Update: April 30, 2020

COVID-19 DIGEST

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

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EPIDEMIOLOGY

LOCAL

As of today there are **46,506 confirmed COVID-19 cases** and **1,873 deaths** in California. In San Francisco there are 1,499 cases and 25 deaths. On Monday San Francisco and the other 6 Bay Area Counties announced the extension of shelter-in-place retrictions through the end of May.

NATIONAL

The United States reached one million cases on Monday and as of today are **1.06 million** cases and over **60,000 deaths**. The epicenter in New York now reports over 300,000 confirmed cases, more than any other individual country, and over 23,000 deaths. However, in continued signs of improvement, new hospital admissions are down 70% and daily deaths down 50% from their peak earlier this month. Many states are starting to re-open their economies. Today we will highlight infection hotspots in food processing plants throughout the United States. Focal outbreaks have occurred at least 80 plants in 26 states, leading to over 4,400 infections and 18 deaths among workers and the death of an inspector for the USDA. The CDC and the Occupational Safety and Health Administration (OSHA) have issued new guidance for meat and poultry processing workers and employers advising increased distance between workers during work and breaktimes, using physical barriers, improving ventilation, and increased handwashing/sanitizing stations. Yesterday President Trump issued an executive order compelling meat processing plants to stay open using the Defense Production Act and cited these plants as part of the critical infrastructure needed to keep people fed.

GLOBAL

Worldwide there are over 3.2 million reported cases of COVID-19 and 231,000 deaths as of this morning. In Spain, the hardest hit country behind the United States with over 230,000 reported infections, children are now allowed to play outside and adults will be able to exercise outside the home starting on May 2. France will start a gradual exit from lockdown on May 11, opening up shops and some business (but not bars or restaurants yet). Countries in Asia which initially oversaw effective responses now seeing a second wave. Singapore has seen a surge of coronavirus cases among migrant workers living in dormitories. As of Tuesday, coronavirus cases linked to migrant worker dormitories accounted for 88 percent of Singapore's 14,446 cases. Japan was initially praised for its early and fast action to mitigate the outbreak, however after lifting restrictions the northern island of Hokkaido has seen an even larger second wave of infections and is now back in lockdown.

DAILY UPDATES

https://www.who.int/emergencies/diseases/novel-coronavirus-2019

UP TO THE MINUTE DISPATCHES

Remdesvir (RDV) Trifecta: There were three major updates from clinical trials of RDV released 4/29/2020

Summary of studies:

ACTT-1 Study: Interim data was presented this fully enrolled, NIH-sponsored, randomized controlled trial evaluating 10 days of RDV vs. placebo in 1063 hospitalized patients. A preliminary DSMB analysis of about 400 patients found: a) 31%

faster time to clinical recovery in those on RDV (11 vs 15 days, p <0.001) and b) a trend towards improved mortality with RDV, 8% vs. 11.6%, (p=0.059). Top-line analysis of the full data set is expected in several weeks.
RCT from China: A similarly designed RCT of RDV vs. placebo conducted in China found no difference in mortality, time to clinical recovery, or adverse events between arms; however, this study was underpowered as enrolled 237 out of 453 planned participants, due to declining COVID cases. Of note, there was no difference in quantitative PCR decline between arms; no viral cultures were done.
SIMPLE trial: This Gilead sponsored study, was an open label study of 5 vs 10 days of RDV in severe disease. They reported no difference in outcomes between arms, suggesting a shorter course of RDV may be possible, which would be welcome given current limitations in available RDV. Both the Chinese study and the SIMPLE trial reported a non-significant trend towards improvement in those treated with RDV within 10 days of symptom onset.

What do these studies tell us? ACTT-1 results are an important proof of concept that RDV can improve recovery from COVID-19 infection. We need more data to understand when and in whom RDV is most effective, what combination strategies are best, and what impact RDV is having on viral clearance.

Should we give RDV to all inpatients with COVID-19 if available? While these data are preliminary, they support use of RDV for hospitalized patients with COVID-19 infection, as more data is forthcoming. RDV has a good safety profile and is the only treatment thus far with a compelling signal for clinical improvement in a placebo controlled RCT.

Will the FDA allow easier access to RDV? RDV is not FDA approved and is only available through clinical trials or Expanded Access/compassionate use programs; an emergency use authorization (EUA) to expand pre-approval access in the US is anticipated.

Update on IL-6 receptor antibodies
IL-6 blockers are an investigational strategy to dampen the heightened inflammatory response seen in COVID-19. A Phase 2/3 randomized controlled trial evaluated two different doses of the IL-6 receptor antibody sarulimab ("Kevzara"), vs placebo in hospitalized patients with severe disease (requiring oxygen) or critical disease (mechanical ventilation, high flow oxygen or ICU level care). Preliminary data from the Phase 2 portion indicated no difference overall in clinical outcome with IL-6R vs. placebo. In a subgroup analysis, those with severe disease did worse if assigned to sarulimab. However, those with critical disease assigned to the higher 400 mg sarulimab dose did better than placebo on a variety of metrics: clinical improvement (59% vs. 41%), off oxygen (58% vs 41%), persistent mechanical ventilation (9% vs 27%). As a result, the DSMB recommended that the Phase 3 study continue with only critically ill patients, at the higher dose of 400 mg vs. placebo. In an intriguing side note, a 4/27 twitter post states that positive data are forthcoming for another IL-6 blocker, tocilizumab; we look forward to the actual data! **Conclusion**: More information is needed to determine the role of IL-6 blockers—if any—for management of COVID-19. Definitive data to inform the safety and efficacy of these drugs is still needed. Use outside of a clinical trial setting is not recommended.

Is mass asymptomatic testing in nursing homes the key to controlling outbreaks?
In an article published in the NEJM last Friday by Arons M et al., the CDC reports on an outbreak of COVID-19 in a skilled nursing facility (SNF) in Washington State. Residents of the SNF were then offered two facility-wide point prevalence screenings for COVID-19 by RT-PCR of nasopharyngeal (NP) swabs a week apart, accompanied by symptom recall. Symptoms were classified into typical (fever, cough, shortness of breath), atypical, and none. Among 76 residents in the point-prevalence surveys, 48 (63%) had positive PCR results, with 27 (56%) essentially asymptomatic, although 24/27 (89%) subsequently developed symptoms, so were reclassified as pre-symptomatic. Quantitative viral loads were similarly high among those who were symptomatic, pre-symptomatic (with viable virus demonstrated by culture 1-6 days prior to symptom development) and those who remained asymptomatic. The mortality from COVID-19 in this setting was high; among 57 residents who tested positive, 26% died. **Conclusion:** More than half of SNF residents in a mass screening campaign were pre-symptomatic/asymptomatic and viral shedding was detected, at high concentrations, even prior to symptom onset. Effective prevention in SNFs (and other congregate settings like jails,

homeless shelter, hospital inpatients, and health care workers) will likely require periodic asymptomatic mass COVID-19 testing to control spread.

FAQ

1. **Should health care workers (HCWs) get universal COVID-19 screening?**
   It is not yet clear whether asymptomatic HCWs should get universal COVID-19 testing by RT-PCR in all settings. This process will likely involve serial testing (e.g. every 1 – 4 weeks), with self-collected nasal swabs being one option. Universal testing would provide important information about infection prevalence and could potentially decrease spread from asymptomatic or pre-symptomatic HCWs to their patients and co-workers. However, it is not clear how much this will add to other measures to combat COVID-19 spread, particularly in communities where the prevalence in HCWs is very low. We support universal testing in high-risk settings, such as skilled nursing facilities, as staff-to-patient and staff-to-staff transmission are well documented, and patient mortality is high. Testing HCWs for COVID-19 using serology should be limited to epidemiologic surveillance and research at this time, since these tests cannot yet be used for decisions regarding individual HCWs.

2. **Could saliva be an effective testing method for the diagnosis of COVID-19?**
   A new study, not yet peer reviewed, suggests that saliva testing for SARS-CoV-2 may have equal or better sensitivity compared to nasopharyngeal (NP) swab sampling. The study evaluated 44 inpatients with COVID-19, 28 of whom had matched NP swab and saliva samples. Saliva was self-collected by patients in sterile urine cups. While test positivity did not differ between sample types, SARS-CoV-2 viral load was consistently higher from saliva. In a subset of 12 patients with longitudinal sampling, saliva provided more consistent viral detection with less temporal variability in test positivity. **Conclusion**: Patient-collected saliva may offer a convenient method for self-collection that reduces healthcare worker exposures, allow for more judicious use of PPE, and provide a means for testing amidst a nationwide swab shortage. More studies are needed to confirm its utility.

3. **What is the utility of chest CT scan in the diagnosis and care of patients with COVID-19?**
   The role of chest CT for diagnosis and care of COVID-19 remains unclear. Unlike RT-PCR, which tests for the presence of the virus itself, CT merely shows evidence of infection or lung injury and cannot be used as a confirmatory test for COVID-19. Currently we use CT mostly as a problem-solving tool in either a) symptomatic patients who have had multiple negative RT-PCR tests (is there some other lung disease we can diagnose?) or b) confirmed COVID-19 patients with fear of a complication (e.g. pulmonary embolism, superimposed bacterial infection). Some centers may consider CT as a "screening" tool but due to the lack of specificity this will likely result in many more false than true positives, especially in a region of relatively low prevalence.

4. **Is SARS-CoV-2 causing distinct systemic inflammatory syndromes in children?**
   While children continue to suffer a lower burden of severe respiratory disease than adults globally, there is rising concern about distinct inflammatory manifestations of COVID-19. Reports of a toxic shock and Kawasaki Disease (KD)-like syndromes in children in the UK and Italy prompted this alert from the Pediatric Intensive Care Society in the UK. Three cases (6 months to 8 years old) in New York City were reported to have cardiac and GI involvement. These add to an already complex picture of cytokine release and thromboembolic inflammatory syndromes seen in adults. Providers should consider SARS-CoV-2 testing in children with toxic shock and KD-like presentations. However, more investigation will be needed to confirm this possible link.

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

This week we interviewed **Dr. Lisa Winston**—the Hospital Epidemiologist for Zuckerberg San Francisco General and Trauma Center.

When did you first recognize that an epidemic was a real possibility for us in San Francisco and what were the actions you recommended to ZSFG leadership?
During the fourth week of February, it became clear that community transmission was occurring in Washington and California in the absence of travel or contact with a known case. Some of the first issues that we had to address were (1) determine isolation precautions, (2) assess our PPE supply, and (3) identify a screening mechanism for patients coming to our healthcare settings. Patient screening was originally focused on symptoms and travel. Testing was very restricted, and we wanted to make sure we could test patients who were eligible.

What have been some of your biggest challenges in this role since the start of the COVID pandemic?
How to keep healthcare workers (HCWs) safe. Early on, we had little information about transmission mechanisms. Frontline HCWs were afraid, and we were afraid for them. Also, all plans we made were constantly changing. Every day, we were rewriting policies and procedures as we had more data and guidance. The pace of change was extraordinary.

What have been some of your biggest success in this role since start of the COVID pandemic?
None of the success have been mine alone and we have worked with amazing multidisciplinary teams. There has been an enormous sense of collegiality and the feeling that everyone working to find solutions together. SF DPH has also worked closely with us, and we partnered with them to help make the right decisions about shelter in place and other strategies to flatten the curve. Universal masking was controversial early on and our resources were limited but we worked with SF DPH leadership to help make that happen. We are very grateful to UCSF Medical Center for providing ZSFG with masks and other support.

How do you think this pandemic has changed the way we will approach infection prevention in the US health care system moving forward?
While I worry that our memories are short, I am optimistic we will be more prepared for future events with respect to the PPE supply chain and emergency reserves. Though the initial roll out of testing was centralized and slow, collaboration between academia and industry allowed the development of high throughput testing to occur at a faster pace than we have ever seen previously. I think we will be more prepared for widespread testing for the next novel pathogen.

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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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