

COVID ROOC
More Information Bank
BLOGS

Note: Not all sources are peer-reviewed whereas some are reviews and interesting blogs. They are not intended in themselves to guide patient management decisions.

The potential problem(s) with a once-a-year COVID vaccine

Marcia Frellick
September, 2022

Comments from the White House this week suggesting a once-a-year COVID-19 shot for most Americans, “just like your annual flu shot,” were met with backlash from many who say COVID and influenza come from different viruses and need different schedules.

Read on at: <https://www.mdedge.com/chestphysician/article/257741/covid-19-updates/potential-problems-once-year-covid-vaccine>

Where Are We with COVID-19 Testing and Diagnostic Methods?

Warren A. Katz, MD
May 2022

Testing for the SARS-Cov-2 virus continues to be essential for the early diagnosis and appropriate treatment of COVID-19. The scope of testing has reached more than six billion people globally. Earlier this year National Geographic magazine revealed that "biochemist Kary Mullis says he was driving from the Bay Area to his cabin in Mendocino in 1983 when suddenly, like a bolt of lightning out of the California sky, he came up with a way to pinpoint a particular stretch of DNA and synthesize an enormous amount of copies." From a technical viewpoint, the reverse transcription-polymerase chain reaction (RT-PCR) test uses RNA as starting material for *in vitro* nucleic acid amplification of the viral antigen. PCR testing is now the benchmark for detecting COVID-19. Because of its advanced technology, the analysis is often not readily available and is expensive. It is associated with relatively few false negatives. Thus, there is still a clear need for reliable, readily available, less expensive, rapid testing for home or point-of-care methods.

Although existing COVID-19 antigen analyses are still limited in some global geographic regions, many other tools will be forthcoming out of research laboratories. The new processes include *quantitative* polymerase chain reaction (qPCR), loop-mediated isothermal amplification (RT-LAMP), recombinase polymerase amplification (RT-RPA), recombinase-aided amplification (RT-RAA), mass spectrometry, and chronoamperometry-based redox cycling assays. Even the popular CRISPR (clustered regularly interspaced short palindromic repeats) technology has been successfully used to develop rapid diagnostic tests for COVID-19 – gaining its first U.S. FDA approval. Artificial intelligence will become more critical when employing these newer methods, hopefully providing greater accuracy in the future.

Although testing gave us a roadmap earlier during the COVID-19 pandemic, the disease still threatens us and has changed the world for the intermediate future. The public is still searching for a more straightforward, widely accepted path back to their former lives. Some federal agencies, TV pundits, and politicians continue to muddy the waters with conflicting information rather than adding clarity. Who would ever think that a modern day plague, including diagnosing it even before the first symptoms, would be do politicized?

The U.S. public health system and those worldwide represent authorities trained to prevent and manage catastrophic infections. According to estimates, over 2,500 local and state public health departments across the U.S. and thousands elsewhere have been involved in the fight against COVID-19. They consist of physicians, nurse, virologists, epidemiologists, public health scholars, and statisticians, who suggest policies to counteract the spread of the coronavirus, in part by aggressive testing. Given the danger and extent of the contagion, one would think that their expert suggestions would be unquestioned. Unfortunately, a new study led by researchers at the Johns Hopkins Bloomberg School of Public Health identified 1,499 unique reports of harassment and denigration of U.S. health departments during the first 11 months of the pandemic, beginning in March 2020. One wonders if many of the one million COVID-related deaths in U.S. could have been averted in the absence of badgering. The authors suggest that training public health officials on how to respond to political and societal conflict and other initiatives are key to reducing acts of harassment

Undoubtedly, these organizations will continue to recognize that it is crucial to rapidly test as many people as possible to return them to pre-pandemic life. Unfortunately, we live in an environment of centuries-old scientific skepticism that undermines the overarching need for widespread testing. Political distrust of key initiatives causes some party leaders to subvert the scientific method, opting instead for populist, ultraconservative, and even religiously inspired false concepts. Also, the anti-vaccination movement and a corollary anti-testing mentality have circulated broadly through social media. Earlier this year, even the U.S. Supreme Court signaled skepticism of the Biden administration's authority to require the workforce of large companies to be vaccinated against COVID-19 or submit to weekly testing.

These attempts to undermine informed expert medical advice disrupt recommended testing goals. As a result, carriers of the virus, overtly sick or not, interact with healthy and immunocompromised people, thus spreading the disease instead of being temporarily quarantined. Still, the hope is that future research in detecting COVID-19 markers will focus on developing widespread portable, harmless, readily available, rapid, and accurate methods that patients can use at home or safe points of care.

Such an assessment would seem to be a prerequisite for minor and significant "normal" economic and social activities such as dining in restaurants, traveling, on-site working, and attending sporting events, large meetings, or private venues. Also, rapid antigen tests have been successful in screening for COVID-19 in congregate settings such as nursing homes, dormitories, homeless shelters, and prisons.

Evidence-based statistics about the prophylactic benefit of pre-event testing remain limited, and the efficacy of this approach is uncertain, particularly with the Omicron variant. As most of us already know, there have been many reports of outbreaks associated with occasions where attendants had negative antigen tests on the same day or day before an outing. An example is the recent White House Correspondents Association Dinner in Washington, DC. There was a requirement for testing negative and proof of vaccination. However, no information has circulated yet about how the tests were performed, the degree of immunization, nor the documentation of the prerequisites. After the dinner, several attendees self-reported developing COVID-19, but apparently the organization did not keep any formal records. Pre-event plans for strict supervision of appropriate vaccination and testing seem to make sense; however, we need more comprehensive data to pursue it as a universal recommendation.

Understanding Risk of COVID-19 in Social and other Interactive Situations

Warren A Katz, MD

October 10, 2021

Few people understand the risk of disease in adults; for them, it's either risky or not – a decision often based on emotions and general misperceptions. Almost every experience is associated with some risk, whether apparent or not. In the case of COVID-19, only when you are hunkered down at home alone, not accepting visitors for ~14 days is your "absolute" risk as low as possible.

However, most of us, fully vaccinated or not, continue to be eager to get out and about. The cautious population will want to know about its chances of getting COVID-19 under various circumstances, such as attending a sizable indoor event compared to just staying home. Some of us routinely weigh the risk of being exposed to the coronavirus by participating in a desired activity (i.e., a wedding) against the probability of infection in a control or reference group (i.e., being home-bound). How much risk people might want to take varies from being ultra-safe based upon science to being reckless based upon cult-like unfounded notions. The absolute risk depends upon the incidence (new cases) or prevalence (existing patients) of COVID-19 in geographic locations. It may also be contingent on the number of vaccinated vs unvaccinated people at an event or venue, masking policies, social distancing, total space, airflow, and, importantly, the amount of virus to which a person is exposed, which reflects the likely number sick people in the area. This conscious calculation may seem impossible; however, if you enter a supermarket that does not have a masking or vaccination policy for its employees or customers, consider the risk that someone in the store has COVID-19 is heightened.

Additional tips on how to evaluate and utilize risk during the COVID-19 pandemic

For the unvaccinated. Unvaccinated people are at a high risk of developing COVID-19 and its complications. They are more likely to spread the disease than the vaccinated! In that COVID-19 continues to be frequent in our communities, the unvaccinated should wear masks (tightly covering the nose and mouth) whenever exposed to anyone outside and when others enter their home. If they are in close contact with people, it would be-considerate to make their unvaccinated status known to ensure proper masking and social distancing for everyone. Otherwise, you must assume that anyone with whom you come in contact is infected with COVID.

For the vaccinated. The original Moderna and Pfizer studies showed that their vaccines protected 90%+ of participants against infections, hospitalizations, intensive care unit admissions, and deaths. In a more

recent study, data from New York State showed that from May 3 to July 25 2021, the overall vaccine efficacy against new COVID-19 cases for all adults declined from 91.7% to 79.8% (Yale Medicine – September 8 2021). As most of us recognize by now, this drop in protection allows for increasing the risk of so-called "breakthrough" COVID-19 infections. The U.S. Centers for Disease Control and Prevention (CDC) indicates though, "The number of COVID-19 vaccine breakthrough infections reported to CDC are an *undercounting* of all SARS-CoV-2 infections among fully vaccinated persons, especially of asymptomatic or mild infections." Vaccinated people with breakthrough infections may spread COVID-19 to others. That is why the World Health Organization (WHO) and the CDC, both sharing the concern about the spread of the coronavirus, sanction the resumption of pre-pandemic activities, yet urge the following to reduce the risk of being infected with the Delta variant and possibly spreading it to others:

- wear a mask indoors in public if you are in an area of substantial or high transmission, [including in vehicles and other forms of transportation]

- wear a mask regardless of the level of transmission if you have a weakened immune system or if, because of your age or an underlying medical condition, you are at increased risk for severe disease

Risk-takers beware! Many supermarkets, restaurants, and other businesses make no demands on their customers nor employees to be vaccinated or even wear masks. Nor do many sporting, entertainment, and social venues! Some individuals with breakthrough COVID-19 infections, despite vaccination, feel miserable, even though treated but not hospitalized. It's more than just a cold! Furthermore, a recent study finds that both vaccinated and unvaccinated sufferers may develop long-hauler syndrome for weeks to months or even longer. Symptoms may include "brain fog," fatigue, persistent loss of smell or taste, hair loss, and extremity numbness.

Deaths are rare among the more than half of Americans, now fully vaccinated. *Concerns are highest in the immunocompromised and the advanced-aged populations when immunity to the virus seems to be dropping. Also, seniors aged ≥65 years account for 87% of deaths from COVID-19 in the vaccinated cohort.* Thus, despite vaccination, this susceptible group needs to pause to assess every out-of-the-ordinary activity. For example, they may have to pass on dining with friends at a crowded restaurant, even outdoors.

Guarding against the Delta strain. A recent study from the Chinese Academy of Medical Sciences has found that viral loads in Delta infections are approximately 1,000 times higher than those caused by previous SARS-CoV-2 variants, the viruses that cause COVID-19 disease. The CDC released new data showing that vaccinated people infected with the Delta variant can carry detectable viral loads (the amount of virus in the upper respiratory tract and elsewhere).

There is also some question about how viable the Delta virus retrieved from vaccinated people is; those who continue to show a high viral load tend to have more severe breakthrough symptoms. A 2008 CDC study revealed that 78% of adults over age 55 years have a least one comorbidity that includes diabetes, chronic obstructive pulmonary disease, asthma, cardiovascular disease, cancer, or arthritis. I advise extra precautions in this group because of the perniciousness of the Delta strain.

Masking in- and outdoors. On September 9, 2021, the CDC recommended that even vaccinated people resume wearing masks in schools and in public indoor spaces in parts of the country where the virus is surging. The incidence of cases continues to be high worldwide during the past month in many countries, most notably the U.S., Brazil, and India. They are working to "flatten the curve" of the coronavirus, which involves reducing the number of new COVID-19 cases from one day to the next. Geographic mask-wearing recommendations and mandates differ.

The CDC recommends that "In areas with high numbers of COVID-19 cases, consider wearing masks in crowded outdoor settings and for activities with close contact with others who are not fully vaccinated,"

Social activities with vaccinated and unvaccinated attendees. The CDC does not offer concrete advice about the intermingling of vaccinated and unvaccinated attendees at social events but infers it. "*Unmasked, unvaccinated people pose a significant risk to others who are unvaccinated. They are an omnipresent risk to vaccinated guests, particularly those with comorbid medical conditions!*" Because we cannot know who is vaccinated and who is not in public settings, we must assume that there's risk of exposure to COVID-19 infected unvaccinated people. The CDC and WHO recommend that all populations wear a mask indoors in public to maximize protection from the Delta variant and to prevent possible spread to others even if you are fully vaccinated. As noted, this advice is most important in an area of substantial or high transmission. The recommendation would be more enforceable if it were a mandate! Some organizations and individuals are already planning Christmas and New Year's Eve parties. Of course, we cannot predict the infection rate by December 2021, but complete compliance with masking is impossible in an indoor restaurant or banquet hall. Now would be an excellent time to become vaccinated if you have not already!

The risk in a crowd when everyone is vaccinated. Yet, even if you have had your shots, the jeopardy still exists in a crowd because we cannot know where everyone has been and their degree of exposure. The risk increases at indoor celebrations, such as on a dance floor, when voices are loud, when singing is loud, and when many attendees drink alcoholic beverages, bringing face-to-face contact closer. For that reason, some cities, such as San Francisco, have taken the high road by requiring that all restaurants, bars, clubs, gyms, and prominent event directors obtain proof of vaccination from patrons and employees to prevent the continued spread of COVID-19.

Additional COVID-19 Vaccinations. We do not yet have guidance about future annual immunizations, like that of the flu. Presently, the CDC has not defined a clear difference between the third COVID-19 vaccine and the "booster shot" except by their indications. It recommends the former for cancer patients and others who have or are at risk for weakened immune systems, especially considering the more contagious Delta variant that is now the most prevalent form.

Booster shots refer to an *additional* COVID-19 vaccination in everyone else, especially others at higher risk; their use remains controversial. Nonetheless, the FDA Advisory Panel recently recommended a booster dose for the following categories:

- People 65 years and older
- Others at significant risk, ostensibly front-line healthcare providers, those with diabetes, and the like.

Notwithstanding this new recommendation, many have already received the booster shot as already advised universally in Great Britain and Israel. Besides building antibodies, boosters may prevent uncomplicated infections, but they are not 100% effective. The risk of transmission in the booster-immunized is not clear. There is no formal CDC guidance yet about the long-term effectiveness of the booster. We know that side effects are usually about the same as after the second vaccination, but gathering more scientific data will address these uncertainties and pave the way for booster shots for everyone who wants them.

What about the Timing of Flu shots in Conjunction with Vaccination This Season?

One of the common excuses offered by Americans for refusing COVID-19 vaccination is that they are awaiting a flu shot first. The CDC has clarified that both the flu and COVID-19 vaccines can be administered *simultaneously*, as with previous other types of vaccinations. Ideally, everyone should become immunized by the end of October. Having both shots should decrease the risks of two potentially serious diseases.

References

CDC. Frequently Asked Influenza (Flu) Questions: 2021-2022 Season. 9/22/21
<https://www.cdc.gov/flu/season/faq-flu-season-2021-2022.htm>

WHO Urges Masking for the Vaccinated, in Split with CDC. 8/11/21
<https://www.nytimes.com/live/2021/06/28/world/covid-vaccine-coronavirus-mask#worried-by-the-delta-variant-who-officials-urged-vaccinated-people-to-keep-wearing-masks>

CDC. COVID-19 Vaccine Breakthrough Case Investigation and Reporting. 9/17/21 <https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html>

CDC. Participate in Outdoor and Indoor Activities. 8/19/21 <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/outdoor-activities.html>

Li B, Deng K, Li K, *et al.* Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 Delta variant. Preprint at medRxiv.7/11/2021.
<https://doi.org/10.1101/2021.07.07.21260122>

CDC. The Possibility of COVID-19 after Vaccination: Breakthrough Infections. 9/7/21. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/why-measure-effectiveness/breakthrough-cases.html>

"A Guide for Covid-19 Risk in Your County." Updated 9/10/21.
<https://www.nytimes.com/interactive/2021/us/covid-risk-map.html>

CDC. Who Is Eligible for a COVID-19 Vaccine Booster Shot? 9/27/21 <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.htm>

COVID-19: "It ain't over till it's over."

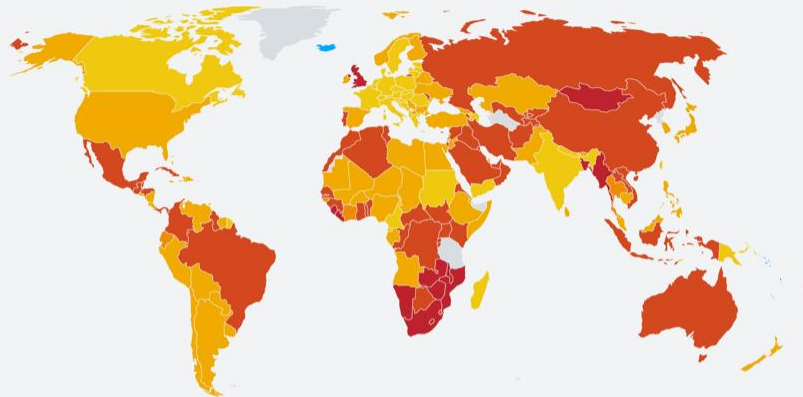
Warren A. Katz, MD

July 3, 2021

We first started developing this curriculum to answer several questions for our target audiences beginning in the Spring of 2020. Was there any relationship between COVID-19 and inflammatory autoimmune diseases, particularly those managed by rheumatologists or dermatologists? Were patients with any of these diseases at greater risk for developing COVID-19? If not, did they have a more severe illness once the coronavirus infected them? Do some immunomodulatory agents increase the risk? If so, why are some such drugs used to treat severe cases of COVID-19?

The COVID ROOC program has attempted to respond to most of these queries. But additional questions are still unanswered. Frankly, one can ask why we continue to promote our curriculum because the prevalence of COVID-19 has dropped significantly since the vaccines have been widely available to the public, at least in the U.S., as of January 2021. The answer is inspired by DW News, a global English-language news and information program from the German public international broadcaster, Deutsche Welle.

Week 25: New COVID-19 cases by country



Countries and territories with

- twice as many new cases**
- more new cases**
- approx. **the same** number of new cases
- fewer new cases**
- less than half** as many new cases
- zero** new cases four weeks in a row
- no data



Source: ECDC, JHU data | DW analysis: comparison of newly reported case numbers in the past 14 days compared to the 14 days before that | For details on methodology see github.com/dw-data/covid19-trend

An article appeared a few days ago indicating that of 188 countries analyzed for the status of the virus, the situation has deteriorated slightly – 71 countries reported more cases in the past two weeks compared with the previous 14 days. Nineteen of them, including Bangladesh, Israel, Mongolia, South Africa, and the United Kingdom, have doubled their cases.

Dr. Anthony Fauci has become the internationally trusted name in COVID-19 messaging. When recently asked when he would return to his immunology research for which he is famous, he replied that it would not be till we squash the pandemic. He indicated earlier last month that he is closely watching "Delta," a new variant first identified in India. A primary concern of his is the millions who are not yet fully vaccinated. Many of them are devout anti-vaxxers, who have yet to come up with a science-driven reason for their avoidance of the vaccine, an intervention that would benefit the world as well as themselves. However, a May 28, 2021, Kaiser Family Foundation post reflected that most vaccine-hesitant people deny they are anti-science or even anti-vaccine. The conspiracy theories of many are nonsense. Approximately 12-15 percent of the population are in a "wait and see" mode because they have concerns about the apparent rapidity in which the vaccines were rushed through, fearing the development was politically motivated. I have tried to make my case in previous writings that coronavirus vaccine studies in reality have been years in the making, and unique modern science has pushed commercialization over the goal line. Hopefully, the forthcoming conversion of FDA "emergency" authorization to a permanent one will be more convincing.

Thanks to the Delta variant, it is time to reconsider if we are as safe as many of the COVID-19 pundits think we are. The current level of vaccine immunity is insufficient to end the pandemic. Since it began, the Delta variant is now responsible for more than one-quarter of COVID cases in the U.S. It has evolved to become far more contagious and deadly than the original virus strain, known as the "wild type." We cannot be complacent because the goal posts move when the virus moves. As a result, all of us who are immunized may soon need a booster.

Here at the Perelman School of Medicine, among others, there is trepidation that a meaningful subset of patients with COVID-19 could be at risk for progression to symptomatic autoimmune syndromes in the future. A recent Penn Medicine email post stated, "As the present pandemic evolved, clinicians and researchers sensed an equation between the sequelae of SARS-CoV-2 infection in COVID survivors—including fatigue, arthralgia, myalgia, and thrombosis—and those of autoimmune disease." Other clinical features of post-COVID patients commonly found in autoimmune diseases include fatigue, sicca syndrome, and rashes. Less common manifestations of autoimmunity have been myocarditis, arthritis, encephalitis, and vasculitis. As noted elsewhere in this curriculum, we now refer to persistent post-COVID-19 symptoms as "long haulers" or "long COVID." In conjunction with the increasing proportion of seemingly recovered patients, these clinical observations suggest that inflammation in response to SARS-CoV-2 infection promotes tissue damage in all phases of the disease.

As we know, *autoantibodies* are a laboratory hallmark of the self-directed aberration of the normal immune response to pathogens that result in cell destruction. Having discovered autoantibodies in patients with COVID-19, E. John Wherry, Ph.D. and Luning-Prak M.D., Ph.D., researchers in the Penn laboratory, and other worldwide researchers searched for candidate target *autoantigens* that could be employed to diagnostic and therapeutic ends. The bottom line is that SARS-CoV-2 causes new-onset IgG autoantibodies in a significant proportion of hospitalized COVID-19 patients and positively correlates with subsequent immune responses to SARS-CoV-2 proteins.

Investigators at the Perelman School of Medicine in Philadelphia, Stanford University School of Medicine in Palo Alto, and the Philipps Universität Marburg in Marburg, Germany, conducted a multi-center study that employed protein assays in 147 COVID-19 patients. They measured hallmark IgG autoantibodies associated with connective tissue diseases, as well as anti-cytokine antibodies and antiviral antibody responses. They found autoantibodies in about half of the hospitalized COVID-19 patients but fewer than 15% of healthy controls. When present, these autoantibodies targeted respective autoantigens associated with uncommon immune disorders such as myositis and systemic sclerosis. A subset of autoantibodies and anti-cytokine antibodies developed in some subjects *de novo* after SARS-CoV-2 infection, placing them at risk for progression to autoimmunity in the future.

Another multinational group of investigators, including one of our faculty, Sokratis Apostolidis, MD, is performing similar research. They concluded that "While the COVID-19 pandemic is leaving a wake of destruction as it progresses, it also provides an unprecedented opportunity to understand how exposure to a new virus could potentially break tolerance to self, potentially giving rise to autoimmunity and other chronic, immune-mediated diseases."

Although most Americans are now at least partially immunized, the rest of the world is not. The danger of illness, hospitalization, and death still looms among the unvaccinated, whereas the vaccinated minimally so. Epidemiological and other scientific investigations must continue. Why? There are vulnerable populations with inherited or acquired immunodeficiencies that cannot mount satisfactory responses to COVID vaccines. It is believed these populations will remain at-risk as long as SARS-CoV-2 circulates in the community. Scientists are exploring whether subgroups of patients with low post-vaccine antibodies still are protected and why. Furthermore, it is likely that SARS-CoV-2 will become an endemic coronavirus and will need to be studied for years to come, just as the influenza virus is.

This insight means that COVID-19 cases will continue to exist, especially in countries with less robust vaccination infrastructure. Take note! A coronavirus epi(pan-)demic is likely to happen again. Of particular importance to rheumatologists and dermatologists is that long-COVID patients, even those with mild clinical manifestations, are likely to exhibit rheumatic and cutaneous manifestations more than any other discipline.

COVID-19 scientists have come a long way in a relatively short time to stem the complication and death rate, mainly because of miracle vaccines. I fear that we still have a way to go. In the words of American baseball and verbal quip legend Yogi Berra, "It ain't over till it's over!"

Sources:

<https://www.mcclatchydc.com/news/politics-government/white-house/article252214508.html>

<https://www.dw.com/en/coronavirus-global-pandemic-trend/a-53954594>

<https://www.penmedicine.org/updates/blogs/penn-physician-blog/2021/february/covid-autoimmunity-article>

<https://www.medrxiv.org/content/10.1101/2021.01.27.21250559v1#p-5>

<https://nymag.com/intelligencer/2021/05/republicans-more-eager-for-vaccine-kaiser-family-foundation.html>

<https://www.news-medical.net/news/20210201/SARS-CoV-2-triggers-development-of-new-onset-IgG-autoantibodies-in-hospitalized-COVID-19-patients.aspx>

<https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-may-2021/>

Thanks to Dr. Sokratis Apostolidis who critically revised this blog and provided critical additions.