COVID-19 Vaccination: The Beginning of the End, or Only the Beginning?

Roshni Sreedharan, MD, FASA, FCCM **David L. Stahl, MD** **Suzanne B. Klainer, MD** **Ronald G. Pearl, MD, PhD, FASA**

COVID-19 has wreaked havoc throughout the health care system and remains the defining zeitgeist of the past year. Anesthesiologists have been an essential resource in the response to COVID, playing pivotal roles in the care of these complex patients, managing ICUs, and staffing airway and vascular access teams. Shortfalls in almost every aspect of health care (ICU beds, ventilators, physicians, nurses, and drugs) compelled investment in innovative strategies to redefine equipment, space, and personnel. While hospitals focused on disease and resource management, patients and the public were challenged with another nemesis: fear. There was a significant decrease in emergency department visits during the pandemic, indicating that patients were not seeking care for serious symptoms (*JAMA Intern Med* 2020;180:1328-33). Patients with cancer created alternate plans with their physicians to avoid hospital admissions at the height of the pandemic (*N Engl J Med* 2020;382:2368-71). Moreover, there was a 55% decrease in percutaneous coronary interventions and a corresponding increase in late-presenting ST-elevation myocardial infarctions (*Catheter Cardiovasc Interv* 2020;96:1080-6). The COVID pandemic had and continues to have a profound impact on non-COVID patients requiring essential care in the hospital, ORs, and clinics.

With the backdrop of over 30 million cases of COVID and over half a million deaths, we now have three FDA-approved COVID vaccines that are safe and effective. Although the antibody response to these vaccines could wane after six to 12 months, we know that the T cell response may provide sustained protection (*ASA Monitor* 2020;84:3). Yes, we may need booster doses, and yes, we may need to get re-immunized every year, but these vaccines are the light at the end of this dark pandemic tunnel. Scientists project that up to 85% of the population may need to be vaccinated to achieve herd immunity, but at this time, only 30% of the United States population is completely vaccinated, and only 43% have received at least one dose (asamonitor.pub/2SBQWX0).

Vaccinations in adults are now limited by people willing to get vaccinated rather than by a shortage of vaccine. Pharmacologic treatment options remain limited, and resistance to behavioral changes (masks, distancing) remains high despite strong evidence to support these

policies (*Nat Commun* 2021;12:2188). While failed organization, policy implementation, and communication have left us in our current reality (*N Engl J Med* 2020;383:1479-80), it is fear and misunderstanding that drive vaccine hesitancy. The same fear has kept people with heart attacks and strokes from coming to the ER for the past year.

Anesthesiologists can play an essential role in addressing this fear, providing accurate information about vaccinations and building patient trust toward vaccine acceptance (*ASA Monitor* 2020;84:3). In today's world where there is rampant misinformation about COVID and its vaccines, we hope that this article will arm physicians with information to help answer questions in their conversations with patients, family members, friends, and those "undecided" if they should be immunized against COVID.

So many options – what are their risks and benefits?

The United States has approved three COVID-19 vaccines under the FDA Emergency Use Authorization (EUA) process. All three vaccines produce both humoral (polyclonal antibodies) and cellular immunity to the spike protein of SARS-CoV-2. Since binding of the spike protein of the virus to the angiotensin-converting enzyme 2 (ACE2) receptor on host cells is required for viral entry into the cells, this immunity prevents and decreases severity of COVID infections.

The Pfizer-BioNTech and Moderna vaccines were the first two vaccines to receive EUA approval. They are both mRNA vaccines. The Johnson & Johnson vaccine is a non-replicating adenovirus with the double-stranded DNA for the coronavirus spike protein added to the DNA of the viral genome. The table lists the various vaccines for COVID-19 available in the U.S., their storage, dosage, mechanisms of action, and efficacy.

Current studies demonstrate that the mRNA vaccines provide high levels of protection against COVID infection, especially severe disease, for at least six months. Longer-term efficacy will be determined with more time. Since the vaccines work by producing humoral and cellular immunity against the spike protein, the development of viral variants with mutations in the spike protein may decrease efficacy (*Science* 2021;371:1306-8), especially with variants that have multiple mutations. The possibility of reduced effectiveness over time and the potential for new variants suggest that annual vaccinations may be needed, similar to the influenza vaccine.

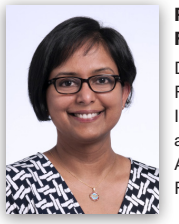
The approved vaccines have a low incidence of significant adverse effects. Both the Pfizer and Moderna vaccine use polyethylene glycol for their lipid encapsulation, and the Johnson & Johnson vaccine has polysorbate, both of which can cause allergic reactions in a small number of people (*Vaccines (Basel)* 2021;9:221). The incidence of anaphylaxis is in the range of one per 100,000, so individuals are observed for at least 15 minutes after vaccination. All three approved vaccines can produce side effects at the site of injection, including pain, redness, and swelling. Systemic reactions can include chills, fever, fatigue, headache, muscle pain, and nausea. These adverse effects are generally mild, occur within the first two days, resolve within several days, and are due to the body's immune response. The "flu-like reactions" are the systemic symptoms of immune response that successful vaccination is intended to induce, so they are a biomarker that the vaccine is working. Side effects frequently are more severe with the second dose of the two-dose vaccines. Individuals vary in how ill they feel when the immune system activates, and a lack of systemic reactions does not indicate decreased efficacy. Even though recent studies have shown that vaccine efficacy is decreased in immunosuppressed patients (*JAMA* 2021;325:1784-6), vaccination is still recommended for all adults who are not allergic to the vaccine components.

Both the Johnson & Johnson and the AstraZeneca vaccines have been associated with an exceptionally rare (approximately one in 250,000) occurrence of thrombosis accompanied by thrombocytopenia (asamonitor.pub/3uJ4u14; asamonitor.pub/2QcxKON). The syndrome clinically resembles heparin-induced thrombocytopenia. Studies have identified anti-platelet factor 4 antibodies in these patients (*N Engl J Med* April 2021). These reactions are so rare that they do not significantly change the risk-benefit ratio of the vaccine since severe morbidity and mortality from COVID-19 infection is a far greater risk. After reviewing the data, regulatory authorities have extended the emergency use authorization for Johnson & Johnson vaccine in the U.S, and the European Medicines Agency continues to recommend the AstraZeneca vaccine in the European Union.

Why I took the vaccine: The authors' perspectives

We believe in science, we believe in public health, and we know that every choice we make has risks, but both data and story tell us that the risk of COVID is in a different galaxy than the risk of this vaccine. We took the vaccine to honor our patients

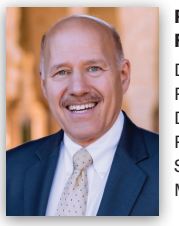
Continued on next page



Roshni Sreedharan, MD, FASA, FCCM
Director, Critical Care Anesthesiology Fellowship, Faculty, Department of Intensive Care and Resuscitation and Department of General Anesthesiology, Cleveland Clinic Foundation.

David L. Stahl, MD
Assistant Clinical Professor and Associate Residency Program Director, Department of Anesthesiology, The Ohio State University Wexner Medical Center, Columbus.

Suzanne B. Klainer, MD
Director of Simulation-Based Education, and Instructor of Anesthesiology, Brigham and Women's Hospital, Harvard Medical School, Boston.



Ronald G. Pearl, MD, PhD, FASA
Dr. Richard K. and Erika N. Richards Professor and Chair, Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University School of Medicine, Stanford, California.

COVID-19 Vaccination

Continued from previous page

who died in the ICU, those we couldn't save, and those who were "so young" and who died alone. We took the vaccine out of fear of leaving our children motherless or fatherless or dying before our parents and grandparents. We took the vaccine for hope, for all the things we used to take for granted: family holidays, school parties, high fives, and hugs. We took the vaccine out of a yearning for normalcy. We took the vaccine for our families, to be able to hug our children without fear of infecting them. We took the vaccine so that grandparents could meet their grandchildren. We took the vaccine to keep our patients safe. We took the vaccine to be part of the solution. We need to see the other side of this disease. We need to know the path forward, the way out of this pandemic. We took the vaccine because in the existential battle between herd immunity and the virus and its variants, as physicians, we choose to believe in science – so we chose the vaccine.

How do I respond when they say...

(asamonitor.pub/2SKMSUB)

… I already had COVID. Why should I get vaccinated?

It's natural to think that having the virus should leave us protected from future infection. But we know that there have been patients who were re-infected after recovering from COVID. Our immune systems can recognize previous infections for some time. It is not clear how long that lasts after the COVID-19 infection. The vaccine triggers a much stronger immune memory to protect you against COVID in the future.

… I got antibodies or plasma when I had COVID. Am I going to have a bad reaction?

There is no evidence that you will have a bad reaction. You should avoid the COVID vaccine if you are currently ill from a COVID infection, and you should wait 90 days if you received antibodies as part of treatment for COVID, but otherwise, there is no reason to delay!

… I'm worried about the vaccine risks to my baby (pregnant or breastfeeding).

There is evidence that pregnant women can not only safely receive the vaccine but that antibodies (proteins you make to fight off infections) triggered by the vaccine in new mothers can be transmitted through the placenta and in breast milk to protect your baby. Apologies for being blunt, but COVID increases the risk of a bad outcome for both mothers and their babies (*JAMA Pediatr* April 2021). The CDC has set up a website to help pregnant woman understand the risks and benefits of vaccination (asamonitor.pub/3hn0waG).

… I'm worried about getting COVID from the vaccine.

Unlike some other vaccines, there is no virus in the vaccine itself. We can say with absolute certainty that you cannot get COVID from the vaccine!

… I'm worried the vaccine will change my DNA.

No, that's not going to happen. The vaccine inserts the recipe for making the "spike protein" into a few of your cells. The recipe is written in the language of biology, using one of two alphabets: DNA or RNA. The cells read the recipe, make the viral "spike protein," and send the protein to the cell surface where it triggers an immune response. Just like all other biological recipes cooking along in the cell, the cell eventually stops reading the recipe and recycles the alphabetic characters. The recipe cannot change your DNA any more than the recipes in your cookbook can change the walls of your house.

… Give it to me straight, which is the best vaccine?

The best vaccine is the one that is in your arm, helping you make antibodies to prevent infection from COVID. All of the FDA-approved vaccines have tremendous evidence that they help keep us safe.

… Why get the vaccine if there are already new variants of the virus?

There are two reasons. First, we know that all three vaccines are effective against all variants. The efficacy is greatest against the original forms of the virus, but none of the variants has complete resistance to the vaccines. Second, each infected person is another bioreactor, creating yet another opportunity for the virus to explore new ways of becoming more infectious. The faster we are all vaccinated, the fewer chances we give the coronavirus to infect other people, mutate, and become resistant. Vaccines are a race against these variants.

… I heard the vaccine won't even last that long.

Most vaccines remain effective for a long time, although many require booster shots to remain effective. There is no reason to think that the COVID vaccine will be any different. Scientists are actively following patients who have been vaccinated. In time we will know how long they stay effective. We might need booster doses in the future. However, we know that works just fine, because regular booster shots are how we have kept influenza and other viruses at bay for decades.

… I'm going to skip the vaccine because herd immunity will protect me.

It is necessary here to explore the individual's understanding (or misunderstanding) of herd immunity and what "protection" means to them. After exploring, it may be worth sharing some of these facts:

- "Herd immunity" does not mean that the virus is gone and everyone is safe. "Herd immunity" means that individual cases don't lead to big outbreaks. SARS-CoV-2 will still be circulating at low levels. Those who get SARS-CoV-2 will still have about a 1% chance of dying, and about a 25% chance of having long-term complications. Counting on herd immunity for protection is like driving without car insurance on the assumption that everyone else's insurance will cover you in the event of a collision.
- Herd immunity requires having enough people immune to the virus so that if someone is infected, no one they come into contact with can get infected from them.
- As highly infectious variants emerge, they may start again circulating in the population despite high levels of immunity. This appears to have happened in Brazil (*Science* April 2021). Those who have not been vaccinated are far more likely to get COVID than those who have been vaccinated and are far more likely to have severe disease and bad outcomes than those who have been vaccinated.
- Even if we get to 100% immunity with adults, at this point, we do not have vaccines available for children, who make up around 20% of the population

Continued on next page

Table

Vaccine	How is it stored?	What does it contain?	What happens after injection?	What is the dose?	How effective is it?
Pfizer-BioNtech	Frozen	Lipid encapsulated single-stranded mRNA that encodes spike protein	mRNA enters cells and gets translated into the spike protein expressed on the surface of the cell. This results in an immune response to the spike protein expressed on the surface of cells.	Two doses 21 days apart (up to 42 days apart)	Prevention of COVID infection – 95% Prevention of severe illness and death – Close to 100%
Moderna	Frozen	Lipid encapsulated single-stranded mRNA that encodes spike protein	mRNA enters cells and translated into the spike protein expressed on the surface of the cell. This results in an immune response to the spike protein expressed on the surface of cells.	Two doses 28 days apart (up to 42 days apart)	Prevention of COVID infection – 95% Prevention of severe illness and death – Close to 100%
Johnson&Johnson	Refrigerated	Non-replicating adenovirus with the double-stranded DNA for the coronavirus spike protein added to the DNA of the viral genome.	Spike protein is DNA taken up by muscle cells and moves into cell's nucleus. Spike protein DNA is then transcribed into mRNA which is translated into the spike protein. This results in an immune response to the spike protein expressed on the surface of cells.	One dose	Prevention of COVID infection – 66% Prevention of severe illness and death – Close to 100%

COVID-19 Vaccination

Continued from previous page

… I want to wait and see what happens to everyone who took the vaccine before I take it.

Millions of people are receiving the vaccine every single day without complications, and worldwide we have surpassed 1 billion doses. We already have so much data and experience showing that it is incredibly safe to get vaccinated. While you are waiting to see what happens with vaccination, you are increasing the likelihood of getting COVID-19. We don't have to wait and see what the risks of COVID infection are: you have a 1% chance of dying and a 25% chance of long-term complications.

… Everyone around me is vaccinated, so I really can't get COVID. Maybe I can wait to get the vaccine?

Even with everyone around you vaccinated, it would only take exposure to one sick person for you to get sick. We know COVID is an incredibly contagious virus, and vaccination is truly the only way to prevent infection. Let me tell you about a patient I had with COVID and how scary it was….

… I heard a vaccine was pulled from the market. How can I be sure that these vaccines are safe?

I view the FDA's response to the rare thrombotic events associated with the Johnson & Johnson vaccine to be reassuring. The FDA was and continues to be extremely thorough in evaluating the risks and benefits associated with the vaccines. After careful evaluation, the FDA again approved the vaccine. The benefits of all three vaccines greatly outweigh the risks.

Should I get the vaccine if I am scheduled for surgery?

With all adult Americans being eligible for the COVID vaccine now, preoperative vaccination protocols for elective surgical patients are an important consideration. Most hospital systems have now caught up with the surgical backlog, despite over 70% of the elective procedures being cancelled with the first wave of COVID (*Br J Surg* 2020;107:1440-9). Although complicated, integration of preoperative vaccination into perioperative pathways can play an important role in reduction in postoperative mortality, pulmonary complications, and health care costs, especially for patients over 70 years of age (*Br J Surg* March 2021).

As anesthesiologists, we are perioperative physicians and, more importantly, patient advocates helping patients and their families navigate the complex perioperative period. It is our responsibility to counsel and provide information to help our patients make sound health care decisions for themselves and everyone around them. Choosing to take an effective vaccine for a deadly illness during a pandemic is one such decision. ■