Update: May 7, 2020

COVID-19 DIGEST

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

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Guest Contributors: Ayesha Appa, MD, Emma Bainbridge, MD, & Monica Fung, MD

EPIDEMIOLOGY: Stats and thank you to all nurses

As of today there are **60,634 confirmed COVID-19 cases** and **2,460 deaths** in California. In San Francisco there are **1,806 cases and 32 deaths**. Demands to re-open California have led to protesters at the state Capitol in Sacramento. While shelter-in-place restrictions are being eased in parts of California on Friday, the Bay Area and LA are taking a more cautious approach as concerns of a second wave of infections arise among health experts. The United States reached one million cases on Monday—as of today there are **1.23 million** cases and over **73,000 deaths**. Worldwide there are over **3.78 million** reported cases of COVID-19 and **264,000 deaths** as of this morning. **National Nurse Appreciation Week began on Wednesday**, now more than ever we would like to take a moment to reflect on the incredible work and sacrifices nurses make daily on the frontlines.

UP TO THE MINUTE DISPATCHES

Did hospitalizations and deaths vary across the New York City boroughs?
Authors conducted a cross-sectional analysis of COVID-19-related hospitalizations and deaths across the five New York City (NYC) boroughs which have known demographic differences. Hospitalizations and deaths per 100,000 population were highest in the Bronx (634 and 224 respectively) and lowest in Manhattan (331 and 122 respectively). Tests performed per 100,000 were also the highest in the Bronx (4599) compared to Manhattan (2844). The population density of Manhattan is more than double that of the Bronx (~71k vs ~34k per square mile, respectively), and both median age and proportion of population over age 65 is higher in Manhattan. However, the Bronx has a median household income half that of Manhattan and the proportion identifying as Black or Hispanic is double.
Conclusion: the NYC borough with the highest rate of poverty and the most racial/ethnic diversity had the highest COVID-19 hospitalization and death rates, while the borough with highest median income (despite highest population density, median age) had the lowest.

A rapidly developed scalable SARS-CoV-2 vaccine shows promise in non-human primates
A pre-print (non-peer reviewed) study reports the small-scale production of a purified, inactivated SARS-CoV-2 virus vaccine candidate, which induced SARS-CoV-2-specific neutralizing antibodies against the S protein in mice, rats, and macaques. These antibodies were effective in neutralizing 10 representative SARS-CoV-2 strains. Vaccination of macaques provided partial to complete protection (as judged by viral loads from various tissues) and lack in clinical symptoms in animals inoculated with SARS-CoV-2 1 week after the 3rd vaccination. The vaccine appeared well-tolerated and safe without any signs of antibody-dependent enhancement of infection, one of the theoretical concerns in SARS-CoV-2 vaccine development. These studies bode well for the rapid clinical development of a SARS-CoV-2 vaccine in humans that would be ready to enter Phase I clinical trials. **Conclusion**: A purified inactivated SARS-CoV-2 virus vaccine candidate confers complete protection in non-human primates against SARS-CoV-2 strains circulating worldwide by eliciting potent humoral responses devoid of immunopathology.

Could human monoclonal antibiotics be effective in the prevention and/or treatment of COVID-19?
Like the antibodies found in sera of patients previously infected with COVID-19, human monoclonal antibodies (mAbs) that effectively neutralize SARS-CoV-2, could potentially be useful for treatment and/or prevention of COVID-19. Two groups have now reported isolating and developing highly promising human mAbs. The first study screened their previously developed collection of antibodies to SARS-CoV and identified an antibody against the Spike (S) protein adept

at neutralizing SARS-CoV-2 in cell culture. A second study (pre-print, not peer-reviewed) isolated and developed two mAbs from memory B cells of patients that had recently recovered from COVID-19. These mAbs also bound to the S protein and were effective in neutralizing infectivity of a non-pathogenic virus that uses the S protein for binding and entry. **Conclusion**: Production of monoclonal, highly neutralizing antibodies to the S protein of SARS-CoV-2 may be a future strategy for prevention and treatment of COVID-19. Scaled-up production and clinical trials would be natural next steps.

FAQ

1. **Are young adults with COVID-19 at risk for stroke?**
   A small case series in NEJM describes five young patients (ages 33-49 years) who were admitted to a New York City hospital over a two-week period with COVID-19 and large vessel ischemic stroke. Three of the patients had comorbidities such as hypertension or diabetes; only one had a history of prior stroke. Notably, two patients had no respiratory symptoms at presentation. Normally this hospital would treat an average of 0.73 patients <50 years with stroke per two-week period (compared to the five reported here). The authors postulate that stroke may be related to coagulopathy or vascular endothelial dysfunction in COVID-19. **Conclusion**: This study, although extremely small is concerning in light of the association of COVID-19 and disorders of coagulation. We need to be alert to and await more data on COVID-19 associated stroke in young patients.

2. **What is our updated understanding of the impact of COVID-19 in organ transplant recipients?**
   Data on COVID-19 among organ transplant recipients are accumulating rapidly. Several case series, including the largest report of 90 organ transplant (kidney, lung, liver, heart, heart-kidney) recipients with COVID-19, suggest that these patients may be at increased risk for severe disease and mortality (range 7-30%). However, select subgroups, including patients earlier after transplant, may have more favorable outcomes. Organ transplant recipients seem to have typical clinical presentation with predominant symptoms of fever, dry cough, dyspnea, and diarrhea. Most have underlying comorbidities associated with COVID-19 such as hypertension, diabetes, obesity, and chronic kidney or lung disease. Decreasing immunosuppression has been a mainstay of treatment, though some patients have recovered without changes. **Conclusion:** Organ transplant recipients with COVID-19 may be at increased risk for complications of COVID-19 but it possible that their other comorbidities may be the driving risk factors for severe disease, not immunosuppression. Prospective studies are needed to guide the management of COVID-19 among organ transplant recipients.

3. **Does the use of biologics for patients with autoimmune diseases increase risk for severe COVID-19?**
   It is unknown whether patients with autoimmune conditions are at increased risk for COVID-19 as a result of biologics, or whether these agents may have a protective effect against the cytokine storm seen in some patients. A recent case series describes 86 patients with immune mediated inflammatory diseases of which 62 (72%) were on biologics or JAK inhibitors. Only 14 (16%) required hospitalization. The percentage of patients on biologics and JAK inhibitors was higher among the ambulatory patients. In a multivariate analysis, hospitalized patients were more likely to be receiving steroids, methotrexate or hydroxychloroquine. Two deaths were reported, neither of these patients were on biologics or JAK inhibitors. When compared to the general population in NY, age-related hospitalization was not increased among this patient population. **Conclusion**: Use of biologics in patients with autoimmune disease and COVID-19 does not seem to be a risk factor for worse outcomes. The COVID-19 Global Rheumatology Alliance has been created with a registry for patients with rheumatologic conditions and COVID-19, an effort led by faculty from UCSF and ZSFG.

4. **How is remdesivir going to be available given the FDA changes?**
   Remdesivir was approved under Emergency Use Authorization on 5/1/2020 for IV administration to hospitalized COVID-19 patients, based on preliminary data from the ACTT-1 study. Per the EUA factsheet, recommended adult dosing is 10 days for critically ill patients (intubated/ECMO) and 5 days for all others, with the ability to extend to

10 days if no clinical improvement. Gilead has donated RDV to the US federal government which will coordinate the distribution. Per the distribution website, hospitals identified by the U.S. government as a recipient for donated remdesivir will be proactively contacted; to find out if your hospital has been designated to receive donated remdesivir, you can email remdesivir@amerisourcebergen.com and provide facility name, ship to address with zip code, Health Industry Number and DEA number.

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

An interview with Joe Derisi, PhD and Steve Miller, MD, PhD on the UCSF and Chan Zuckerberg BioHub collaboration to provide a rapid scale up of COVID-19 testing to UCSF and the Bay Area.

Dr. Steve Miller is the Director of the UCSF Microbiology Laboratory and Professor of Laboratory Medicine at UCSF

Dr. Joe DeRisi is Co-Preident of the Chan Zuckerberg BioHub and Professor of Biochemistry and Biophysics at UCSF

At the beginning of the epidemic, at what point do you recognize that you were going to need significant support to ramp up testing?

Dr. Miller: In late January/early February, we became aware of the urgent need to develop and implement COVID-19 testing, but FDA regulations essentially precluded laboratories from developing their own assays. Fortunately, on March 2 the regulations were modified to allow academic laboratories to pursue emergency use authorization. On March 9, we went live with a modified version of the CDC assay for COVID-19 RNA detection. Given the increasing spread it became apparent we would need high-throughput testing, and we began exploring all potential options. Normally, commercial test manufacturers would take the lead in doing this, but since these were taking time and we were seeing shortages of supplies and reagents, we started looking at options to convert research testing facilities and resources into clinical use.

How did you conceive of the idea of using the CZ BioHub for testing and what were some barriers to creating this partnership between UCSF and CZ Biohub?

Dr. DeRisi: The question was "how can we mobilize a huge, and highly trained workforce (our graduate students and postdocs) that otherwise would be forced to stay at home?" Originally, the idea was to engage in "research only" activities - testing that would not return a result back the patient. The fact that results would not be returned to patients was inherently dissatisfying, since those who were asymptomatic and possibly positive for the virus would not be informed of their status. The barriers to actual clinical testing are significant. In this case, a key barrier, having to do with personnel requirements, was suspended by an Executive Order by the Governor on March 12th. This immediately cleared the way for us to consider utilizing volunteers and space UCSF had been leasing next to the Biohub as a "pop up" CLIA lab expansion, together with the Clinical Lab here at UCSF. That effort began in earnest on March 12th. With the help of a huge number of volunteers and Biohub staff, the SARS-CoV-2 real time assay was validated and "go live" on March 20th. This incredible speed would not have been possible without a close partnership with Ed Thornborrow and Steve Miller!

What is the present testing capacity on what testing mechanisms are being used?
Dr. Miller: Currently the clinical laboratories at China Basin and the hospital sites have 5 different assay platforms running with a total potential throughput of > 1,000 samples per day. With the addition of the testing available at CZ Biohub, there is capacity to perform an additional 2,000 tests per day. We are overcoming several barriers to achieving that capacity, notably the shortage of swabs and tubes to collect samples, ability to handle and process large numbers of samples, and reporting of results through electronic means. Our partners have also had to ramp up their capacity to collect patient samples, and as all of this improves, we are increasing the utilization of that testing capacity. The Biohub's peak throughput for a 72-hour period was 3,245 samples tested during the COVID-19 Mission Study led by Diane Havlir.

How do you foresee this work enhancing the UCSF-CZBioHub partnership in the future?
Dr. Miller: We anticipate continuing to work closely together to support the clinical mission and perform research studies related to COVID-19 epidemiology, pathogenesis, tests development, and other areas. As commercial manufacturers and other laboratories build their testing capacity, there will be less of a need for Biohub to perform clinical testing, and eventually there will be an end declared to the COVID emergency, at which point the regulatory changes that enable clinical testing at Biohub will revert to their prior form. Currently, we are working to help our partners at other institutions and DPH to enable their testing, and much of this work can continue as needed. Over time, we will focus on other emerging infectious threats and use the experience gained to improve our ability to detect and respond to emerging agents.

Dr. DeRisi: Together with UCSF, the Biohub will dramatically ramp up our molecular epidemiology efforts, including full genome sequencing of positives from within San Francisco and throughout the State. In collaboration with CDPH, the Biohub and UCSF have a major role to play as a force to improve public health by providing surge testing capacity, advanced analytics, and genomics services.

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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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