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Medical Intelligence Report

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Topic: COVID-19 Research Update

Recommendations from the CDC for Fully Vaccinated Individuals

The CDC released new recommendations for individuals who have been fully vaccinated for COVID-19 (CDC, 2021).

People are considered fully vaccinated:

- 2 weeks after their second dose in a 2-dose series, like the Pfizer-BioNTech or Moderna vaccines
- 2 weeks after a single-dose vaccine, like Johnson & Johnson's vaccine

In public places where a number of individuals not from your household may be present, the CDC still recommends wearing a mask, staying 6 feet apart from others, and avoiding crowds and poorly ventilated spaces.

The changes to the recommendations include:

- Fully vaccinated individuals can gather indoors with other fully vaccinated people without wearing a mask.
- Fully vaccinated individuals can gather indoors with unvaccinated people from **one** other household (for example, visiting with relatives who all live together) without masks, unless any of those people or anyone they live with has an increased risk for severe illness from COVID-19.
- Vaccinated individuals who have been in close contact with someone who has COVID-19 do not need to stay away from others or get tested unless you have symptoms.

Everyone, including those who are fully vaccinated, should continue to use measures to prevent transmission in places including in public, gatherings with unvaccinated people from more than one other household, and when visiting with an unvaccinated person who is at increased risk of severe illness or death from COVID-19 or who lives with a person at increased risk.

Additionally, medium and large gatherings should still be avoided. Air travel should be delayed if possible, and if necessary, CDC recommendations for reducing transmission should continue to be followed.

There is a possibility of getting COVID-19 after being fully vaccinated, and fully vaccinated individuals should continue to be aware of possible symptoms associated with the virus and avoid others if symptoms develop.

COVID-19 Vaccine Updates

Johnson and Johnson Vaccine receives Emergency Use Authorization

The FDA issued a third Emergency Use Authorization (EUA) for use of the Johnson and Johnson COVID-19 vaccine in individuals over the age of 18 (FDA, 2021). The vaccine delivers a DNA copy of the SARS-CoV-2 spike protein that is encased in the shell of an adenovirus.

The Johnson & Johnson vaccine is able to provide protection from COVID-19 with only a single dose, rather than the two doses required for the other authorized vaccines.

The vaccine can also be shipped at temperatures above freezing, unlike the other available vaccines, because of the protection from the adenovirus shell. These two characteristics are expected to simplify the vaccination process in comparison to earlier vaccines.

In the studies used to support the EUA, the Johnson & Johnson vaccine reduced the risk of moderate to severe COVID-19 by 66.1%. Researchers at the FDA also evaluated the frequency of hospitalization for COVID-19 that occurred 28 days or more after vaccination (Herper and Branswell, 2021). The 28-day time period allows for evaluation of participants who have more fully developed an immune response to the vaccination.

In the vaccinated group, there were NO hospitalizations of individuals 28 days or more after vaccination while there were 16 in the placebo group.

Importantly, the clinical trials of the Johnson & Johnson vaccine were conducted after the emergence of the new variants, B.1.351 and P.1, of SARS-CoV-2, and there were trial sites for the study in South Africa and Brazil, where the variants were spreading rapidly.

The results from the trials show that the vaccine has a 100% efficacy in prevention of hospitalizations even in areas with community spread of the SARS-CoV-2 variants.

As mentioned in previous *PCI COVID-19 Updates*, the efficacy of the vaccine varied based on the geographic area evaluated. In areas where variants that affect the immune response to the virus were actively spreading (e.g. South Africa), the efficacy was 58%. However, in the United States, where the variants were not yet common, the vaccine had a 72% efficacy in reducing the risk of moderate to severe or critical COVID-19.

The clinical trials for the Johnson & Johnson vaccine also included periodic testing of participants, allowing for detection of asymptomatic cases.

In participants who received the vaccine, there was a 65.5% reduction in the number of people who were infected with COVID-19.

This characteristic was not reported for the other authorized vaccines because testing of asymptomatic individuals was not included in the initial clinical trials.

Reports from Johnson & Johnson indicate that production of the vaccine has been lower than originally anticipated. However, the drug company Merck has arranged to participate in the manufacture of the Johnson & Johnson vaccine to help boost the production. Based on information from government officials, the additional production assistance is expected to double the amount of this vaccine available (McGinley and Rowland, 2021).

Skin Reactions to Moderna Vaccine

Based on the Phase 3 clinical trial of the Moderna COVID-19 vaccine, 84.2% of participants had an immediate reaction in the skin surrounding the injection site while delayed skin reactions, those that developed eight days or more after vaccination, occurred in 0.8% of participants (Blumenthal et al., 2021). Researchers from Massachusetts General Hospital have reported 12 individuals who had large, delayed skin reactions to the vaccine. The reactions varied greatly between individuals, but included reddening of the skin and tenderness at the location. The largest were over 10 centimeters in diameter. All of the individuals went on to receive their second dose of the vaccine, and six did not have a reaction to the second shot while three had a similar reaction and three had a reduced reaction to the second shot. All of the reactions were able to be treated with ice and antihistamines except one individual who also required corticosteroids. The visible signs of the reaction resolved in a median of 6 days with a range of two to eleven.

Individuals who have this type of delayed, hypersensitivity reaction can receive the second dose of the vaccine safely and can be treated conservatively by their primary care provider.

Effect of a Single Dose of Vaccine in Individuals with a Previous SARS-CoV-2 Infection

A study of healthcare workers at the University of Maryland Medical Center investigated the response to vaccination in three groups: (1) those with a negative antibody test for COVID-19, (2) those with a positive antibody test for COVID-19 who did not have symptoms, and (3) those with a positive antibody test for COVID-19 that had symptoms associated with the illness (Saadat et al., 2021). The 59 participants in the study were vaccinated with either the Pfizer-BioNTech vaccine or the Moderna vaccine, and evaluations occurred directly before vaccination, seven days after vaccination, and 14 days after vaccination with a single dose. The study time period was from December of 2020 to January of 2021. The amount of antibodies produced as well as the ability of antibodies to neutralize vaccine were evaluated.

The amount of antibodies present in individuals with a previous infection was higher at all time-points compared to those who had not previously had COVID-19. The level of neutralization was also higher at all time points in both groups with a previous SARS-CoV-2 infection compared to those without a previous infection.

Based on the results, the researchers suggest that a single-dose vaccination strategy may be appropriate for those with a prior COVID-19 diagnosis, or these individuals could be placed lower on the vaccination priority list until larger supplies are available.

Delay of Second Dose of AstraZeneca-Oxford Vaccine Increased Efficacy

The combined results from four randomized and controlled trials in the United Kingdom, Brazil, and South Africa investigating the efficacy of the AstraZeneca-Oxford vaccine were published in The Lancet (Voysey et al., 2021). The vaccine was initially designed to be administered as a single dose, but a booster dose was added after Phase 1 trials. Some participants had initially agreed to participate in the single dose study and chose not to receive a second dose. Additionally, manufacturing issues led to a delay in the second dose for a subset of the participants who received two doses, allowing for an analysis of the result with differing length of time between the doses.

In the report, the outcome of 17,178 participants was evaluated, and 8948 participants were in the trial in the United Kingdom, 6753 were in the trial in Brazil, and 1477 were in the trial in South Africa. There were 332 total cases of symptomatic COVID-19 within 14 days of the second dose of the vaccine or placebo, which corresponded to 1.0% of the vaccinated group and 2.9% of the placebo group. Based on this information, the overall efficacy of the vaccine was 66.7% in reducing the risk of symptomatic COVID-19.

Vaccine efficacy for the prevention of hospitalization calculated 22 days after the FIRST dose was 100% with no one in the inoculated group requiring treatment in the hospital.

There were 22 individuals admitted to the hospital for treatment of COVID-19 in the group that received the placebo, and three were considered to have severe symptoms.

The analysis of the efficacy of the vaccine based on the length of the time between boosters showed that efficacy was high when the booster was given at 2 months and increased with longer intervals.

The vaccine efficacy after two standard doses was 55.1% with an interval of less than 6 weeks and 81.3% when the two doses were more than 12 weeks apart.

When information from participants who received a single dose was analyzed, a single standard dose of vaccine provided protection against symptomatic COVID-19 in the first 90 days with an efficacy of 76.0%. There was no waning of protection observed during the study period after only a single dose.

While there was no waning of protection observed over the course of the study period, the amount of antibodies detected did decrease over time. The amount of antibodies peaked at day 28 and then decreased by 34% by 90 days after vaccination and 64% by 180 days after vaccination.

The trial that was conducted in the United Kingdom included periodic PCR-based testing regardless of symptoms, allowing for an assessment of the prevention of transmission based on the amount of asymptomatic and symptomatic cases. The protection from asymptomatic or symptomatic infection after the second dose was 49.5%.

Based on the available information, the authors conclude that the AstraZeneca-Oxford vaccine provides protection from COVID-19 with dosing intervals that range from less than 6 weeks to 12 weeks or more and that a longer interval before the booster dose provides better protection and does not compromise the available protection in the 3-month period before the second dose is administered.

Results from On-Going Vaccination Campaigns

The effects of on-going vaccination campaigns are starting to become evident as the number of individuals fully vaccinated increases.

Nursing Home Deaths decline with Vaccination

As of February 25, 2021 in the United States, the number of cases and deaths from COVID-19 at nursing homes has been decreasing (Conlen et al., 2021).

Between late December and early February, the number of new cases at nursing homes fell by 80% while deaths dropped by 65%.

The reduction in the number of new cases and deaths occurred even with increases in general population of the United States. The effect is thought to be due to vaccination of residents and staff of the facilities. Based on records from the CDC, about 4.5 million residents and staff at the facilities had received at least one dose of vaccine by late February with 2.1 million fully vaccinated.

Results from Israel's Vaccination Campaign

Israel has been able to vaccinate an estimated 84% of their population that is over the age of 70 as of February, 2021 (Rinott et al., 2021). In order to determine the effect of vaccination, researchers evaluated the rate of mechanical ventilation in individuals over the age of 70 and those under the age of 50. The vaccination rate for those under the age of 50 was the lowest in the country with 9.9% having had both doses of the vaccine. The ratio of individuals with COVID-19 over the age of 70 who required mechanical ventilation declined 67% compared to those aged less than 50 years between December of 2020 and February of 2021.

The researchers state that "these findings provide preliminary evidence of the effectiveness of vaccines in preventing severe cases of COVID-19 at the national level."

A second study evaluated the effect of vaccination of 596,618 individuals in Israel with the Pfizer-BioNTech vaccine compared to the same number of similar individuals who did not receive the vaccine (Dagan et al., 2021). Information on individuals was obtained from medical records provided by Clalit Health Services, which is one of the four integrated healthcare organizations in Israel and covers approximately 53% of the country's population. The outcomes assessed by the researchers were: documented SARS-CoV-2 infection, symptomatic COVID-19, hospitalization for treatment of COVID-19, severe illness from COVID-19, and death from COVID-19.

The participants were over the age of 16 and had not had a previous, documented case of COVID-19. The group included participants who were vaccinated between December 20, 2020, and February 1, 2021. Overall, the participants were younger than the general population because there were few older individuals available who had not yet been vaccinated for inclusion in the comparison group. The median age of the participants was 45 with a range from 35 to 62. Evaluation of the medical records of participants indicated that 96% received a second dose of the vaccine, and 95% received their second dose before day 24. The variant B.1.1.7, was becoming increasingly prevalent during the study period, and by the end up to 80% of tested samples were B.1.1.7. B.1.351 was still rare in Israel at the time of the study. The results of the analysis is listed in Table 1.

Table 1. Effectiveness of Pfizer-BioNTech in Israel

	14-20 Days after First Dose	21-27 Days after First Dose	7 Days after Second Dose
Effectiveness in prevention of documented infection	46%	60%	92%
Effectiveness in preventing symptomatic COVID-19	57%	66%	94%
Effectiveness in preventing hospitalization for COVID-19	74%	78%	87%
Effectiveness in preventing severe illness	62%	80%	92%
Effectiveness in preventing death	72%	84%	Not Reported

The effectiveness of the vaccine in preventing death after the second dose was not reported because there were too few individuals in the vaccinated group for a statistically relevant analysis.

The effectiveness of the vaccine against asymptomatic infection was found to 29% within 14 to 20 days after the first dose, 52% during days 21 to 27 after the first dose, and 90% 7 days or more after the second dose.

The effectiveness of the vaccine was found to be similar across the age groups included in the study while there was a slightly lower effectiveness in individuals with multiple co-existing chronic conditions. The number of symptomatic infections observed in the trial began to diverge between the vaccinated group and unvaccinated group around 12 days after inoculation, which suggests that protection begins around this time. A similar trend was observed in the Phase 3 clinical trial.

With the high level of interest in the protection afforded by a single dose of the vaccine, the researchers also determined the efficacy during the period between the first and second dose, which was 29% as mentioned above. In the clinical trial of the Pfizer-BioNTech vaccine, the estimated efficacy to prevent infection between the first dose and the second dose was higher, at 52%. The difference in the level of prevention is thought to be due to the high level of transmission in the country at the time of this study. The higher amount of transmission would mean that participants had a higher risk of exposure in the first weeks of this study when the immune response is still weak when compared to conditions during the earlier clinical trial. To exclude the infections that may have occurred before the immune response, the researchers also determined the effectiveness of the vaccine to prevent COVID-19 14 to 20 days after the first dose and found it was 57%, which is similar to that observed in the clinical trial.

Results from England's Vaccination Campaign

A study from Public Health England, called the SARS-CoV-2 Immunity and Reinfection Evaluation (or SIREN) Study, is investigating the effectiveness of previous infection on immunity from SARS-CoV-2 as well as the effectiveness of available vaccines (Hall et al., 2021). The participants in the study are healthcare workers and support staff in publicly funded hospitals in the United Kingdom. As of December 7, 2020, there were 29,378 participants in the SIREN study, and 23,324 of those qualified for this analysis. Out of this group, 35% had had a previous positive test for COVID-19, based on both antibody tests and PCR-based RNA tests. The vaccines administered in this study were from Pfizer-BioNTech and AstraZeneca-Oxford.

At least one dose of either vaccine was administered to 89% of participants by February 5, 2021. Most of the individuals (or 94%) received the vaccine from Pfizer-BioNTech. Only 8% of the participants had received a second dose by February 5. Of those who received two doses, the median length of time between doses was 23 days with a range from 19 to 28 days. The researchers found that protection from infection began from day 10 after vaccination and increased after that point.

Participants in the study were tested for COVID-19 every two weeks for at least two months after being vaccinated due to their roles in hospital settings. During the study, there were 977

new infections from SARS-CoV-2. Within the 21 days after the first dose of vaccine, there were 71 new infections in vaccinated participants, and there were nine infections in the seven days after the second dose in those who were fully vaccinated. The effectiveness of a vaccine in preventing both asymptomatic and symptomatic cases allows for the estimation of the reduction in transmission.

When only those participants who had not tested positive for COVID-19 before vaccination were included in the analysis, the effectiveness 21 days after the first dose was 72%, and it was 86% seven days after the second dose.

There was not enough information to determine the protection for the individuals who had had a positive COVID-19 test before inoculation, but previous investigations indicate that this group of participants had 90% protection from re-infection based on the immune response from natural infection.

This study occurred during a time when the B.1.1.7 variant was widespread in the United Kingdom and shows that the Pfizer-BioNTech vaccine is effective in prevention of COVID-19 from the variant.

The small number of people who had been vaccinated with the AstraZeneca vaccine prevented an analysis of the effectiveness in the time period of this study.

Another report of the vaccination of healthcare workers at Cambridge University Hospitals was released as a pre-print (Weekes et al., 2021). Researchers compared the number of positive tests for unvaccinated workers with those less than 12 days after the first vaccine dose and those more than 12 days after their first dose. There were 26 positive tests out of 3,252 unvaccinated individuals tested, 13 positive tests out of 3,535 individuals tested less than 12 days after the first dose, and 4 positive tests out of 1,989 individuals tested more than 12 days after the first dose.

The researchers estimated that there is a four-fold decrease in the risk of asymptomatic SARS-CoV-2 infection amongst healthcare workers 12 days or more after vaccination with one dose.

A third report of the vaccination campaign in the United Kingdom targeting elderly individuals was also provided by Public Health England (Bernal et al., 2021). The researchers evaluated the PCR-based testing data between October 26, 2020 and February 21, 2021 from individuals with symptoms that were not healthcare professionals. There were 156,930 individuals who were tested during the study period that also had vaccination records available, and in this group, 28.4% of the tests were positive for COVID-19.

In individuals 80 years or older who received the Pfizer-BioNTech vaccine, the odds of testing positive for COVID-19 began to decrease ten to 13 days after the first dose. The odds continued to decrease after that and plateaued between 28 and 34 days after the first dose and remained steady after that. When compared to individuals who were not vaccinated, the vaccine effectiveness for this period was 70%. From 14 days after the second dose, evaluation of the odds of a positive COVID-19 test indicated a vaccine effectiveness of 89%.

After January 4, 2021, the age limits for eligibility expanded to include individuals over the age of 70. The vaccine effectiveness for the Pfizer-BioNTech vaccine increased in a similar manner until 28 to 34 days after vaccination and then plateaued at 61%. During this time, it was also decided to delay the second dose of vaccination to increase the number of individuals in the United Kingdom who were at least partially vaccinated so no second doses were given.

The AstraZeneca-Oxford vaccine also was authorized and put into use on January 4, 2021. In individuals over the age of 70, the odds of testing positive for COVID-19 began to decrease 14 to 20 days after the first dose. The odds continued to decline until 28 days after the first dose, and the effectiveness at this time was calculated to be 60%. At 35 days after vaccination the odds were still decreasing, and the calculated effectiveness was 73%. The second dose was also delayed in this group.

In addition to the protection from symptomatic disease, the researchers also observed protection from emergency hospitalization and death after vaccination with both vaccines. The Pfizer-BioNTech vaccine provided a 43% reduction in the risk for hospitalization within 14 days of a positive COVID-19 test, and a 51% reduction in the risk of death within 21 days of a positive COVID-19 test. The AstraZeneca vaccine provided a 37% reduction in the risk for hospitalization within 14 days of a positive test. The risk of death associated with the AstraZeneca-Oxford vaccine could not yet be determined due to the length of time from its authorization.

These results were determined at the time B.1.1.7 became the predominant strain in the country, suggesting that both vaccines are also effective against the variant.

Based on the study, the authors conclude that combined with the effect against symptomatic disease, a single dose of either vaccine is approximately 80% effective at preventing hospitalization, and a single dose of the Pfizer-BioNTech vaccine is 85% effective at preventing death from COVID-19.

Immune Response to Prevent Re-Infection with SARS-CoV-2

Questions about the length of protection from the immune response after SARS-CoV-2 infection remain, in part, because of the newness of the virus. Researchers at the National Cancer Institute, a section of the United States National Institutes of Health, evaluated results from commercial testing laboratories to determine the proportion of individuals who tested positive for COVID-19 after having a previous positive antibody test (Harvey et al., 2021).

The researchers surmised that if few people who were positive for SARS-CoV-2 antibodies later tested positive for COVID-19 via PCR-based testing, they could estimate the risk for re-infection from SARS-CoV-2.

The information for the analysis came from 70 different commercial companies and includes de-identified laboratory information, electronic health records, and other data describing COVID-19 status. The information collected represents more than 50% of the commercial diagnostic and antibody testing in the United States. The study included evaluation of 3,257,478 unique individuals who received results from an antibody test on or after January 1, 2020 with the end

of the study period on August 26, 2020. Within this group, 88.3% received negative antibody results, 11.6% had positive antibody results, and 0.1% had inconclusive results.

Over the study period, 2.6% of those with an initial positive antibody test had a subsequent antibody test, allowing for assessment of the length of the antibody response to COVID-19. There were 12.4% of the individuals who had a negative antibody test within 30 days after a previous positive test. The proportion of individuals with a negative antibody test increased to 18.4% within 90 days of the initial test.

These results are consistent with previous studies indicating that antibody levels wane in a modest fraction of individuals over a period of months after initial detection.

The researchers then looked at the risk of having a positive PCR-test after an initial positive antibody test. As the time from the initial positive antibody test increased, fewer participants received a positive PCR-based test. Within 30 days of the initial antibody test, 11.3% had a subsequent positive PCR-based test, which was attributed to prolonged shedding of viral RNA as has been reported previously. Of the measurements 31 to 60 days after a positive antibody test, 2.7% had a positive PCR-based test. Testing 61 to 90 days after the positive antibody test produced 1.1% positive PCR-based tests, and testing 90 days or more after the antibody test resulted in 0.3% positive PCR-based tests. Over the entire length of the study period, the rate of positive PCR-based tests from individuals who had a negative antibody test at the start of the study was relatively consistent around 3%, suggesting a stable background infection rate over the course of the study.

Based on the ratio of positive PCR COVID-19 tests in those with and without antibodies, the researchers report an approximate 10-fold decrease in infections in those with evidence of a previous SARS-CoV-2 infection, suggesting a protective effect from antibodies produced.

A similar reduction in the risk of re-infection was apparent when the researchers analyzed the data based on different regions of the United States. The overall level of reduction of the country was similar to the reduction observed in the different regions, suggesting that the reduction was not from local differences in testing or transmission rates.

In an accompanying editorial, Mitchell H. Katz from NYC Health and Hospitals in New York, New York, discusses how to advise individuals who have tested positive for antibodies to COVID-19 (Katz, 2021). He mentions that there have been questions about the accuracy of tests used to detect antibodies as well as concerns about how long and how well an immune response to a previous infection with SARS-CoV-2 protects an individual. He also indicates that the results reported in the study from Harvey and colleagues are reassuring in regards to both concerns.

Based on the study, the antibody tests appeared to be accurate and able to identify those who were protected from re-infection.

The results reported by Harvey and colleagues also agree with another study of healthcare workers with a positive antibody test who had a lower risk of re-infection.

The question that has still not been answered, however, is how long the protection will last. Review of the available information led Dr. Katz to recommend that:

All individuals should be vaccinated regardless of evidence of previous infection from antibodies or diagnostic testing.

Re-Infection at Nursing Homes

Officials from the Kentucky Department of Public Health investigated two COVID-19 outbreaks that occurred at a skilled nursing facility three months apart in October, 2020 and in July, 2020 (Cavanaugh et al., 2021). There were five residents of the facility that tested positive for COVID-19 during both outbreaks. The five individuals ranged in age between 67 and 99, and each had more than three chronic, underlying conditions. None were immunocompromised or were taking immunosuppressive medications.

Three of the five individuals were asymptomatic during their first illness, and two had mild symptoms that had resolved before the start of the second outbreak. Testing samples from the first outbreak were not retained, so that it was not possible to compare the genomic sequence and confirm two separate infections. However, all five individuals had at least four consecutive negative PCR-based tests between the two outbreaks, suggesting that the second positive test was not re-activation of the first infection.

During the second outbreak, all five experienced symptoms, and the two residents who had mild symptoms with their first infection experienced more severe symptoms during the second infection. One resident required hospitalization for treatment and subsequently died.

The authors of the study suggest that the mild cases of COVID-19 experienced during the first outbreak may not have produced sufficiently robust immune response to prevent re-infection.

Individuals also experience a decline in immune system function with age that might be related to the re-infection with COVID-19. Overall, it has been found that re-infection with SARS-CoV-2 seems to be rare, but the characteristics associated with a poor immune response to the virus are not known.

The authors conclude that steps to protect this population from the ongoing potential of SARS-CoV-2 exposures should be implemented, including among those who have previously had a COVID-19 diagnosis.

SAR-CoV-2 Transmission

The FDA and USDA released a statement reiterating that there is no evidence of food or food packaging acting as a source of viral transmission of SARS-CoV-2 (FDA-USDA, 2021). Based on experience over the last year, the groups stress that food and packaging are highly unlikely to spread SARS-CoV-2. There have been studies that detected SARS-CoV-2 on packaging, but most use PCR-based testing that detects the viral RNA and not live virus.

The officials stated that "Given that the number of virus particles that could be theoretically picked up by touching a surface would be very small and the amount needed for infection via oral inhalation would be very high, the chances of infection by touching the surface of food packaging or eating food is considered to be extremely low."

Transmission at Gyms

Researchers at the CDC reported two instances of rapid spread of SARS-CoV-2 at exercise facilities, suggesting that improved protocols may be necessary to control transmission in these environments.

The first instance occurred in Hawaii in June and July, 2020 (Groves et al. 2021). An instructor at two Honolulu fitness facilitates tested positive for COVID-19 after teaching several classes. Based on contact tracing, 21 COVID-19 cases were linked to the instructor. At the time of the incident**,** masks were not required in fitness facilities.

Approximately 60 hours (more than two days) before symptom onset, the instructor taught a yoga class while wearing a mask, zero of 33 people in the class became ill. None of the participants reported wearing a mask during the class. Around 40 hours (1 to 2 days) before his symptoms started, the instructor taught a one-hour high-intensity cycling class for 10 participants. Neither the instructor nor the participants wore masks, but the cycling stations were six feet of more from each other. Four of the participants only had exposure to the instructor in this class, and none of the four became ill. Six participants had a second exposure to the instructor the next day. The day that his symptoms began, or about four hours before symptoms onset, the instructor taught a one-hour cycling class with 10 participants in the same facility and room as the class the previous day. Again, no one wore a mask, but the cycle stations were six feet or more from each other.

All 10 participants in the second cycling class received a positive SARS-CoV-2 PCR test within the next week, which corresponds to an attack rate of 100%.

One of the participants in the second cycling class was also a fitness instructor who subsequently taught classes after being exposed. Two days after his exposure in the cycling class, and more than two days before his symptoms started, he taught five personal training and small-group kickboxing sessions. During the morning sessions both the instructor and the participants wore masks, but in the afternoon, no one wore a mask. One participant had a negative COVID-19 test and five individuals had no symptoms over the next 14 days, but were not tested. Four of the individuals had additional exposure at another time.

Approximately 36 hours before his symptoms began, the instructor provided personal training to four different participants, and no one wore a mask. One of the participants in this group tested positive for COVID-19 five days later.

On the same day his symptoms began, or around 12 hours before symptom onset, the second instructor taught 10 participants (one personal training and three kickboxing sessions with nine participants) with the caregiver present for a total of 11 exposed individuals, and the instructor did not wear a mask. Four of those participating on this day had been exposed previously. Two participants wore masks, but both were infected. Overall, ten out of the eleven people exposed tested positive for COVID-19, which corresponds to an attack rate of 91%.

Out of the 21 secondary cases linked to the first instructor, 20 had symptoms during their illness, and two were hospitalized.

The timing of exposure to the onset of symptoms for the instructors was associated with the attack rate in the classes. Individuals who were exposed on the same day both instructors' symptoms started were more likely to become ill.

The timing of exposure and attack rate for both instructors:

- Exposure more than two days before symptom onset had an attack rate of 0% (0 out of 33)
- Exposure 1 to 2 days before symptoms onset had an attack rate of 13% (1 out of 8)
- Exposure on the same day as symptom onset had an attack rate of 95% (20 out of 21)

The authors conclude that the rate of transmission was highest on the day of symptom onset for both instructors, which is consistent with findings from previous studies.

Transmission in the facilities in Hawaii was likely facilitated by not wearing face masks, extended close contact, and poor room ventilation. The transmission in the community was considered low at the time of the incident, reiterating that specific environments are more likely to lead to transmission of the virus.

The second incidence of rapid spread in an exercise facility occurred in Chicago, Illinois between August 24 and September 1, 2020 (Lendaki et al., 2021). The facility offered four to eight high-intensity indoor classes daily with classes at less than 25% capacity, or 10 to 15 people. Mask use, temperature checks, and symptom screenings were required on entry, but masks were not required during exercise. During the classes, patrons brought their own mats and weights and were stationed more than six feet apart.

The first reported case at the facility was diagnosed on September 1, 2020, and the individual had last attended a class on August 28, which was also the day of their symptom onset. The facility then closed for 13 days. There were 81 individuals identified that had attended classes

between August 24 and September 1. There were 55 cases of COVID-19 identified, with 60% confirmed by testing and 7% probable based on symptoms and exposure.

Of those identified with COVID-19, 78% participated in multiple classes while potentially infectious.

The frequency of mask use during the classes was also investigated, and 76% reported infrequent mask use.

A number of the individuals reported symptoms during their illness with 40% reporting a fever. Two of those that became sick were treated at the emergency department for their symptoms, and one individual required hospitalization. No deaths were reported.

The Chicago Department of Public Health attributed this outbreak to the high proportion of attendees with COVID-19 who participated in class while symptomatic or asymptomatic and infectious.

Transmission in Schools

The regional and state public health departments in Georgia investigated and reported on an outbreak in eight public elementary schools that occurred between December 1, 2020 and January 22, 2021 (Gold et al., 2021). During the time frame of the investigation, 2,600 students and 700 staff members attended elementary school in person, which correlates to approximately 80% of the district's elementary school students. The transmission rate in the county increased by approximately 300% during the same time frame. In total, nine clusters were identified that included 13 educators and 32 students occurring at six schools.

The educator was the index patient for four clusters, a student was the index patient for one cluster, and it could not be determined who the index patient was in four clusters.

Eight of the clusters included educator-to-student transmission, and four clusters included student to student transmission. There were two clusters where educator to educator transmission during in-person meetings or lunches was followed by educator to student transmission. This scenario of educator to student transmission led to 48% of the school associated cases.

Officials also found that conditions in the schools were not optimal for the prevention of transmission. For example, students were separated by plastic shields, but were sitting less than three feet from each other due to the high capacity and classroom layouts. There was also evidence of transmission between educators and students during small group interactions with close proximity between participants. Mask use was mandated at all times except while eating, and reported and observed compliance was high.

There were five reported instances of inadequate mask use that may have contributed to clusters of transmission. Students ate in the classrooms where distancing was difficult. There

were also interactions between staff during lesson planning and lunches where less safe interactions were noted.

The authors conclude that educators can play an important role in in-school transmission and that in-school transmission can occur when physical distancing and mask compliance are not optimal.

Other studies in Europe have indicated that the type of transmission that occurs most often in schools is between educators. The researchers of the current study state that promotion of measures to prevent transmission between educators will likely reduce in-school transmission.

SARS-CoV-2 Variant Updates

The long period with high transmission has led to the detection of several variants, including two in the United States.

P.1

Researchers have published a pre-print of a study describing the characteristics of the variant P.1 that was first detected in Brazil (Scheuber and van Elsland, 2021). Seventeen mutations were found in the variant with three of interest in the spike protein, K417T, E484K, and N501Y. The N501Y mutation was previously identified in B.1.1.7 and is thought to increase the transmissibility of the virus.

Indeed, the researchers determined that P.1 is between 1.4 and 2.2 times more transmissible than early variants of SARS-CoV-2.

Based on modeling in the study, P.1 increased from 0% of cases to 87% of cases in seven weeks (CIDRAP, 2021). The three mutations were also found to increase the binding of the spike protein to the ACE2 receptor, the protein on human cells used by the virus to infect a cell.

Other changes in the spike protein, such as E484K, in P.1 cause antibodies produced by the body to bind poorly to the spike protein, and **from 25% to 61% of previously infected people may be susceptible to re-infection**, which was apparent in the high re-infection rates recently observed in the Brazilian city of Manaus. Researchers also determined that the P.1 variant is associated with a **1.1 to 1.8 times increase in risk of mortality** compared to previously circulating variants.

In another pre-print, researchers also described the effect of P.1 virus on antibody binding and activity (Souza et al., 2021). The researchers used live P.1 virus and measured the ability of convalescent plasma from individuals infected with earlier variants of SARS-CoV-2 and antibodies from individuals vaccinated with the CoronaVac vaccine (developed by Sinovac) to neutralize the virus. The antibodies in the convalescent plasma had a 6-fold lower neutralizing ability for P.1 compared to previous versions of SARS-CoV-2. Additionally, antibodies produced after vaccination with CoronaVac failed to efficiently neutralize the P.1 virus.

B.1.526

Two groups have identified a new variant that is becoming more prevalent in the Northeast and specifically New York City (West et al., 2021 and Annavajhala et al., 2021). The variant is in the lineage B.1.526 and contains several of the mutations also observed in the B.1.351 variant. Most concerning is the presence of the E484K mutation that reduces the effect of antibodies. The N501Y mutation that was first observed in the B.1.1.7 mutation is not present in B.1.526.

The first instances of the B.1.526 variant were detected in November, 2020, and the proportion of cases rose to 12.3% in the last two weeks of February, 2021 according to Annavajhala and colleagues. The other research group, West and colleagues, detected higher levels of the new variant with approximately 25% of the coronavirus genomes sequenced and deposited from New York during February 2021.

The individuals with B.1.526 were found to be older than individuals infected with the initial form of the virus, 58.1 years versus 52.4 years, but there was no difference in the gender, race, or ethnicity between individuals with the two variants.

Individuals with B.1.526 were more likely to require treatment in the emergency department or be admitted to the hospital, 85.9% versus 70.8%.

B.1.427/B.1.429

The variant referred to as B.1.427 or B.1.429 was first identified in Southern California, but has now been found to make up more than 50% of the samples collected in 44 counties in the state Wadman, 2021). Researchers have found that it is more contagious than previous versions of the virus and also associated with higher rates of admission to the intensive care unit. There is also evidence that the mutations in B.1.427/B.1.429 allow it to evade the immune system, and potentially lead to re-infections as observed with B.1.351 and P.1. The surge observed with this variant was noteworthy, however, the increase in the rate of transmission seems to be below the level of B.1.1.7, the variant responsible for surges in Europe (Achenbach and Johnson, 2021).

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