PINNACLECARE

Medical Intelligence Report

Date: June 9, 2021

Topic: COVID-19 Research Update

COVID-19 Pandemic Trends

In the United States, ten states (Pennsylvania, Vermont, Hawaii, New Hampshire, Massachusetts, Connecticut, Maine, New Jersey, Rhode Island, and New Mexico) had reached the goal of 70% of eligible residents having at least one dose of a COVID-19 vaccine as of May 27, 2021 (Soucheray, 2021b). There are an additional ten states that had reached 65% coverage and were approaching the 70% goal outlined by the White House. At least 25 states have fully vaccinated at least 50% of their adult residents (Soucheray, 2021).

The increase in the number of people who are vaccinated has led to decreases of 23% in the number of new daily reported COVID-19 cases in the United States with associated deaths falling by 9.1% and COVID-related hospitalizations falling by 10.5%.

There have been large decreases in the number of COVID-19 related deaths at long-term care facilities as well (Bao and De Jesus, 2021). At this time last year, more than 43% of the COVID-19 deaths in the United States were associated with long-term care facilities, and now the deaths of people connected to the facilities has dropped to 31% of the COVID-19 deaths in the United States. In mid-January of 2021, there were more than 5,000 deaths a week in long-term care facilities in the United States. In March of 2021 the number of reported deaths had fallen to fewer than 300 deaths a week.

However, when the number of cases occurring in individuals who have not been vaccinated is separated from those who are vaccinated, the case rate, or daily, new reported cases per 100,000 people, is nearly as high in some areas as it was during the national surge that occurred in December, 2020 and January, 2021 (Keating and Shapiro, 2021). Nationally, the vaccination rate is approaching the 70% goal, but when looking at state populations or smaller locales, there are areas with much lower rates of vaccination (Jiménez, 2021). For example, there are 15 states where 50% or less have received at least one dose of vaccine. Mississippi has the lowest vaccination rate in country with 34% of the population having received at least one dose, and in some parishes in Louisiana, less than 20% of people have received even one dose.

The rate of new cases is 73% higher for unvaccinated individuals compared to the national average, which includes the rate for both vaccinated and unvaccinated individuals.

The rate of hospitalization and death for unvaccinated people also remains high, at levels nearly the same as it was two to three months ago.

In other words, the pandemic is spreading as fast among the unvaccinated as it did during the winter surge.

There are six states where the average new daily deaths per one million unvaccinated residents is 50% higher than the overall national rate that includes both vaccinated and unvaccinated individuals. Additionally, the death rate for unvaccinated individuals has remained at the same level, rather than declining as it has in those who have been vaccinated, meaning that unvaccinated people are not safer.

Data from Maryland indicates that unvaccinated young adults in the state have the same infection rate as they had during the January surge in COVID-19 cases. Furthermore, **the risk of hospitalization among those who are infected is more than double the risk reported in January**, which is thought to be due to the spread of variants of the virus. Officials in Washington state have also reported an increased risk of hospitalization for unvaccinated residents. For example, unvaccinated individuals over 65 years old were 11-times more likely to be hospitalized and those 45 to 64 were 18-times more likely to require hospitalization for COVID-19.

The CDC has a COVID-19 surveillance system that monitors laboratory-confirmed COVID-19–associated hospitalizations in 99 counties across 14 states, accounting for approximately 10% of the population of the United States (Havers et al., 2021). In order to better understand potential changes in the infection rates for individuals aged 12 to 15 who are now eligible for vaccination, the CDC examined the COVID-19–associated hospitalizations among adolescents aged 12 to 17 years between January 1 and March 31, 2021. During this time period, there were 204 adolescents hospitalized primarily for COVID-19 with 31.4% also requiring treatment in the intensive care unit and 4.9% requiring mechanical ventilation.

Between March 1, 2020 and April 24, 2021, hospitalizations for adolescents rose to the highest level in January of 2021 at 2.1 per 100,000, which corresponds to a surge of cases in COVID-19 in the United States. The number of hospitalizations declined in March, 2021 to 0.6 per 100,000, but increased again in April to 1.3 per 100,000.

The authors report that the "cumulative COVID-19–associated hospitalization rates during October 1, 2020 to April 24, 2021, were 2.5 to 3.0 times higher than were influenza-associated hospitalization rates from three recent influenza seasons."

Updates on Variants

Naming of Variants

In order to simplify the naming of emerging variants of SARS-CoV-2, the WHO announced a new naming convention that utilizes the Greek alphabet (WHO, 2021). This system allows for an easy-to-remember name without the possible negative association for names tied to geographic areas. As the scientific nomenclature is becoming increasingly complex due to genomic branching of the variants, it has become difficult to use in everyday discussions. The new names and the previous names of the current variants of concerns are listed in Table 1 (WHO, 2021).

Table 1. The new nomenclature from the WHO.

WHO Label	Pango Lineage	GISAID Clade or Lineage	Nextstrain Clade	Earliest Documented Samples	Date of Designation
Alpha	B.1.1.7	GRY (GR/501Y.V1)	20I/S:501Y.V1	United Kingdom,Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J/S:501Y.V3	Brazil,Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/452R.V3	21A/S:478K	India,Oct-2020	

Spread of Variants

The Delta variant, previously known as B.1.617.2, has spread to numerous countries and branched into at least three subtypes that have been identified (Adam, 2021). Delta has been found to be more transmissible than the initial form of SARS-CoV-2 from the start of the pandemic and also more transmissible than the Alpha variant, previously known as B.1.1.7.

Based on early estimates, researchers have stated that Delta may be 50% more transmissible than Alpha.

In England, approximately 50% of infections are from the Delta variant, replacing Alpha as the most prevalent form. Genomic sequencing suggests that the number of infections with the Delta variant could be growing by 13% more than Alpha infections each day. Fortunately, there has not been a large rise in the overall number of cases in the United Kingdom. Rather, one variant is replacing the other as the most dominant observed.

Public Health England released the results from a new study that shows that two doses of either the Pfizer-BioNTech or AstraZeneca-Oxford vaccines were effective against the Delta variant of SARS-CoV-2 (PHE, 2021). A single dose of the vaccines gave only partial protection, however.

Results from the study of Delta variant

- The Pfizer-BioNTech vaccine was 88% effective against symptomatic disease caused by the Delta variant two weeks after the second dose compared to 93% effective against the Alpha variant.
- The AstraZeneca-Oxford vaccine was 60% effective against symptomatic disease caused by the Delta variant two weeks after the second dose compared to 66% effective against the Alpha variant.
- Both vaccines were 33% effective against symptomatic disease from the Delta variant after the first dose compared to 50% effective against the Alpha variant.

Mechanism of Increased Transmission of the Alpha variant

The Alpha variant, previously known as B.1.1.7, has been shown to be more transmissible than the initial forms of SARS-CoV-2 present at the beginning of the pandemic. Initial assessments showed that some of this increase was due to changes in the spike protein of the virus, but researchers have also found changes in other parts of the virus that contribute to the increased ability to infect susceptible individuals (Thorne et al., 2021). Two other viral proteins, Orf9b and Orf6, are known to suppress the innate immune response during infection. The researchers found mutations in Orf9b and Orf6 that led to changes in human cellular responses. The changes in the cellular responses seem to lead to a larger suppression of the innate immune response, which is the non-specific response of immune cells to all pathogens, allowing the Alpha variant to replicate better and increase the duration of infection.

Updates on Vaccination

Vaccination in Individuals with Cancer

Individuals who are being treated for cancer often have a lower immune response and are more susceptible to infections, and they have also been found to have poorer outcomes after infection with SARS-CoV-2. Therefore it is important to determine if the lowered immune response also changes the response to COVID-19 vaccination in individuals being treated for solid tumors. Researchers performed a clinical trial that included 102 adult participants with solid tumors who were undergoing active intravenous-anticancer treatment as well as 78 healthy individuals who both received the second dose of the Pfizer-BioNTech vaccine at least 12 days before the start of the study (Massarweh et al., 2021).

The researchers measures the antibodies in the bloodstream of the participants, and 90% of those being treated for cancer had detectable antibodies against the SARS-CoV-2 spike protein after the second vaccine dose. In the healthy control group, all of the individuals had detectable levels of antibodies. The median level of antibodies in the group of participants being treated for cancer was lower than that in the healthy individuals, and the only variable that was significantly

associated with lower antibody levels was treatment with chemotherapy plus immunotherapy (or antibody based cancer therapy).

The authors conclude that vaccination of individuals with solid tumors is important and effective, even during anti-cancer therapy.

Breakthrough Infections

After authorizing the use of three vaccines for use against COVID-19, the CDC has been monitoring for breakthrough infections, or infections that occur after vaccination for a virus (CDC Breakthrough Investigation Team, 2021). The surveillance began on January 1, 2021 and ended on April 30, 2021, and at the end of the surveillance, the investigation team published a report on the information that had been collected. As of May 1, 2021, data is only being collected on individuals who are hospitalized or die from COVID-19 in order to focus on the cases of highest clinical and public health significance.

There were a total of 10,262 breakthrough cases of COVID-19 reported from 46 states and territories as of April 30, 2021.

This number is most likely an underrepresentation of the actual number of breakthrough infections due to an expected high number of asymptomatic cases where an individual may not have known they were ill.

Of the officially reported breakthrough cases, 27% were asymptomatic, 10% of patients were hospitalized, and 2% died.

Not all of the individuals who were hospitalized were hospitalized for the treatment of COVID-19. Some were tested upon admission and found to be positive through standard testing procedures. Of the 995 individuals with breakthrough infections who were hospitalized, 29% were asymptomatic or hospitalized for a reason unrelated to COVID-19. The median age of individuals who died was 82 years with a range from 71 to 89, and 18% died from a cause that was unrelated to COVID-19.

Interestingly, 66% of the breakthrough infections were found to be due to one of the forms of SARS-CoV-2 classified as variants of concern by the WHO and listed in Table 1.

The Alpha variant, previously known as B.1.1.7, was the most prevalent at 56% of the variants of concern identified as a breakthrough infection. The Beta variant, previously B.1.351, and Gamma variant, previously P.1, were present at low levels, 8% and 4%, respectively.

On a state level, breakthrough infections were also found to be associated with variants of SARS-CoV-2 (McEwan et al., 2021). Researchers at the University of Washington performed genomic sequencing on 20 samples from cases of vaccine breakthrough infections identified at their institutions and partners. The median range in age for the individuals was 43 with a range from 23 to 65 years. All 20 of the samples were found to be variants of concern. As with the

national-level data, the Alpha variant was the most prevalent in 40% of the samples. The Beta variant made up 10% of the samples, and Gamma was present in 5%.

For comparisons sake, the researchers also looked at the proportions of the different variants in the cases in Washington state that were sequenced at the university lab. Overall, 68% were found to be variants of concern with a 31% rate of the Alpha variant, 1% rate of the Beta variant, and 7% of the Gamma variant.

Based on this analysis, variants of concern made up a higher proportion of the breakthrough cases compared to all COVID-19 cases, with an increased frequency of 1.47-times more in the breakthrough infections than in regular infections.

When evaluated by itself, the Alpha variant was 3.38-times more common in breakthrough infections compared to regular infections.

Myocarditis after Vaccination

Public health officials in Israel have issued a press release describing several incidences of myocarditis, or inflammation of the heart muscles, after vaccination for COVID-19 with the Pfizer-BioNTech vaccine (IMOH, 2021). Based on the report, the myocarditis was usually a mild illness characterized by chest pains, shortness of breath, or rapid heart palpitations. There have been 275 cases of myocarditis reported in Israel between December, 2020 and May, 2021, and 148 of these cases occurred at a time near vaccination for COVID-19, making them potentially associated with vaccination.

Characteristics of individuals with myocarditis around the time of COVID-19 vaccination

- 27 cases occurred after the first dose
- 121 cases occurred after the second dose
- Those were affected were mainly younger men between 16 and 19
- Most cases were treated in the hospital for up to 4 days
- 95% were considered mild cases

The officials conclude that “There is some probability for a possible link between the second vaccine dose and the onset of myocarditis among young men aged 16 to 30.”

Cases of myocarditis around the time of vaccination for COVID-19 have also been reported in the United States (Soucheray, 2021). Based on the data collected, the cases are mild, often follow the second dose of mRNA vaccine, and are seen more often in males than females. Less information has been released than in the report from Israel. However, there were also reports from the United States Department of Defense of 14 cases of myocarditis, and the European Medicines Agency (The European equivalent to the FDA, said they had received 107 reports of myocarditis following vaccination with the Pfizer-BioNTech vaccine (Vogel and Couzin-Frankel, 2021).

Researchers and physicians mention that the side effect seems to be very rare and is treatable, but that parents and pediatricians should be aware of youngsters with chest pain, shortness of breath, or rapid heart palpitations that occur after vaccination for COVID-19.

Immune Response to SARS-CoV-2

Researchers have determined that individuals who have been infected with SARS-CoV-2 have long-lived cells that produce antibodies to the virus both circulating in the blood and in bone marrow (Turner et al, 2021). In a study with 77 participants who had experienced mild cases of SARS-CoV-2, the level of antibodies to the virus were detectable, but declined rapidly in the first four months after infection and more slowly in the following seven months. While the levels declined, antibodies against SARS-CoV-2 remained detectable for the eleven months of the research study.

Importantly for long-term immunity, stable plasma cells (the cells that produce antibodies) were found in the bone marrow seven to eight months after infection, suggesting life-long production will occur.

Immune Protection Levels

When a disease is new, the extent of the response of the immune system to the pathogen to prevent reinfection must be determined. This threshold is important to ascertain the levels of immune components necessary for long-term protection after infection and after vaccination. With clinical studies from seven COVID-19 vaccines available and numerous studies of individuals who have recovered from COVID-19, researchers have been able to make the first estimates of the immune protection levels required for protection against infection from SARS-CoV-2 (Khoury et al, 2021).

Based on this information, in order to get 50% protection from SARS-CoV-2 infection (or a 50% efficacy), the neutralization level of antibodies produced in reaction to the vaccine needs to be at 20% of the mean level produced by individuals recovered from COVID-19. In order to get a 50% protection from a severe infection, a much lower level of neutralization is required, 3%. These values can be used in future research studies to screen potential vaccines for efficacy without the need of large trials early trials to determine efficacy.

Based on the decay rate of antibodies that occurs after vaccination that has been observed thus far, the researchers predict that vaccinated individuals will have a large loss in the protection from infection with the virus within about a year, but there will continue to be sufficient antibodies to prevent severe disease.

Changes to the Menstrual Cycle from COVID-19 or Vaccination

There are an increasing number of anecdotal reports of changes in women's menstrual cycles after infection with SARS-CoV-2 or vaccination. There is currently only a single published study on the effects of SARS-CoV-2 infection on women's reproductive systems, but it is reasonable that the inflammatory changes observed throughout the body during COVID-19 could also affect the reproductive organs, including the lining of the uterus (Youn, 2021).

In the study, the laboratory information from 237 women of child-bearing age was evaluated, and the menstrual data from 177 of group was also analyzed (Li et al., 2021).

Of the participants with menstrual data, 25% had changes in menstrual volume, and 28% had changes in the length of their menstrual cycle.

The most common changes were a decreased menstrual volume (in 20%) and a prolonged cycle (in 19%).

There was not a difference in the proportion of participants with a menstrual volume change between those with mild and those with severe COVID-19. However, individuals who had had a severe case of COVID-19 were more likely to have a longer menstrual cycle than those with mild disease. For example, 19% of participants who were mildly ill had a cycle longer than 37 days while 34% of those who had had severe COVID-19 had a cycle longer than 37 days.

There were no differences in hormone levels or ovarian reserve between individuals who had had COVID-19 and a healthy comparator group.

The participants in the study were checked on by telephone two months after discharge, and eight of the 36 with decreased menstrual volume had not returned to normal and two had improved symptoms. In those with disrupted cycle times, all had normalized except for one 44-year-old individual who may have been close to perimenopause.

The authors concluded that there were various changes in menstruation during and after COVID-19, including changes in volume and the length of cycles. While increases in the menstruation volume occurred less frequently in this group, it was more prevalent in those who had had COVID-19 than in the comparison group who had not had a SARS-CoV-2 infection. The follow-up observation in this study suggests that most changes that occur will be temporary. Previous research has shown that systemic complications are strongly correlated with menstrual changes, and "menstrual changes, which were often neglected by clinicians," may be likely to occur in those who have had an illness like COVID-19 that leads to multisystem dysfunction.

Importantly, there were no significant changes in sex hormone concentrations, suggesting that the ovarian endocrine system of female individuals with COVID-19 is not seriously affected.

There has also been misinformation circulating about an effect of vaccination on fertility of both women and men. In response to these false claims, The Association of Reproductive and Clinical Scientists and the British Fertility Society published guidance stating that there is no link between vaccines and fertility (Iacobucci, 2021).

The guidance states "There is absolutely no evidence, and no theoretical reason, that any of the vaccines can affect the fertility of women or men."

There have been cautions about getting vaccinated right before some in vitro fertilization steps because doctors will not perform the procedures if a patient has a fever, which could be a sign of infection. There are no other considerations that would affect the procedure or timing of vaccination.

CDC Recommendation Updates

The CDC updated their recommendations for the operation of day and overnight camps for children over the summer (CDC Guidance, 2021).

If it is possible for all participants and staff to be vaccinated, camps can operate at full capacity, without masking, and without physical distancing in accordance with the CDC's guidance for fully vaccinated individuals.

However, since there is no authorized vaccine for individuals under the age of 12, most summer camps will need to continue to implement safeguards to prevent transmission of SARS-CoV-2. As has been shown in multiple studies and different situations, consistent use of complementary and layered prevention strategies can help reduce the spread of COVID-19 and protect people who are not fully vaccinated including campers, staff, and their families.

The key prevention strategies that have been identified as reducing the risk of transmission of SARS-CoV-2 include

- Promoting vaccination for eligible individuals
- Correctly and consistently using well-fitted masks that cover the nose and mouth
- Physical distancing and staying in groups throughout the day to reduce exposure
- Handwashing and covering coughs and sneezes
- Avoiding crowded and/or poorly ventilated indoor activities
- Engaging in outdoor activities if possible and increasing ventilation when indoors
- Routine cleaning to help maintain healthy facilities
- Staying home when an individual has symptoms of a respiratory illness
- Testing for COVID-19 as recommended by the CDC with regards to symptoms or exposure to an infected individual.
- Contact tracing in combination with isolation and quarantine of sick individuals.
- Screening testing to detect asymptomatic cases.

The CDC has also updated their recommendations for mask use. As has been stated previously, consistent and correct mask use by people who are not fully vaccinated is especially important indoors and in crowded settings, when physical distancing cannot be maintained. However, there is limited evidence of transmission of SARS-CoV-2 outdoors due to the diluting effect of the air currents.

The recommendations for mask use remains the same for indoor activities with **all** unvaccinated individuals over the age of 2-years strongly encouraged to wear a mask.

Based on the low risk of infection outdoors, people do not need to wear masks outdoors.

One possible exception where unvaccinated individuals are still encouraged to wear masks is in locales with high virus transmission rates while in crowded outdoor settings or during outdoor activities that involve sustained close contact with other people of unknown vaccination status.

Symptoms of COVID-19

Researchers at the University of Washington at Seattle investigated the symptoms associated with outcomes from hospitalization for COVID-19 (Chatterjee et al., 2021).

They found that individuals with blood oxygen levels, under 92%, who had fast, shallow breathing had elevated death rates, suggesting that individuals who are sick with COVID-19 at home should watch for these signs.

Additionally, almost all of the individuals with this combination of symptoms required supplemental oxygen and glucocorticoids.

However, only 10% of hospitalized individuals in the study reported shortness of breath or cough, which are two of the main symptoms listed on the WHO and CDC websites for COVID-19. The authors state that this finding underscores “that respiratory symptoms are uncommon and by themselves may not accurately identify at-risk patients.” They also found that body temperature, heart rate, and blood pressure were not associated with death, but a higher body mass index was linked to lower blood oxygen and faster respiratory rate.

Treatments for COVID-19

The FDA issued an Emergency Use Authorization for an antibody treatment called sotrovimab for mild-to-moderate COVID-19 in adults and pediatric patients 12 years of age and older who are at high risk for progression to severe COVID-19, including hospitalization or death (FDA, 2021). As with other antibody treatments, it must be administered early in the infection and before hospitalization or oxygen is needed.

The final analysis was published of the Phase 3 clinical trial for remdesivir (Olender et al., 2021). In the report, all of the participants had completed the final 28 day observation period after use of the drug, allowing for a final assessment of the effects. Based on the analysis, the 14-day clinical recovery rate was higher in individuals taking remdesivir than in those receiving only standard care, 65.2% compared to 57.1%. Additionally, the mortality rate 28 days after

receiving remdesivir was lower than in those receiving only standard care, 12.0% compared to 16.2%.

References

Adam D. What scientists know about new, fast-spreading coronavirus variants. *Nature*. Published May 24, 2021. Accessed May 25, 2021 at https://www.nature.com/articles/d41586-021-01390-4

Bao B, De Jesus Y. U.S. nursing home deaths fall sharply as older Americans are vaccinated. *The New York Times*. Published June 3, 2021. Accessed on June 3, 2021 at https://www.nytimes.com/live/2021/06/03/world/covid-vaccine-coronavirus-mask

Branswell H. The name game for coronavirus variants just got a little easier. *STAT News.* Published May 31, 2021. Accessed June 1, 2021 at https://www.statnews.com/2021/05/31/the-name-game-for-coronavirus-variants-just-got-a-little-easier/

Callaway E. Had COVID? You'll probably make antibodies for a lifetime. *Nature*. Published May 26, 2021. Accessed May 28, 2021 at https://www.nature.com/articles/d41586-021-01442-9

CDC. Guidance for Operating Youth Camps. Updated May 28, 2021. Accessed June 4, 2021 at https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/summer-camps.html

CDC COVID-19 Vaccine Breakthrough Case Investigations Team. COVID-19 Vaccine Breakthrough Infections Reported to CDC - United States, January 1-April 30, 2021. *MMWR Morb Mortal Wkly Rep*. 2021 May 28;70(21):792-793. doi: 10.15585/mmwr.mm7021e3. PMID: 34043615.

Chatterjee NA, Jensen PN, Harris AW, Nguyen DD, Huang HD, Cheng RK, Savla JJ, Larsen TR, Gomez JMD, Du-Fay-de-Lavallaz JM, Lemaitre RN, McKnight B, Gharib SA, Sotoodehnia N. Admission respiratory status predicts mortality in COVID-19. *Influenza Other Respir Viruses.* 2021 May 24. doi: 10.1111/irv.12869. Epub ahead of print. PMID: 34028169.

FDA. Coronavirus (COVID-19) Update: FDA Authorizes Additional Monoclonal Antibody for Treatment of COVID-19. Published May 26, 2021. Accessed on May 27, 2021 at https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-additional-monoclonal-antibody-treatment-covid-19

Havers FP, Whitaker M, Self JL, et al. Hospitalization of Adolescents Aged 12–17 Years with Laboratory-Confirmed COVID-19 — COVID-NET, 14 States, March 1, 2020–April 24, 2021. *MMWR Morb Mortal Wkly Rep*. ePub: 4 June 2021.

Iacobucci G. Covid-19: No evidence that vaccines can affect fertility, says new guidance. *BMJ*. 2021 Feb 19;372:n509. doi: 10.1136/bmj.n509. PMID: 33608302.

Israeli Ministry of Health. Surveillance of Myocarditis (Inflammation of the Heart Muscle) Cases Between December 2020 and May 2021 (Including). Published June 2, 2021. Accessed June 2, 2021 at https://www.gov.il/en/departments/news/01062021-03

Jiménez J. The South may see a Covid surge this summer as vaccination rates lag. *The New York Times.* Published June 6, 2021. Accessed June 6, 2021 at https://www.nytimes.com/live/2021/06/07/world/covid-vaccine-coronavirus-mask

Keating D, Shapiro L. The unseen covid-19 risk for unvaccinated people. *The Washington Post*. Published May 21, 2021. Accessed May 28, 2021 at https://www.washingtonpost.com/health/interactive/2021/covid-rates-unvaccinated-people/

Khoury DS, Cromer D, Reynaldi A, Schlub TE, Wheatley AK, Juno JA, Subbarao K, Kent SJ, Triccas JA, Davenport MP. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med.* 2021 May 17. doi: 10.1038/s41591-021-01377-8. Epub ahead of print. PMID: 34002089.

Li K, Chen G, Hou H, Liao Q, Chen J, Bai H, Lee S, Wang C, Li H, Cheng L, Ai J. Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age. *Reprod Biomed Online*. 2021 Jan;42(1):260-267. doi: 10.1016/j.rbmo.2020.09.020. Epub 2020 Sep 29. PMID: 33288478; PMCID: PMC7522626.

Massarweh A, Eliakim-Raz N, Stemmer A, Levy-Barda A, Yust-Katz S, Zer A, Benouaich-Amiel A, Ben-Zvi H, Moskovits N, Brenner B, Bishara J, Yahav D, Tadmor B, Zaks T, Stemmer SM. Evaluation of Seropositivity Following BNT162b2 Messenger RNA Vaccination for SARS-CoV-2 in Patients Undergoing Treatment for Cancer. *JAMA Oncol*. 2021 May 28. doi: 10.1001/jamaoncol.2021.2155. Epub ahead of print. PMID: 34047765.

McEwan AE et al. Variants of concern are overrepresented among post-vaccination breakthrough infections of SARS-CoV-2 in Washington State. *medRxiv*. Published May 25, 2021. Accessed on May 26, 2021 at https://www.medrxiv.org/content/10.1101/2021.05.23.21257679v1

Olender SA et al. Remdesivir versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection: An Analysis of 28-Day Mortality. *Open Forum Infectious Disease*. Published May 26, 2021. Accessed May 28, 2021 at https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofab278/6285231

Public Health England. Vaccines highly effective against B.1.617.2 variant after 2 doses. Published May 22, 2021. Accessed May 26, 2021 at https://www.gov.uk/government/news/vaccines-highly-effective-against-b-1-617-2-variant-after-2-doses

Soucheray S. COVID-19 cases drop sharply across US. *CIDRAP News*. Published May 24, 2021. Accessed May 25, 2021 at https://www.cidrap.umn.edu/news-perspective/2021/05/covid-19-cases-drop-sharply-across-us

Souceray S. Ten states reach 70% COVID-19 vaccination goal. *CIDRAP News*. Published May 27, 2021. Accessed May 28, 2021 at https://www.cidrap.umn.edu/news-perspective/2021/05/ten-states-reach-70-covid-19-vaccination-goal

Thorne LG et al. Evolution of enhanced innate immune evasion by the SARS-CoV-2 B.1.1.7 UK variant. *bioRxiv*. Published June 7, 2021. Accessed June 7, 2021 at https://www.biorxiv.org/content/10.1101/2021.06.06.446826v1

Turner JS, Kim W, Kalaidina E, Goss CW, Rauseo AM, Schmitz AJ, Hansen L, Haile A, Klebert MK, Pusic I, O'Halloran JA, Presti RM, Ellebedy AH. SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. *Res Sq* [Preprint]. 2020 Dec 31:rs.3.rs-132821. doi: 10.21203/rs.3.rs-132821/v1. Update in: Nature. 2021 May 24;: PMID: 33398264; PMCID: PMC7781328.

Vogel G, Couzin-Frankel J. Israel reports link between rare cases of heart inflammation and COVID-19 vaccination in young men. *Science*. Published June 1, 2021. Accessed on June 2, 2021 at https://www.sciencemag.org/news/2021/06/israel-reports-link-between-rare-cases-heart-inflammation-and-covid-19-vaccination

WHO. Tracking SARS-CoV-2 variants. https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

Youn S. These women say covid-19 changed their periods. They're calling for more research. *The Washington Post*. Published May27, 2021. Accessed on June 1, 2021 at https://www.thelily.com/these-women-say-covid-19-changed-their-periods-theyre-calling-for-more-research/