Good morning. I have much to share.

Under COVID-19 News I review the CDC guidance on preventing Covid-19 in (K)-12 schools. Next a brief discussion on booster doses, and last the new warning added to the J&J vaccine for GBS.

Under Journal Review I start by reviewing three prepublication articles from the UK summarizing the risk of Covid-19 in children 18 years and younger. Next an article from Nature confirming the importance of the second shot in protecting against VOC. Last, investigators analyzed milk samples to determine if vaccine-related mRNA was detectable in human milk after vaccination.

Have a wonderful Tuesday

Ed

COVID-19 News

CDC Guidance for COVID-19 Prevention in Kindergarten (K)-12 Schools
July 9, 2021
Highlights
Major changes:
No masks required for vaccinated students, faculty, and staff
Masks should be worn indoors by all individuals ages 2 and older who are not fully vaccinated against Covid-19. In general people do not need to wear masks when outdoors.
The CDC also stated that those who are fully vaccinated no longer need to wear a mask or physically distance in any setting, including while participating in extracurricular activities or while eating. However, it noted that based on the needs of the community, a school may opt to make mask use universally required regardless of vaccination status.
Updated to emphasize the need for localities to monitor community transmission, vaccination coverage, screening testing, variants, and occurrence of outbreaks to guide decisions on the level of layered prevention strategies. This could include moving back to universal masking if there is an increase or high Covid-19 transmission within the school or surrounding community. See testing.

Physical distancing:
CDC now recommends that schools maintain at least 3 feet of physical distance between students within classrooms to reduce transmission risk.

Screening Testing:
Increased emphasis on screening testing, especially for unvaccinated faculty/staff and athletes. CDC guidance provides that people who are fully vaccinated do not need to participate in screening testing and do not need to quarantine if they do not have any symptoms, though decisions regarding screening testing may be made at the state or local level. Screening testing may be most valuable in areas with substantial or high community transmission levels, in areas with low vaccination coverage, and in schools where other prevention strategies are not implemented. Screening testing should be offered to students who have not been fully vaccinated when community transmission is at moderate, substantial, or high levels (Table below); at any level of community transmission, screening testing should be offered to all teachers and staff who have not been fully vaccinated. To be effective, the screening program

should test at least once per week, and rapidly (within 24 hours) report results. Screening testing more than once a week might be more effective at interrupting transmission.

	Low Transmission[1] Blue	Moderate Transmission Yellow	Substantial Transmission Orange	High Transmission Red
Students	Do not need to screen students.	**Offer screening testing for students** who are not fully vaccinated at least once per week.		
Teachers and staff	**Offer screening testing for teachers and staff** who are not fully vaccinated at least once per week.			
High risk sports and activities	**Recommend screening testing for high-risk sports[2] and extracurricular activities[3]** at least once per week for participants who are not fully vaccinated.		**Recommend screening testing for high-risk sports and extracurricular activities** twice per week for participants who are not fully vaccinated.	**Cancel or hold high-risk sports and extracurricular activities virtually** to protect in-person learning, unless all participants are fully vaccinated.
Low- and intermediate-risk sports	Do not need to screen students participating in low- and intermediate-risk sports.[2]	**Recommend screening testing for low- and intermediate-risk sports** at least once per week for participants who are not fully vaccinated.		

[1] Levels of community transmission defined as total new cases per 100,000 persons in the past 7 days (low, 0-9; moderate 10-49; substantial, 50-99, high, ≥100) and percentage of positive tests in the past 7 days (low, <5%; moderate, 5-7.9%; substantial, 8-9.9%; high, ≥10%.)

HH, ventilation, staying home when sick, contact tracing, and cleaning/disinfection are also part of guidance. They now say cleaning once a day is adequate in most circumstances.

Comments: This guidance has been written to be flexible based on local conditions. They do provide some guidance based on levels of community spread which is welcomed. Schools may opt to require universal masking if local cases were rising or if a school could not determine how many of its students and staff members were vaccinated. Children have made up 14 percent of all cases to date, up from around 7 percent this time last year, according to the AAP, but serious illness and death among them remains rare. Around 2 percent or less of all COVID-19 cases in children result in hospitalization, and even fewer — .03 percent of cases or less — result in death. (See articles below) Young children are also less likely to transmit the virus to others compared to teenagers and adults. There is still concern for the rare complication of MIS-C and some children can have prolonged symptoms after infection has resolved. Then there is the question about the impact of the Delta variant as children and teachers return to the classroom this fall. There is a companion document that reviews the science supporting the recommendations which I highly recommend.

CDC, FDA Say Booster Doses are Not Needed at this Time

Federal officials said booster doses are not necessary yet. They point to data that fully vaccinated people are in fact protected against serious illness, hospitalizations, and deaths from all current SARS-CoV-2

viruses including VOC (includes delta). They claim they are prepared to recommend booster doses when the science demonstrates they are needed.

Comment: Currently almost 50% of Americans are fully vaccinated. The elderly have the highest vaccination rate, at 80%. It is people who are not vaccinated that currently are at greatest risk. Only 38% of people ages 18 to 29 years have received at least one vaccine dose, the lowest rate among any age group eligible to get immunized, according to the CDC. Let me be clear – although young adults are not at high risk of developing severe Covid-19, they can spread the virus without knowing they are infected if they are not vaccinated or do not take precautions. The literature also clearly shows the risk of long-term effects in young people who contract the virus, such as shortness of breath, fatigue, and cognitive dysfunction. We also know that people with immune dysfunction may not be fully protected even if fully vaccinated. Therefore, it becomes even more important for everyone who is eligible to be vaccinated.

As the data evolves prioritizing booster doses maybe partially based on such factors as age and underlying medical conditions. There is already some data that suggests a third dose may be useful in certain populations such organ transplants. [Review in the Briefing several weeks ago] Israel has announced they will offer boosters to persons with a weakened immune system. Rather than talk about booster doses, let us boost vaccination rates now for all eligible persons. Over 95% of deaths have been in unvaccinated individuals.

J&J Vaccine
Federal officials have identified 100 suspected cases of Guillain-Barré (GBS) among recipients of J&J one-dose shot through VAERS that relies on patients and health care providers to report adverse effects of vaccines. There have been 12.8 million persons vaccinated with the J&J vaccine. Although regulators have found that the chances of developing the condition are low, they appear to be higher among recipients of the J&J vaccine than among the general population in the US. Most cases were reported about two weeks after vaccination and mostly in men, many of them aged 50 years and older. The FDA added that it "continues to find the known and potential benefits clearly outweigh the known and potential risks" of the vaccine. The European medicine's regulator recommended language about a possible link between the AZ vaccine and GBS.

Comment: The new safety concern comes at a critical moment in the US fight against Covid-19. The pace of vaccinations has slowed considerably as a new, more transmissible variant Delta is spreading quickly especially in under vaccinated areas. This worries me since this report only serves to reinforces the lack of confidence or hesitancy that some people already had. GBS has previously been linked to other vaccines, including the 1976 swine flu vaccine and more recently this year with GlaxoSmithKline's shingles vaccine, Shingrix. The FDA also attached warnings to the Pfizer-BioNTech and Moderna vaccines earlier this year. One of the major advances in public in the past century has been the marked reduction of vaccine preventable diseases. On balance the benefits of Pfizer, Moderna, and J&J vaccines far outweigh the risks. If life is to return to "normal", vaccinations are our ticket to control and shorten the pandemic. To remind everyone, the 1918 pandemic lasted two years.

Journal Review

Risk Factors for Intensive Care Admission and Death Amongst Children and Young People Admitted to Hospital with COVID-19 and PIMS-TS in England During the First Pandemic Year
medRxiv published online July 5, 2021

doi: https://doi.org/10.1101/2021.07.01.21259785

Deaths in Children and Young People in England Following SARS-CoV-2 Infection During the First Pandemic Year: A National Study Using Linked Mandatory Child Death Reporting Data

medRxiv published online July 8, 2021

doi: https://doi.org/10.1101/2021.07.07.21259779

Which Children and Young People are at Higher Risk of Severe Disease and Death After SARS-CoV-2 Infection: A Systematic Review and Individual Patient Meta-Analysis

medRxiv published online July 8, 2021

doi: https://doi.org/10.1101/2021.06.30.21259763

These three prepublication articles from the UK show in children 18 years and younger the risk of Covid-19 deaths and serious illness was extremely low. During the pandemic, the mandatory National Child Mortality Database (NCMD) was linked to Public Health England (PHE) testing data to identify CYP (<18 years) who died with a positive SARS-CoV-2 test. A clinical review of all deaths from March 2020 to February 2021 was undertaken to differentiate between those who died of SARS-CoV-2 infection and those who died of an alternative cause but coincidentally tested positive. In this paper SARS-CoV-2 was very rarely fatal in CYP, even among those with underlying comorbidities. Some 99.995% of the 469,982 children in England who were infected during the year examined by investigators survived. In another study underlying health conditions, especially serious brain- or nerve-related disabilities, increased the risk of dying of Covid-19. Fifteen of the 25 children in the UK who died because of Covid-19 had underlying serious illnesses, while four had chronic underlying conditions. Three of the deaths were due to MIS-C. Six of the children who died due to Covid-19 didn't appear to have an underlying health condition. No child with a stand-alone diagnosis of asthma, diabetes, epilepsy, or Down syndrome died from Covid-19.

Underlying health conditions also raised the risk of severe illness, the two other papers reported. One study found a higher risk of admission to intensive care among children with health conditions such as diabetes, asthma, and cardiovascular disease. Those with multiple conditions had the highest risk. Even so, the absolute risk was exceedingly small.

Comment: These studies all related to time periods before the emergence of the delta variant, but the authors said there was yet no evidence that the variant causes more severe illness or death among children. Public health officials will need to decide whether to recommend vaccinations for children of younger ages. (< age 12) The decision would involve balancing the risks and benefits of vaccination with the low risk of serious illness and death from Covid-19 especially since young children are also less likely to transmit the virus to others compared to teenagers and adults.

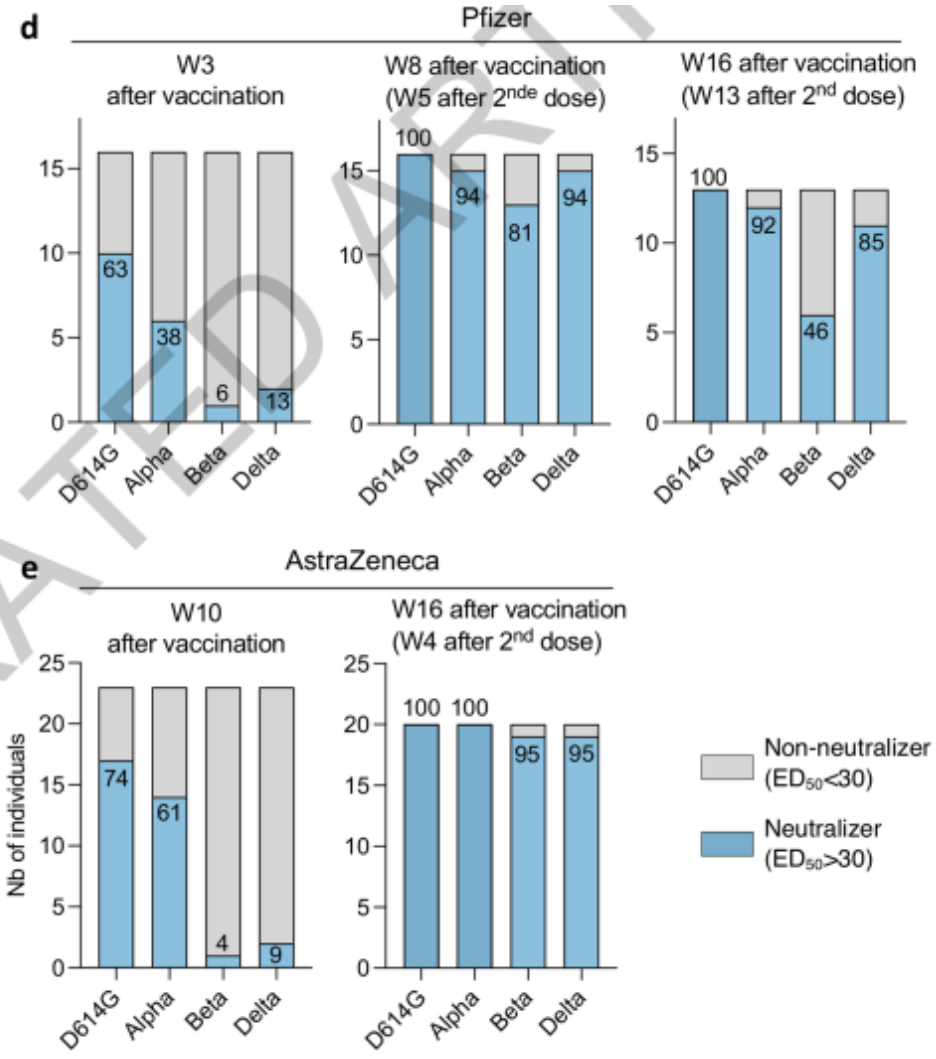
Reduced Sensitivity of SARS-CoV-2 Variant Delta to Antibody Neutralization

Nature published online July 8, 2021

https://doi.org/10.1038/s41586-021-03777-9

The investigators isolated a Delta strain from a traveler returning from India. They examined its sensitivity to monoclonal antibodies (mAbs) and to antibodies present in sera from COVID-19 convalescent individuals or vaccine recipients, in comparison to other viral strains. The lineage includes three main subtypes (B1.617.1, B.1.617.2 and B.1.617.3), harboring diverse Spike mutations in the N-terminal domain (NTD) and the receptor binding domain (RBD) which may increase their immune evasion potential. Delta from this traveler was resistant to neutralization by some anti-NTD and anti-RBD mAbs including Bamlanivimab, which were impaired in binding to the spike protein. Sera from convalescent patients collected up to 12 months post symptoms were 4-fold less potent against variant Delta, relative to variant Alpha (B.1.1.7). Sera from individuals having received one dose of Pfizer or

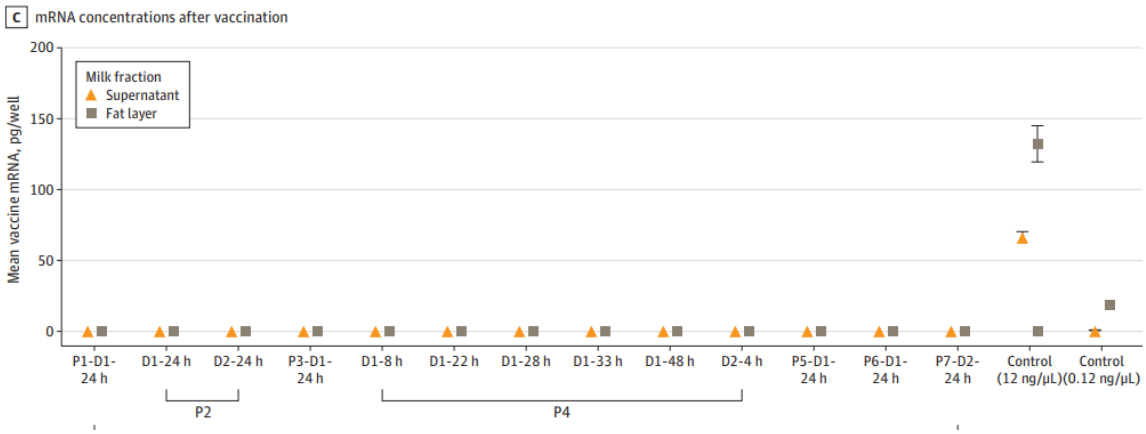
AstraZeneca vaccines barely inhibited variant Delta. Administration of two doses generated a neutralizing response in 95% of individuals, with titers 3-to-5-fold lower against Delta than Alpha.



Comment: A single shot of a two-dose vaccine offers little if any protection. However, the study also found that fully vaccinated people, two doses of the Pfizer or AstraZeneca vaccine, should retain significant protection against the delta variant. This has been verified by other studies. In addition, we should abandon the Lilly monoclonal for early treatment and selectively use the Regeneron combination mAbs.

Evaluation of Messenger RNA From COVID-19 BTN162b2 and mRNA-1273 Vaccines in Human Milk
JAMA Pediatr published online July 6, 2021
doi:10.1001/jamapediatrics.2021.1929
The investigators analyzed milk samples to determine if vaccine-related mRNA was detectable in human milk after vaccination. Self-collected milk samples were kept on ice or immediately frozen (at home) until arrival in the laboratory. Samples were collected prior to vaccination and at varied time points up to 48 hours after vaccination. Total RNA was isolated from milk components using the RNeasy Mini Kit (Qiagen). We performed real-time quantitative polymerase chain reaction assay targeting the mRNA

used in the COVID-19 mRNA-based vaccines. A total of 7 breastfeeding mothers (mean [SD] age, 37.8 [5.8] years) volunteered for this study (Table). Their children ranged in age from 1 month to 3 years. Postvaccination milk samples were collected 4 to 48 hours after administration of the Pfizer (n = 5) or Moderna (n = 2) vaccines. Analysis of 13 human milk samples collected 24 hours after vaccination, including multiple timepoints (4 to 48 hours) from a single participant, revealed that none of the samples showed detectable levels of vaccine mRNA in any component of the milk.



Comment: Vaccine-associated mRNA was not detected in 13 milk samples collected 4 to 48 hours after vaccination from 7 breastfeeding individuals. These results provide important early evidence to strengthen current recommendations that vaccine related mRNA is not transferred to the infant from lactating individuals who receive the COVID-19 mRNA-based vaccine. This study supports the WHO recommendation that breastfeeding individuals be vaccinated and does not advise cessation of breastfeeding following vaccine administration. Limitation of this study is the small sample size.