

COVID-19 DIGEST

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

Members: Joanne Engel, MD, PhD, Harry Lampiris, MD, Lisa Winston, MD, Annie Luetkemeyer, MD, Chaz Langelier, MD, PhD, Vivek Jain, MD, MAS, Deborah Yokoe, MD, MPH, Sarah Doernberg, MD, MAS, Jennifer Babik, MD, PhD, Monica Gandhi, MD, MPH, Rachel Bystritsky, MD, Ted Ruel, MD, Lynn Ramirez, MD, Charles Chiu, MD, PhD, Bryn Boslett, MD & Chesa Cox, MPH; **Co-Chairs & Digest Editors:** Brian Schwartz, MD & Diane Havlir, MD;

Guest Contributors: Lillian Brown, MD, PhD, Andrew Kerkhoff MD, PhD, and Catherine DeVoe, MD

EPIDEMIOLOGY

LOCAL

[In San Francisco](#) there are currently **2,437 cases** and **40 deaths**. [California](#) crossed the 100,000 case threshold as there were **102,106 confirmed COVID-19 cases** and **3,921 deaths** reported as of Thursday, May 28. Statewide almost half of the reported cases and more than half of the reported deaths are in Los Angeles County, where 48,700 cases and 2,195 deaths have been reported. [Imperial County](#), a rural county on the Mexican border, has the highest concentration of cases at 760 cases per 100K population (compared to 258 per 100K statewide, 482 per 100K in Los Angeles County, and 277 cases per 100K in San Francisco). This surge is partly due to American retirees living in Mexico, dual citizens, and Americans working or visiting family in Mexico crossing the border from Mexico for medical care. The rural health care system has been overwhelmed; last week the only two hospitals in the county had to temporarily [turn away COVID-19 patients](#). The first case among an [immigrant at the ICE detention center](#) in the border town Calexico, CA in Imperial County was confirmed last Friday and [6 staff members](#) have also tested positive for COVID-19.

NATIONAL

The [United States](#) crossed the 100,000 death mark; as of Thursday May 29 there are over **1.7 million cases** and **101,123 deaths** from COVID-19 reported. The enormous scale of this tragic loss of life in less than three months is impossible to comprehend. [Excerpts from obituaries](#) from around the country reveal a glimpse into the humans that make up this staggering number. New cases and deaths have decreased significantly in New York, with [only 1,044 new cases and 103 deaths](#) reported on May 26, the lowest daily totals since mid-March.

GLOBAL

[Worldwide](#) there are currently over **5.9 million** reported cases of COVID-19 and **357,000 deaths**. India, which imposed the [world's largest pandemic lockdown](#) on all 1.3 billion citizens on March 25, is seeing sharp rise in new infections. [India](#) currently has more than 158,000 infections and 4,500 deaths and ranks fourth in the world in number of daily new infections behind the United States, Russia, and Brazil. [Mumbai](#), India's financial capital and the second most densely populated city in the world, is the country's epicenter with more than 33,000 cases. The coronavirus wards are already full in many hospitals in Mumbai, and the local government has asked other states for [doctors and nurses](#). As travel restrictions ease there is concern that [cases will spike in rural areas of the country](#) as millions of migrant laborers return to their home states.

UP TO THE MINUTE DISPATCHES

Preliminary report on the efficacy of Remdesvir (RDV) in a randomized control trial

The ACTT-1 study randomized 1063 hospitalized patients to IV remdesvir (up to 10 days during hospitalization) vs. a blinded placebo control. In a [preliminary report](#), RDV significantly shortened time to recovery to 11 days vs. 15 days with placebo ($p < 0.001$) and was associated with a trend toward decreased mortality: 7.1% vs. 11.9%. The largest impact was seen in patients requiring oxygen but not intubated, with a recovery rate ratio of 1.47 (95%CI 1.17-1.84). There was not a significant difference in time to recovery in ICU patients; however critically ill individuals may take many weeks to reach recovery and this group was underpowered. No difference was seen in those with mild-moderate disease (5 days

to recovery both arm); it is not clear how many days of RDV these participants received before discharge. Starting RDV more than 10 days after symptom onset did not significantly impact time to recovery. Less serious adverse events occurred in those who received RDV (21%) vs. placebo (27%). Approximately 30% of participants had not yet reached the recovery endpoint or the study end (Day 29); a final analysis is forthcoming. The [Gilead SIMPLE-Severe RCT](#) found equivalent clinical outcomes at day 14 with 5 vs. 10 days of RDV in 397 hospitalized, non-intubated patients; there was no control arm. These data are reflected in [RDV prescriber information](#) recommending 5 days for non-ICU patients, with an extension to 10 days if poor clinical response. **Conclusion:** RDV improves clinical outcomes and may reduce mortality and thus should be the current standard of care for hospitalized COVID patients. We need more data to understand the impact of RDV in critically ill patients and in those with milder disease hospitalized for only a few days; the latter may not be prioritized for treatment during ongoing RDV shortages. Given the 7% mortality even with RDV treatment, we clearly need additional effective strategies.

Difference in nasal expression of ACE-2 in children vs. adults, a possible reason for children to be less likely infected with SARS-CoV-2?

Since early [reports](#) from China, children have represented a minority of reported COVID-19 cases. We have [learned](#) that children experience milder disease compared to adults, but it has remained unclear if children are also less likely to acquire or [transmit](#) SARS-CoV-2 infection. A [recent publication](#) sheds light on a potential biological piece to this puzzle. For a study of asthma biomarkers, investigators had previously characterized gene expression in nasal epithelium of participants aged 4 to 60 years in New York City. Recognizing that SARS-CoV-2 relies on the ACE2 receptor to enter cells, investigators re-examined their data and found nasal epithelial ACE2 gene expression was significantly lower in children; the lowest (2.40 log₂ counts per million; 95%CI, 2.07-2.72) was found in children 4-10 years (n=45) and the highest (3.09 ; 95% CI, 2.83-3.35) in older adults (25-60 years, n = 29). **Conclusion:** While this study is not able to directly link ACE2 receptor expression to risk of COVID-19 or transmission, it provides an intriguing biologic pathway that could explain trends suggested in epidemiologic data.

Initial data on efficacy and safety of convalescent plasma in patients with severe COVID-19

The goal of convalescent plasma therapy is to use antibodies from recovered patients to treat patients with active infection. To date, evidence for convalescent plasma for COVID-19 is limited to case reports. A recent [case-control study](#) (pre-print, not peer reviewed) examined the impact of convalescent plasma on clinical outcomes: 39 patients with severe COVID-19 received two units of convalescent plasma from donors with high spike-antibody titers ($\geq 1:320$) and were matched to 156 control patients with severe COVID-19 who did not receive plasma. Patients who received plasma had small improvements in 14-day oxygenation status (82.0% vs. 75.7%; p=0.028) and a lower 30-day mortality than matched controls (12.8% vs. 24.4%; p=0.039). In adjusted analyses, non-intubated COVID-19 patients who received plasma had substantially lower mortality (hazard ratio=0.19 [95%CI, 0.05-0.72]), while intubated patients who received plasma did not (hazard ratio = 1.24 [95%CI, 0.33-4.67]). A [second study](#) (pre-print, not peer reviewed) of more than 5,000 patients with COVID-19 who received convalescent plasma found the incidence of serious adverse events in the first 4 hours of transfusion to be <1%. **Conclusion:** Convalescent plasma is safe and may improve clinical outcomes in hospitalized COVID-19 patients, especially when given earlier during the course of the disease. Confirmatory data from randomized controlled trials on convalescent plasma are needed.

FAQ

1. What are we learning about patients with severe COVID-19 who receive IL-6 blockers?

Some institutions have been using IL-6 blockers for the treatment of patients with severe COVID-19. Thus far, there have been no published randomized controlled trials to assess the risks and benefits of IL-6 for patients with severe COVID-19. A [small case-control study](#) (pre-print, not peer reviewed) of hospitalized patients with COVID-19, included 21 tocilizumab treated patients demonstrated a significant reduction in short-term mortality. However, a [small cases series](#) (pre-print, not peer reviewed) of 11 patients treated with tocilizumab found no improvement in fevers and oxygenation in most patients. Another recent [case-control study](#) (pre-print, not peer reviewed) of critically ill

patients found that use of tocilizumab was associated with an increased risk of secondary infections.

Conclusion: While IL-6 blockers may improve outcomes for patients with COVID-19, to date there is no conclusive data to support their use and there are concerns about secondary toxicities. Until more robust clinical data is available, the use of these agents should be limited to clinical trials.

2. What is our updated understanding of the utility of hydroxychloroquine (HCQ) in prevention and treatment of COVID-19?

In vitro activity and early uncontrolled case series generated excitement about the use of hydroxychloroquine (HCQ) for prevention and treatment of COVID-19, but benefit has not been proven in larger studies. A recent [multinational registry analysis](#) compared outcomes in 14,888 patients who received HCQ or chloroquine (CQ) within 48 hours of COVID-19 diagnosis, with or without a macrolide, with 81,144 who did not. After controlling for confounders including disease severity, the investigators found that HCQ/CQ use was associated with increased risk of both ventricular arrhythmias and in-hospital mortality. With regard to a possible role in prevention, a [retrospective analysis](#) (pre-print, not peer reviewed) examined the incidence and severity of COVID-19 in 722 patients with autoimmune conditions, 290 of whom were taking HCQ; no significant difference in incidence was found. The World Health Organization has [temporarily paused the HCQ arm in the SOLIDARITY trial](#) while the recently-published data undergoes review. **Conclusion:** These data point to the importance of HCQ/CQ only being utilized in the setting of carefully conducted clinical trials to insure possible serious adverse effects can be measured against any possible benefits and to definitively address the role of HCQ/CQ in COVID-19 treatment and prevention.

3. What have we learned from postmortem examinations of patients who die from COVID-19?

A [study](#) of 7 patients who died from COVID-19 were compared to 7 patients who died of Influenza A (H1N1) and age matched controls. COVID-19 and H1N1-infected lungs exhibited diffuse alveolar damage, perivascular T cell infiltration, and increased ACE2 protein. However, only COVID-19 cases exhibited severe endothelial injury, widespread thrombosis and microangiopathy of the pulmonary vessels, and increased pulmonary vascular angiogenesis. In a separate [study](#), 10 consecutive patients who died of COVID-19 related complications were autopsied, of which 6 did not undergo mechanical ventilation. Diffuse alveolar damage was detected in all the lungs, along with signs of exudative early-phase acute diffuse alveolar damage. Myocarditis and epicarditis were detectable in 4 and 2 of the cases, respectively. Minimal fibrosis was detected in some of the livers. SARS-CoV-2 was detectable in the respiratory tracts of all the autopsied patients. No signs of encephalitis or CNS vasculitis was detected, and CSF PCR were negative. **Conclusion:** COVID-19 pulmonary disease may be distinct from other viral respiratory infections with widespread thrombosis and microangiopathy. The viral and host response that contribute to these distinctive features are important areas of future study.

FRONTLINE: Interviews with Leaders Responding to the COVID-19 Epidemic

Prevention and Care for Patients with COVID-19 within the VA Health Care System with Harry Lampiris, MD and Jennifer Mulliken, MD



Harry Lampiris, MD
Chief, Infectious Diseases Section at SFVAHCS
Professor of Medicine, UCSF



Jennifer Mulliken, MD
Medical Director of
Antimicrobial Stewardship, SFVAHCS
Assistant Professor of Medicine, UCSF

What are some unique challenges facing our veterans during the COVID-19 epidemic?

Our patients are disproportionately affected by aging and multiple medical/psychosocial comorbidities as well as spread out far across Northern California. Our outpatient clinics reach as far as the Oregon border, which means immediate access to healthcare is often difficult for our patients. As a result, COVID-19 testing and patient triage have been challenging, as has coordination between the hospital and multiple health departments. This has led to the need for more robust telephone care and telemedicine options, which are rapidly expanding at our medical center. Despite these challenges, we think patients receiving care in our system have certain advantages – they benefit from excellent coordination of care from inpatient to outpatient settings, robust case management of community-based geriatric and marginally housed patient populations, and committed staff who have worked incredibly hard to make changes in healthcare delivery as a result of the pandemic.

How much of the COVID-19 prevention and treatment planning at the VA is dictated on the national level versus at the San Francisco VA Health Care System (SFVAHCS)?

National VA directives and guidance reflect evidence-based practices and standards of care, which are rapidly changing as new information about COVID-19 becomes available. Usually the directives are relatively broad and allow for flexibility in implementation. Our local leadership has responded swiftly to help our laboratory medicine service develop processes and gain access to multiple platforms of COVID-19 testing, which are not available at many other VAs. Our hospital incident command system has also introduced new systems of care, including an outpatient respiratory screening clinic and remodeled inpatient and intensive care units for COVID-19 patients.

The SFVAHCS has a skilled nursing facility on site. What have been specific challenges that the facility has brought during your COVID-19 planning/care?

One of the greatest challenges has been the facility's strict visitor policy and restricted activities for residents, both of which have caused great stress and anxiety for residents and family members. In addition, any residents who develop symptoms compatible with COVID-19 are required to be transferred to acute care, which increases the risk of delirium, rapid deconditioning, and other complications. As a result of these challenges, new practices have been developed around COVID-19 surveillance and enhanced psychosocial and emotional support for our veterans and their families. National VA guidelines have been vague about frequency of testing for veterans and staff at nursing facilities, but our hospital has taken an aggressive approach to screening asymptomatic patients and healthcare

workers. After repeatedly testing about 80 patients and 200 healthcare workers in our facility, we are fortunate that there has been no evidence of sustained transmission to staff or patients.

What do you see as your biggest successes at the SFVAHCS during the COVID-19 epidemic?

Thanks to multidisciplinary collaborations within the SFVAHCS, we have successfully operationalized many new practices related to PPE, laboratory testing, screening of patients and healthcare workers, and monitoring of vulnerable patient populations in the community. We are proud of how tirelessly everyone in our ID division has worked to provide excellent care to our veterans, and as a result, state of the art laboratory testing and a variety of treatment options (both experimental and approved) have been made available to our patients.

INSTITUTIONAL CONTACTS FOR CLINICAL OPERATIONS

ZSFG Hospital - Infection Control Team: Lisa Winston, MD (lisa.winston@ucsf.edu) and Vivek Jain, MD, MAS (vivek.jain@ucsf.edu) *Program Manager:* Elaine Dekker (elaine.dekker@ucsf.edu)

UCSF Health - COVID-19 Preparedness Leadership Team - Infection Prevention Team: Deborah Yokoe, MD, MPH (deborah.yokoe@ucsf.edu), Lynn Ramirez, MD, MPH (lynn.ramirez@ucsf.edu), Chaz Langelier, MD, PhD (chaz.langelier@ucsf.edu), and Amy Nichols (amy.nichols@ucsf.edu)

UCSF Benioff Childrens Hospital Oakland – Infection Prevention & Control Team: Ann Petru, MD (Ann.Petru@ucsf.edu), Charlotte Hsieh, MD (Charlotte.Hsieh@ucsf.edu), *Program Manager:* Amanda Lucas, MS RN CIC (Amanda.Lucas@ucsf.edu)

SFVAHCS - Infection Control Team: Harry Lampiris, MD (harry.lampiris@va.gov), Shelley Dwyer, RN (shelley.dwyer@va.gov), Alma Pipkin, RN (alma.pipkin@va.gov), and Scott Miller, RN (dean.miller2@va.gov)

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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