TGIF!

Today I have chosen a diverse group of articles starting out with the Pew report on COVID and overuse of antibiotics. The next article looks at antibody resistance to some mutants. The next article tries to answer if infection with the B.1.1.7 (UK) variant is more lethal. The last article looks at antibody response to mRNA vaccines in persons vaccinated who have had prior COVID-19 infection.

I hope everyone has a wonderful weekend.

Ed

Could Efforts to Fight the Coronavirus Lead to Overuse of Antibiotics?
Pew Charitable Trust Report March 2021
Using IBM Watson Health's electronic health records database, investigators analyzed data on 5,898 unique US hospital admissions from February through July 2020, representing 4,980 patients. Nearly half of the admissions involved patients aged 56 and older, 52% were women, and most admissions involved patients in the Midwest (84%) and the South (14%). Fifty-nine percent of the hospitalizations lasted 1 to 3 days. Around 58% of the admissions occurred in June (18%) and July (40%).

Within the study population, 52% of admissions resulted in at least one antibiotic being prescribed, with 82% of those patients receiving antibiotics at admission and 96% within the first 48 hours of hospitalization. Thirty-six percent of admissions resulted in more than one antibiotic prescription. Only 7% of COVID-19 admissions were found to have positive bacterial culture results from blood, urine, and respiratory samples. More than half of the COVID-19 admissions received an empiric antibiotic. On a positive note, the analysis also found that far fewer patients—15% of the admissions—received additional antibiotics after 48 hours, which suggests that once clinicians did have test results there was some degree of de-escalation of antibiotic prescribing.

Comment: The findings of the study, which is the largest study to date on antibiotic use in US COVID-19 patients, add to the growing body of research on antibiotic prescribing during the pandemic. Studies to date have estimated that anywhere from 55% to 98% of hospitalized COVID patients around the world were treated with antibiotics, while <5% had a bacterial co-infection that would require their use. This has led to widespread concern about unnecessary antibiotic use during the pandemic. This is similar to other studies reviewed in the last several months in the Daily Briefing. The findings are an important reminder about why antibiotic stewardship programs are necessary.

Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7
Nature published online March 8, 2021
doi.org/10.1038/s41586-021-03398-2
For the study, the researchers examined all mutations in the spike protein of the 2 variants. The researchers created SARS-CoV-2 pseudoviruses with the 8 mutations found in the UK variant and the 9 mutations found in the South African variant. They then measured the sensitivity of these pseudoviruses to monoclonal antibodies developed to treat patients with coronavirus disease 2019 (COVID-19), convalescent serum from patients who were infected earlier in the pandemic, and serum from patients who have been vaccinated with the Moderna or Pfizer vaccine.

The study measured the neutralizing activity of 18 different monoclonal antibodies, including the antibodies in 2 products authorized for use in the United States by the FDA. Against the UK variant, most

antibodies were still potent, although the neutralizing activity of 2 antibodies in development was modestly impaired. For the South Africa variant, the neutralizing activity of 4 antibodies was completely or markedly abolished. Those antibodies included bamlanivimab (LY-CoV555) and casirivimab, which is 1 of the 2 antibodies in an approved antibody cocktail (REGN-COV). The second antibody in the cocktail, imdevimab, retained its neutralizing ability, as did the complete cocktail. Convalescent plasma from most patients who had recovered from COVID-19 earlier in the pandemic had 11-fold less neutralizing activity against the South Africa variant and 4-fold less neutralizing activity against the UK variant.

Investigators found that antibodies in blood samples taken from people inoculated with the Moderna or Pfizer vaccine were less effective at neutralizing variants B.1.1.7 and B.1.351. Against the UK variant (B.1.1.7), neutralization dropped by roughly 2-fold, but against the South Africa variant (B.1.351), neutralization dropped by 6.5- to 8.5-fold. Novavax vaccine reported on January 28, 2021, that the vaccine was nearly 90% effective in the UK part of the trial, but only 49.4% effective in the South Africa part of the trial, where most cases of COVID-19 are caused by the B.1.351 variant.

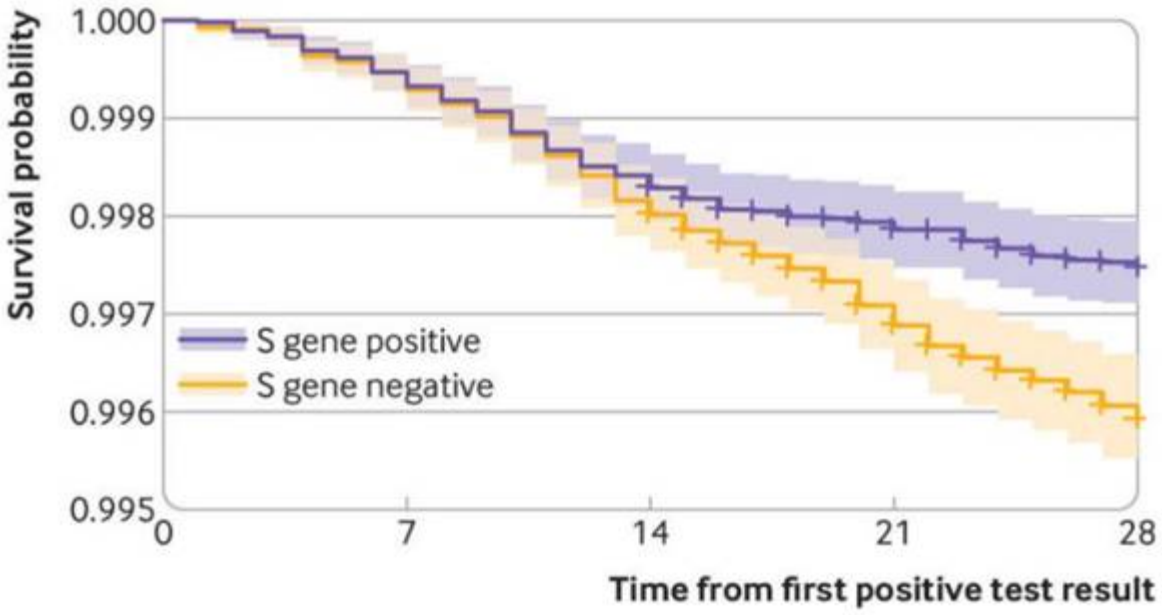
Comment: Both SARS-CoV-2 variants B.1.1.7 and B.1.351 are raising concerns not only because of their increased transmissibility but also because of their extensive mutations in spike that could lead to antigenic changes detrimental to mAb therapies and vaccine protection. This virus is changing in a direction that could ultimately lead to escape from our current therapeutic and prophylactic interventions (mAB, vaccines) directed to the viral spike. If increased spread of some virus variants continues and more critical mutations accumulate, then we may have to chase after the evolving SARS-CoV-2 continually, as we have long done for influenza virus. Such considerations require that we stop virus transmission as quickly as is feasible, by redoubling our mitigation measures and by expediting vaccine rollout. Vaccine manufacturers are already looking at the next generation of vaccines.

Risk of Mortality in Patients Infected with SARS-CoV-2 Variant of Concern 202012/1: Matched Cohort Study

BMJ published online March 10, 2021
doi.org/10.1136/bmj.n579

The investigators sought to establish whether there is any change in mortality from infection with a new variant of SARS-CoV-2, (B.1.1.7) compared with prior strains. The mortality hazard ratio associated with infection with B.1.1.7 compared with infection with previously circulating variants was 1.64 (95% confidence interval 1.32 to 2.04) in patients who tested positive for covid-19 in the community. In this comparatively low risk group, this represents an increase in deaths from 2.5 to 4.1 per 1000 detected cases.

Cycle threshold values were lower in participants who were S gene negative (variant) than in those who were S gene positive. Low values for the N gene cycle threshold implied that the viral load in participants at the time of sampling was higher with the variant. The higher mortality could be associated with the higher viral load in S gene negative participants because of the intrinsic properties of the B.1.1.7 mutation. This may also explain a higher Ro associated with the variant.

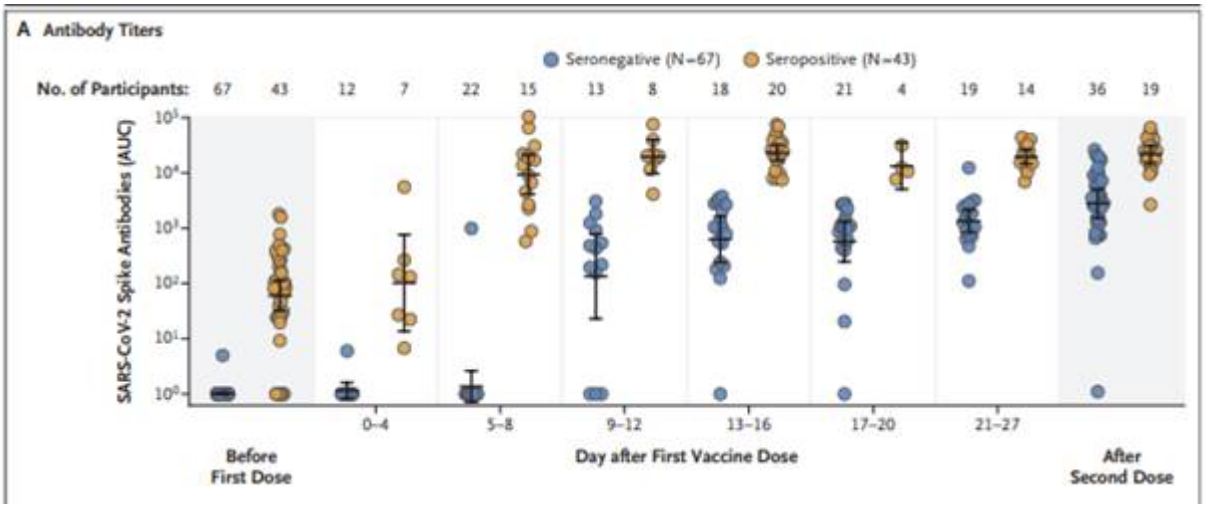


S gene negative =new variant

Comment: Healthcare capacity planning and national and international control policies are all impacted by this finding. The good news is that current vaccines are still high efficacious against the B.1.1.7(UK) variant.

Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine
N Engl J Med published March 10, 2021
DOI: 10.1056/NEJMc2101667
Investigators sampled an ongoing study of 110 participants in the longitudinal Protection Associated with Rapid Immunity to SARS-CoV-2 (PARIS) study. All received one dose of the Pfizer or Moderna vaccine in 2020. 39.0% were seropositive for COVID-19 antibodies prior to vaccination. Eighty-eight participants received the Pfizer vaccine, and 22 had the Moderna vaccine. Mean patient age was 40 years.

The antibody titers of vaccinees with preexisting immunity were 10 to 45 times as high as those of vaccinees without preexisting immunity at the same time points after the first vaccine dose (e.g., 25 times as high at 13 to 16 days) and exceeded the median antibody titers measured in participants without preexisting immunity after the second vaccine dose by more than a factor of 6. Although the antibody titers of the vaccinees without preexisting immunity increased by a factor of 3 after the second vaccine dose, no increase in antibody titers was observed in the Covid-19 survivors who received the second vaccine dose. No substantial difference was noted in the dynamics of antibody responses elicited by the Pfizer and Moderna vaccines after the first dose. The most common side effects were pain, swelling, and redness at the injection site, and the most-reported systemic adverse effects were fatigue, headache, chills, muscle pain, fever, and joint pain.



Comment: The investigators found that a single dose of mRNA vaccine elicited rapid immune responses in seropositive participants, with postvaccination antibody titers that were like or exceeded titers found in seronegative participants who received two vaccinations. COVID-19 survivors may not need a second dose of mRNA-based vaccine to prevent subsequent symptomatic infections.