**Update: October 16, 2020**

# COVID-19 DIGEST

## *From the Cross-Campus Infectious Diseases COVID-19 Task Force*

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## EPIDEMIOLOGY

**LOCAL**

California now reports **869,722 confirmed COVID-19 cases** and **16,856 deaths**. The positive test rate statewide continues to decrease and was 2.6% over the last week. As of October 16, **11,782 positive cases** and **130 deaths** have been reported in San Francisco. New cases and test positivity continue to decline; over the last 7 days, an average of 26 new cases were diagnosed per day and the positive test rate was 0.8%, with over 5,000 tests being performed in the city per day. San Francisco continues to meet the state's criteria for the Orange Tier ('Moderate Risk') and this week 2 additional Bay Area Counties, Santa Clara and Alameda, also moved into the Orange Tier. All nine Bay Area counties met the State's Health Equity metric this week. On October 14 the >180 public playgrounds in San Francisco opened again to the public with extensive guidelines on use.

**NATIONAL**

The United States currently reports over **8.0 million cases of** COVID-19 diagnosed and more than **218,000 deaths.** One of these cases is President Trump, who announced that he and his wife had tested positive on October 1; currently at least 39 additional infections have been linked to the White House since September 30th. Across the country daily testing, reported daily cases, and hospitalizations are currently increasing, and overall cases have increased more than 10% over the last week in 36 states. The current surge is most pronounced in rural areas of the Midwest and West and currently the per capita cases and deaths in North Dakota, South Dakota, and Montana exceed those seen in the Sunbelt states during their summer surges. The CDC director has warned that small household gatherings are contributing to increased spread, possibly as these have moved indoors due to colder weather in many parts of the country.

This week we highlight the impact of COVID-19 on Filipino Americans, who make up 4% of nurses in the United States, many whom have been on the front lines taking care of COVID-19 patients throughout the epidemic. A recent report by the National Nurses United union found that Filipino Americans account for over 30% of the deaths among nurses due to COVID-19. In California, where they make up 20% of the nurse work force, 70% of COVID-19 deaths among nurses have been among Filipino Americans. Filipino American nurses and their families are at particular risk in the United States where they are concentrated in in-patient, critical care roles, many work second jobs in long term care facilities, and many live in large, intergenerational households.

**GLOBAL**

There are currently over **39 million** reported cases of COVID-19 and roughly **1.1 million deaths** globally. Europe is experiencing a second surge, with an average of over 100,000 infections per day over the last week and accounting for 1/3 of the world's new infections. The ongoing surge has prompted France to declare a public health emergency and impose a curfew on Paris, Germany to impose a curfew on bars and restaurants, limit the sizes of gatherings, and restrict travel, and the UK to announce a 3-tiered system of restrictions based on levels of local spread.

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## UP TO THE MINUTE DISPATCHES

**Treating COVID with Monoclonal Antibodies (mAbs)—What's New?**

Laboratory-generated monoclonal antibodies that target a single part of SARS-CoV-2 (typically the "spike protein") aimed at reducing levels of virus and accelerating disease recovery are being tested in patients with mild to severe COVID disease. A Regeneron press release reported on 275 COVID infected outpatients randomized to a combination of two mAbs (low or high dose) vs. placebo. Levels of the virus were lower after 7 days, and symptom resolution was faster among antibody recipients (6-8 days) vs. placebo recipients (13 days). The effect was largely seen in those without COVID antibodies at the time of mAb infusion. In a similar study of 268 outpatients with mild-moderate COVID, participants receiving dual mAbs made by Lilly showed reduced viral load, faster symptom resolution and a lower hospitalization rate (0.9% vs 5.8%, p= 0.049), compared to placebo. These mAbs intravenous infusions have been generally safe, however, an ongoing study of mAbs in hospitalized patients has been paused as of 10/13/2020 to evaluate a safety concern. **Conclusion**: Investigational monoclonal antibodies hold great promise for both treatment and prevention; a single infusion has a half-life of weeks to months. One of the challenges for early treatment is that patients will need to be identified as soon as possible after infection in order to gain the maximal benefit. This means testing access, results turnaround and linkage to care all need to occur in a shorter period of time than what currently happens in most of the U.S. Further, a subcutaneous formulation (vs intravenous) would greatly facilitate access by reducing current logistics of treatment.

**Reinfection with SARS-CoV-2: the fifth case report**

As the SARS-CoV-2 pandemic prolongs, we have begun to see reports of re-infection. To date, there are four published or preprint case reports of re-infection with a phylogenetically distinct SARS-CoV-2, from Nevada, Hong Kong, Ecuador and Belgium. Among these, half report lessened severity and half increased severity of disease with secondary infection. This pre-print case report from Seattle provides a fifth example, here with a milder infection.

This was an elderly patient in a skilled nursing facility with oxygen-dependent emphysema developed severe COVID-19 in March 2020. He had two negative PCRs soon after infection. In July 2020 he developed dyspnea/cough and a repeat SARS-CoV-2 PCR test was positive with viral sequencing demonstrating a distinct strain (D614G clade from Europe) from the first infection (D614 from Wuhan). SARS-CoV-2 antibodies were detectable at reinfection, but at low levels. Repeat antibody measurement 42 days after reinfection showed increase of neutralizing antibodies to both viral strains. B-cell expansion was low during the patient's reinfection, indicative of some immune recognition of the prior infection. Overall, these findings suggest that poorly developed or waned antibodies against the D614 virus formed after primary infection were not protective against reinfection with the D614G variant. **Conclusion**: Like with other seasonal coronaviruses, immunity to the first infection may wane over time or may not be protective against new variants. These findings have implications for vaccine development and duration of vaccine protection. The rarity of documented re-infections to date, however, provide hope while awaiting advancements in vaccines.

**SARS-CoV-2 Mutation Leading to Possible Remdesivir Resistance in an Immunocompromised Patient**

Remdesivir is the primary antiviral for treatment of SARS-CoV-2 infection. Remdesivir resistance has not been identified to date. A recent case report describes a 76-year-old woman with CLL complicated by secondary B-cell-deficiency who was hospitalized for 2 months for COVID-19 complicated by persistent SARS-CoV-2 viremia. She was treated with remdesivir for 5 days at week 6 of illness without improvement in viremia or hypoxia. She then received convalescent plasma around week 8 which was temporally correlated with clinical improvement and resolution of viremia. Molecular analysis revealed a mutation in the viral RNA-dependent RNA-polymerase (RdRP), the site of action of remdesivir, in a blood sample collected after remdesivir administration. Neither respiratory or blood samples prior to remdesivir treatment revealed this mutation. Although phenotypic studies were not performed, the authors postulate that this mutation may have led to remdesivir resistance. The combination of immunosuppression, prolonged shedding, high viral burden (given presence of viremia) may have led to the selection of this mutation. **Conclusion**: Point mutations in RdRP may develop while on remdesivir. This case raises the question of whether a longer duration of remdesivir or use of combination antiviral therapy would be a beneficial strategy for COVID treatment in immunocompromised patients.

**COVID-19 Transmission in US Child Care Programs**

There remains much debate but limited data about whether transmission in schools and childcare centers facilitate the

community spread of SARS-CoV-2. There have been concerning examples of outbreaks and cases of transmission. But the closing of centers as incidence rose across the United States has made robust epidemiologic analysis challenging. A recent study took an innovative approach, surveying 57,335 child care providers about the period of April-May, 2020. Childcare centers remained open, or reopened, for half of respondents; 427 cases of COVID-19 were reported. In multivariate logistic regression modelling, community death rates, race, and some personal behaviors were predictive of infection, but exposure to childcare center was not (OR, 1.06; 95% CI, 0.82 to 1.38; P = 0.66). In a separate case-control analysis, being a home-based childcare provider was associated with COVID-19 (OR, 1.59; 95% CI, 1.14 to 2.23; P < 0.01), but exposure to childcare was not (p=0.64). **Conclusion**: These data suggest that at least during this early phase of the pandemic, with variable implementation of preventative measures, exposure to childcare centers was not a key driver in spread of SARS-CoV-2 infection. These are encouraging data about childcare centers but intermittent reports of spread in some settings underscore the need for persistent vigilance to preventative measures.

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## FAQ

1. **Do face masks impair gas exchange in healthy patients with COPD?**
   Universal masking is a key strategy for controlling the COVID-19 pandemic while awaiting a vaccine. Mask hesitancy has been a barrier to universal masking and complaints have been made that masks cause build-up of carbon dioxide ($CO_2$). To assess whether masks causes $CO_2$ retention, researchers used capnography and pulse oximetry to assess changes in end-tidal $CO_2$ and $O_2$ saturation before and after wearing a surgical mask in 15 patients with severe COPD (mean age 72 years, FEV1 44±22%). They found no change in the end-tidal $CO_2$ concentration at rest or after a 6-minute walk test. Arterial $O_2$ saturation did not change at rest but they were unable to conduct a walk test in masked vs. unmasked state due to COVID-19 restrictions. A decline in arterial $O_2$ saturation and the arterial $PaO_2$ did occur in two patients which was interpreted as being consistent with the advanced severity of COPD. **Conclusion**: $CO_2$ retention did not occur at rest or after 6 minutes of walking while wearing a face mask, and there was no decline in oxygen saturation at rest. This small study can be used to help discourage mask hesitancy for patients who have COPD and other underlying lung disease are concerned about $CO_2$ retention.

2. **What are we learning about the safety of remdesivir in patients with renal insufficiency?**
   Remdesivir, has proven beneficial for patients with COVID-19 disease and serious adverse events occur at similar rates to patients receiving placebo. However, clinical trials and the compassionate use program excluded patients with creatinine less than or equal to 30 mL/min. Recently, the European Medicines Agency's Pharmacovigilance Risk Assessment Committee released information about a safety signal related to renal failure. Remdesivir itself is unlikely nephrotoxic but the drug is formulated with a sulfobutylether-b-cyclodextrin (SBECD) vehicle because of low water solubility. In animal models, SBECD causes renal tubule obstruction at very high doses. Studies suggest that continuous renal replacement therapy and intermittent hemodialysis both readily remove SBECD. Further studies and post-marketing reports of remdesivir's safety in patients with renal failure both on and off renal replacement therapy will be critical. **Conclusion:** Until further data become available, existing evidence suggests that the amount of SBECD in each dose of remdesivir is low enough to consider this medication to patients with renal failure, particularly given the short course of remdesivir therapy. If possible, the lyophilized powder form should be provided as it contains half the amount of SBECD than the solution (3g vs. 6g per 100 mg dose).

3. **Can SARS-CoV-2 survive on human skin?**
   From the early days of the COVID-19 outbreak there have been questions about the modes of SARS-CoV-2 transmission. A recent investigation sought to better understand the stability of SARS-CoV-2 on human skin, using a model system with cadaveric human skin samples. Whereas SARS-CoV-2 had reduced survival times on human skin compared to other surfaces (metal, glass, and plastic), virus survival times were consistently prolonged for SARS-CoV-2 compared to influenza A. Both viruses were inactivated within 15 seconds when the surfaces were treated with 80% ethanol. A strength of this study is its use of viral culture methods to detect viable virus, rather than

relying on molecular testing (i.e. PCR) which may detect both non-viable and viable virus. **Conclusion**: Given the potentially greater stability on skin and environmental surfaces of SARS-CoV-2 compared with influenza A, the risk of transmission of SARS-CoV-2 via direct contact or via fomites may be higher than with influenza. Consistent hand hygiene remains prudent.

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## The Post-COVID Clinic
### An interview with Dr. Neeta Thakur and Dr. Lekshmi Santhosh

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**Can you provide a description of your post-COVID care clinic? What type of health care providers, what type of care is provided?**
*The UCSF OPTIMAL and ZSFG Critical Illness Recovery clinics aim to facilitate the recovery of COVID-19 survivors by creating a multidisciplinary hub that allows for comprehensive evaluation of patient's needs, streamlined access to multiple specialties, standardized care based on anticipated consequences from COVID-19, and iterative adaptation through knowledge gained. At UCSF-OPTIMAL, the team comprises of pulmonary/critical care physician faculty members, a trained psychologist specializing in trauma, a psychiatry research coordinator, and a pharmacy trainee, with collaborations with geriatrics, cardiology, neurology, integrative medicine, and research groups across UCSF. At the ZSFG Critical Illness Recovery Clinic, the team comprises of pulmonary/critical care physician faculty members, pulmonary/critical care fellows, a clinical nurse, and a faculty psychiatrist with collaborations with physical and occupational therapy, infectious disease, cardiology, and neurology.*

**Based on the published literature, what are the most common symptoms that patients suffer following COVID?**
*Studies from China, Italy, and the US show that patients suffer from a wide range of symptoms after infection with SARS-CoV-2, including persistent pulmonary, physical, cognitive, and mental health symptoms. Particularly, persistent dyspnea, fatigue, and chest pain are extremely common. Neurological manifestations have also been increasingly recognized, ranging from mild encephalopathy to delirium, strokes, fatigue, neuropathy, anosmia, as well as depression, anxiety, and PTSD.*

**How common are these symptoms post-COVID and how long do they last?**
*Studies from China, Italy, and the US have shown differences in how long these symptoms persist post-COVID. Patients who were hospitalized and/or in ICU may have longer persistent symptoms, while even patients who were not*

*hospitalized show delays in return to usual state of health. Some patients have been dubbed 'long-haulers' who report persistent symptoms weeks to months after initial diagnosis.*

**In your experience, are you seeing similar findings in your patients? Have there been surprising findings?**
*In our experience, our findings mirror the published data, with the majority of patients reporting persistent dyspnea and fatigue. A large proportion of patients also report cognitive and mental health impairments. The published data is limited in that most studies do not have a dedicated control group and have not been compared with historical controls such as prior data looking at survivors of ARDS. Further research is urgently needed to document the variety and severity of impairments in these patients.*

*One surprising finding we are noting in clinics at both sites is the extreme shame and stigma attached to a coronavirus diagnosis. Unlike survivors of ARDS from pneumonia or influenza, a proportion of patients with COVID express feelings of guilt, blame, shame, and stigma. At the UCSF OPTIMAL Clinic, seeing healthcare workers afflicted with COVID has been particularly gut-wrenching, as these feelings are magnified even more intensely. At the ZSFG Critical Illness Recovery Clinic, may patients who have had COVID feel isolated and, despite on average being younger than what we have seen in the published literature, the majority have not been able to return to work, even three to six months out, highlighting the long-lasting economic consequences of critical illness.*

*Personally, the patient encounters have been incredibly rewarding–seeing a patient survive a lengthy ICU stay and seeing them in clinic returning to normalcy has brought many of us to tears. Sharing back of the patient stories, with permission, to other ICU providers, including nursing and the respiratory care staff, has been an unexpected source of motivation and inspiration during this prolong pandemic.*

**How do you think we can best help transition patients hospitalized with COVID into the outpatient setting?**
*Anticipatory guidance from the inpatient setting and guidance on how to navigate the morass of post-discharge resources is key. Explicit linkage to outpatient care, in particular, rehabilitation services and mental health support, is essential to help patients seamlessly navigate the transition from inpatient to outpatient care. Our clinics aim to help shepherd patients through this difficult transition.*

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**UCSF Hospital Epidemiology and Infection Prevention COVID-19 webpage:**
https://infectioncontrol.ucsfmedicalcenter.org/ucsf-health-covid-19-resources
**San Francisco DPH link:** https://www.sfcdcp.org/infectious-diseases-a-to-z/coronavirus-2019-novel-coronavirus

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