TGIF to all

Today I have chosen 6 articles of interest.
The first 2 highlight the challenges of vaccinating cancer and transplant patients. The next article looks at COVID-19 associated pulmonary aspergillosis. The 4th article looks at COVID symptoms, symptom clusters, and predictors for becoming a "long-hauler". The last 2 articles look at the widespread and effective vaccination among healthcare workers.

Have a great weekend – have some great articles for Monday!

Ed

Interim Results of the Safety and Immune-Efficacy of 1 Versus 2 Doses of COVID-19 Vaccine BNT162b2 for Cancer Patients in the Context of the UK Vaccine Priority Guidelines
medRxiv published online March 17, 2021
doi.org/10.1101/2021.03.17.2125313
This study presents data on the safety and immune efficacy of Pfizer (BNT162b2) vaccine in 54 healthy controls and 151 mostly elderly patients with solid and hematological malignancies, respectively, and compares results for patients who were boosted with BNT162b2 at 3 weeks versus those who were not. Immune efficacy was measured as antibody seroconversion, T cell responses, and neutralization of SARS-CoV-2 Wuhan strain and of a variant of concern B.1.1.7 (UK). They also collected safety data for the BNT162b2 vaccine up to 5 weeks following first dose. Antibody seroconversion was the primary assay for vaccine efficacy. They used an ELISA test to measure IgG antibodies specific for the SARS-CoV-2 S protein that was included in the vaccine. The study was conducted in the UK.

The vaccine was largely well tolerated. However, in contrast to its very high performance in healthy controls (>90% efficacious), immune efficacy of a single inoculum in solid cancer patients was strikingly low (below 40%) and very low in hematological cancer patients (below 15%). Of note, efficacy in solid cancer patients was greatly and rapidly increased by boosting at 21-days (95% within 2 weeks of boost). Too few hematological cancer patients were boosted for clear conclusions to be drawn.

Comment: The UK initial rollout was to vaccinate as many people as possible with at least one dose, however, delayed boosting potentially leaves most solid and hematological cancer patients wholly or partially unprotected, with implications for their own health; their community and the evolution of variant strains. Prompt boosting of solid cancer patients [second dose] quickly overcomes the poor efficacy of the primary inoculum in solid cancer patients.

Immunogenicity of a Single Dose of SARS-CoV-2 Messenger RNA Vaccine in Solid Organ Transplant Recipients
JAMA published online March 15, 2021
doi:10.1001/jama.2021.4385
Transplant recipients across the US were recruited though social media to participate in this prospective cohort and those who underwent SARS-CoV-2 vaccination between December 16, 2020, and February 5, 2021, were included. Samples were tested using the anti–SARS-CoV-2 S enzyme immunoassay (Roche Elecsys) that tests for antibodies against the receptor-binding domain of the SARS-CoV-2 spike protein.

There were 436 transplant recipients included in the study. None had a prior PCR-confirmed diagnosis of COVID-19. The median age was 55.9 years (interquartile range [IQR], 41.3-67.4 years), 61% were

women, and 89% were White transplant recipients; 52% received the Pfizer vaccine and 48% received the Moderna vaccine. Median time since transplant was 6.2 years (IQR, 2.7-12.7 years). The maintenance immunosuppression regimen included tacrolimus (83%), corticosteroids (54%), mycophenolate (66%), azathioprine (9%), sirolimus (4%), and everolimus (2%).

At a median of 20 days (IQR, 17-24 days) after the first dose of vaccine, antibody was detectable in only 76 of 436 participants (17%; 95% CI, 14%-21%). Transplant recipients receiving anti-metabolite maintenance immunosuppression therapy were less likely to develop an antibody response than those not receiving such immunosuppression therapy (37% vs 63%, respectively). Older transplant recipients were less likely to develop an antibody response (adjusted IRR, 0.83 [95% CI, 0.73-0.93] per 10 years, P = .002). Those who received Moderna were more likely to develop an antibody response than those receiving Pfizer (69% vs 31%, respectively: adjusted IRR, 2.15 [95% CI, 1.29-3.57], P = .003).

Comment: These findings in this publication of inadequate antispike antibody responses in organ transplant recipients after the first dose of mRNA vaccines suggest that such patients may remain at risk for COVID-19 despite vaccination. Further studies characterizing memory B-cell and T-cell responses, will be important in determining vaccination strategies as well as immunologic responses after the second dose. Should persons who are immunosuppressed be tested after vaccination to determine antibody response? If they do not have an antibody response, what should we advise? Please remember if you do test persons post vaccination please order anti–SARS-CoV-2 S. This study only examined a single dose. The study above suggests a much better response with the second dose.

COVID-19 Associated Pulmonary Aspergillosis (CAPA) in Mechanically Ventilated Patients
Clin Infect Dis published online March 9, 2021
doi.org/10.1093/cid/ciab223
A retrospective cohort study of adult mechanically ventilated COVID-19 patients admitted to five Johns Hopkins hospitals was conducted between March and August 2020. Starting in April, all patients admitted to ICU on MV were screened with serum aspergillus EIA, serum BDG, and fungal cultures. Probable CAPA was defined as having one of the following conditions: presence of new cavitary lung lesion(s) on chest CT without alternative explanation, positive serum GM EIA or positive BAL for aspergillus. [others use other criteria]

People with CAPA had similar severity of illness compared to controls on admission. Amongst the cohort of 396 people, 39 met criteria for CAPA. Compared to those without, patients with CAPA were more likely to have underlying pulmonary vascular disease (41% vs 21.6%, p=0.01), liver disease (35.9% vs 18.2%, p=0.02), coagulopathy (51.3% vs 33.1%, p=0.03), solid tumors (25.6% vs 10.9%, p=0.017), multiple myeloma (5.1% vs 0.3%, p=0.027), corticosteroid exposure during index admission (66.7% vs 42.6%, p=0.005), and had a lower BMI (median 26.6 vs 29.9, p=0.04). People with CAPA had worse outcomes as measured by ordinal severity of disease scores, requiring longer time to improvement p<0.001, and advancing in severity twice as fast(p<0.001). People with CAPA were intubated twice as long as those without (p <0.001) and longer LOS (median 41 vs 18.5 p<0.001).

Comment: Depending on definitions applied, the incidence of recognized CAPA ranged from 5 to 10%. People with CAPA had different underlying diseases, especially with regards to BMI, pulmonary, liver, and oncologic diseases prior to COVID-19, compared with those who did not develop CAPA. Regardless of definitions used, people with CAPA had uniformly worse outcomes compared to those without,

especially with regards to severity of illness, ventilatory and hemodynamic support, and duration of hospitalization.

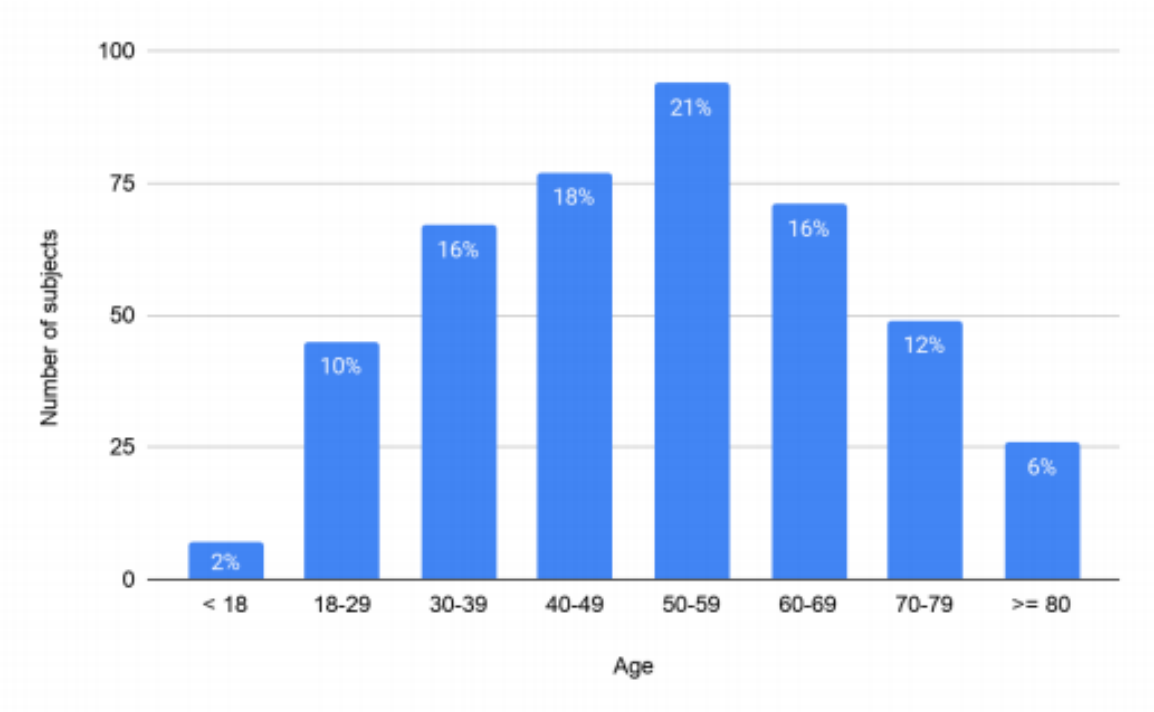
Aspergillosis as a complication of severe viral infection has been best documented in people with influenza. Several large cohort studies have showed that rates of pulmonary aspergillosis in influenza patients requiring ICU admission range from 7-30%, depending on methods applied to diagnostic screening, seasonal viral epidemiology, and definitions applied to report "influenza associated aspergillosis". [Lancet Resp Med 2018;6:782-792] Early in the COVID-19 pandemic, European centers reported similarly high rates of pulmonary aspergillosis associated with COVID-19; rates have similarly varied depending on diagnostic methods and definitions. [Clin Infect Dis published online July 28, 2020] It has been suggested that risks for both airway and invasive aspergillosis in this setting occur due to viral-mediated damage in airway fungal clearance and concurrent suppression of secondary immunologic defenses. Receipt of corticosteroids, particularly hydrocortisone, during admission appeared to be associated with increased risks for CAPA. Based on the RECOVERY Trial almost all patients in the ICU on MV will be on steroids.

COVID Symptoms, Symptom Clusters, and Predictors for Becoming a Long-Hauler: Looking for Clarity in the Haze of the Pandemic

medRxiv published online March 5, 2021

doi.org/10.1101/2021.03.03.21252086

The presence of persistent symptoms after apparent resolution from COVID-19 have frequently been reported throughout the pandemic by individuals labeled as "long-haulers". Recent data indicate that only about 10% of patients hospitalized with COVID-19 become "long-haulers" in fact most cases in this study did not require hospitalization. With that in mind the purpose of this study was to assess for symptoms at days 0-10 and 61+ among subjects with PCR-confirmed SARS-CoV-2 infection. The University of California COVID Research Data Set (UC CORDS) was used to identify 1407 records that met inclusion criteria. Symptoms attributable to COVID-19 were extracted from the electronic health record. A model was developed predictive for becoming a long-hauler based on symptoms. 27% reported persistent symptoms after 60 days. Women were more likely to become long haulers, and all age groups were represented with those aged 50 ± 20 years comprising 72% of cases. Presenting symptoms included palpitations, dysgeusia, chills, insomnia, hyperhidrosis, anxiety, sore throat, and headache among others. Twenty-seven percent (n = 382) of "community dwelling" patients with COVID-19 had persistent symptoms that lasted more than 60 days after diagnosis and were considered "long-haulers. The researchers reported that many "long-haulers" — approximately 32% — did not have symptoms at the time of testing for SARS-CoV-2. They identified 5 symptom clusters at day 61+: chest pain-cough, dyspnea-cough, anxiety-tachycardia, abdominal pain nausea, and low back pain-joint pain.



Comment: Further research is needed to understand the underlying pathophysiology including host phenotypes associated with aberrant innate and adaptive immune responses following SARS-CoV-2 infection. Additional studies are urgently needed that focus on the physical, mental, and emotional impact of long term COVID-19 survivors who become "long-haulers".

SARS-CoV-2 Infection after Vaccination in Health Care Workers in California
N Engl J Med published online March 23, 2021
DOI: 10.1056/NEJMc2101927
University of California researchers evaluated COVID-19 infection rates in 36,659 HCWs on the San Diego and Los Angeles campuses vaccinated with at least one dose of the Moderna or Pfizer vaccine from Dec 16, 2020, to Feb 9, 2021. In that timeframe, 28,184 (77%) received the second dose of vaccine. On December 2, in addition to defining a low threshold for testing of symptomatic persons, UCSD mandated that asymptomatic health care workers undergo weekly testing by polymerase chain-reaction (PCR) assay of nasal swabs. On December 26, UCLA instituted an optional testing program for asymptomatic health care workers with PCR assay of nasal swabs. This program has allowed for increased detection of asymptomatic SARS-CoV-2 infections after vaccination.

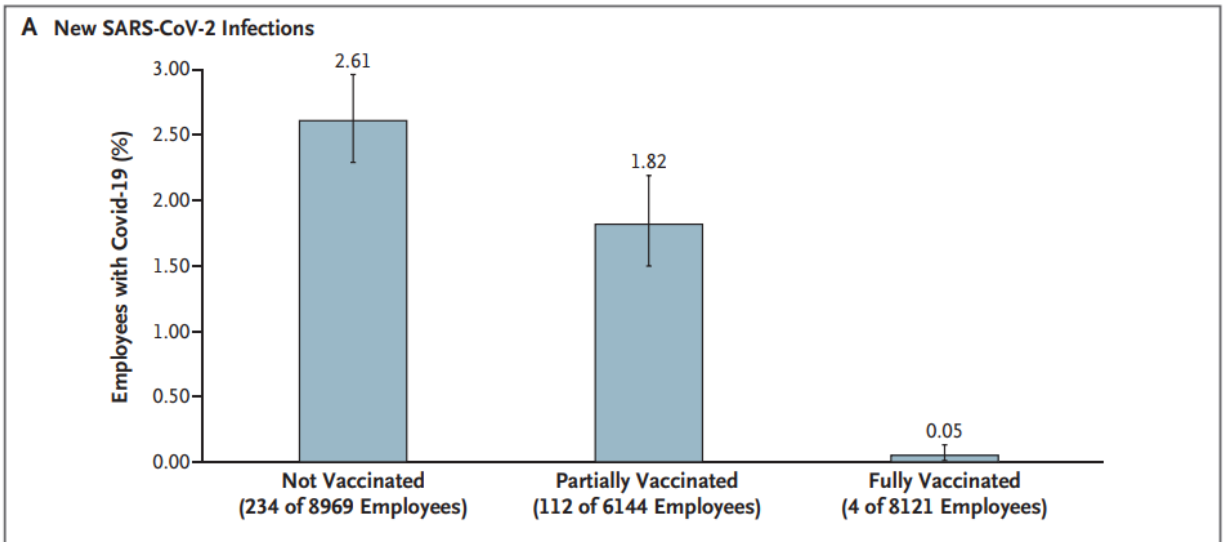
Of the 36,659 vaccinated HCWs, 379 (1.0%) tested positive for COVID-19 1 or more days after vaccination, 71% of them within the first 2 weeks after the first dose. Of the 28,184 HCWs who received their second dose, 37 (0.1%) tested positive, 22 of them 1 to 7 days later. Eight tested positive 8 to 14 days later, and 7 did so at least 15 days later.

With 5,455 HCWs at the San Diego campus and 9,535 at the Los Angeles campus who received their second vaccine dose at least 2 weeks before testing, the findings correspond to a 0.05% positivity rate. The absolute risk of infection after vaccination was 1.19% among San Diego HCWs and 0.97% among those in Los Angeles.

Comment: The rarity of positive test results 14 days after administration of the second dose of vaccine is encouraging and suggests the efficacy of these vaccines in real world settings. With the emergence of new variants, the authors still recommend continued public health mitigation measures (masking, physical distancing, daily symptom screening, and regular testing), even in environments with a high incidence of vaccination, until herd immunity is reached at large. Despite concern over variants, this report and the one below supports the incredible effectiveness of current vaccines.

Early Evidence of the Effect of SARS-CoV-2 Vaccine at One Medical Center
N Engl J Med published online March 23, 2021
The authors report data from the University of Texas Southwestern Medical Center (UTSW), which initiated a program on December 15, 2020, to offer vaccine against SARS-CoV-2 to its frontline employees in phase 1a of vaccination. The launch of the vaccination effort coincided with a rapid surge in numbers of new SARS-CoV-2 infections in North Texas. This escalation led to the largest surge to date in the region and strained health systems.

In the initial 31 days of the vaccination campaign, 59% of 23,234 UTSW employees received a first dose of either one of the mRNA vaccines and 30% received a second dose. Between December 15, 2020, and January 28, 2021, a total of 350 of the 23,234 employees (1.5%) who were eligible to receive the vaccine were identified as being newly infected with SARS-CoV-2. 2.61% of unvaccinated employees developed the infection versus 1.82% of partially vaccinated workers and 0.05% of fully vaccinated employees. In addition, vaccinations preserved their workforce. They observed a greater than 90% decrease in the number of employees who are either in isolation or quarantine.



Comment: These studies demonstrate that widespread and effective vaccination among healthcare workers provides a safe environment even in the presence of a high rate of SARS-CoV-2 infection in the community. Furthermore, it protects our workforce critical to patient safety. The HCW acceptance rate for vaccination in this study was close to 80%. Other organizations have reported 60-70% acceptance rate which is very disappointing. Perhaps reports as the 2 reviewed here will encourage everyone to get vaccinated.