





# ANA Investigates: Neurological Complications of COVID-19 Vaccines

Adeline L. Goss, MD <sup>1</sup>, Rohini D. Samudralwar, MD <sup>2</sup>, Rohit R. Das, MD, MPH <sup>3</sup>, and Avindra Nath, MD <sup>4</sup>

As more patients gain access to the coronavirus disease 2019 (COVID-19) vaccines, neurologists are facing questions about potential neurological complications, benefits, and timing of vaccination. The latest *ANA Investigates* podcast took these questions to Dr. Avindra Nath, intramural Clinical Director of the National Institute of Neurological Disorders and Stroke (NINDS).

Four major vaccine mechanisms have been explored for the COVID-19 vaccines: DNA-based vaccines, mRNA-based vaccines, protein-based vaccines, and inactivated virus. DNA-based vaccines introduce the DNA coding for the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) spike protein into cells using viral vectors, inducing cells to produce spike proteins. The mRNA vaccines similarly introduce mRNA into cells, usually via a lipid nanoparticle. Protein-based vaccines are based on the Spike protein or its fragments. Finally, several vaccines are based on inactivated SARS-CoV-2 virus.

Concern about neurological complications from COVID-19 vaccines escalated in the fall of 2020, when 2 patients developed transverse myelitis after receiving the Oxford/AstraZeneca vaccine.<sup>1</sup> One case was ultimately deemed unlikely to be related to the vaccination (the patient had pre-existing multiple sclerosis), whereas the other was determined to be possibly related.<sup>2</sup> Data from the mRNA vaccine clinical trials showed that 7 cases out of 37,000 vaccine recipients developed Bell's palsy and none developed Guillain-Barré syndrome (GBS). The US Food and Drug Administration (FDA) concluded that the rate of Bell's palsy was not higher than expected in the

general population.<sup>3</sup> In the DNA-based Johnson & Johnson vaccine trial, one patient each in the vaccinated and placebo group developed GBS.<sup>4</sup> Similarly, no association between COVID-19 infection and GBS has been found.<sup>5</sup>

Any patient or healthcare provider can report side effects of vaccines through the Centers for Disease Control (CDC) Vaccine Adverse Event Reporting System (VAERS); patients, providers, and manufacturers can also report complications to the FDA Adverse Event Reporting System (FAERS). As of March 2, 2021, 51,755,447 dosages of the vaccines have been administered in the United States and 9,442 reports of adverse reactions to the vaccines have been submitted to VAERS. The most common neurological symptoms included dizziness, headache, pain, muscle spasms, myalgia, and paresthesias, which are expected to occur as acute, transient effects of the vaccination. Rare cases of tremor, diplopia, tinnitus, dysphonia, seizures, and reactivation of herpes zoster have been reported. There are also cases of stroke (17 cases), GBS (32 cases), facial palsy (190 cases), transverse myelitis (9 cases), and acute disseminated encephalomyelitis (6 cases) in the VAERS database. However, this does not suggest a causal link with the vaccination. The CDC published a more detailed analysis of this database from the first month of vaccination and did not find any safety concerns.<sup>6</sup> An important limitation of the VAERS database is that it is based on passive surveillance and is thus subject to reporting bias and may contain errors. Additionally, because of the large numbers of patients being vaccinated and the background rate of neurological conditions in a population, some cases of neurological conditions

View this article online at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/ana.26065). DOI: 10.1002/ana.26065

Received Mar 4, 2021, and in revised form Mar 9, 2021. Accepted for publication Mar 10, 2021.

Address correspondence to Adeline L. Goss, MD, Neurohospitalist Fellow, Department of Neurology, University of California San Francisco, 505 Parnassus Avenue, Box 0114, San Francisco, CA 94143. E-mail: [adeline.goss@ucsf.edu](mailto:adeline.goss@ucsf.edu)

From the <sup>1</sup>Department of Neurology, University of California San Francisco, San Francisco, CA; <sup>2</sup>Department of Neurology, University of Texas Health Science Center at Houston, Houston, TX; <sup>3</sup>Department of Neurology, UT Southwestern Medical Center, Dallas, TX; and <sup>4</sup>National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD

will occur within the post-vaccination window by chance alone. To date, there has not been a signal suggesting higher rates of neurological disease associated with the COVID-19 vaccines.

No neurological condition is an absolute contraindication to COVID-19 vaccination,<sup>7</sup> but there are special considerations around COVID-19 vaccines for patients who take immunosuppressive medications. These patients might be at increased risk for severe COVID-19, making vaccination particularly important. Yet some of these immunosuppressive medications may attenuate immune responses to vaccine antigens.<sup>7</sup> Therefore, timing of the vaccine may play an important role in balancing immune response in these patients. Recent guidelines for patients with multiple sclerosis taking certain disease-modifying therapies suggest timing the vaccine to before the start of treatment or near the end of a treatment cycle in order to maximize immune response.<sup>8,9</sup> The GBS/Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) Foundation provides the following guideline: for the rare person who develops GBS within 4 to 6 weeks of receiving an immunization, it seems prudent to avoid that vaccination in the future. For those whose GBS did not follow soon after a vaccination, there are no reliable data to indicate the risk of developing GBS after a vaccination.<sup>10</sup>

Overall, both at an individual and a population level, the benefits of COVID-19 vaccination far outweigh the risks of a neurological complication. Prospective research will be needed to establish any association between COVID-19 vaccines and neurological complications, particularly as new strains of the virus emerge and new vaccines are developed to combat them.

### Also in the Podcast Episode

- COVID-19 vaccine considerations for patients who have previously suffered a neurological condition after receiving a different vaccine.
- Recent research into homology between the SARS-CoV-2 spike protein and the human genome.
- Suggested directions for early career investigators interested in COVID-19 vaccine research.

[https://hwcdn.libsyn.com/p/c/f/0/cf0ae47ebb9ef2c9/S2\\_Ep4\\_NeuroCompCOVIDVaccine\\_Feb2021.mp3?c\\_id=95950106&cs\\_id=95950106&expiration=1616599631&hwt=dd26dd187bc7af20d73351eb28562b8e](https://hwcdn.libsyn.com/p/c/f/0/cf0ae47ebb9ef2c9/S2_Ep4_NeuroCompCOVIDVaccine_Feb2021.mp3?c_id=95950106&cs_id=95950106&expiration=1616599631&hwt=dd26dd187bc7af20d73351eb28562b8e)



## Acknowledgment

The authors would like thank Dr. Walter Koroshetz, NINDS at the National Institutes of Health (NIH) for his helpful comments.

## Author Contributions

A.G. conducted the podcast interview, edited, and produced the podcast episode, and wrote the manuscript. R.S. and R.D. drafted questions for the podcast and edited the manuscript. A.N. participated in the podcast interview and edited the manuscript.

## Potential Conflicts of Interest

The authors declared no conflict of interest.

## References

1. Allen A, Szabo L, Kaiser Health News. NIH "Very Concerned" about Serious Side Effect in Coronavirus Vaccine Trial [Internet]. Scientific American 2020. Available at: <https://www.scientificamerican.com/article/nih-very-concerned-about-serious-side-effect-in-coronavirus-vaccine-trial/>. Accessed February 27, 2021.
2. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397:99–111.
3. Ledford H. US authorization of first COVID vaccine marks new phase in safety monitoring. *Nature* 2020;588:377–378.
4. CDC. COVID-19 Vaccination Considerations for Persons with Underlying Medical Conditions [Internet]. Centers for Disease Control and Prevention 2021. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/underlying-conditions.html>. Accessed March 11, 2021.
5. Keddie S, Pakpoor J, Mousele C, et al. Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome. [date unknown];24.
6. Gee J. First Month of COVID-19 Vaccine Safety Monitoring — United States, December 14, 2020–January 13, 2021 [Internet]. *MMWR Morb Mortal Wkly Rep* 2021;70. Available at: <https://www.cdc.gov/mmwr/volumes/70/wr/mm7008e3.htm>. Accessed March 10, 2021.
7. IDSA COVID-19 Real Time Learning Network Editorial Staff. COVID-19 Real-Time Learning Network: Vaccines FAQ [Internet]. 2021. Available at: <https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information-faq/>. Accessed February 27, 2021.
8. Ciotti JR, Valtcheva MV, Cross AH. Effects of MS disease-modifying therapies on responses to vaccinations: a review. *Mult Scler Relat Disord* 2020;45:102439.
9. Timing MS Medications with COVID-19 mRNA Vaccines [Internet]. National Multiple Sclerosis Society [date unknown]. Available at: <https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/covid-19-vaccine-guidance/Timing-MS-Medications-with-COVID-19-mRNA-Vaccines>. Accessed February 27, 2021.
10. Foundation Global Medical Advisory Board statement on COVID vaccines for CIDP and MMN [Internet]. GBS/CIDP Foundation International 2021. Available at: <https://www.gbs-cidp.org/2021/01/21/foundation-global-medical-advisory-board-statement-on-covid-vaccines-for-cidp-and-mmn/>. Accessed February 27, 2021.