Update: May 21, 2020

COVID-19 DIGEST

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

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EPIDEMIOLOGY

LOCAL

As of Wednesday there are **83,859 confirmed COVID-19 cases** and **3,407 deaths** in California. In San Francisco there are 2,185 cases and 37 deaths. Three new testing sites are scheduled to open in the city this week: one in Bayview, one at SF City College, and the first mobile testing site which opened at its first stop in the Tenderloin on Wednesday.

NATIONAL

In the United States over **1.5 million** cases and over **82,000 deaths** from COVID-19 have been reported. All 50 states have started easing COVID-19 related restrictions, even as many do not meet federal benchmarks for re-opening and many have increasing case counts. Texas, which was one of the first states to re-open, reported its highest single-day increase in new cases last weekend.

GLOBAL

Worldwide there are currently over **5 million** reported cases of COVID-19 and **330,000 deaths**. **Brazil** has emerged as a new epicenter of the epidemic with over 271,000 reported cases and 18,000 deaths becoming the country with the third highest number of infections worldwide (behind the United States and Russia). The current estimated effective reproductive number (R_0) in Brazil is over 2.0, the highest in the world, based on ongoing modeling and analysis of active transmission of COVID-19 by Imperial College. The health care system is already severely strained – on Wednesday officials in São Paolo, Brazil's hardest hit state, said they expected their overstretched health care system to collapse within 3 weeks and in the state of Amazonas some towns have no ICU beds and hospitals in the capital Manaus have had to turn patients away. It is heart wrenching to see this explosive epidemic in Brazil. This calls for swift and global national and international action.

UP TO THE MINUTE DISPATCHES

Prone positioning in non-intubated patients with severe COVID-19

A study prior to the COVID-19 epidemic showed mortality benefit for proning intubated patients with severe ARDS. COVID-19 patients are at high risk for ARDS and mechanical ventilators are in limited supply, therefore, providers have been trying prone positioning in non-intubated patients as well. Two studies examined prone positioning in non-intubated COVID-19 patients. A prospective single-center French study of 24 awake, non-intubated COVID-19 patients found 6 patients responded to prone positioning with significantly increased PaO2 (mean of 73.6 to 94.9 mmHg) during proning. After 10 days, 5 patients required intubation, 4 of whom couldn't tolerate proning for more than 1 hour. 10 patients reported back pain, otherwise, no complications arose. A cross-sectional single-center Italian study of 15 patients undergoing non-invasive ventilation in the prone position found all patients had improved SpO2 and P:F ratio during pronation, with 12/15 sustaining improvement after pronation. After 14 days, 1 patient required intubation and 1

patient died. **Conclusion:** Two small, non-randomized single-center trials demonstrate feasibility of awake non-intubated proning. Limitations include selection bias for patients who could tolerate awake proning. Awake proning can be carefully considered to temporize in the right patient, while we await 2 larger ongoing RCTs.

High asymptomatic seroconversion rate in patients and HCWs in a universally-masked dialysis unit after a single case of COVID-19

Dialysis units have been identified as high-risk areas for transmission of COVID-19. A recent study performed a mass testing campaign (PCR and serology) in patients and health care workers (HCWs) in a pediatric hemodialysis unit in Indiana following a patient testing positive. Patients and HCWs wore surgical masks at all times, and HCWs had temperatures checked before and after shifts. On day 0, a single patient with symptoms of COVID-19 tested positive by PCR; that patient was dialyzed in an isolation room throughout the study period. Between day 0-7, 2 HCWs experienced COVID-19 symptoms but tested negative by PCR. Between days 7-21, all 38 patients and HCWs had IgM and IgG testing every 7 days. By day 21, 3/13 patients (23%) and 11/25 HCWs (44%) become seropositive, although none displayed symptoms. Interestingly, no HCWs who cared for the known COVID-19 positive patient seroconverted, but 2/11 healthcare workers that cared for patients who demonstrated subclinical seroconversion also seroconverted (and 1 had a positive PCR at the time of seroconversion). In total, 14/38 (37%) patients and HCWs had seroconversion after a single exposure to a positive patient in a masked hemodialysis unit, but all remained asymptomatic. **Conclusion:** From a single symptomatic patient with COVID-19 a high rate of exposure of patients and HCWs was described despite universal masking in a pediatric dialysis unit. It is possible that the low rate of symptoms could represent a lower inoculum of exposure from universal masking. Other health care environment or community transmission cannot be ruled out as cause of seroconversion.

Did stay-at-home orders decrease COVID-19 transmission in the Midwestern United States?

Iowa was one of 5 states that did not issue stay-at-home orders during the COVID-19 epidemic. It is not known what impact the failure to implement stay-at-home orders may have had on continued COVID-19 transmission. To evaluate this question, researchers utilized a difference-in-differences design to compare the daily changes in COVID-19 cases per 10,000 residents in 8 Iowa counties with that of 7 bordering Illinois counties before-and-after implementation of Illinois' stay-at-home order on March 21, 2020. The authors found similar trends in cumulative COVID-19 cases per 10,000 in neighboring Iowa and Illinois counties before Illinois issued stay-at-home orders, however after that timepoint, cases increased more rapidly in Iowa, while they clearly slowed in Illinois. Within one month, Iowa was estimated to have an excess of 217 COVID-19 cases attributable to the lack of stay-at-home order – this accounted for nearly one-third of the 716 COVID-19 cases confirmed during this period. Estimates accounting for differences in population density and poverty rates between Iowa and Illinois counties as well as differences in the timing of school and nonessential business closures showed similar results. This data suggests that stay-at-home orders may have helped to limit the transmission of COVID-19 in Iowa and builds upon evidence from California demonstrating the positive public health impact associated with early implementation of stay-at-home orders during the COVID-19 epidemic.

FAQ

1. **How often do we see false-negative PCR tests for COVID-19?**
   PCR assay is widely used to diagnose or rule out COVID-19 infection and guide decision-making, including use of isolation precautions. Data are evolving regarding test performance. A pooled analysis of seven studies estimated the false-negative testing rates by day since infection using PCR results from 1330 upper respiratory tract samples and data on time since symptom onset or exposure. Between day of exposure and typical symptom onset on day 5, the false negative rate ranged from 100% on day 1 to 67% on day 4, suggesting a window period between transmission and detectable viral load, during which PCR has less diagnostic value. **Conclusion**: Given the high false-negative rate early in infection, negative PCR results in an asymptomatic patient cannot reliably be used to rule out COVID-19.

2. **Is prior BCG vaccination protective against COVID-19?**
   The bacillus Calmette–Guérin (BCG) vaccine is used to prevent severe tuberculosis (TB) infection, however, epidemiologic studies suggest that BCG vaccination may induce a "trained immunity" that confers protection against viral infections. This has led to speculation that BCG vaccination might also prevent COVID-19. A recent study from Israel reviewed COVID-19 test results from 72,000 residents. They found that there was a comparable proportion of positivity among those born in the 3 years before and after the introduction of universal newborn BCG vaccination (10.4% vs 11.7%; p=0.09). Conclusion: Prior BCG vaccination is unlikely protective against COVID-19 but ongoing trials of BCG in healthcare workers will provide a more robust evaluation.

3. **Can clinicians predict which patients will develop severe COVID?**
   A recent meta-analysis of 45 studies and >4000 patients showed that predictors of severity in patients with COVID-19 (ICU admission, ARDS, mortality) included elevations in leukocyte count, transaminases, LDH, and procalcitonin. A retrospective study has also evaluated the use of chest radiography (CXR) in predicting clinical outcomes in patients presenting with COVID-19. The study evaluated the initial CXR in 338 patients <50 years old. Each CXR was divided into six zones and one point was assigned for each zone containing opacities; a total "CXR severity score" was then calculated from 0 to 6. A higher CXR severity score was associated with hospital admission and intubation. Multiple other studies have also looked at predictors of disease severity in COVID-19. **Conclusion:** Laboratory markers and radiographic testing may be useful to determine which patient develop severe COVID-19 and can be considered when determining triage of patients.

4. **What is a COVID-19 antigen test and how might be useful in patient care?**
   The first SARS-CoV-2 antigen test has received FDA emergency use authorization. The test, manufactured by Quidel corporation, detects the nucleocapsid protein using a laminar flow fluorescence technology that returns a result within 15 minutes using a specialized instrument. Compared to a gold standard of SARS-CoV-2 PCR, the antigen test is 80% sensitive and 100% specific according to the manufacturer's package insert. **Conclusion**: The antigen is less sensitive than PCR. This antigen assay may have a role in settings where rapid turnaround is critical. A negative test does not rule out COVID-19.

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

Interview with Bryn Boslett, MD. Lead for COVID-19 Ambulatory Operations at UCSF Health and Director of the HIV Clinic at UCSF Medical Center

Can you share a little about your day to day as work as the leader for the COVID-19 ambulatory response at UCSF Health?
My role is very unique in that I get to work with many different teams – Population Health, Hospital Epidemiology and Infection Prevention, Clinical Informatics / Apex, Occupational Health, Clinical Laboratories, and more – to create, modify and implement our COVID-19 screening, triage and testing policies and algorithms across UCSF Health. I have also helped to author of many of our patient and provider-facing communications for the UCSF website and Apex smart phrases.

Can you share the evolution of the ambulatory COVID-19 testing program at UCSF Health?
When we started the COVID-19 testing program in early March, we were initially quite limited by lack of testing supplies and safe spaces to see patients. Ambulatory leadership was able to rapidly create several new programs to meet the growing need, including the COVID-19 Hotline, Video Acute Care Clinic, Respiratory Screening Clinics, and Accelerated Care Units. As our testing resources grew, we were able to expand testing to anyone presenting with a COVID-19 compatible clinical syndrome via our Mobile Testing Site at Laurel Heights. By late April, we were able to add asymptomatic screening of patients being scheduled for surgery or certain higher-risk procedures, as well as any planned hospital admission.

What are the biggest challenges to reopening the ambulatory setting?
One of the biggest challenges is fear. Both patients and staff are worried about coming to a place where there are sick people. It's very understandable, but at some point, patients and providers need to see each other. We have put into place a very robust set of safety procedures that minimize risks for anyone who enters our buildings: we provide masks for all patients and employees, screen every patient and employee for COVID-19 symptoms before they enter, arrange COVID-19 testing for all pre-surgical patients and patients admitted to the hospital, and we have detailed infection prevention guidance for almost any scenario one can imagine. I believe that our COVID-19 polices have made UCSF Health one of the safest places in the city.

Do you foresee a long-term need for the use of telehealth for our patients and providers at UCSF?
Yes, I expect there to be an ongoing need for telehealth as one of the strategies to reduce traffic in the clinics and promote physical distancing. I believe it's an overall good thing, so long as we are being fairly reimbursed for these visits. We've had this technology available to us for a few years, but many providers and patients were slow to embrace it. Now that we have been forced to adopt telehealth, I think that most people can see the benefits – no

driving through city traffic, no parking fees, improved access for our more remote patients, etc. There are difficulties too, and nothing really replaces a face-to-face interaction, but for the right scenario the benefits cannot be denied.

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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/

Previous digests can be found: hividgm.ucsf.edu/covid-19
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