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COVID-19 DIGEST

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

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EPIDEMIOLOGY

LOCAL

As of today, there are **40,812 confirmed COVID-19 cases and 1594 deaths in California**. Today, California Governor Gavin Newsom announced a new program for local governments to provide restaurant delivery service to older Californians. In San Francisco, there are **1340 confirmed COVID-19 cases and 22 deaths**. This week, San Francisco increased testing capacity for all essential workers and symptomatic residents. This weekend, UCSF investigators, the San Francisco DPH, and community partners will launch a massive testing project in the Mission district, one of the hardest hit neighborhoods in the municipality of San Francisco.

NATIONAL

There are now over **924,402 cases reported and 52,168 deaths in the United States**. New York State remains the epicenter of the epidemic, both in the United States and worldwide with New York continuing to report more coronavirus cases than any other country worldwide. New York State has 263,000 cases and 15,740 deaths to date. An early antibody testing project in New York City suggested that 20% of residents may have now had exposure to the virus, which would make the case fatality rate much lower than previously calculated. Today, we highlight the jail and prison system in the United States, where there have been many COVID-19 outbreaks. Earlier this week, a prison in Marion, Ohio, became the largest-known source of coronavirus cases in the country, with more than 1,800 inmates testing positive (with two inmates and one staff member now dead from the infection) during a mass testing campaign. In response, many jails around the country have initiated mass testing campaigns and have released prisoners to thin the population.

GLOBAL

There are currently **2,827,981 million cases of COVID-19 and 197,074 deaths** reported around the world. The US continues to lead the world in the total numbers of infections. In brief updates from around the other regions, countries in Latin America are increasingly affected with Ecuador and Panama leading the region in terms of both infections and deaths, although both are likely underreported. Germany has opened up cautiously, but continue to be concerned that long-standing social distancing will be necessary. Coronavirus cases are increasing across the African continent, although testing capacity remains limited, and there is increasing concern about concomitant hunger and the rise of other infectious diseases-related deaths, such as from malaria, with the pandemic. Coronavirus cases are rising in Singapore, a region in which they were previously controlled, likely due to neglect of marginalized communities and migrant workers. And, although mortality rates in India are rising from coronavirus, the lockdown continues and the spread has been less than anticipated from earlier estimates.

UP TO THE MINUTE DISPATCHES

How do antibody-based tests perform in the lab or at the point-of-care for diagnosis of COVID-19?

Identification of viral nucleic acid via PCR has been the primary method for diagnosing COVID-19, but there is increasing interest in the use of antibody-based testing to assess exposure. Researchers in the UK (pre-print) evaluated a panel of antibody-based COVID-19 tests – a novel Enzyme-linked immunosorbent assay (ELISA) in the lab and 9 commercially-developed Lateral-Flow Assays (LFAs) to be used at the point of care. Serum of patients diagnosed with COVID-19 served

as the positive controls and serum of patients in UK before December 2019 served as negative controls. ELISA identified COVID-19 IgM or IgG antibodies in 34/40 cases and 0/50 controls, yielding a sensitivity and specificity of 85% and 100%. The sensitivity of ELISA IgG improved to 100% when restricted to patients exhibiting symptoms for ≥10 days. No patients were IgM positive but IgG negative by ELISA. LFA had a sensitivity of 55-70% with a specificity of 95-100%. IgG titers rose for 3 weeks post symptom onset and began to fall by 8 weeks, but remained above the detection threshold. This small study was limited by small sample sizes and has not yet been peer reviewed. **Bottom line:** This study suggests ELISA is best used to identify COVID-19 exposure 10 or more days following symptoms. Despite being available at point of care, currently available LFAs have variable sensitivity. Whether a positive antibody test to COVID-19 by one of these tests correlates with immunity is not known.

Gaining insight into ARDS mechanisms in COVID-19

Two recent papers seek to uncover the mechanisms behind the development of acute respiratory distress syndrome (ARDS) in a subset of COVID-19 patients often >7 days after onset of symptoms. Blanco-Mello et al compared the transcriptional response of SARS-CoV-2 to other respiratory viruses including Influenza A in a variety of immortalized tissue culture cells, infection of primary airways cells, in vivo samples derived from SARS-CoV-2 infected ferrets, and finally from post-mortem samples collected from the lungs of humans who died with SARS-CoV-2 or normal lung biopsies. These studies, together with serum profiling in the ferret model, revealed a unique and inappropriate inflammatory response characterized by low levels of type I and type III interferons, elevated chemokines, and elevated IL-6 expression. Giamarellos-Bourboulis et al compared 28 patients with COVID-19 and ARDS to 26 patients COVID-19 without ARDS. Control groups included patients with 2009 H1N1 Influenza A and patients with community acquired pneumonia-associated sepsis. Some patients with COVID-19 associated-ARDS had macrophage activation syndrome, and most had immune dysregulation characterized by low expression of HLA-DR on a subset of monocytes (CD14 positive) that is triggered by monocyte hyperactivation, excessive IL-6 release, and profound lymphopenia. This pattern is distinct from ARDS-associated bacterial sepsis or 2009 H1N1 influenza. Together, these studies suggest that COVID-19 associated ARDS may be characterized by both a reduced innate immune response coupled with an exaggerated inflammatory cytokine response.

FAQ

1. **Is hepatic injury common in patients with COVID-19?**
   Elevated transaminases (AST and/or ALT) are relatively common in COVID-19. Multiple studies from China showed that transaminases were elevated in up to 35% of patients with COVID-19. Two recent large studies from New York City show that this number may be even higher (up to 39% for ALT and 58% for ALT). One study form China showed that transaminase elevations were mild in the majority of cases, although more significant elevations were associated with a higher risk of severe COVID-19 disease. It is not clear if liver injury is related to direct infection in the hepatobiliary system versus indirect effects of inflammation. **Conclusion:** Mild transaminitis is common in patients with COVID; more significant elevations are unusual but associated with more severe disease.

2. **What do we know seasonal spread of common human coronaviruses and how might that influence our predictions of future spread of COVID-19 in future seasons?**
   Prior outbreaks of animal coronaviruses (SARS-CoV, MERS-CoV) did not result in prolonged and sustained human spread as we are seeing with SARS-CoV-2. It is possible that spread of SARS-CoV-2 may ultimately follow a similar pattern as the four human coronaviruses (OC43, 229E, HKU1, NL63). A longitudinal study of respiratory illnesses in Michigan explored the transmission dynamics of human coronaviruses. Spread began in December, with a peak incidence in January/February followed by a decline in March. Transmission in June to September represented only 2.5% of total cases. Household transmission was confirmed in a quarter of cases and children < 5 years had the most disease. **Conclusion**: It is unknown if SARS-CoV-2 will follow the same seasonal transmission pattern as common

human coronaviruses and we should prepare for that. However, this is a new virus with its own unique transmissibility, and only time will tell.

3. **Are patients on ACE-Inhibitors (ACE-I) or Angiotensin-Receptor Blockers (ARBs) at increased risk for severe COVID-19?**
   As mentioned in an earlier digest, SARS-CoV-2 binds to cells via the ACE-II receptor, therefore there has been speculation that the use of an ACE-Is or ARBs might impact the course of disease in COVID-19. Researchers at a large hospital in Wuhan, China, performed a retrospective study of 1178 patients admitted with COVID-19 between January-March 2020. 362 (31%) admitted patients had hypertension with an in-hospital mortality rate of 21% (vs. 6.5% non-hypertension). Among patients with hypertension on ACE-I/ARBs, there was no difference in rates of severe/non-severe disease nor any difference in mortality, when compared to those with hypertension not on ACE-I/ARBs. Differences were not seen between ACE-Is and ARBs either. **Conclusion**: Use of ACE-I/ARBs does not seem to increase risk for poor outcomes in patients with hypertension and COVID-19. This data supports present guidelines that patients with ACE-I/ARBs should continue treatment during COVID-19 epidemic.

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

This week we interviewed **Dr. Becky Martinez**—an anesthesiologist on the front line at New York Presbyterian-Columbia University Irving Medical Center in New York City. We asked her about the Obstetric Intensive Care Unit "OBICU" (O-BIK-U). Editorial disclosure: She is Diane Havlir's daughter and starting critical care fellowship at UCSF in the summer.

Why did the OBICU start? Let me start a step back from that. In March, one of our OB patients requiring intrapartum intubation unexpectedly tested COVID positive. The number of exposures was enormous, and this served as a wake-up call for us. We tested 210 pregnant women presenting for delivery and to our surprise found 13.7 % women PCR positive, 88% of which had no symptoms. As a result, on March 22, we starting COVID screening all labor and delivery patients. The practice of care for OB patients requiring intensive care at that time was to transfer them to the main medical or surgical ICU. It was imminently clear that capacity in these units was going to be a challenge so we decided to establish an OB ICU for any peripartum patient with critical care needs on labor ward of the hospital.

How does the OBICU work? The unit is led by OB anesthesia. We have a multi-disciplinary team that rounds multiple times a day and includes OB physicians, nurses, pharmacists and ancillary services. Although a family member can be present at delivery, only medical personnel are allowed in the unit. We still have over 250 patients with a primary diagnosis of COVID19 in various ICUs at our hospital. We are in communication and always sharing updates and insights. Every day we learn something new.

What are some of the complications you are seeing? We are seeing most of the same complications in the OBICU as we find in the other ICUs—hypoxia, hypotension, and high fevers. We are aggressively managing respiratory distress and have avoided invasive ventilation to date. Clots are a big concern, in particular because of the increased susceptibility of our OB population. We have not seen a dramatic increase in pre-eclampsia. I am happy to say we have not had any deaths.

Any final comments? I am proud to be a member of the medical community. Any support we can give each other during this time, no matter how small or big can really make a difference. One night when I was on call, a dinner food delivery arrived from the UCSF residents. You should have seen the smile on everyone's faces! Thank you so much.

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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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