Update: June 25, 2020

COVID-19 DIGEST

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

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EPIDEMIOLOGY

LOCAL

As of today, **3,297 positive cases** and **48 deaths** have been reported in San Francisco. Since February 28, **129,617 test results** have been reported (positive test rate 3%) and only 1.5% of COVID-19 tests performed in June are positive to date. California now reports **195,897 confirmed COVID-19 cases** and **5,723 deaths**, with Los Angeles County (89,490 total cases and 886 cases/100K) and Imperial County (5,549 total cases and 3,079 cases/100K) continuing as hotspots in Southern California. The positive test rate statewide was 4.8% last week. As of June 23, 5,399 persons were hospitalized statewide, the highest level since early April. We are very pleased to report that on June 18 Governor Gavin Newsom issued a statewide order for face coverings to be worn in all public places. Uptake of face coverings continues to be variable and contentious in the state despite data supporting their value.

NATIONAL

On Wednesday, the United States reported the highest single-day increase with more than 36,000 new cases reported. In the United States there are now more than **2.3 million reported cases** of COVID-19 and more than **122,000 deaths** with the majority of new cases concentrated in the Southeast and Western US. Cases, positive test rate, and hospitalizations are all increasing in Texas, Arizona, Florida, South Carolina, and Georgia. The surge in hospitalizations is severely straining capacity in Texas; in Houston 97% of ICU beds are occupied and Texas Children's Hospital has started admitting adult patients. Arizona's ICU beds are currently at 88% capacity. No post-protest surges have been seen in New York, Boston, Minneapolis, and an analysis across 315 US cities did not find evidence of an increase in cases following Black Lives Matter protests.

GLOBAL

Worldwide there are currently over **9.3 million** reported cases of COVID-19 and **almost half a million deaths**. In addition to the United States, global hotspots in India, Latin America, and Africa are experiencing accelerating epidemics. Record numbers of new cases have been reported in India nearly every day in the last week, public hospitals in the urban centers of New Delhi and Mumbai are overflowing, and the geographic spread is increasing with infections reported in nearly all of India's districts. Brazil has the second-highest death toll in the world (behind the United States), with more than 52,000 deaths and 1.1 million reported cases. In Mexico a staggering 59% of tests were positive over the last 7 days. Over 326,000 cases are reported across the African Continent, with almost a third in South Africa where there are over 106,000 cases and 2,100 deaths.

UP TO THE MINUTE DISPATCHES

What is the prevalence of antibodies among different age groups in Geneva, Switzerland?

Repeated testing for anti-COVID-19 antibodies (serosurvey) in an unselected population yields more accurate estimates of the true burden of COVID-19 and allows for monitoring of COVID-19 transmission dynamics in communities over time. Investigators undertook anti-COVID-19 IgG antibody testing between April 6 and May 9 (a period of declining

hospitalizations and public health measures to reduce transmission) among 2,766 randomly selected individuals (≥5 years) living in Geneva, Switzerland who were previously enrolled in a population-representative study. Bayesian logistic regression was used to estimate the weekly seroprevalence of COVID-19 accounting for the antibody test performance and adjusted for the age and sex distribution of Geneva's population. Preliminary results showed a seroprevalence in the first, second, third, fourth and fifth weeks of 4.8% (95% CI: 2.4–8.0), 8.5% (5.9–11.4), 10.9% (7.9–14.4), 6.6% (4.3–9.4), and 10.8% (8.2–13.9), respectively. Using individuals 20-49 years as a reference, children 5-9 years old were substantially less likely to have detectable anti-COVID-19 antibodies (relative risk [RR] = 0.32 [95%CI:0.11-0.63]), as were adults ≥65 (RR=0.50 [0.28-0.78]). Only a single child <10 years old had detectable COVID-19 antibodies, despite 17% of children <10 years old living in households where at least one other infection had occurred. Authors estimated that for each confirmed COVID-19 case ascertained through their health systems, there were in fact nearly 12 community infections. **Conclusion:** These results provide interesting insights on cumulative disease burden at the tail-end of the first phase of the COVID-19 epidemic in Geneva, and highlight differences among age groups that may reflect either biological differences in susceptibility to infection and also behavioral changes that may have protected older adults at risk.

Genome-wide Association Study of Severe Covid-19 with Respiratory Failure

There is considerable variation in disease severity among patients with COVID-19. Researchers in Europe conducted a genome-wide association study (GWAS) to try and identify genetic factors associated with severe disease. They included ~8.5 billion single nucleotide polymorphisms of 2 case control panels of patients. Group 1: 835 patients with severe COVID-19 and 1255 uninfected controls from Italy, and Group 2: 775 patients with severe COVID-19 and 950 uninfected controls from Spain. The study identified 2 loci with statistically significant associations with severe disease. One loci spanned a region which encodes an amino acid transporter that may interact with the COVID-19 receptor on human epithelial cells, angiotensin converting enzyme 2 (ACE-2), as well as genes encoding the chemokines CCR9 and CXCR6. CXCR6 may regulate lung-resident memory CD8 T cells in response to airway pathogens. The second significant locus coincided with the ABO blood group, with a higher risk of severe infection in blood group A and a protective effect in blood group O, consistent with another recent pre-print study. A limitation of the study is that the control groups were comprised primarily of patients not exposed to COVID-19 rather than patients who were exposed and were not-infected or asymptomatic. **Conclusion**: This study suggests some provocative associations with loci that may interact with ACE-2, chemokines, and the ABO blood group. Verification of this study with broader populations including infected controls with asymptomatic or mild COVID-19. The definitive link between a gene and a COVID-19 outcome may also require testing in animal models, model organisms, and/or cell culture.

Upper Airway Gene Expression Differentiates COVID-19 From Other Acute Respiratory Illnesses and Reveals Suppression of Innate Immune Responses by SARS-CoV-2

A recent study (pre-print, not peer reviewed) from researchers at UCSF and Chan Zuckerberg Biohub examined the host gene response to SARS-CoV-2 by metagenomic sequencing. They used swabs from 238 patients with acute respiratory illnesses who underwent testing for COVID-19. 94 tested positive for COVID-19, 41 for other pathogenic respiratory viruses and 103 had no virus detected. They found that when compared to other viral respiratory infections, patients with COVID-19 demonstrated a diminished innate immune response, with reduced expression of genes involved in toll-like receptor signaling, interleukin signaling and chemokine binding, neutrophil degranulation and recruitment of immune cell types. **Conclusion**: Infection with SARS-CoV-2 is associated with a suppressed innate immune response in the upper airway when compared to infection with other pathogenic respiratory viruses, in patients tested for COVID-19. This finding may be an important factor underlying the early, asymptomatic viral replication and infectiousness observed in COVID-19. Future longitudinal studies will be required to understand the underlying mechanisms and temporal dynamics of this observation throughout the course of SARS-CoV-2 infection.

FAQ

1. **What are the recommendations for prevention of COVID-19 in dental settings?**
   San Francisco DPH has a detailed health directive. Elements include posting signage, social distancing, symptom screening for patients and personnel, screening for close exposures within 14 days, face coverings for all (including

patients when not receiving care), and hand hygiene protocols. The directive is to minimize aerosol generating procedures (AGPs), and PCR testing within 7 days of a non-emergent AGP is "strongly recommended." For AGPs, four-handed dentistry, high evacuation suction, and dental dams are recommended. CDC guidance additionally recommends that personnel wear surgical masks + eye protection + gloves + gowns if there may be splashing or splattering, with N95s or higher level respirators used for AGPs in those assumed to be non-infectious. Only emergent procedures should be performed if COVID-19 positive.

2. **What is our updated understanding of the seroprevalence of SARS-CoV-2 infection in Southern California?** Our present understanding of the prevalence of COVID-19 infection is based mostly on PCR testing. Antibody testing is helpful since it would detect patients who had previously asymptomatic or milder infection who may have not been tested. In order to better understand the seroprevalence of COVID-19 in LA County researchers conducted a study offering antibody (IgM/IgG) testing to a random sample of patients at 6 study sites as well as in-home testing. 1,952 people were invited and 865 (50.6%) were tested. 35 individuals tested positive resulting in an overall adjusted seroprevalence of 4.65%. Amongst different race/ethnic groups prevalence was Black (6.94%), White (4.42%), Hispanic (2.10%). The study respondents were disproportionately white, affluent, and female in this investigation; the authors attempted to adjust for differing characteristics for study participants versus the general LA County population. **Conclusion**: This study suggests a much higher number of COVID-19 cases have occurred in LA county than had been reported (367,000 versus 8,430 as of 4/10/20). Ongoing surveillance is needed to understand the impact of COVID-19 throughout the state and in particular among vulnerable populations.

3. **What is our updated understanding of smell and taste dysfunction in patients with COVID-19?** A recent article reported results of a telephone survey in 204 patients with COVID-19. Patients reported a reduction in taste (in 55%) and smell (in 42%) at a median of 4 days before diagnosis (40% had both, and it was severe in 35-40%). Only 15-17% of patients with severe reduction in taste/smell reported severe nasal obstruction, suggesting that the pathophysiology may be a direct effect of the virus on the olfactory nerve rather than solely due to nasal inflammation and obstruction. Overall, this study adds to a growing body of (mostly retrospective) studies showing that disorders of taste and smell are very common in COVID-19, ranging from 34% to 89% depending on the study. **Conclusion**: Disorders of taste and smell are common presenting symptoms of COVID-19 and can occur without nasal congestion.

4. **Does neighborhood and dwelling matter for COVID-19 risk?** A previous study in New York revealed significant disparities in hospitalization and death rates across the city boroughs, with highest rates in Queens and the Bronx. This cross-sectional study of pregnant women investigated associations between the "built environment" (large households, household crowding, and low socioeconomic status) and neighborhood among pregnant women delivering at NY-Presbyterian hospitals after implementation of a universal SARS-CoV-2 PCR testing campaign. Of 396 women tested, 71/396 (17.9%) of patients were infected with SARS-CoV-2. Odds of infection (all odds ratios presented as interdecile) were lower among women living in buildings with more residential units (OR, 0.34 [95% CI, 0.16-0.72]), higher appraised values (OR, 0.29 [95% CI, 0.10-0.89]), and in neighborhoods with higher median incomes (OR, 0.32 [95% CI, 0.12-0.83]). Odds of infection were higher among women residing in neighborhoods with higher unemployment rates (OR, 2.13 [95 CI, 1.18-3.83]), large household membership (OR, 3.16 [95% CI, 1.58-6.37]), and greater household crowding (OR, 2.27 [95% CI, 1.12-4.61]). Limitations of the study include small sample size and specialized patient population (pregnant women). **Conclusion**: This study provides empirical evidence for the hypothesis that variation in the urban environment, including overcrowding and poverty, are important social determinants of SARS-CoV-2 transmission. Support for those unable to socially distance under these conditions will be important for curbing the COVID-19 pandemic in the U.S.

Reflections on the human experience during COVID-19

The human experience of the frontline health providers during pandemics is one chronicled throughout history in

journals and portrayed in powerful works of fiction. As we are in the midst of this pandemic, we wanted to call out an insightful piece published in JAMA written by Dr. Allison Bond, one of our infectious disease fellows at UCSF. Excerpts of her reflections are below.

Now we are left to care for patients in the hospital as if in a vacuum; we wonder who they and their loved ones truly are. I never got to meet the partner of the patient who was pregnant and sick with COVID-19, a recent immigrant who had sought medical care when she could no longer bear the sensation of impending suffocation. She lived with 7 other people in a small apartment, and I found myself wondering about her partner in particular. Had he discouraged her from going to the hospital, or had he called the ambulance? Was he supportive, neglectful, or even abusive? We were left guessing about details that had important implications for her care. I fear that if enough time passes, we might forget how important visitors are not only to patients but also to the care we provide. Worse, we may decide it's more convenient to do without them.

We navigate these uncharted waters together, my colleagues, patients, and I, yet we are unable to truly see each other. It has been a surreal trip into a parallel dimension in which we may be together, but too often feel utterly alone. I'm not sure it will ever be the same again. In fact, I worry that it won't be.

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LATE BREAKING NEWS

Dexamethasone: A step forward for critically-ill COVID patients

The RECOVERY trial is an open-label pragmatic randomized controlled trial of over 11,000 participants conducted by the UK National Health service, representing 15% of UK hospitalized COVID patients. The study randomizes participants 2:1 to usual care (no placebo) vs. one of 4 active COVID treatments; the hydroxychloroquine arm was stopped due to lack of efficacy. In a preprint analysis of the dexamethasone arm, 2104 patients were randomized to up to 10 days of 6 mg of dexamethasone vs. 4321 participants eligible for dexamethasone and assigned to usual care. Overall, significantly fewer patients assigned dexamethasone died within 28 days than those in the control group, a difference driven by a marked one-third mortality reduction in those on mechanical ventilation (29% vs 40.7%, RR 0.65 [95% CI, 0.51 to 0.82]) and a one-fifth reduction in those requiring oxygen but not intubated (21.5% vs 25%, RR 0.80 [0.70 to 0.92]). Hospitalized, non-hypoxic patients saw no benefit (17% vs 13.2%, RR 1.21 [0.93 to 1.61]). No participants received remdesivir or convalescent plasma; a small number (4-6%) underwent a second randomization to tocilizumab vs. control due to clinical deterioration. 7% of control arm patients received dexamethasone. Data were not presented on adverse events attributed to steroid use nor on which patients were excluded from this intervention. **Conclusions:** Given the results of this study in patients with COVID-19, dexamethasone should be used for critically-ill patients, should be considered for some hospitalized hypoxic patients not requiring mechanical ventilation, and be avoided in non-hypoxic patients. Outcomes of hospitalized patients treated with steroids in conjunction with antivirals will be examined in ongoing studies.

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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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