Good morning. As I mentioned last Tuesday, my wife and I will be gone on vacation starting this Monday. I may occasionally send updates, but officially back December 4th. As a dear colleague Dick Hamrick wrote me last Tuesday: Margaret Lewis used to say – "It will be here when you get back." You also liked the idea of expanding the Briefing to an ID Newsletter in 2022. Thanks for the feedback. This has been a labor of love and it has truly been a privilege to serve our community in this small way during the pandemic.

Today under COVID-19 News the French have advised against Moderna vaccine for people under 30. The other news was the report from Regeneron that their MCA reduced the risk of contracting the disease by 81.6% compared with a placebo in a long-term study.

Under Journal Review I start with two articles on coronaviruses in bats and deer. The third article is a study of lactating parents and the pattern of IgA and IgG antibodies in human milk between COVID-19 infection vs mRNA vaccination out to 90 days. The last article is the evaluation of the Pfizer vaccine phase 2/3 trial in children 5-11.

I hope everyone has a wonderful weekend.

Ed

COVID-19 News

French Health Authority Advises Against Moderna COVID-19 Vaccine for Under 30s

On Monday France's public health authority has recommended people under 30 be given Pfizer's COVID-19 vaccine when available instead of Moderna, which carried comparatively higher risks of heart-related problems. The Haute Autorite de Sante (HAS), which does not have legal power to ban or license drugs but acts as an advisor to the French health sector, cited "very rare" risks linked to myocarditis, that had shown up in recent data on the Moderna vaccine and in a French study published on Monday. [I cannot find an English version of study yet] Within the population aged under 30, this risk appears to be around five times lower with Pfizer's vaccine compared to Moderna's.

Comment: The decision in Paris came after regulators in several other countries, including Canada, Finland and Sweden, had also taken a more defensive stance on Moderna over heart-related safety concerns affecting younger people. The FDA has repeatedly said, the benefits of vaccination far outweigh the risks. The risk of myocarditis is much greater with natural infection. Myocarditis after vaccination tends to be mild and short lived. The study from Epi-Phare, an independent medicines safety research group that works closely with the French government, confirmed previous findings -- while noting cases are rare and do not cast doubt on the effectiveness of the shots.

Regeneron's MCA Cut Risk of Covid-19 by 82%
Regeneron Pharmaceuticals announced its monoclonal antibody drug continued to provide strong protection against Covid-19 infection for up to eight months, reducing the risk of contracting the disease by 81.6% compared with a placebo in a long-term study.

Comment: This announcement showed their MCA can provide long-lasting temporary immunity against Covid-19, which could make it an attractive option for people who don't respond to vaccines because they have impaired immune systems. AstraZeneca announced last month they had an MCA that provides protection for up to a year. [see Briefing last month]

Journal Review

A Novel SARS-CoV-2 Related Coronavirus in Bats from Cambodia
Nat Commun published online November 12, 2021
doi.org/10.1038/s41467-021-26809-4
To date, the closest relatives to SARS-CoV-2 have been detected in Rhinolophus bats sampled in the Yunnan province, China. Here the investigators describe the identification of SARS-CoV-2 related coronaviruses in two Rhinolophus shameli bats sampled in Cambodia in 2010. Metagenomic sequencing identifies nearly identical viruses sharing 92.6% nucleotide identity with SARS-CoV-2. Most genomic regions are closely related to SARS-CoV-2, except for a region of the spike, which is not compatible with human ACE2-mediated entry. The discovery of these viruses in a bat species not found in China indicates that SARS-CoV-2 related viruses have a much wider geographic distribution than previously reported and suggests that SE Asia represents a key area for future surveillance for coronaviruses.

Comment: NPR just reported that a novel coronavirus, likely originating in dogs, is infecting people in Malaysia and Haiti. The virus is likely the eighth coronavirus known to cause disease in people. Back in May, investigators at Duke University reported they had detected a nearly identical coronavirus in children at a Malaysian hospital. The researchers found the virus in the upper respiratory tract of 3% of the 301 patients they tested in 2017 and 2018. The genetic sequence of the Malaysian virus suggested it likely originated in dogs and then jumped into people. See next article.

Multiple Spillovers and Onward Transmission of SARS-CoV-2 in Free-Living and Captive White-Tailed Deer (*Odocoileus virginianus*)

bioRxiv posted online November 1, 2021
doi.org/10.1101/2021.10.31.46667

White-tailed deer (*Odocoileus virginianus)*, the predominant cervid in North America, are susceptible to SARS-CoV-2 infection, and experimentally infected fawns transmit the virus to other captive deer. To test the hypothesis that SARS-CoV-2 may be circulating in deer, the investigators evaluated 283 retropharyngeal lymph node (RPLN) samples collected from 151 free-living and 132 captive deer in Iowa from April 2020 through December of 2020 for the presence of SARS-CoV-2 RNA.

Up to 80 percent of deer sampled from April 2020 through January 2021 in the state were infected. Notably, between Nov 23, 2020 and January 10, 2021, 80 of 97 (82.5%; 95% CI 73.7, 88.8) RPLN samples had detectable SARS-CoV-2 RNA by RT-PCR. Whole genome sequencing of the 94 positive RPLN samples identified 12 SARS-CoV-2 lineages, with B.1.2 (n = 51; 54.5%), and B.1.311 (*n* = 19; 20%) accounting for ~75% of all samples. The geographic distribution and nesting of clusters of deer and human lineages strongly suggest multiple zooanthroponotic spillover events and deer-to-deer transmission. There is no evidence that deer have passed the virus back to humans.

Comment: The findings pose worrisome implications for the spread of the coronavirus, although they were not able to identify how the deer might have contracted the virus from humans. Researchers and outside experts characterized the study's findings as worrisome. Widespread infection among North America's most common game species could make eradicating the pathogen even more difficult, especially if they became a reservoir for mutations that eventually spilled back over to humans. The study raises a multitude of questions that investigators will be keen to examine, including whether other wild animals can also carry the virus. The more species capable of carrying the virus, the greater the chances it can evolve in ways that threaten human health.

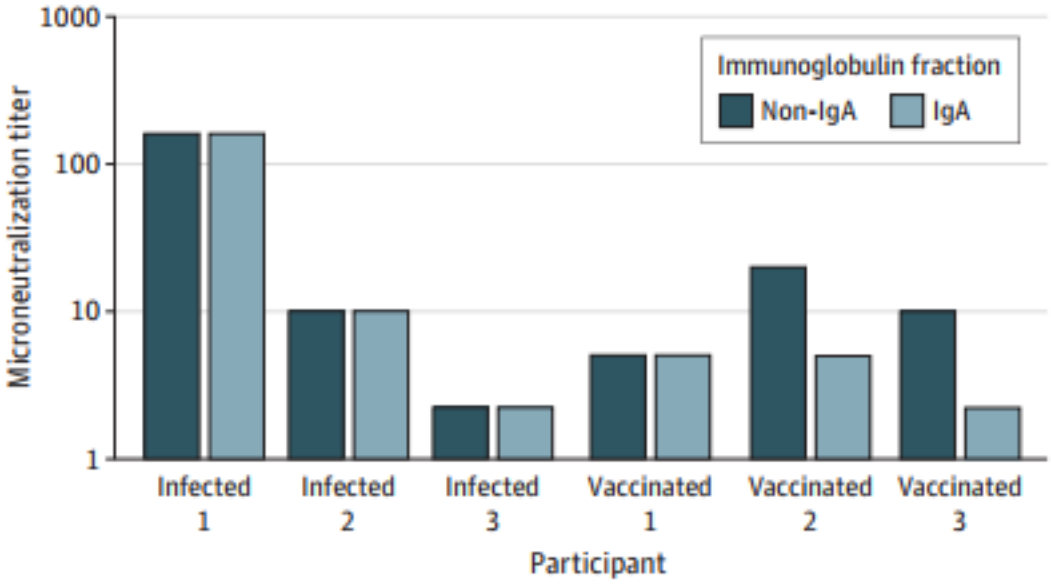
Association of Human Milk Antibody Induction, Persistence, and Neutralizing Capacity With SARS-CoV-2 Infection vs mRNA Vaccination

JAMA Pediatr published online November 10, 2021
doi:10.1001/jamapediatrics.2021.4897

Convenience sampling observational cohort (recruited July to December 2020) of lactating parents with infection with human milk samples collected at days 0 (within 14 days of diagnosis), 3, 7, 10, 28, and 90. The observational cohort included vaccinated lactating parents with human milk collected prevaccination, 18 days after the first dose, and 18 and 90 days after the second dose.

In this cohort study of a convenience sample of 47 lactating parents with infection and 30 lactating parents who were vaccinated, antibody response in milk after infection was IgA dominant and highly variable while vaccination was associated with a robust IgG response, which began to decline by 90 days after the second vaccine dose. Milk from both groups showed neutralization activity against live SARS-CoV-2 virus, which can be attributed to IgA and IgG SARS-CoV-2 antibodies.

Figure 4. Anti-SARS-CoV-2 Microneutralization Activity in the IgA vs Non-IgA Fractions of Human Milk

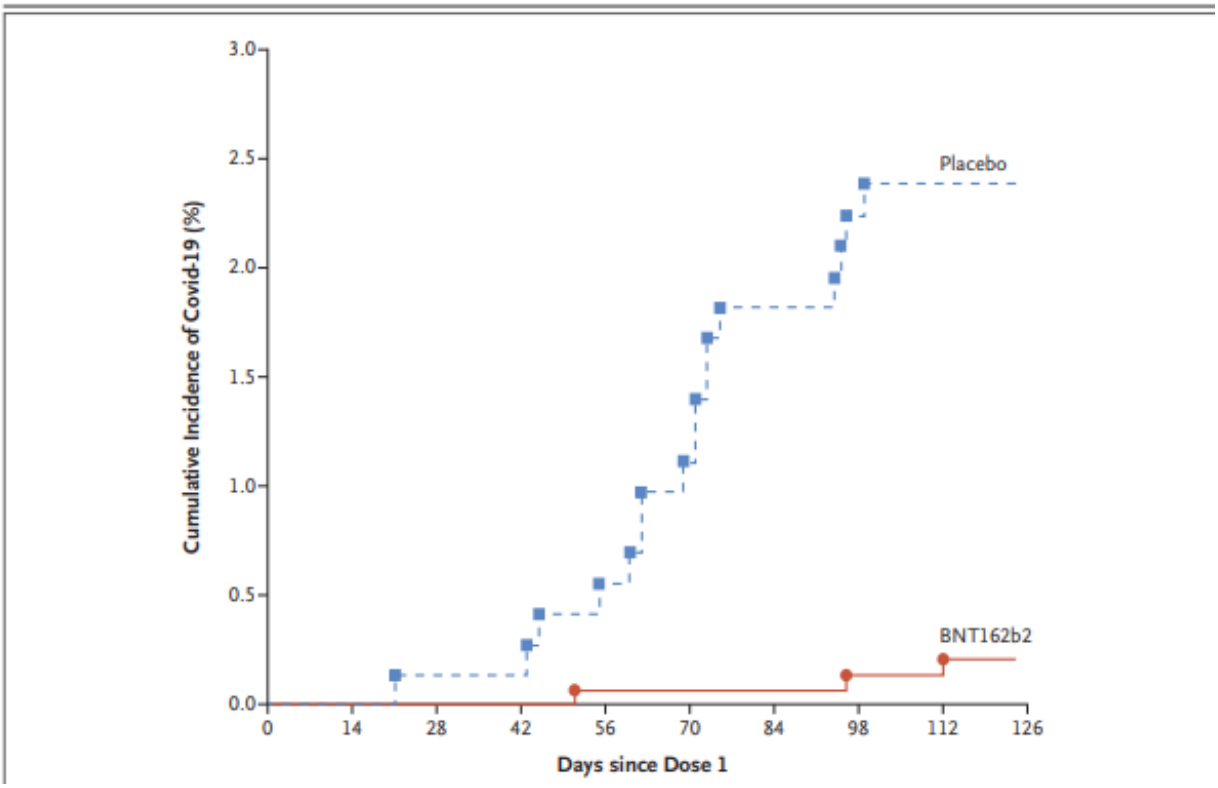


Comment: In this study of lactating parents, the pattern of IgA and IgG antibodies in human milk differed between COVID-19 infection vs mRNA vaccination out to 90 days. While infection was associated with a highly variable IgA-dominant response and vaccination was associated with an IgG-dominant response, both were associated with having human milk that exhibited neutralization activity against live SARS-CoV-2 virus. Importantly whether a dominant IgA or IgG response, both infection and vaccination generated human milk with neutralizing activity. The vaccinated group demographics were limited, given that the vaccine was only available to HCWs at the time of recruitment. This explains the older age and higher education level of the vaccinated group and introduces bias to the study. This study presents the longest published follow-up of human milk postvaccination.

Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age
N Engl J Med published online November 9, 2021
DOI: 10.1056/NEJMoa2116298
This study presents results for 5-to-11-year-old children in the phase 2-3 trial. Participants were randomly assigned in a 2:1 ratio to receive two doses of either the Pfizer vaccine at the dose level identified during the open-label phase 1 study or placebo. In 5-to-11-year-olds, a vaccination regimen involved intramuscular (deltoid) injection of two doses of Pfizer vaccine administered 21 days apart and was initiated at a 10-µg dose level. VE against confirmed Covid-19 with onset at least 7 days after the second dose was described both in participants without evidence of previous SARS-CoV-2 infection.

In the phase 2-3 trial, a total of 2268 children were randomly assigned to receive the Pfizer vaccine (1517 children) or placebo (751 children). At data cutoff, the median follow-up was 2.3 months. In the 5-to-11-year-olds, as in other age groups, the Pfizer vaccine had a favorable safety profile. No vaccine-related serious adverse events were noted. One month after the second dose, the geometric mean ratio of SARS-CoV-2 neutralizing titers in 5-to-11-year-olds to those in 16-to-25-year-olds was 1.04 (95%

confidence interval [CI], 0.93 to 1.18), a ratio meeting the prespecified immunogenicity success criterion. Covid-19 with onset 7 days or more after the second dose was reported in three recipients of the Pfizer vaccine and in 16 placebo recipients (VE, 90.7%; 95% CI, 67.7 to 98.3).



Comment: A Covid-19 vaccination regimen consisting of two 10-µg doses of the Pfizer vaccine administered 21 days apart was found to be safe, immunogenic, and efficacious in children 5 to 11 years of age. Limitations of the study include the lack of longer-term follow-up to assess the duration of immune responses, efficacy, and safety. However, longer-term follow-up for this study will continue for 2 years. This study was also not powered to detect potential rare side effects of the Pfizer vaccine in 5-to-11-year-olds such as myocarditis. However, the safety of the Pfizer vaccine observed in this study combined with widespread use of Pfizer vaccine in older populations should provide reassurance of the vaccine's VE and safety.