ANA Investigates: Neurological Complications of COVID-19 Vaccines

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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.1 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.2 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.3 In the DNA-based Johnson & Johnson vaccine trial, one patient each in the vaccinated and placebo group developed GBS.4 Similarly, no association between COVID-19 infection and GBS has been found.5

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.6 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...
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, 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. 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. 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.

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&expiration=1616599631&hwt=dd26dd187bc7af20d73351eb28562b8e

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**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.

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