TRANSMISSION PATTERNS

COVID-19 patients in earlier stages exhaled millions of SARS-CoV-2 per hour

Ma et al. collected exhaled breath condensate (EBC) samples from 49 COVID-19-positive patients and 15 COVID-19-negative controls. Air samples and environmental samples were collected from the hospitals, personal belongings, and hotels where participants were quarantined. Sample analysis by qRT-PCR found that 26.9% of EBC specimens were positive for SARS-CoV-2, demonstrating evidence that the virus may be released directly into the air when COVID-19 patients breathe. Surfaces (5% positivity) and air samples (4% positivity) had lower positive rates than the EBC samples, though of the positive surfaces, the toilet area had the highest positivity rate (17%) followed by hospital floors (13%). A swab specimen of an air duct by a COVID-19 patient's bed was also positive. Based on cycle threshold values, viral RNA breath emission rates were highest during earlier stages of COVID-19, with an estimated emission rate of up to 10^5 viruses released into the air per minute. Additionally, the authors found that swab samples of surfaces frequently touched by COVID-19 patients, including mobile phones and door handles, were rarely positive (9% of phone swabs and 0% of handles). This study has implications for the role of airborne spread of COVID-19, highlighting the importance of ventilation and face coverings to minimize risk of airborne infection.

Outbreak of COVID-19 in a nursing home associated with aerosol transmission as a result of inadequate ventilation

This letter to the editor, in response to the article “It is Time to Address Airborne Transmission of COVID-19” describes a COVID-19 outbreak investigation in a Dutch nursing home possibly due to inadequate ventilation. There are 7 wards within the nursing home: in 1 of the 7 wards, 81% of residents and 50% of healthcare workers were diagnosed with confirmed COVID-19, in contrast all the tests of residents and healthcare workers in the other wards were negative. The outbreak happened at a time were low community transmission was happening in the country, As a previous precaution, all HCWs had been assigned to a specific ward and wore surgical masks, residents were housed individually but did spend some time in shared spaces. Due to the outbreak, the ventilation systems were investigated, and they found that the system in the affected ward had been renovated with a CO2 energy-efficient ventilation system that recirculated indoor air without filtration if CO2 levels were below 1000 ppm. This ward was also cooled by air conditioning units that recirculated air, the other wards had units that ventilated with outside air. The data suggest the outbreak was caused by aerosol transmission of COVID-19.
BCG vaccination in infancy does not protect against COVID-19. Evidence from a natural experiment in Sweden

In April 1975, Sweden stopped vaccinating newborns with the BCG vaccine, resulting in a decrease in vaccination rate from 92% to 2%. de Chaisemartin et al. used this change in vaccination pattern to conduct a regression discontinuity and assessed the effect of the BCG vaccine on COVID-19 cases, hospitalization, and deaths per capita. No moderate effect in cases and hospitalizations were seen in their results between the cohort with high BCG vaccine coverage and the cohort with low coverage (1·0005 (CI95: [0·8130 – 1·1881]) and 1·2046 (CI95: [0·7532 – 1·6560]) respectively), and no significant data for deaths was achieved. These results suggest that differences in the severity of COVID-19 across countries cannot be attributed to childhood BCG vaccination, and further investigation with clinical trials may not be necessary.

Keywords: bcg, covid-19, regression discontinuity

PATHOPHYSIOLOGY

Humoral Immune Response to SARS-CoV-2 in Iceland

The goal of this study was to assess SARS-CoV-2 seroprevalence and changes in antibody levels four months after a SARS-CoV-2 infection in the population of Iceland. SARS-CoV-2 antibodies were tested in 30,576 individuals with six assays which targeted pan-immunoglobulin (IgG, IgM, IgA). Results showed that assays measuring pan-Ig antibodies had a low number of false positives. Due to the low prevalence of SARS-CoV-2 infection in Iceland, seropositive individuals must have had positive results from both pan-Ig antibody assays. Of the 1797 individuals who recovered from SARS-CoV-2, 1215 were tested and 1107 were seropositive. Of those with unknown exposure, 0.3% were seropositive and of those quarantined, 2.3% were positive. The majority (56%) of SARS-CoV-2 infections were diagnosed with qPCR in Iceland, 30% occurred in individuals outside of quarantined who were not tested with qPCR, and 14% occurred in quarantined individuals not tested with qPCR. This study provides evidence that antiviral antibodies against SARS-CoV-2 did not decline within 4 months of SARS-CoV-2 diagnosis.

Pathophysiology of COVID-19-associated acute respiratory distress syndrome: a multicentre prospective observational study

Grasselli et al. conducted a prospective observational study to examine the functional and morphological features of invasively ventilated patients with COVID-19-related acute respiratory distress syndrome (ARDS). A total 301 patients older than 18 years admitted to ICUs of seven Italian hospitals between March 9 and March 22, 2020 with confirmed COVID-19 who were on mechanical ventilation and met the Berlin criteria for ARDS were enrolled. Results indicate that patients with COVID-19-related ARDS have lung morphology and respiratory mechanics that match those of classical ARDS. In addition, a subgroup of patients with COVID-19-related ARDS have disease characterized by low static compliance of the respiratory system and increased D-dimer concentrations. These individuals with high D-dimers, low compliance had significantly increased mortality (56% 28-day morality) compared to those patients with low D-dimers (22% 28-day mortality among those with low D-dimers and low compliance and 27% among those with low D-dimers and high
compliance). The results suggest that classical protective ventilatory strategies are recommended for patients with COVID-19-related ARDS. Furthermore, the identification of the phenotype of both low static compliance and increased D-dimer concentrations has implications for future clinical trials.

A comment published in The Lancet Respiratory Medicine highlighted the findings of the above study by Grasselli et al. as well as a second study regarding COVID-19 associated ARDS by Sinha et al., entitled "Prevalence of phenotypes of acute respiratory distress syndrome in critically ill patients with COVID-19: a prospective observational study". Comment author Lorraine Ware suggests that collectively, these studies demonstrate the complex nature of the pathophysiology of COVID-19 associated ARDS, reinforcing the need for further high-quality studies on the subject.

**PEDIATRIC PRESENTATION**

*Clinical characteristics of children and young people admitted to hospital with COVID-19 in United Kingdom: prospective multicentre observational cohort study*

This study aimed to characterize the features of children and young people (aged <19 years) who were hospitalized with SARS-CoV-2 in the UK between January 17 and July 3, 2020. Multisystem inflammatory syndrome in children and adolescents temporarily related to COVID-19 (MIS-C), a severe COVID-19 phenotype that has been found to occur in children and young people and classified by the World Health Organization (WHO), was also evaluated. The median age of the 651 children and young people included in this study was 4.6 (IQR 0.3 – 13.7 years). Forty-two percent (42%) had at least one comorbidity, and 18% were admitted to critical care. Eleven percent (11%) met the WHO MIS-C criteria; those who met the criteria were of older age, were more likely to be of non-white ethnicity, and were five times more likely to be admitted to critical care. These patients were also more likely to have associated fatigue, headache, myalgia, sore throat, lymphadenopathy, and a low platelet count than those who did not have MIS-C. The results provide additional insight into MIS-C presentation and epidemiology and further demonstrates the overall less severe COVID-19 in children and young people than adults.

**CLINICAL PRESENTATION AND MANAGEMENT**

*COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing*

In this study, authors performed whole genome sequencing on respiratory specimens collected during two distinct episodes of SARS-CoV-2 infection in the same individual, with the second infection occurring 142 days after the patient first became symptomatic. A comparative genome analysis found that the viral genomes from posterior oropharyngeal saliva specimens obtained during the first and second episodes of COVID-19 belong to different clades/lineages: the first virus genome was phylogenetically closely related to strains collected in the USA and England between March-April of 2020, while the second virus genome was closely related to strains collected in England and Switzerland between
July-August of 2020. The results indicate that the patient experienced re-infection, rather than persistent viral shedding from the first infection. Based on these findings, the authors suggest that SARS-CoV-2 may continue to circulate among human populations despite herd immunity from natural infection or vaccination.

MENTAL HEALTH

Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic

Using two nationally representative population-based surveys of adults aged 18 or older, Ettman et al estimate the prevalence of depression symptoms in the US during the COVID-19 pandemic compared to before the pandemic and identified the associated risk factors. The during-COVID-19 sample included 1441 participants with 27.8% showing depression symptoms, while the before-COVID-19 sample included 5065 participants with 8.5% showing depression symptoms. Increased risk of depression symptoms persisted across all demographic groups during COVID-19, while the distribution of depression symptoms within categories was consistent with that observed prior to the pandemic. During COVID-19, lower social and economic resources and higher COVID-19 stressor scores were risk factors for experiencing depression symptoms. Authors call for policy attention for economically and socially marginalized groups, as they bear most of this mental health burden.

NON-PHARMACEUTICAL/PUBLIC HEALTH INTERVENTIONS

Rapid real-time tracking of non-pharmaceutical interventions and their association with SARS-CoV-2 positivity: The COVID-19 Pandemic Pulse Study

This study aimed to capture data surrounding non-pharmaceutical intervention adoption, access to SARS-CoV-2 testing, and observe associations with self-reported SARS-CoV-2 positivity in Maryland using electronic surveys. The final sample size included 1,030. The majority of participants were White (60%), Black/African American (23%), and Hispanic/Latino (7%). Overall, 66% of participants had visited friends or family, 68% followed strict social distancing guidelines and 53% masking indoors. Results showed that 72% of Black participants reported always wearing a mask outdoors compared to 44% of Whites. SARS-CoV-2 infection was more common among young, male Hispanic/Latino or Black/African American individuals (P<0.05). SARS-CoV-2 infection was also more common among individuals who reported attending a location of worship, public transportation, visiting friends or family, attending a gathering of more than 10, and visiting indoor and outdoor venues where people gather (p<0.05). A history of SARS-CoV-2 infection was negatively associated with strict social distancing. These results provide additional evidence that strict social distancing reduce the SARS-CoV-2 transmission and further considerations are needed for indoor activities with large gatherings (public transportation and locations of worship).
Preventing and Mitigating SARS-CoV-2 Transmission — Four Overnight Camps, Maine, June–August 2020

In this report, the authors detail the outcomes of non-pharmaceutical interventions used to prevent and mitigate SARS-CoV-2 transmission in four overnight camps in Maine. All four camps utilized a multilayered approach of testing and quarantining all staff and campers before and after arrival. Attendees were quarantined in cohorts and tested after camp arrival, regardless of pre-camp screening. Three of the four camps required the submission of test results before entry into camps and RT-PCR testing was repeated on average 4-9 days after the attendees arrived at camp. Furthermore, daily screening was used to identify a total 12 attendees with COVID-19 symptoms who were isolated, and their cohorts quarantined until those symptomatic individuals received negative test results. In addition to testing and quarantining measures, the camps required all participants to wear face coverings, practice social distancing, and engage in other preventative measures such as staggered or cohorted bathroom use. The additional testing following arrival at camp led to the successful identification of three attendees who had been asymptomatic but were found positive by RT-PCR for SARS-CoV-2 infection. Because attendees had quarantined with their cohorts, these three asymptomatic cases did not lead to any secondary transmission. These findings suggest the employed methodologies have implications for SARS-CoV-2 transmission prevention in settings where individuals are entering settings with different levels of exposure, i.e. camps and schools.

Mask Wearing and Control of SARS-CoV-2 Transmission in the United States

This study utilized survey data to understand the effect of personal mask wearing habits, statewide mask mandates, and social distancing on community transmission of SARS-CoV-2 in the United States. Analysis of 378,207 responses to serial cross-sectional surveys revealed a significant association between the percent of a community reporting mask wearing habits and controlling community transmission such that the effective reproductive number fell below one (R<1). Specifically, a 10% increase in reported mask wearing habits was associated with an increased odds (OR: 3.53 (95% CI: 2.03, 6.43) of controlling transmission (R<1). The study found that non-white or Hispanic, women, elderly, and lower income respondents were more likely to report face mask wearing. Using a multivariate logistic model, the authors determined that communities practicing high levels of social distancing and high levels of mask wearing have the greatest probability of a controlled epidemic. Mask wearing trends increased between June 3 and July 31; however, analyses found no significant change in mask usage between the two weeks before and after statewide government mask mandates. These findings suggest a need for supplemental public health interventions to encourage widespread mask adoption.

*Please note all studies published in medRxiv and bioRxiv are preprints and have not yet undergone a rigorous peer review process.
PHARMACEUTICAL INTERVENTIONS

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients with COVID-10: A Meta-analysis

This study aims to estimate the association between corticosteroid administration and 28-day all-cause mortality, compared with usual care or placebo, for critically ill COVID-19 patients. A total of 1703 critically ill patients from seven randomized clinical trials in 11 countries were included in the prospective meta-analysis. Overall, mortality was lower among patients randomized to corticosteroids (dexamethasone, hydrocortisone, or methylprednisolone), with OR=0.66 [95% CI, 0.52-0.82] compared to patients randomized to usual care or placebo. Serious adverse events were more common among patients receiving usual care or placebo. (other paper)

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, Shivali Joshi, and Guntas Padda contributed to these summaries. This work is volunteer based.

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