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COVID-19 DIGEST

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

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EPIDEMIOLOGY

LOCAL

California now reports **122,238 confirmed COVID-19 cases** and **4,444 deaths**. In San Francisco there are currently **2,644 cases** and **43 deaths**. 6 Bay Area counties are among the 7 counties statewide who have not moved into advanced Stage 2 re-opening (which allows retain and dine-in restaurants). San Francisco issued an updated Health Order on face coverings was issued on May 28; Face coverings are now required whenever leaving the home and whenever anyone other than members of their household or living unit are within 30 feet (unless they meet certain exceptions).

NATIONAL

In the United States there are now more than **1.8 million reported cases** of COVID-19 and more than **108,000 deaths**. This week as millions across the country protest police brutality and structural racism, the COVID-19 pandemic continues to highlight longstanding health disparities in the United States. Black and Latinx populations in the United States are more likely to get infected and to be hospitalized from COVID-19 than White populations (see dispatch below) and have suffered a greater economic impact. Areas that report COVID-19 data by race/ethnicity show pervasive disparities in case rates: 48% of reported cases in San Francisco are among Latinx (15% of the population); in Chicago reported case rates are 3.8 times higher among Latinx and 2.4 times higher among Black populations compared to White populations; and in Minnesota 22% of reported cases are among Blacks (6.6% of the population) and 20% are among Hispanics (5.5% of the population). Nationally, age-adjusted hospitalization rates among non-Hispanic Blacks are 4.5 times that of non-Hispanic Whites, while rates among Hispanic/Latinx are approximately 3.5 times that of non-Hispanic Whites. And while just 13% of the US population is Black, 24% of the deaths from COVID-19 are among the Black population. A recent report by the Economic Policy Institute on the economic impact of the epidemic on black workers found that Black workers were both more likely to have lost their jobs as a result of the pandemic *and* more likely to be employed in front-line essential jobs than white workers.

GLOBAL

Worldwide there are currently over **6.5 million** reported cases of COVID-19 and **385,000 deaths**. While the United States continues to be the global epicenter of the pandemic that threatens millions of persons on multiple continents around the globe, last Friday the United States withdrew from the World Health Organization. Mexico, where currently over 101,000 cases and almost 12,000 deaths have been reported, began re-opening its economy on Monday the same day it reported the highest daily total of new infections. Hospitals in Mexico city are currently operating at 80% of capacity raising concerns that increasing cases could overwhelm the system.

UP TO THE MINUTE DISPATCHES

A prospective study of venous thromboses among critically ill patients with COVID-19

Multiple reports have suggested that COVID-19 is associated with an increased risk of venous and arterial thrombotic events, though the underlying mechanisms remain uncertain. Of note, ARDS and critical illness have been associated with coagulopathy, and reports during the H1N1 influenza epidemic documented a substantial incidence of venous

thromboembolism (VTE). In order to quantify the burden of VTE among ICU patients with COVID-19, a prospective study of 34 patients admitted to a French ICU. All underwent routine lower extremity ultrasounds at time of ICU admission, and studies were repeated after 48 hours if no thrombi were found initially. The investigators found that 65% of participants had lower extremity DVTs at time of ICU admission, increasing to 79% of participants by 48 hours following ICU admission. Eighteen patients (53%) had bilateral thrombosis, and 9 patients (26%) had proximal thrombosis. **Conclusion**: VTE is very common among critically-ill persons with COVID-19, but not all venous thrombi may be clinically significant. Randomized controlled studies are needed to determine whether more than routine VTE prophylaxis would be beneficial.

A Randomized Trial of Hydroxychloroquine (HCQ) as Post-Exposure Prophylaxis for COVID-19 shows no benefit
A randomized controlled trial used social media to recruit 821 asymptomatic subjects with self-reported household or occupational exposure to a confirmed case of COVID-19. Participants were randomized to a 5-day course of HCQ versus placebo within 4 days of a high- or moderate-risk exposure; there was no significant difference between groups (11.8% vs 14.3%) in development of illness compatible with COVID-19 by day 14. Adverse events mild in severity were more frequent in the HCQ group (40.1%) compared to placebo (16.8%). Limitations of the study included monitoring (everything done remotely by self-report), its largely clinical definition of the primary outcome (only 18.7% of infections were PCR-confirmed); the relatively long interval between exposure and HCQ initiation (≥3 days in most subjects, which some argue is too late); and its young (median age 40) cohort. In addition, an observational study on HCQ/chloroquine use that had demonstrated no benefit was retracted by the Lancet following significant concerns were raised about the statistical analysis and data integrity. **Conclusion**: HCQ post-exposure prophylaxis did not prevent development of symptoms compatible with COVID-19. Other ongoing trials will determine whether HCQ has a place in treatment of COVID-19. HCQ should only be used for COVID-19 treatment in the setting of a clinical trial in light of accumulating data.

Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: insights and knowledge gaps
A meta-analysis evaluating the efficacy of respiratory protection (N95 respirators or surgical masks), physical distancing, and eye protection has been interpreted as indicating that N95s are more protective than surgical masks when caring for patients with COVID-19. The studies included were highly variable in setting, design, and quality and focused on 3 different pathogens (SARS-CoV-1, MERS, and SARS-CoV-2). A subgroup analysis of 10 studies compared the impact of N95s to surgical masks had limitations. Limitations included that 4 studies compared N95s vs. no masks and 6 studies surgical masks vs. no masks; no studies compared N95s to surgical masks. In addition, only one study focused on COVID-19 and was from a single hospital in Wuhan that compared 2 convenience provider groups: Group 1 used N95s/frequent hand hygiene and Group 2 used no masks/"only occasional hand hygiene." Results showed a significantly lower odds ratio for acquiring COVID-19 for Group 1. **Conclusion**: This meta-analyses with data from very diverse sources and settings supports physical distancing, the use of respiratory protection and eye protection to prevent COVID-19 transmission. It does not inform the N95s vs surgical masks debates.

How do hospitalization and mortality differ among Black versus White patients with COVID-19?
This retrospective cohort study compared hospitalizations and mortality rates among non-Hispanic Black and White patients with RT-PCR confirmed COVID-19 in care through an integrated healthcare delivery system in Louisiana between March 1-April 11th, 2020. Although Black patients make up just one third (31%) of the population in this database, they represented the majority (70.4%) of the 3,841 COVID cases diagnosed. Black individuals also comprised the majority of COVID patients requiring hospitalization (76.9% of 1,382 patients) and of those who died (70.6% of 336 patients). Compared with their White counterparts, Black individuals with COVID-19 were more likely to be insured by Medicaid (15.0% vs 5.0%), to reside in low-income parts of the state (56.9% vs 29.0%), and to have comorbidities -- including obesity (53.9% vs 39.5%), diabetes (18.9% vs 10.0%), and hypertension (33.8% vs 23.9%). In adjusted multivariate models, Black race was independently associated with risk of hospitalization from COVID-2019 (OR 1.96, 95% CI 1.62-2.37). In a time-to-event, Black race was not independently associated with an increased risk of in-hospital death when adjusted for other sociodemographic and clinical characteristics. **Conclusion:** Black race was not found to be an independent risk factor for in-hospital mortality. However, there is a disproportionate impact COVID-19 on Blacks

who were more likely to be both infected and hospitalized for SARS-CoV-2, underscoring this important health disparity being seen around the US.

FAQ

1. **How common are co-infections in patients with COVID-19?**
   Early data from China suggested that co-infection with other respiratory pathogens was rare in patients with COVID-19. A recent systematic review and meta-analysis (pre-proof, not peer reviewed) of thirty studies including 3,834 patients with COVID-19 demonstrated that bacterial co-infection was present in 7% of hospitalized patients and that rates were higher in the ICU compared to the non-ICU ward setting (14% vs. 4%). The pooled proportion of viral co-infections in this study was 3%, with RSV and influenza A being the most common pathogens. Another recent study examined nasopharyngeal specimens from 1,206 patients in northern California and found that among 116 laboratory confirmed cases of COVID-19, viral co-infection was present in 24 (20.7%) specimens. RSV and rhinovirus/enterovirus were the most common co-pathogens. **Conclusion**: Rates of bacterial co-infection in patients with COVID-19 are overall low, which has important implications for antibiotic stewardship in the hospital. Rates of viral co-infection differ widely between studies, which likely reflects differences in sample size as well as seasonal and geographic trends.

2. **Updated understanding of the impact of COVID on patients with cancer**?
   Cancer patients appear to be at increased risk of COVID-19 as well as severe complications. Earlier reports from China demonstrated an increased prevalence of malignancy among COVID-19 patients and COVID-19 among cancer patients. Subsequent larger studies from China, the U.S. (including New York City), and the U.K. have also found that patients with cancer and COVID-19 are at increased risk for severe disease (requiring intensive care or mechanical ventilation) and death with reported case fatality rates ranging 20-29%. Amongst this population, the highest risk for severe disease and mortality included patients with other known risk factors COVID-19 complications (older age, male gender, hypertension, cardiovascular disease), advanced malignancy, recent chemotherapy, and hematologic malignancy. **Conclusion**: Patients with cancer and COVID-19 are increased risk for severe disease. Further studies are needed to determine whether behavioral (frequent healthcare exposure) vs. clinical (myelosuppression/ immunosuppression) risk factors are most associated with these poor outcomes.

3. **What are the outcomes of patients undergoing surgery with perioperative COVID-19?**
   A recent international multicenter cohort study examined 30-day mortality and rate of pulmonary complications in a cohort of 1128 patients diagnosed with COVID-19 in the 7 days before (26.1%) or 30 days after (71.5%) undergoing surgery. Most (74%) operations were emergent and 74.6% were classified as major. Thirty-day mortality was 23.8% and pulmonary complications occurred in 51.2%, accounting for 82.6% of deaths. Risk factors for mortality included male sex, age≥70, malignancy, and emergent or major surgery. Limitations of this study are: 1) no control group; 2) lack of universal testing may have biased the cohort toward those with more severe or symptomatic COVID-19; 3) many centers limited lower-risk/elective surgeries during this time period, biasing towards higher risks of morbidity and mortality. **Conclusion:** Patients with perioperative COVID-19 appear to have a higher risk of poor outcomes than is generally reported for most surgeries. Decisions around delaying surgery must account for this risk but should also balance risks of progression of underlying disease. Studies of outcomes in patients with asymptomatic infections undergoing surgery will be informative.

4. **What do we know about HIV increasing or decreasing the risk of COVID-19?**
   Researchers in Spain have now completed the largest prospective cohort study to date of 51 consecutive HIV positive patients admitted COVID-19 to a single hospital in Madrid. Compared with a cohort of 1,288 people living with HIV (PWH) without COVID-19, those who were diagnosed with COVID-19 were more likely to have a higher BMI (25.5 vs 23.7, $p<0.05$), to have hypertension, diabetes, chronic kidney disease, chronic liver disease, and to have been on tenofovir-based anti-retroviral therapy (ART) prior to their COVID diagnosis, although the majority of

patients were on tenofovir. There were no differences in clinical features, laboratory abnormalities, and radiographic changes among PWH and those without HIV from other series. PWH with CD4 counts <200 cells/mm^3 did not exhibit differences in clinical outcomes compared to those with higher CD4 counts. ART regimen did not change the risk of mild, moderate or severe COVID-19. **Conclusion:** Most data to date suggest persons with HIV are not at increased risk of COVID-19 susceptibility or severe disease—however the studies are small like this one. Whether any ART regimen protects from COVID-19 is still an open question.

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

Epidemiology and characteristics of COVID-19 in children with Drs. Ted Ruel and Lynn Ramirez

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Are children getting COVID-19?

Overall children continue to be a small proportion of reported COVID-19 cases. But, compared to earlier in the pandemic, the proportion of reported COVID cases is increasing in those 0-18 years of age. Currently, among reported COVID-19 cases children in: San Francisco account for 7% of cases, California account for 5.8% of reported cases with 70% of these occurring in LatinX, and US account for 4% of cases with 50% of these occurring in LatinX. The increased burden of COVID-19 in children can be reflective of increased access to testing over time including testing those with mild/no symptoms. Continued vigilance of the pediatric COVID-19 trends is needed.

How often are we seeing symptomatic COVID-19 at BCH-SF?

COVID-19 has been relatively uncommon at BCH-San Francisco. The BCH-San Francisco overall COVID-19 positivity testing rate is about 1% and the symptomatic rate is 1.5% (0-18 years of age).

How clear is the correlation between Multisystem Inflammatory Syndrome in Children and COVID-19?

The evidence of a link between SARS-CoV-2 and a syndrome being referred to as Multisystem Inflammatory Syndrome (MIS) is increasingly strong. The first suggestion came simply from the timing of presentation: increased numbers of MIS-like syndromes were diagnosed in European children weeks after the surge of COVID-19 in adults.

In the USA, we have also seen MIS-like cases following surges on the East Coast. And using newly available testing, we are finding that most children with MIS also have antibodies to SARS-CoV-2, pointing to prior infection.

However, in areas of lower COVID-19 incidence like ours, we must remain equally alert to the possibility of other infections and inflammatory conditions in children that could look similar and lead to harm if not diagnosed and treated promptly.

What do you foresee school will look like for kids this fall? Is there a way to make it safe?
I am cautiously optimistic that we will be able to open schools this Fall in a safe, albeit modified, way. It will depend on what happens to COVID-19 incidence as we relax restrictions and learn from summer camps. In our region, we have proactive school and public health officials who work closely with epidemiologists, and we have shown that we are able to control infections with sheltering policies.

We should expect modified schedules, limitation in group size, certain activities (e.g. close contact sports, singing) and a surveillance strategy. While published data are a little mixed, several studies have shown that when opened with proper surveillance, schools can operate and limit transmission to adult and other children.

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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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