New Research

*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see Digital Commons

Basic Science / Virology / Pre-clinical


   Findings: In February 2020 the World Health Organization (WHO) assembled an international panel of experts to develop animal models for COVID-19 to accelerate testing of vaccines and therapeutics. This review summarizes the findings to date and provides relevant information for preclinical testing of COVID-19 vaccine candidates and therapeutics.

Clinical Syndrome


   Findings: We conducted a multicenter study in the US of 112 adult LT recipients with COVID-19. The median age was 61 years, 54.5% (n=61) were male, and 39.3% (n=44) Hispanic. The mortality rate was 22.3% (n=25); 72.3% (n=81) were hospitalized and 26.8% (n=30) admitted to the ICU. Analysis of peak values of alanine aminotransferase (ALT) during COVID-19 showed moderate liver injury in 22.2% (n=18) and severe liver injury in 12.3% (n=10). Compared to age and gender matched non-transplant patients with CLD and COVID-19 (n=375), the incidence of acute liver injury was lower in LT recipients (47.5% vs. 34.6%). Variables associated with liver injury in LT recipients were younger age, Hispanic ethnicity, metabolic syndrome, vasopressor use and antibiotic use. Reduction in immunosuppression (49.4%) was not associated with liver injury (p= 0.156) or mortality (p= 0.084). Liver injury is associated with higher mortality and ICU admission in LT recipients with COVID-19. Hence, monitoring liver enzymes closely can help in early identification of patients at risk for adverse outcomes. Reduction of immunosuppression during COVID-19 did not increase risk for mortality or graft failure.

Findings: This study found a higher rate of gastrointestinal complications, including mesenteric ischemia, in critically ill patients with COVID-19 compared with propensity score–matched patients without COVID-19, suggesting a distinct phenotype for COVID-19 compared with conventional ARDS. High expression of angiotensin-converting enzyme 2 receptors along the epithelial lining of the gut that act as host-cell receptors for SARS-CoV-2 could explain involvement of abdominal organs. Higher opioid requirements and COVID-19–induced coagulopathy may also explain the disproportionately high rate of ileus and ischemic bowel disease. Differences in duration of illness did not seem to explain the differences in gastrointestinal complications.


Findings: We performed a retrospective cohort study of adult patients admitted to NYU Langone Health system between March 1 and April 27 2020 with a positive nasopharyngeal swab polymerase chain reaction test result and presence of primary nontraumatic intracranial hemorrhage or hemorrhagic conversion of ischemic stroke on neuroimaging. Among 3824 patients admitted with COVID-19, 755 patients had neuroimaging and 416 patients were identified after exclusion criteria were applied. The mean age was 69.3 (16.2), 35.8% were women, and 34.9% were on therapeutic anticoagulation. ICH occurred in 33 (7.9%) patients. Older age, non-Caucasian race, respiratory failure requiring mechanical ventilation, and therapeutic anticoagulation were associated with ICH on univariate analysis (p < 0.01 for each variable). In adjusted regression models, anticoagulation use was associated with a five-fold increased risk of ICH. ICH was associated with increased mortality. Anticoagulation use is associated with increased risk of ICH in patients with COVID-19.


Findings: In 89 consecutive patients hospitalized for Covid-19 infection we found a 20% prevalence of protein S deficiency and a very high prevalence of antiphospholipid antibodies: mainly lupus anticoagulant. The presence of PS deficiency or antiphospholipid antibodies was not linked with a prolonged aPTT nor with D-dimer, fibrinogen or C-reactive protein concentrations. These coagulation abnormalities are also not linked with thrombotic clinical events occurring during hospitalization nor with mortality. We assess a high prevalence of positive tests detecting thrombophilia in Covid-19 infections. However, in our series, these acquired thrombophilias are not correlated with the severity of the disease nor with the occurrence of thrombotic events. Albeit the strong thrombotic tendency in Covid-19 infections, the presence of frequent acquired thrombophilia may be part of the inflammation storm of Covid-19 disease and should not systematically modify our strategy on prophylactic anticoagulant treatment which is already revised upwards in this pathology.

Findings: The frequency of PE in COVID patients attending the ED is 6.64‰, which was more than 7-fold higher than that in the non-COVID ED population. This relatively high rate suggests that during the COVID period, the ED population comprised more patients with suspected and diagnosed PE, due, in part, to a higher suspicion by emergency physicians and also to fewer ED visits for other complaints. However, some study limitations impose caution in interpreting our findings. In many cases the diagnosis of COVID was based on clinical/radiological findings, with no microbiological confirmation. Further PE was only counted for study purposes if a CTPA was performed in the ED. During the COVID-19 pandemic, emergency physicians had a lower threshold for ordering CTPA although CTPA positivity for PE did not differ between periods, confirming that SARS-COV-2 is not associated with a higher incidence of PE among high risk patients. However, a higher proportion of ED patients were diagnosed with PE during the COVID period and among COVID patients when all ED comers were taken into account. Patient-related or disease-related factors could have accounted for such increased rates, as the characteristics of the patients attending the ED could be dissimilar between periods, although the similar rates observed for non-COVID patients in both periods does not support this possibility.

**Diagnostics & Screening**


Findings: The CovidNudge platform was a sensitive, specific, and rapid point of care test for the presence of SARS-CoV-2 without laboratory handling or sample pre-processing. The device, which has been implemented in UK hospitals since May 2020, could enable rapid decisions for clinical care and testing programmes.


Findings: The ArchitectTM test had a specificity of 100 % and sensitivity of 99.1 % and 93.9 % when excluding or including immunocompromised patients, respectively for specimens collected >14 days post symptom onset or >5 days post-RNA testing. The PanbioTM test had 99.3 % agreement to ArchitectTM. Notably, N = 6 immune-compromised individuals were identified that did not develop detectable antibodies by day 30. There is good concordance between the ArchitectTM SARS CoV-2 IgG Assay and PanbioTM COVID-19 IgG/IgM Rapid Test Device for the detection of SARS CoV-2 IgG.

Findings: The repeatability verification results of the A, B, C, and D systems are all qualified. D-Ab performed best (92% sensitivity and 99.23% specificity), and B_IgM performed worse than the other systems. Except for the A_IgM and C_IgG systems, the optimal diagnostic thresholds and cutoff values of the other kits and their recommendations are inconsistent with each other. B_IgM had the worst AUC, and C_IgG had the best diagnostic accuracy. More importantly, the B_IgG system had the highest false positive rate for testing patients with AIDS, tumours and pregnancies. The A_IgM system test showed the highest false positive rates among elderly individuals over 90 years old. COVID-2019 IgM/IgG antibody test systems exhibit performance differences. The D-Ab serum diagnosis kit is the most reliable detection system for anti-SARS-CoV-2 antibodies, which can be used as an alternative method for nucleic acid testing.


Findings: Dried blood spot (DBS) samples can be used for the detection of severe acute respiratory syndrome coronavirus 2 spike antibodies. DBS sampling is comparable to matched serum samples with a relative 98.1% sensitivity and 100% specificity. Thus, DBS sampling offers an alternative for population-wide serologic testing in the coronavirus pandemic.


Findings: In this mass-screening study including 1,924 individuals, the sensitivity of nucleic acid amplification testing with nasopharyngeal and saliva specimens were 86% and 92%, respectively, with specificities greater than 99.9%. The true concordance probability between the nasopharyngeal and saliva tests was estimated at 0.998 on the estimated airport prevalence at 0.3%. In positive individuals, viral load was highly correlated between NPS and saliva. Both nasopharyngeal and saliva specimens had high sensitivity and specificity. Self-collected saliva is a valuable specimen to detect SARS-CoV-2 in mass screening of asymptomatic persons.

Epidemiology & Public Health

Findings: In this retrospective case-control study, we found that ED co-location with Covid-19 patients is not associated with Covid-19 acquisition. Our findings provide reassurance that SARS-CoV-2 transmission occurs uncommonly in EDs. Emergency Departments have implemented various strategies to limit SARS-CoV-2 transmission, including use of personal protective equipment such as face masks and eye protection, cohorting patients with respiratory symptoms, social distancing, and limiting visitors. The EDs in this study may have implemented different infection control precautions at different times, and we are unable to comment on which strategies are most effective for reducing SARS-CoV-2 transmission.


Findings: Among 4,002 patients, 264 (6.6%) had ibuprofen prescription claims before COVID-19. Age, sex and comorbidities were comparable between the two study groups. Standardized absolute risks of the composite outcome for ibuprofen-prescribed versus non-ibuprofen patients were 16.3% versus 17.0%. In conclusion, in this nationwide study, there was no significant association between ibuprofen prescription claims and severe COVID-19.


Findings. When standardised to the US dialysis population, seroprevalence ranged from 3·5% (3·1–3·9) in the west to 27·2% (25·9–28·5) in the northeast. Comparing seroprevalent and case counts per 100 000 population, we found that 9·2% (8·7–9·8) of seropositive patients were diagnosed. When compared with other measures of SARS-CoV-2 spread, seroprevalence correlated best with deaths per 100,000 population. Residents of non-Hispanic Black and Hispanic neighbourhoods experienced higher odds of seropositivity (odds ratio 3·9 and 2·3, respectively) compared with residents of predominantly non-Hispanic white neighbourhoods. Residents of neighbourhoods in the highest population density quintile experienced increased odds of seropositivity (10·3 [8·7–12·2]) compared with residents of the lowest density quintile. County mobility restrictions that reduced workplace visits by at least 5% in early March, 2020, were associated with lower odds of seropositivity in July, 2020 (0·4 [0·3–0·5]) when compared with a reduction of less than 5%. During the first wave of the COVID-19 pandemic, fewer than 10% of the US adult population formed antibodies against SARS-CoV-2, and fewer than 10% of those with antibodies were diagnosed. Public health efforts to limit SARS-CoV-2 spread need to especially target racial and ethnic minority and densely populated communities.

Findings: COVID-19 patients often develop severe hypoxemic acute respiratory failure and ARDS requiring high levels of ventilator support. Current SNS ventilators were unable to fully support all COVID-19 patients, and only about half of newly ordered ventilators have the capacity to support the most severely affected patients; ventilators with less capacity for providing high level support are still of significant value in caring for many patients. Current SNS ventilators and those on order are capable of supporting most but not all COVID-19 patients. Technologic, logistic, and educational challenges encountered from current SNS ventilators are summarized, with potential next generation SNS ventilator updates offered.

Findings: The impact of COVID-19 on U.S. HCP was first described using national case surveillance data in April 2020. Since then, the number of reported HCP with COVID-19 has increased tenfold. This update describes demographic characteristics, underlying medical conditions, hospitalizations, and intensive care unit (ICU) admissions, stratified by vital status, among 100,570 HCP with COVID-19 reported to CDC during February 12-July 16, 2020. HCP status was available for 571,708 (22%) of 2,633,585 cases reported to CDC. Most HCP with COVID-19 were female (79%), aged 16-44 years (57%), not hospitalized (92%), and lacked all 10 underlying medical conditions specified on the case report form (56%). Of HCP with COVID-19, 641 died. Compared with nonfatal COVID-19 HCP cases, a higher percentage of fatal cases occurred in males (38% versus 22%), persons aged ≥65 years (44% versus 4%), non-Hispanic Asians (Asians) (20% versus 9%), non-Hispanic Blacks (Blacks) (32% versus 25%), and persons with any of the 10 underlying medical conditions specified on the case report form (92% versus 41%). From a subset of jurisdictions reporting occupation type or job setting for HCP with COVID-19, nurses were the most frequently identified single occupation type (30%), and nursing and residential care facilities were the most common job setting (67%).

Findings: Hospital admissions in the US fell dramatically with the onset of the COVID-19 pandemic. However, little is known about differences in admissions patterns among patient groups or the extent of the rebound. In this study of approximately 1 million medical admissions from a large nationally representative hospitalist group, we found that declines in non-COVID-19 admissions from February to April 2020 were generally similar across patient demographic subgroups and exceeded 20% for all primary admission diagnoses. By late June/early July 2020, overall non-COVID-19 admissions had rebounded to 16% below prepandemic baseline volume (8% including COVID-19 admissions). Non-COVID-19 admissions were substantially lower for patients residing in majority-Hispanic neighborhoods (32% below
baseline) and remained well below baseline for patients with pneumonia (-44%), COPD/asthma (-40%), sepsis (-25%), urinary tract infection (-24%) and acute ST-elevation myocardial infarction (STEMI), -22%.

**Laboratory Results**


**Findings:** A total of 1641 patients were included in the study (mean age 62 years; 886 men [54%]; 740 White individuals [45%] and 497 Hispanic individuals [30%]; 276 nonsurvivors [17%]). Elevated RDW (>14.5%) was associated with an increased mortality risk in patients of all ages. Patients who had levels above normal range were nearly three times as likely to die from COVID-19.


**Findings:** We recently reported a patient with COVID-19 reinfection. Here, we showed that serum neutralizing antibody could be detected during the first episode but not at presentation of the second episode. During reinfection, neutralizing antibody and high avidity IgG were found within 8 days after hospitalization, while IgM response was absent.


**Findings:** Interindividual clinical variability in the course of SARS-CoV-2 infection is immense. We report that at least 101 of 987 patients with life-threatening COVID-19 pneumonia had neutralizing IgG auto-Abs against IFN-ω (13 patients), the 13 types of IFN-α (36), or both (52), at the onset of critical disease; a few also had auto-Abs against the other three type I IFNs. The auto-Abs neutralize the ability of the corresponding type I IFNs to block SARS-CoV-2 infection in vitro. These auto-Abs were not found in 663 individuals with asymptomatic or mild SARS-CoV-2 infection and were present in only 4 of 1,227 healthy individuals. Patients with auto-Abs were aged 25 to 87 years and 95 were men. A B cell auto-immune phenocopy of inborn errors of type I IFN immunity underlies life-threatening COVID-19 pneumonia in at least 2.6% of women and 12.5% of men.


**Findings:** Clinical outcome upon infection with SARS-CoV-2 ranges from silent infection to lethal COVID-19. We have found an enrichment in rare variants predicted to be loss-of-function (LOF)
at the 13 human loci known to govern TLR3- and IRF7-dependent type I interferon (IFN) immunity to influenza virus, in 659 patients with life-threatening COVID-19 pneumonia, relative to 534 subjects with asymptomatic or benign infection. By testing these and other rare variants at these 13 loci, we experimentally define LOF variants in 23 patients (3.5%), aged 17 to 77 years, underlying autosomal recessive or dominant deficiencies. We show that human fibroblasts with mutations affecting this pathway are vulnerable to SARS-CoV-2. Inborn errors of TLR3- and IRF7-dependent type I IFN immunity can underlie life-threatening COVID-19 pneumonia in patients with no prior severe infection.

Prognosis


Findings: In this national cohort of VA patients, most SARS-CoV-2 deaths were associated with older age, male sex, and comorbidity burden. Many factors previously reported to be associated with mortality in smaller studies were not confirmed, such as obesity, Black race, Hispanic ethnicity, chronic obstructive pulmonary disease, hypertension, and smoking.


Findings: Paired nasopharyngeal and plasma samples were included from 85 patients. The median age was 55 years, and individuals with RNAemia were older than those with undetectable SARS-CoV-2 RNA in plasma (63 vs 50 years). Comorbidities were frequent including obesity (37.6%), hypertension (30.6%), and diabetes mellitus (22.4%). RNAemia was detected in 28/85 (32.9%) of patients, including 22/28 (78.6%) who required hospitalization. In models adjusted for age, RNAemia was detected more frequently in individuals who developed severe disease including ICU admission (32.1 vs 14.0%) and invasive mechanical ventilation (21.4% vs 3.5%). All 4 deaths occurred in individuals with detectable RNAemia. An additional 121 plasma samples from 28 individuals with RNAemia were assessed longitudinally, and RNA was detected for a maximum duration of 10 days. This study demonstrated a high proportion of SARS-CoV-2 RNAemia, and an association between RNAemia and clinical severity suggesting the potential utility of plasma viral testing as a prognostic indicator for COVID-19.


Findings: Median patient age was 64 years (range, 1 to 108 years); 47% were women, 40% were Black, 16% were Latinx, and 21% were nursing home residents. Among all patients, 131 (16%) died and 694 (83%) were discharged (523 [63%] had mild to moderate disease and 171 [20%] had severe disease). Of deaths, 66 (50%) were nursing home residents. Of 787 patients admitted with mild to moderate disease, 302 (38%) progressed to severe disease or death: 181
(60%) by day 2 and 238 (79%) by day 4. Patients had markedly different probabilities of disease progression on the basis of age, nursing home residence, comorbid conditions, obesity, respiratory symptoms, respiratory rate, fever, absolute lymphocyte count, hypoalbuminemia, troponin level, and C-reactive protein level and the interactions among these factors. A combination of demographic and clinical variables is strongly associated with severe COVID-19 disease or death and their early onset. The COVID-19 Inpatient Risk Calculator (CIRC), using factors present on admission, can inform clinical and resource allocation decisions.

Findings: After adjustment for patient and clinical characteristics, older age was the strongest predictor of death, exceeding comorbidities, abnormal vital signs, and laboratory test abnormalities. That coronary artery disease, but not chronic lung disease, was associated with death among hospitalized patients warrants further investigation, as do associations between certain antihypertensive medications and death.

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2771090?resultClick=1
Findings: There are limited data on the characteristics and outcomes of cardiac arrest in patients hospitalized with COVID-19 in the US. In our study of 54 patients with COVID-19, there was a 100% mortality rate following CPR. The initial rhythm was nonshockable for 52 patients (96.3%), with pulseless electrical activity being the most common (44 [81.5%]). Despite 29 patients (53.7%) achieving ROSC, none survived to discharge. The high mortality following CPR is likely multifactorial. The overall survival to discharge before the outbreak was 25%, with it being 11% in patients with a nonshockable rhythm. Given that most of the patients in this study developed a nonshockable rhythm, the outcome was likely to be poor. Additionally, at the time of cardiac arrest, many patients were either receiving mechanical ventilation, kidney replacement therapy, or vasopressor support, all factors previously shown to be associated with a poor outcome following IHCA. These outcomes warrant further investigation into the risks and benefits of performing prolonged CPR in this subset of patients, especially because the resuscitation process generates aerosols that may place health care personnel at a higher risk of contracting the virus.

Findings: Of 1629 consecutive hospitalized adult patients with confirmed COVID-19 from March 1st thru March 31, 2020, 1461 patients were included in final analysis. 327 patients died during hospitalization and 1134 survived to discharge. Median age was 62 years (IQR 50.0, 74.0) with 56% of hospitalized patients under the age of 65. 47% were female and 63% identified as African American. Most patients (55%) had either no or one comorbidity. In multivariable
analysis, older age, admission respiratory status including elevated respiratory rate and oxygen saturation ≤ 88%, and initial laboratory derangements of creatinine > 1.33 mg/dL, alanine aminotransferase > 40 U/L, procalcitonin > 0.5 ng/mL, and lactic acid ≥ 2 mmol/L increased risk of in-hospital death. This study is one of the largest analyses in an epicenter for the COVID-19 pandemic. Older age, low oxygen saturation and elevated respiratory rate on admission, and initial lab derangements including renal and hepatic dysfunction and elevated procalcitonin and lactic acid are risk factors for in-hospital death.

**Survivorship & Rehabilitation**


To address the rehabilitation wave, we describe a spectrum of interventions that start in the ICU and continue through all the appropriate levels of care. This approach requires organized rehabilitation teams including physical therapists, occupational therapists, speech-language pathologists, rehabilitation psychologists/neuropsychologists, and physiatrists collaborating with acute medical teams. Here, we also discuss administrative factors that influence the provision of care during the COVID-19 pandemic. The services that can be provided are described in detail to allow the reader to understand what services may be appropriate locally. We have been learning and adapting real-time during this crisis and hope that sharing our experience facilitates the work of others as the pandemic evolves.

**Therapeutics**


Findings: Baseline characteristics were very similar in the two groups, with no significant difference in age, sex, comorbidities, medicines taken, and disease severity. Also, groups were similar in laboratory tests and chest CT scan findings. Sixteen patients (23.9%) in the Placebo group were submitted to endotracheal intubation and mechanical ventilation, compared to 14 patients (20.6%) in the NAC group (p=0.675). No difference was observed in secondary endpoints. **CONCLUSION:** Administration of NAC in high doses did not affect the evolution of severe Covid-19.


Findings: 10 studies (all on tocilizumab) comprising 1358 patients were included. Meta-analysis showed that the tocilizumab group had lower mortality than the control group. The risk ratio
(RR) was 0.27 95%CI 0.12 to 0.59 and the risk difference (RD) was 12% 95%CI 4.6% to 20% in favour of the tocilizumab group. With only a few studies available there were no differences observed regarding side effects. Our results showed that mortality was 12% lower for COVID-19 patients treated with tocilizumab compared to COVID-19 patients who were not treated with tocilizumab. The number needed to treat was 11, suggesting that for every 11 (severe) COVID-19 patients treated with tocilizumab 1 death is prevented. These results require confirmation by randomized controlled trials.


Findings: Favipiravir is an oral broad-spectrum inhibitor of viral RNA-dependent RNA polymerase that is approved for treatment of influenza in Japan. We conducted a prospective, randomized, open-label, multicenter trial of favipiravir for the treatment of COVID-19 at 25 hospitals across Japan. Eligible patients were adolescents and adults admitted with COVID-19 who were asymptomatic or mildly ill and had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Patients were randomly assigned at a 1:1 ratio to early or late favipiravir therapy (the same regimen starting on day 6 instead of day 1). The primary endpoint was viral clearance by day 6. The secondary endpoint was change in viral load by day 6. Exploratory endpoints included time to defervescence and resolution of symptoms. Eighty-nine patients were enrolled, of whom 69 were virologically evaluable. Viral clearance occurred within 6 days in 66.7% and 56.1% of the early and late treatment groups (adjusted hazard ratio [aHR], 1.42; 95% confidence interval [95% CI], 0.76-2.62). Of 30 patients who had a fever (≥37.5°C) on day 1, time to defervescence was 2.1 days and 3.2 days in the early and late treatment groups (aHR, 1.88; 95%CI, 0.81-4.35). During therapy, 84.1% developed transient hyperuricemia. Favipiravir did not significantly improve viral clearance as measured by RT-PCR by day 6 but was associated with numerical reduction in time to defervescence. Neither disease progression nor death occurred to any of the patients in either treatment group during the 28-day participation.


https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30563-2/abstract

Findings: Of 1717 patients with COVID-19 evaluated, 513 patients were included in the study; of these 170 (33%) were treated with corticosteroids. During the hospitalization 166 (34%) patients reached the primary outcome [60/170 (35%) in the corticosteroid group and 106/343 (31%) in the non-corticosteroid group]. At multivariable analysis corticosteroid treatment was not associated with lower 30-day mortality rate. After inverse probability of treatment weighting, corticosteroids were not associated to lower 30-day mortality. However, subgroup analysis revealed that in patients with PO2/FiO2 < 200 mmHg at admission [135 patients, 52 (38%) treated with corticosteroids] corticosteroid treatment was associated to a lower risk of
30-day mortality. Our study shows that the effect of corticosteroid treatment on mortality might be limited to critically ill COVID-19 patients.


Findings: Ten patients were assigned to the therapeutic enoxaparin and ten patients to prophylactic anticoagulation. There was a statistically significant increase in the PaO2/FiO2 ratio over time in the therapeutic group (163 at baseline, 209 after 7 days, and 261 after 14 days). In contrast, we did not observe this improvement over time in the prophylactic group (184 at baseline, 168 after 7 days, and 195 after 14 days). Patients of the therapeutic group had a higher ratio of successful liberation from mechanical ventilation and more ventilator-free days (15 days versus 0 days when compared to the prophylactic group. Therapeutic enoxaparin improves gas exchange and decreases the need for mechanical ventilation in severe COVID-19.


Findings: Data for 1035 patients with COVID-19 who received ECMO support were included in this study. Of these, 67 (6%) remained hospitalised, 311 (30%) were discharged home or to an acute rehabilitation centre, 101 (10%) were discharged to a long-term acute care centre or unspecified location, 176 (17%) were discharged to another hospital, and 380 (37%) died. The estimated cumulative incidence of in-hospital mortality 90 days after the initiation of ECMO was 37·4% (95% CI 34·4–40·4). Mortality was 39% (380 of 968) in patients with a final disposition of death or hospital discharge. The use of ECMO for circulatory support was independently associated with higher in-hospital mortality (hazard ratio 1·89, 95% CI 1·20–2·97). In patients with COVID-19 who received ECMO, both estimated mortality 90 days after ECMO and mortality in those with a final disposition of death or discharge were less than 40%. These data from 213 hospitals worldwide provide a generalisable estimate of ECMO mortality in the setting of COVID-19.

Transmission / Infection Control


Findings: In 213 patients with SARS-CoV-2 infection, 41 (19%) had remained asymptomatic from potential exposure to laboratory confirmation and admission; of them, 39 (95%) underwent follow-up RT-PCR testing after a median 13 days. In 172 symptomatic patients, 144 (84%) underwent follow-up RT-PCR testing. Twenty-one (54%) asymptomatic individuals and 92 (64%) symptomatic patients tested positive for SARS-CoV-2 at follow-up. Asymptomatic individuals and symptomatic patients did not show any significant differences in the mean Ct values of the
E (31.15 vs 31.43; p>0.99), RdRp (32.26 vs 32.93; p=0.92) and N (33.05 vs 33.28; p>0.99) genes. Approximately one-fifth of the individuals without severe symptoms were asymptomatic, and their viral loads were comparable to those in symptomatic patients. A large proportion of mildly symptomatic patients with COVID-19 or asymptomatic individuals with SARS-CoV-2 showed persistent positive upper respiratory RT-PCR results at follow-up.


Findings: Single fabric layers blocked a range of ultrafine particles. When fabrics were layered, a higher percentage of ultrafine particles were filtered. The average filtration efficiency of single layer fabrics and of layered combination was found to be 35% and 45%, respectively. Non-woven fusible interfacing, when combined with other fabrics, could add up to 11% additional filtration efficiency. However, fabric and fabric combinations were more difficult to breathe through than N95 masks. Our findings suggest that face masks made from layered common fabric can help filter ultrafine particles and provide some protection for the wearer when commercial face masks are unavailable.


Findings: Of the 2900 employees, 50.9% participated in the study, revealing a positive SARS-CoV-2 seroprevalence of 4.9% (72/1476), [95% CI of 4.04% - 5.89%]. There were no statistically significant differences in the presence of antibody based on gender, age, frontline worker status, job title, performance of aerosol generating procedures or exposure to known patients with coronavirus infectious disease 2019 (COVID-19) within the hospital. Employees who reported exposure to a known COVID-19 case outside of work had a significantly higher seroprevalence at 14.84% (23/155) compared to those that did not 3.70% (48/1296). Notably, 29% of seropositive employees reported no history of symptoms for SARS-CoV-2 infection. Seroprevalence of SARS-COV-2 among employees was not significantly different among those who provided direct patient care and those who did not, suggesting facility-wide infection control measures based were effective. Employees who reported direct personal contact with COVID-19 positive persons outside of work were more likely to have SARS-CoV-2 antibodies. Employee exposure to SARS-CoV-2 outside of work may introduce infection into hospitals.


Findings: Many scientific reports document that asymptomatic and presymptomatic individuals contribute to the spread of COVID-19, probably during conversations in social interactions. Droplet emission occurs during speech, yet few studies document the flow to provide the transport mechanism. This lack of understanding prevents informed public health guidance for
risk reduction and mitigation strategies, e.g., the "6-foot rule." Here we analyze flows during breathing and speaking, including phonetic features, using orders-of-magnitude estimates, numerical simulations, and laboratory experiments. We document the spatiotemporal structure of the expelled airflow. Phonetic characteristics of plosive sounds like "p" lead to enhanced directed transport, including jet-like flows that entrain the surrounding air. We highlight three distinct temporal scaling laws for the transport distance of exhaled material including 1) transport over a short distance (<0.5 m) in a fraction of a second, with large angular variations due to the complexity of speech; 2) a longer distance, ∼1 m, where directed transport is driven by individual vortical puffs corresponding to plosive sounds; and 3) a distance out to about 2 m, or even farther, where sequential plosives in a sentence, corresponding effectively to a train of puffs, create conical, jet-like flows. The latter dictates the long-time transport in a conversation. We believe that this work will inform thinking about the role of ventilation, aerosol transport in disease transmission for humans and other animals, and yield a better understanding of linguistic aerodynamics, i.e., aerophonetics.


Findings: To make the physics of person-to-person virus transmission from emitted droplets of oral fluid while speaking easily understood, we present simple and transparent algebraic equations that capture the essential physics of the problem. Calculations with these equations provide a straightforward way of determining whether emitted droplets remain airborne or rapidly fall to the ground, after accounting for the decrease in droplet size from water evaporation. At a relative humidity of 50%, for example, droplets with initial radii larger than about 50 μm rapidly fall to the ground, while smaller, potentially virus-containing droplets shrink in size from water evaporation and remain airborne for many minutes. Estimates of airborne virion emission rates while speaking strongly support the proposal that mouth coverings can help contain the COVID-19 pandemic.

Women & Children


Findings: SARS-CoV-2 test positivity in individuals in labor was associated with a higher prevalence of preeclampsia and lower prevalence of induction of labor. COVID-19 is primarily a respiratory infection but also has systemic effects that may resemble preeclampsia. The absence of an increased prevalence of preterm birth is concordant with results of 2 previous studies using comparators. The lack of difference in Apgar scores and birth weight for gestational age between groups is similar to that in a US study. In light of other accumulating data, it is already clear that COVID-19 is less severe in pregnancy than the 2 previous coronavirus infections SARS and MERS. Nevertheless, there are reports of pregnant persons requiring critical care, and there have been other reports of both mother and infant deaths in association with COVID-19.
41. The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19.
Findings: We apply systems-level analyses of blood immune cells, cytokines, and autoantibodies in healthy children, children with Kawasaki disease enrolled prior to COVID-19, children infected with SARS-CoV-2, and children presenting with MIS-C. We find that the inflammatory response in MIS-C differs from the cytokine storm of severe acute COVID-19, shares several features with Kawasaki disease, but also differs from this condition with respect to T cell subsets, interleukin (IL)-17A, and biomarkers associated with arterial damage. Finally, autoantibody profiling suggests multiple autoantibodies that could be involved in the pathogenesis of MIS-C.

42. Characterizing Coinfection in Children with COVID-19: A Dual Center Retrospective Analysis.
Findings: Recent reports have shown pediatric COVID-19 coinfection rates as high as 51%. However, our dual center study found that viral coinfection rates in pediatric COVID-19 patients are low. This analysis was performed at a time of year when respiratory viral transmission, most notably influenza, was declining. During the study period, the Illinois Department of Public Health tracked a decrease in influenza positive tests from 14.9% for the week ending March 14, 2020 to 1.8% for the week ending April 25, 2020 [6]. The stay at home order issued in the state of Illinois on March 9, 2020 also may have played a role in the reduction of seasonal respiratory viral transmission. During seasons of low rates of respiratory viral transmission, our data suggest that testing for other viruses among COVID-19 patients may not be warranted.

43. Rates of Maternal and Perinatal Mortality and Vertical Transmission in Pregnancies Complicated by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Systematic Review.
Findings: Of the 99 articles identified, 13 included 538 pregnancies complicated by SARS-CoV-2 infection, with reported outcomes on 435 (80.9%) deliveries. Maternal ICU admission occurred in 3.0% of cases (8/263) and maternal critical disease in 1.4% (3/209). No maternal deaths were reported (0/348). The preterm birth rate was 20.1% (57/284), the cesarean delivery rate was 84.7% (332/392), the vertical transmission rate was 0.0% (0/310), and the neonatal death rate was 0.3% (1/313). With data from early in the pandemic, it is reassuring that there are low rates of maternal and neonatal mortality and vertical transmission with SARS-CoV-2. The preterm birth rate of 20% and the cesarean delivery rate exceeding 80% seems related to geographic practice patterns.

44. Distinguishing Multisystem Inflammatory Syndrome in Children from Kawasaki Disease and Benign Inflammatory Illnesses in the SARS-CoV-2 Pandemic.
Corwin DJ, Sartori LF, Chiotos K, et
Findings: We describe 3 groups with inflammatory syndromes during the SARS-CoV-2 pandemic. The initial profile of lymphopenia, thrombocytopenia, hyponatremia, and abnormal creatinine may help distinguish critically ill MIS-C patients from classic/atypical KD or more benign acute inflammation.

Findings: A total of 32 studies comprising 41,640 children and adolescents and 268,945 adults met inclusion criteria, including 18 contact-tracing studies and 14 population screening studies. The pooled odds ratio of being an infected contact in children compared with adults was 0.56 (95% CI, 0.37-0.85), with substantial heterogeneity (I² = 94.6%). Three school-based contact-tracing studies found minimal transmission from child or teacher index cases. Findings from population screening studies were heterogenous and were not suitable for meta-analysis. Most studies were consistent with lower seroprevalence in children compared with adults, although seroprevalence in adolescents appeared similar to adults. In this meta-analysis, there is preliminary evidence that children and adolescents have lower susceptibility to SARS-CoV-2, with an odds ratio of 0.56 for being an infected contact compared with adults. There is weak evidence that children and adolescents play a lesser role than adults in transmission of SARS-CoV-2 at a population level. This study provides no information on the infectivity of children.

GUIDELINES & CONSENSUS STATEMENTS


FDA / CDC / NIH / WHO Updates

ECRI: N95-Style Mask Testing Program - Report: Use of Imported N95-Style Masks, without NIOSH Certification or Independent Lab Validation, May Put Healthcare Workers and Patients at Risk during the COVID-19 Pandemic

**Providence continues to supply N95s, NIOSH and FDA approved respirators. Learn about how Providence is ensuring we have safe and effective masks to protect our caregivers and patients HERE.**
Covid-19: CDC publishes then withdraws information on aerosol transmission. Tanne JH. BMJ. 2020 Sep 24;370:m3739. doi: 10.1136/bmj.m3739.

Johnson & Johnson Initiates Pivotal Global Phase 3 Clinical Trial of Janssen’s COVID-19 Vaccine Candidate

F.D.A. to Release Stricter Guidelines for Emergency Vaccine Authorization

Novavax Initiates Phase 3 Efficacy Trial of COVID-19 Vaccine in the United Kingdom


*author’s reply


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