Update: June 11, 2020

COVID-19 DIGEST

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

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EPIDEMIOLOGY

LOCAL

California now reports **140,390 confirmed COVID-19 cases** and **4,869 deaths**, with ongoing hotspots in Southern California, notably Los Angeles County and Imperial County. In San Francisco there are currently **2,840 cases** and **44 deaths**. Hospitalizations across San Francisco have been steadily declining since late March/early April and currently **38 people** were hospitalized with COVID-19 citywide. An analysis of the genomic epidemiology of SARS-CoV-2 in the Bay Area and Northern California from 36 patients presenting in late January – mid-March 2020 across 9 Counties and the Grand Princess Cruise ship demonstrate at least 7 distinct SARS-CoV-2 lineages in circulation and likely limited transmission between communities at that point in time.

NATIONAL

In the United States there are now more than **2 million reported cases** of COVID-19 and more than **113,000 deaths**. Last week the Department of Health and Human Services announced that beginning on August 1 all labs will be required to include detailed demographic data when they report the results of coronavirus tests to the federal government, including race and ethnicity. Texas is one of 21 states currently reporting increasing case counts of COVID-19. Statewide **77,253 cases** and **1,853 deaths** were reported in Texas as of June 9, with increasing numbers of new confirmed cases, test positivity rate, and new COVID-19 hospitalizations over the last 2 weeks.

GLOBAL

Worldwide there are currently over **7.4 million** reported cases of COVID-19 and **over 418,000 deaths**. Iran, which emerged as an early epicenter of transmission, experienced rising numbers of reported infections throughout May after relaxing restrictions in April. There are currently over **178,000 officially reported infections** and **8,500 deaths** in Iran, however these numbers likely underestimate the true toll. While the initial outbreak was centered in Tehran, the second wave of infections has been concentrated primarily in Khuzestan province where overwhelmed hospitals and a water shortage have challenged efforts to contain the epidemic.

UP TO THE MINUTE DISPATCHES

Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients with Severe and Life-threatening COVID-19 A Randomized Clinical Trial

More than 20,000 US COVID-19 patients have received convalescent plasma (plasma from patients with resolved COVID-19) to treat COVID-19, however data to support use remain limited and largely observational. In an open label randomized controlled trial conducted in Wuhan, 103 patients with severe or life threatening COVID-19 were randomized to a single infusion of convalescent plasma vs. standard of care. Of the 55 with severe disease (hypoxia but no intubation or organ failure), there was a trend towards efficacy of convalescent plasma vs. no treatment; 91% vs 68% (HR 2.15, p=0.03) with clinical improvement at day 28, the primary endpoint. In the 59 with life-threatening disease (intubated or organ failure), there was no difference in improvement with plasma vs. no treatment: 20.7% vs 24.1% (HR 0.88, p=0.83). Limitations of this study include bring underpowered (closed early due to the end of the local epidemic), heterogenous background treatment including use of human immunoglobulin in 28%, and a median 30 interval between

symptom onset and treatment, which may impact efficacy. **Conclusion**: Convalescent plasma may improve outcomes in non-ICU COVID patients. Ongoing trials will provide much needed data on optimal timing and populations who may benefit most, including use in ICU patients, outpatients and as prevention. At UCSF, the randomized controlled CAPRI trial is evaluating the efficacy of convalescent plasma to reduce disease progression in hospitalized patients with COVID-19, contact annie.luetkemeyer@ucsf.edu for more information.

Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing
Most testing for COVID-19 involves healthcare worker administered nasopharyngeal (NP) swab testing. This approach necessitates PPE use due to the potential for aerosol generation from sneezing or coughing induced by the collection process and limits the accessibility of testing to those with access to a healthcare facility testing site. A single center study compared matched samples obtained by clinicians from the nasopharynx with self-collected samples from one or more other sites in 530 patients. Using healthcare worker collected NP swabs as a gold standard, the authors observed a sensitivity of 94.0% and 96.2% for patient collected nasal and mid-turbinate swabs, respectively. **Conclusion**: Patient-collected SARS-CoV-2 swab tests are likely an adequate substitute for clinician-collected tests, findings with important implications as broader self-collected testing could enable expanded access to COVID-19 diagnostics, reduce healthcare worker exposure, and support stewardship of PPE.

Are children with SARS-CoV-2 as infective as adults?
Uncertainty remains regarding the extent to which children act as a source of spread of SARS-CoV-2. A recent study revealed that expression of the angiotensin converting enzyme-2 in the nasal epithelium is less in children than adults. Some hypothesized that this may result in reduced risk of infection in children. However, we don't know if difference in age impact infectivity once they are infected. A German study (pre-print, not peer reviewed) analyzed PCR data from 3303 patients with SARS-CoV-2 across the lifespan to assess the relationship between age and viral load. Two different PCR systems were used, the first (LC480) at the beginning of cluster-based testing campaigns a second (the Roche Cobas system) after mid-March. The authors established a viral load of >250,000 copies as "infectious" based on prior data comparing viral load and positive viral culture. They found no differences in infectivity by age with the LC480 platform, but samples tested via the Cobas system did show a small reduction in infectivity with younger age. **Conclusion**: SARS-Co-V viral loads did not differ dramatically across age strata suggesting among children who do get infected may be as infective as older persons. Further studies using culture-based techniques will help answer this question more definitively.

FAQ

1. **Updated understanding of neurologic disease in patients with COVID-19**
   A recent Spanish study surveyed a range of neurologic complications among 841 inpatients with COVID-19. In this cohort, 57.4% were found to have some neurologic symptom or disorder, though nonspecific problems such as myalgias were also counted. Of greater concern, 1.3% of participants suffered an ischemic stroke and 0.4% developed intracranial hemorrhage. Approximately 5% developed taste disturbance or loss of smell, which has been described previously. Other complications such as seizure or encephalitis were diagnosed in <1%. In 4.1% of cases, death was attributed to neurologic complications. **Conclusion**: Persons with COVID-19 may experience a range of neurologic complications such as stroke. Determining which are directly related to COVID-19 as opposed to general physiologic derangements, concomitant medications, or critical illness can be challenging. Prospective registries will provide greater clarity.

2. **How does mode of delivery impact maternal and fetal outcomes in pregnant women with COVID-19?**
   After early data showed an increased risk of maternal complications in pregnant women with COVID-19, researchers in Spain sought to determine whether mode of delivery was associated with maternal or neonatal complications. In a recent study, 82 pregnant women with lab-confirmed COVID-19 were stratified by symptom severity at admission. Forty-one (53%) patients delivered vaginally, and 37 (47%) delivered by c-section. In the latter group, 8 (21.6%) had increased oxygen needs after delivery, and 5 (13.5%) required ICU admission. Among the infants, only 2 developed

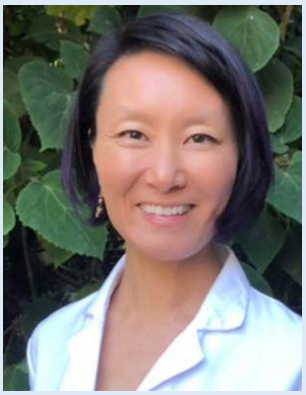
symptomatic lab-confirmed COVID-19; symptoms for both resolved within 48 hours. After adjusting for potential confounding factors, the authors found that c-section was independently associated with both increased maternal oxygen requirements after delivery and increased risk of NICU admission. **Conclusion**: While c-section delivery was independently associated with worse maternal and neonatal outcomes, the conclusions that can be drawn from this small study are limited. More research is needed to better understand the consequences of maternal COVID-19 on maternal and neonatal outcomes.

3. **How has recent data influenced our understanding of PIMS?**
   Two recent studies provide important insight into COVID-19 associated multisystem inflammatory syndrome in children (MIS-C). In one study from the UK of 58 children with MIS-C, 15 (26%) had a positive COVID-19 PCR and 87% (40 of 46 tested) had positive COVID-19 IgG. Twenty-six (50%) had shock but there was only one death. Eight (14%) were identified to have coronary artery aneurysms. When compared to a large database of children with KD and KD-shock in the US, children with MIS-C and aneurysms were older and had higher markers of inflammation and cardiac injury. Another report of 17 children with MIS-C in New York City found patterns of cytokine expression similar to that reported with KD. **Conclusion**: These studies suggest MIS-C is similar to KD but there are some clinical and potentially pathophysiological differences. Additional research will be needed to identify children at risk for coronary aneurysms and optimal treatment.

4. **Updates in clinical trials using HCQ for treatment of COVID-19?**
   In a preliminary DSMB analysis, the multi-arm UK Recovery trial found no difference in 28 day mortality in 1542 COVID-19 patients randomized to hydroxychloroquine vs. 3132 randomized to standard of care; 25.7% vs 23.5% (HR 1.1 (95% CI 0.98-1.26) p=0.1). There was no evidence of a beneficial effect of HCQ on length of hospital stay or other outcomes. **Conclusion**: These results continue to build on the body of literature suggesting that HCQ may not be effective for prevention or treatment of COVID-19.

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

Dr. Lee and Dr. Peluso are the leads on the sister studies, COVID-19 Host Immune Response Pathogenesis (CHIRP) and Long-term Impact of Infection with Novel Coronavirus (LIINC). These studies are investigating acute (CHIRP) and convalescent (LIINC) COVID-19, respectively.



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As experts in observational cohort studies in HIV, how has your prior experience influenced the design of your studies in COVID-19?

Our work with the UCSF HIV SCOPE cohort and performing translational infectious diseases studies helped provide the experience and infrastructure needed to efficiently develop these COVID-19 cohorts as the epidemic was unfolding. When it became clear that COVID-19 would become a pandemic, we quickly pivoted our HIV study infrastructure to recruit COVID-19 positive individuals with the overall goal of understanding the determinants of COVID-19 severity and long-term sequelae of COVID-19. The experienced clinical research staff and the rich collaborations with investigators from within UCSF and across the country allowed us to make this transition smoothly. Our experience with HIV taught us that carefully constructed and deeply characterized observational cohorts with longitudinal follow up are of real value in understanding complex diseases and allowed us to have a head start in implementing these studies.

Can you please briefly describe the overarching goals of your study?
Dr. Lee: The COVID-19 Host Immune Response Pathogenesis (CHIRP) Study is a prospective longitudinal cohort study of acute COVID-19. The purpose of the study is to rapidly enroll people who are acutely COVID+ (as well as close contacts exposed to COVID+ people) to understand the clinical, demographic, behavioral, immunologic, and genetic risk factors associated with COVID-19 severity and transmission. These patients will be followed longitudinally with collection of DNA samples as well as immunologic (cellular and humoral) and virologic data (SARS-CoV-2 viral shedding, infectivity).

Dr. Peluso: The Long-term Impact of Infection with Novel Coronavirus (LIINC) study is a prospective observational cohort of COVID-19 convalescence. The major immunologic goal of the study is to characterize the humoral and cellular immune responses to COVID-19 over the two years after the initial infection and to determine whether these responses are durable and protective. Our primary virologic goal is to determine whether individuals who had prior COVID-19 continue to shed into the chronic phase and whether it is possible for them to get re-infected, as determined by a documented repeat infection or a substantial change in the immune response. We also have a strong interest in characterizing the long-term sequelae of acute infection which includes both biomedical and psychosocial sequelae.

What are two of the questions you are most excited to see answered by your studies?
Dr. Lee: We hope that the proposed acute COVID-19 study will help answer (1) what host genetic and immunologic mechanisms determine COVID-19 disease severity and transmission? and (2) how can these mechanisms be leveraged to inform SARS-CoV-2 vaccine development and potential immunotherapies.

Dr. Peluso: Beyond characterizing the immune response over time, LIINC is particularly interested in determining whether the potency or durability of that response will differ between subpopulations. I am personally quite interested in whether the immune response in those with asymptomatic SARS-CoV-2 or people with HIV and SARS-CoV-2 co-infection will differ from that in the general population.

If providers have patients who might be a good fit for your studies how can they get them involved?
Dr. Lee: Individuals interested in CHIRP may directly contact the study coordinator, Ellen Stein (ellen.stein@ucsf.edu), or Study PI, Sulggi Lee (sulggi.lee@ucsf.edu). Patients should be informed that it is an intensive translational study with 5 in-person visits done early in infection

Dr. Peluso: LIINC can enroll anyone with PCR-confirmed COVID-19 at any stage of recovery. More information can be found at http://www.liincstudy.org/; interested participants can sign up on the website, email LIINC@ucsf.edu, or leave a voicemail at 628-206-4148.

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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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