CLINICAL PRESENTATION AND MANAGEMENT

Extrapulmonary manifestations of COVID-19:
In this review article, authors synthesised emerging literature surrounding the extrapulmonary manifestations of COVID-19. This area of research was founded on the molecular premise that ACE2 receptors (entry receptor for COVID-19) are knowingly expressed in extrapulmonary tissues, therefore consideration must be given to the virus’ multi-system effects. Here, we provide additional insight on the hepatobiliary and endocrine manifestations specifically.

- **Hepatobiliary.** ACE2 receptors are present on cholangiocytes this allows SARS-CoV-2 to cause direct damage. Hepatocellular injury has been seen in 14-53% of critically-ill COVID-19 patients, manifesting most commonly as elevated aminotransferases, elevated bilirubin and low serum albumin. At present, guidelines do not recommend further investigation with this finding, unless patients have additional concerning features (↑ bilirubin, hepatomegaly, RUQ pain). LFTs should be regularly monitored though, particularly for patients on remdesivir, lopinavir and tocilizumab.

- **Endocrine.** ACE2 receptors have been found in the endocrine pancreas. Diabetes mellitus (DM) and obesity are associated with more severe COVID-19 illness (24% of hospitalized patients have pre-existing DM). Conversely, COVID-19 exacerbates the risk of diabetic complications such as hyperglycaemia and ketoacidosis. Given this, HbA1C should be used to screen hyperglycemic or ketotic COVID patients for underlying diabetes. Avoid oral anti-hyperglycemics due to renal dysfunction, hypoglycemia and delayed gastric emptying. Remote glucose monitoring should be employed as a strategy to reduce contact frequency between diabetic patients with COVID-19 and healthcare workers.

PEDIATRIC PRESENTATION

Age-Related Differences in Nasopharyngeal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Levels in Patients With Mild to Moderate Coronavirus Disease 2019 (COVID-19):

The researchers sampled patients age 65 or younger between March 23 and April 27 from various outpatient, inpatient, emergency department, and drive-through testing sites across Chicago, Illinois. A total of 145 patients who tested positive for SARS-CoV-2 infection by reverse transcriptase PCR were enrolled in the study. Participants were separated into three groups: children under five years of age, older children between five and 17 years, and adults over 18 years. The PCR amplification cycle threshold values indicate that young children have higher amounts of viral RNA in their nasopharynx compared to older children and adults. Although this measures viral RNA and not infectious virus, previous findings demonstrate that levels of RNA correlate with ability to culture infectious virus. The study results suggest that young children can be important drivers of COVID-19 spread in the general population.

PHARMACEUTICAL INTERVENTIONS
Drug treatments for covid-19: living systematic review and network meta-analysis

This publication is a living systematic review that the authors will continually update to provide the most recent data on pharmaceutical interventions for COVID-19. This first analysis, which was conducted June 26, 2020, included 23 randomized controlled trials from US Centers for Disease Control and Prevention COVID-19 Research Articles Downloadable Database and Chinese databases to compare drug treatments for COVID-19. The analysis determined that glucocorticoids were the only intervention that may reduce mortality and mechanical ventilation compared with standard care. Use of Remdesivir provided benefits for duration of mechanical ventilation and time to symptom resolution; however, the drug’s effect on mortality is unknown. Hydroxychloroquine may increase risk for adverse effects, may not reduce mortality, and may increase length of hospital stay. Beyond the discussion of the three drugs, the study highlighted the lack of certainty regarding effectiveness of interventions, as data availability is sparse, imprecise, and risk of bias was high due to a lack of study blinding.

NON-PHARMACEUTICAL INTERVENTIONS

The role of telehealth during COVID-19 outbreak: a systematic review based on current evidence

Monaghesh et al. conducted a systematic review to determine the role of telehealth in controlling and treating COVID-19 infection. Telehealth was defined as the use of services such as telephone, live video conferencing and email. Eight studies were selected for analysis and demonstrated the benefits of telehealth during the global COVID-19 pandemic. Key themes highlighted were that telehealth avoids physical contact between patients and healthcare staff (known as medical distancing), decreases gatherings in waiting rooms, and can reduce morbidity and mortality of Covid-19. Additionally, the authors found that telehealth demonstrated value for diagnosing patients with the disease, medicine check-ups, triaging, appointments in some cancer settings, and mental health services during the pandemic. Thus, the authors suggest that telehealth is a useful service to avoid exposure, prevent the spread of Covid-19, and reduce burden on the healthcare system.

REGION-SPECIFIC LESSONS LEARNED

COVID-19 epidemic doubling time in the United States before and during stay-at-home restrictions

The authors used surveillance data from the COVID-19 repository at Johns Hopkins University to compare COVID-19 doubling time before and during stay-at-home restrictions. The University of Oxford Coronavirus Government Response Tracker stringency index was used to identify the start point of stay-at-home orders, but the effects of the orders were measured 14 days after implementation. Results indicate that nationally, doubling time increased by 82.13%, with a mean doubling time of 2.68 to 15.00 days. Among the 45 states that implemented stay-at-home orders, all had a significant increase in doubling time, except for Minnesota, with a relative average increase of 72.65%. The five states that did not issue stay-at-home orders showed a slower increase in doubling time. Results indicate that stay-at-home orders combined with CDC-recommended practices and travel restrictions likely contributed to reducing the growth rate of the epidemic. Future success will depend on effective testing, tracing, and isolation as restrictions are lifted.

The first 100 days of SARS-CoV-2 control in Vietnam

This study utilized clinical and demographic data paired with Apple and Google mobility data to determine the efficacy of COVID-19 control measures used by the Vietnam Government.
Vietnam’s effective containment of SARS-CoV-2 can be attributed to rapid government action and isolation of all contacts of known cases. The Vietnamese government sought to rapidly educate the public, close spaces of mass gathering, restrict international travel and impose strict quarantine, and implement case and contact tracing starting January 2020. 60% of cases in Vietnam were imported. Vietnam’s policy identified and isolated all direct contacts of COVID-19 cases regardless of symptoms for 14-days. This was particularly effective as most (43%) of those infected in Vietnam did not develop symptoms.

TRANSMISSION PATTERNS

**SARS-CoV-2 in rural Latin America. A population-based study in coastal Ecuador**

Brutto et al. assessed the prevalence, distribution, and risk factors in middle-aged and older populations associated with SARS-CoV-2 seropositivity in the Atahualpa Project’s population-based prospective pre-existing cohort. SARS-CoV-2 antibodies were identified using a lateral flow antibody test. Antibodies were identified in 303 out of 673 Ecuadorian adults. Clinical manifestations of disease was reported by 77% of seropositive individuals (positive response to IgM and/or IgG) and 15% of seronegative individuals. Seropositive persons were also more spread across the village and reported greater use of open latrines. The authors suggest that the high seroprevalence of disease (45%) across the village confirms concerns of widespread transmission of SARS-CoV-2 in rural Latin America and suggests fecal-oral transmission cannot be excluded.

**Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study**

This study aimed to understand the risk of COVID-19 among healthcare workers compared to the general population, as well as understand how PPE equipment affects risk. The COVID Symptom Study app was used to track 2,135,190 participants from both the UK and the USA, of whom, 99,795 participants were front-line healthcare workers. The authors found that front-line healthcare workers had a twelvefold increase in risk of a positive COVID-19 test compared to the general community, with the association being stronger in the UK compared to the US. It was also found that Black, Asian, and minority healthcare workers had an increased risk of COVID-19 (adjusted hazard ratio 1.81, 95% CI 1.45 - 2.24) compared to non-Hispanic white healthcare workers. Additionally, healthcare workers who reuse PPE or have inadequate PPE had an increased risk of COVID-19 (adjusted hazard ratio 1.46, 95% CI 1.21 - 1.76). Overall, this study suggests the importance of ensuring proper use and availability of PPE to protect healthcare workers who are at increased risk of infection, particularly those from Black, Asian and minority ethnic backgrounds.

**Human mobility and coronavirus disease 2019 (COVID-19): a negative binomial regression analysis**

Oztig et al. studied the effect of human mobility via airline travel on the prevalence of COVID-19 infection in 144 countries, hypothesizing that Schengen countries (area comprising 26 European countries that have officially abolished all passport and all other types of border control at their mutual borders), countries with higher mobility, and countries with a higher number of airports could be positively associated with a higher number of infections. Using negative binomial regression, the number of airline passengers and infections (using WHO data) were analyzed and results showed that countries with a higher population density, percentage of elderly, airline passengers, and airports were associated with more cases. Schengen countries were also shown to be positively associated. These results demonstrate the effect higher mobility can have on the transmission of Covid-19 and that well-connected
locations are more likely to be infected both quicker and more severely with a high number of initial cases.

NON-CLINICAL TRENDS

Prevalence of Health Care Worker Burnout During the Coronavirus Disease 2019 (COVID-19) Pandemic in Japan

Matsuo et al. investigated rates of burnout among interdisciplinary healthcare workers treating patients with COVID-19 at a tertiary hospital in Tokyo, Japan. An online survey (n=312) evaluating the three major domains of burnout (emotional exhaustion, cynicism and professional efficacy) revealed the overall burnout prevalence to be 31.4%. Factors associated with increased levels of burnout included female gender, younger age, less experience, anxiety because of unfamiliarity with PPE, decreased sleep and fewer vacation days. Nurses (46.8%; n=126), radiology technicians (36.4%; n=22) and pharmacists (36.8%; n=19) were most likely to report burnout. Participants who reported burnout were significantly more likely to have intentions of dropping out of their profession (74.5% vs 24.3%; P=.01). Despite being a single-center analysis, this study represents an important step towards evaluating the post-pandemic impacts of COVID-19 on the mental health of frontline healthcare workers.

COVID-19 Pandemic: Disparate Health Impact on the Hispanic/Latinx Population in the United States

A multi-tiered approach was used to analyze literature on disparities Latinx populations face in the COVID-19 pandemic in the United States. Hispanics comprise 18% of the U.S. population, but 28.4% of COVID-19 cases. Mortality data is sparse but as per the CDC: mortality rates are two-folds higher in age-adjusted death rate for the Hispanic population (204.6 per 100,000 vs. 90.4 per 100,000) as of May 14, 2020. Among 14 states, Hispanics disproportionately constituted 14.2% of hospitalizations. Similarly, only 31 states and D.C. have reported COVID-data for Hispanic populations. Hispanics, similarly, have a higher burden of chronic conditions like obesity, diabetes, and renal disease and the highest uninsured rate (19.8%) in the United States. These disparities are coupled with pre-existing risk factors that affect both acquisition and progression of COVID 19 and access to quality care. These factors include but are not limited to immigration status, healthcare system mistrust, language barriers. This population is also affected by unfavorable working conditions: a quarter of them work in key service occupations and only 16.2% of workers held jobs that would allow them to work from home. Similarly, the Hispanic poverty rate is 19.4% in the United States which impedes access to medication and food and exacerbates comorbid disease and likely, COVID-19. Additionally, Hispanics often live in multi-generational homes and remain a disproportionate percentage in detention centers, prisons, and amongst those experiencing homelessness making adherence to social distancing protocol difficult. To address the COVID-19 disparities among Latinx populations, the article suggests improving COVID-19 information dissemination that is linguistically and socio-culturally tailored and trauma-informed, ensuring trust in optimal linkage to high quality care for COVID and prevention of comorbid disease, equitable access to testing, increased access to emergency care via Medicaid expansion, and improved national, state, and district level data collection in order to further analyze disparities faced and inform future prevention and control and unwire pre-existing determinants of health such as income, housing, and education.
Assessment of SARS-CoV-2 Screening Strategies to Permit the Safe Reopening of College Campuses in the United States

This study aimed to assess different screening strategies in order to allow safe reopening of universities in the United States. An epidemic model was used that captured the epidemiology of SARS-CoV-2, the natural history of COVID-19 illness, and regular mass screening to detect and contain the virus in a college setting. The hypothetical cohort included 5,000 students, with 4,990 students without SARS-CoV-2 and 10 with undetected, asymptomatic SARS-CoV-2 at the start of the semester. With screening every 1, 2, 3, or 7 days with a 70% sensitivity and 98% specificity, the result was 162, 243, 379, and 1840 infections, respectively. In the cost-effectiveness analysis, it was found that the screening costs using a test with 70% sensitivity would amount to $470, $910, $120 per student per 80-day period in the base-case (screening every 2 days), worst-case (daily screening), and best-case scenario (weekly screening). It is important to note that the specificity of the test is much more important than the sensitivity. Overall, this study suggests that a fast, inexpensive and poorly sensitive test (>70%) with an R<sub>t</sub> of < 2.5 combined with strict adherence to prevention measures is cost-effective and can control the number of COVID-19 infections to allow students to safely return to campus. However, some challenges include the number of false-positives that may overburden housing capacity for isolation.

ADDITIONAL RESOURCES
UCSF Library COVID-19 Research and Information Resources
UCSF Institute for Global Health Sciences COVID-19 Resources
UC Davis One Health Institute COVID-19 FAQs
Harvard Viswanath Lab Myths vs Facts

Note on this Document: This document was assembled by graduate and doctoral students attending the University of California, San Francisco with the intent of facilitating the rapid dissemination of information to the global community in order to help during this time. James Feng, Carina Ashkar, Shivali Joshi, Anika Kalra, Hannah Thomas, and Caihla Petiprin contributed to these summaries. This work is volunteer based.

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