quantify adverse drug reactions following anti-SARS-CoV-2 vaccinations.<sup>[9]</sup>

To conclude, with the increase in reports of adverse reactions following anti-SARS-CoV-2 vaccinations, there is a need for quantification of such association through standardized tools. Nevertheless, the majority of the data favor a possible

correlation of anti-SARS-CoV-2 vaccinations with uveitis rather than a coincidental occurrence. In addition, while assessing such associations, one should keep in mind that the benefits of vaccination far outweigh such risks.

**Parthopratiim Dutta Majumder**

Medical and Vision Research Foundations, Sankara Nethralaya, Chennai, Tamil Nadu, India

**Correspondence to:** Dr. Parthopratiim Dutta Majumder, Department of Uvea, Sankara Nethralaya, 18, College Road, Nungambakkam, Chennai - 600 006, Tamil Nadu, India. E-mail: drparthopratiim@gmail.com

## References

1. Bellamkonda N, Lambe UP, Sawant S, Nandi SS, Chakraborty C, Shukla D. Immune response to SARS-CoV-2 vaccines. *Biomedicine* 2022;10:1464.
2. Safary A, Esalatmanesh K, Eftekharsadat AT, Jafari Nakjavani MR, Khabbazi A. Autoimmune inflammatory rheumatic diseases post-COVID-19 vaccination. *Int Immunopharmacol* 2022;110:109061.
3. Dutta Majumder P, Prakash VJ. Retinal venous occlusion following COVID-19 vaccination: Report of a case after third dose and review of the literature. *Indian J Ophthalmol* 2022;70:2191-4.
4. Agarwal M, Dutta Majumder P, Babu K, Konana VK, Goyal M, Touhami S, *et al.* Drug-induced uveitis: A review. *Indian J Ophthalmol* 2020;68:1799-807.
5. Chew MC, Wiryasaputra S, Wu M, Khor WB, Chan ASY. Incidence of COVID-19 vaccination-related uveitis and effects of booster dose in a tertiary uveitis referral center. *Front Med* 2022;9:925683.
6. Ng XL, Betzler BK, Testi I, Ho SL, Tien M, Ngo WK, *et al.* Ocular adverse events after COVID-19 vaccination. *Ocul Immunol Inflamm* 2021;29:1216-24.
7. Nangia P, Prakash VJ, Dutta Majumder P. Retinal venous occlusion in a child following Corbevax COVID-19 vaccination. *Indian J Ophthalmol* 2022;70:3713-5.
8. The use of the WHO-UMC system for standardised case causality assessment. Available from: <https://www.who.int/publications/m/item/WHO-causality-assessment>. [Last accessed on 2022 Dec 06].
9. Cunningham ET, Moorthy RS, Agarwal M, Smit DP, Zierhut M. Ocular complications following COVID-19 vaccination-coincidence, correlation, or causation? *Ocul Immunol Inflamm* 2022;30:1031-4.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online	
<b>Quick Response Code:</b>	<b>Website:</b> www.ijo.in
	<b>DOI:</b> 10.4103/ijo.IJO_2279_22

**Cite this article as:** Dutta Majumder P. Commentary: The good vaccine, the bad virus, and the ugly inflammation. *Indian J Ophthalmol* 2023;71:1035-6.