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 this study, we used a cell-based infection assay to screen more than 3,000 agents used in humans and animals, including 2,855 small molecules and 190 traditional herbal medicines, and identified 15 active small molecules in concentrations ranging from 0.1 nM to 50 μM. Two enzymatic assays, along with molecular modeling, were then developed to confirm those targeting the virus 3CL protease and the RNA-dependent RNA polymerase. Several water extracts of herbal medicines were active in the cell-based assay and could be further developed as plant-derived anti-SARS-CoV-2 agents. Some of the active compounds identified in the screen were further tested in vivo, and it was found that mefloquine, nelfinavir, and extracts of Ganoderma lucidum (RF3), Perilla frutescens, and Mentha haplocalyx were effective in a challenge study using hamsters as disease model.

Clinical Syndrome


   Findings: This prospective study included 94 COVID-19 patients. Smell and taste tests were applied to all patients. Ten days after the first test, a second test was applied to the patients with an impaired sense of smell to compare the results. Of the 94 patients, there were 67 patients with smell and taste impairment, of whom 34 (50.7%) had smell impairment only, 3 (4.4%) had taste impairment only, and 30 (44.7%) had both smell and taste impairment. It was found that the smell scores of 55 patients with smell and taste impairment in the first evaluation were significantly higher at the second measurement; and their tasting period was significantly shortened compared to the first measurement. COVID-19 patients may present to medical centers with a broad variety signs and symptoms. This study shows that impairment in...
the senses of smell and taste is common in this disease and strongly associated with COVID-19 infection. However, smell and taste impairment is mostly temporary and improves during the recovery period.


Findings: While tachyarrhythmias seem most common, we describe four cases of COVID-19 patients who developed a transient high-degree atrioventricular (AV) block during the course of their hospitalization. All four patients who developed a high-degree AV block during their hospitalization with COVID-19 did not require permanent pacing. Similarly to most AV blocks associated with infectious organisms and given its transient nature, this case series suggests that conservative management strategies should be preferred in COVID-19 patients who develop complete heart block.


Findings: 119 patients were randomly selected from the 372 admitted to one tertiary hospital in Valencia (Spain) for COVID-19 infection during the period of study. Despite a high level of pharmacological thromboprophylaxis (89%), the incidence of PE was 35.6%, mostly with a peripheral location and low thrombotic load. Multivariate analysis showed that heart rate, room-air oxygen saturation (spO2), D-dimer, and C-reactive protein (CRP) levels at the time of admission were independent predictors of incident PE during hospitalization. A risk score was constructed with these four variables showing a high predictive value of incident PE. Our findings confirmed a high incidence of PE in hospitalized COVID-19 patients. Heart rate, spO2, D-dimer, and CRP levels at admission were associated with higher rates of PE during hospitalization.


Findings: From April to September 2020, we enrolled 61 consecutively admitted COVID-19 patients, 35 (57%) of whom required ICU management for respiratory failure. Forty-one CNS/PNS complications were identified in 28 of 61 (45.9%) patients and were more frequent in ICU compared to non-ICU patients. The most common CNS complication was encephalopathy (n = 19, 31.1%), which was severe in 13 patients (GCS ≤ 12), including 8 with akinetic mutism. Length of ICU admission was independently associated with encephalopathy (OR = 1.22). Other CNS complications included ischemic stroke, a biopsy-proven acute necrotizing encephalitis, and transverse myelitis. The most common PNS complication was critical illness polyneuromyopathy (13.1%), with prolonged ICU stay as independent predictor (OR = 1.14).
Treatment-related PNS complications included meralgia paresthetica. Of 41 complications in total, 3 were para/post-infectious, 34 were secondary to critical illness or other causes, and 4 remained unresolved. Cerebrospinal fluid was negative for SARS-CoV-2 RNA in all 5 patients investigated. CNS and PNS complications were common in hospitalized COVID-19 patients, particularly in the ICU, and often attributable to critical illness. When COVID-19 was the primary cause for neurological disease, no signs of viral neurotropism were detected, but laboratory changes suggested autoimmune-mediated mechanisms.


Findings: In this multicenter, retrospective study, 476 patients with COVID-19 were enrolled from a consecutive series. The main symptoms observed in the study included fever on admission, cough, fatigue, and shortness of breath. The most common comorbidities were hypertension and diabetes mellitus. Patients with lower CD4+ T cell level were older and more often male compared to those with higher CD4+ T cell level. Reduced CD8+ T cell level was an indicator of the severity of COVID-19. Both decreased CD4+ T and CD8+ T cell levels were associated with in-hospital death in COVID-19 patients, but only the decrease of CD4+ T cell level was an independent predictor of in-hospital death in COVID-19 patients. Reductions in lymphocytes and lymphocyte subsets were common in COVID-19 patients, especially in severe cases of COVID-19. It was the CD8+ T cell level, not the CD4+ T cell level, that reflected the severity of the patient’s disease. Only reduced CD4+ T cell level was independently associated with increased in-hospital death in COVID-19 patients.

**Diagnostics & Screening**


Findings: In a cohort of 1091 symptomatic COVID-19 patients, initial chest CT was normal in 5.2% of cases. • Normal chest CT in confirmed COVID-19 is frequent even when onset of symptoms is greater than 3 days. • The outcome of COVID-19 patients with initial normal chest CT, while better than those with abnormal CT, was not entirely benign with 5.3% death and/or mechanical ventilation.


Findings: Patients infected with SARS-CoV-2, influenza A (flu A), influenza B (flu B), and respiratory syncytial virus (RSV) have overlapping clinical presentations, but the approaches to
treatment and management of infections caused by these viruses are different. Therefore, rapid diagnosis in conjunction with infection prevention measures is important to prevent transmission of the diseases. Recently, a new Xpert Xpress SARS-CoV-2/Flu/RSV (Xpert 4-in-1) assay enables the detection and differentiation of SARS-CoV-2, flu A, flu B, and RSV in upper respiratory tract specimens. In this study, we evaluated the performance of the Xpert 4-in-1 assay by comparing it with the Xpert Xpress SARS-CoV-2 and Xpert Xpress Flu/RSV assays for the detection of the four viruses in nasopharyngeal (NP) specimens. A total of 279 NP specimens, including 66, 56, 64 and 53 positive specimens for SARS-CoV-2, flu A, flu B and RSV respectively, were included. The Xpert 4-in-1 assay demonstrated high concordance with the comparator assays, with overall agreement for SARS-CoV-2, flu A, flu B, and RSV at 99.64%, 100%, 99.64%, and 100%, respectively, and a high kappa value ranging from 0.99 to 1.00, indicating an almost perfect correlation between assays. The cycle threshold value association between positive samples also showed a good correlation between assays. In conclusion, the overall performance of the Xpert 4-in-1 assay was highly comparable to that of the Xpert SARS-CoV-2 and Xpert Flu/RSV assays for the detection and differentiation of SARS CoV-2, flu A, flu B, and RSV in NP specimens.


Findings: Self-collected saline gargle and an oral-anterior nasal swab have a similar sensitivity to a nasopharyngeal swab for the detection of SARS-CoV-2. These alternative collection techniques are cheap and can eliminate barriers to testing, particularly in underserved populations. The adjusted sensitivity of the saline gargle was 0.90, the oral swab was 0.82 and the combined oral-anterior nasal swab was 0.87 as compared to a nasopharyngeal swab, which demonstrated a sensitivity of around 90% when all positive tests were the reference standard. The median cycle threshold values for the SARS-CoV-2 E-gene for concordant and discordant saline gargle specimens were 17 and 31, for the oral swabs were 17 and 28 and oral-anterior nasal swabs were 18 and 31.


Findings: This study compared the clinical performance of five AD tests, including four rapid AD (RAD) tests (biotical, Panbio, Healgen, and Roche) and one automated AD test (VITROS). For that purpose, 118 (62.8%) symptomatic patients and 70 (37.2%) asymptomatic subjects were tested, and results were compared to RT-PCR. Results: The performance of the RAD tests was modest and allowed us to identify RT-PCR positive patients with higher viral loads. For Ct values ≤25, the sensitivity ranged from 93.1% to 96.6%, meaning that some samples with high viral
loads were missed. Considering the Ct value proposed by the CDC for contagiousness (i.e., Ct values ≤33) sensitivities ranged from 76.2% to 88.8% while the specificity ranged from 96.3% to 99.1%. The VITROS automated assay showed a 100% sensitivity for Ct values ≤33 and had a specificity of 100%; Conclusions: Compared to RAD tests, the VITROS assay fully aligned with RT-PCR for Ct values up to 33, which might allow a faster, easier and cheaper identification of SARS-CoV-2 contagious patients.

Epidemiology & Public Health

Findings: Among patients with COVID-19-related critical illness admitted to ICUs of a learning health system in the United States, mortality seemed to decrease over time despite stable patient characteristics. Mortality decreased over time, from 43.5% to 19.2% between the first and last 15-day periods in the core adjusted model, whereas patient acuity and other factors did not change. Further studies are necessary to confirm this result and to investigate causal mechanisms.

Findings: Mitigation policies, including closure of nonessential businesses, restrictions on gatherings and movement, and stay-at-home orders, have been critical to controlling the COVID-19 pandemic in many countries, but they come with high social and economic costs. European countries that implemented more stringent mitigation policies earlier in their outbreak response tended to report fewer COVID-19 deaths through the end of June 2020. These countries might have saved several thousand lives relative to countries that implemented similar policies, but later. Earlier implementation of stringent mitigation policies, even by just a few weeks, appears to be important to prevent widespread COVID-19 transmission and reduce the number of deaths.

Findings: A more highly transmissible variant of SARS-CoV-2, B.1.1.7, has been detected in 10 U.S. states. Modeling data indicate that B.1.1.7 has the potential to increase the U.S. pandemic trajectory in the coming months. CDC’s system for genomic surveillance and the effort to expand sequencing will increase the availability of timely U.S. genomic surveillance data. The increased transmissibility of the B.1.1.7 variant warrants universal and increased compliance with mitigation strategies, including distancing and masking. Higher vaccination coverage might
need to be achieved to protect the public. Genomic sequence analysis through the National SARS-CoV-2 Strain Surveillance program will enable a targeted approach to identifying variants of concern in the United States.


Findings: SARS-CoV-2 antibody levels decrease with time, but the nature and quality of the memory B cells that would be called upon to produce antibodies upon re-infection has not been examined. Here we report on the humoral memory response in a cohort of 87 individuals assessed at 1.3 and 6.2 months after infection. We find that IgM, and IgG anti-SARS-CoV-2 spike protein receptor binding domain (RBD) antibody titres decrease significantly with IgA being less affected. Concurrently, neutralizing activity in plasma decreases by fivefold in pseudotype virus assays. In contrast, the number of RBD-specific memory B cells is unchanged. Memory B cells display clonal turnover after 6.2 months, and the antibodies they express have greater somatic hypermutation, increased potency and resistance to RBD mutations, indicative of continued evolution of the humoral response. Analysis of intestinal biopsies obtained from asymptomatic individuals 4 months after the onset of coronavirus disease-2019 (COVID-19), using immunofluorescence, or polymerase chain reaction, revealed persistence of SARS-CoV-2 nucleic acids and immunoreactivity in the small bowel of 7 out of 14 volunteers. We conclude that the memory B cell response to SARS-CoV-2 evolves between 1.3 and 6.2 months after infection in a manner that is consistent with antigen persistence.

**Healthcare Delivery & Healthcare Workers**


Findings: Seven hundred and nine participants completed the surveys comprising 291 (41%) doctors, 344 (49%) nurses and 74 (10%) other healthcare staff. Over half (59%) reported good well-being; however, 45% met the threshold for probable clinical significance on at least one of the following measures: severe depression (6%), PTSD (40%), severe anxiety (11%) or problem drinking (7%). Thirteen per cent of respondents reported frequent thoughts of being better off dead, or of hurting themselves in the past 2 weeks. Within the sample used in this study, we found that doctors reported better mental health than nurses across a range of measures. We found substantial rates of probable mental health disorders, and thoughts of self-harm, amongst ICU staff; these difficulties were especially prevalent in nurses. Whilst further work is needed to better understand the real level of clinical need amongst ICU staff, these results indicate the need for a national strategy to protect the mental health, and decrease the risk of functional impairment, of ICU staff whilst they carry out their essential work during COVID-19.

Findings: This study compared the provision of additional capacity to no intervention from a societal perspective. A decision model was developed using, e.g. information on age-specific fatality rates, ICU costs and outcomes, and the herd protection threshold. The net monetary benefit (NMB) was calculated based upon the willingness to pay for new medicines for the treatment of cancer, a condition with a similar disease burden in the near term. The marginal cost-effectiveness ratio (MCER) of the last bed added to the existing ICU capacity is €21,958 per life-year gained assuming full bed utilization. The NMB decreases with an additional expansion but remains positive for utilization rates as low as 2%. In a sensitivity analysis, the variables with the highest impact on the MCER were the mortality rates in the ICU and after discharge. This article demonstrates the applicability of cost-effectiveness analysis to policies of hospital pandemic preparedness and response capacity strengthening.


Findings: In this cohort study of 8516 patients with COVID-19 admitted to 88 US Veterans Affairs hospitals, strains on critical care capacity were associated with increased COVID-19 mortality. Among patients with COVID-19, those treated in the ICU during periods of peak COVID-19 ICU demand had a nearly 2-fold increased risk of mortality compared with those treated during periods of low demand. These findings suggest that public health officials and hospital administrators should consider interventions that reduce COVID-19 ICU demand to improve survival among patients with COVID-19 in the ICU.

**Laboratory Results**


Findings: Hypoxemia is readily detectable by assessing SpO2 levels, and these are important in optimizing COVID-19 patient management. Hyperlactatemia is a marker of tissue hypoxia, particularly in patients with increased oxygen requirement and microvascular obstruction. We monitored peripheral venous lactate concentrations in hospitalized patients with moderate to severe COVID-19 (n = 18) and in mild ambulatory COVID-19 patients in home quarantine (n = 16). Whole blood lactate decreased significantly during the clinical course and recovery in hospitalized patients (P = 0.008). The blood lactate levels were significantly higher in hospitalized patients than ambulatory patients (day 1: hospitalized versus ambulatory patients P = 0.002; day 28: hospitalized versus ambulatory patients P = < 0.0001). Elevated lactate levels may be helpful in risk stratification, and serial monitoring of lactate may prove useful in the care of hospitalized COVID-19 patients.
**Prognosis**


*Findings:* Controversy surrounds the circulating cytokine/chemokine profile of COVID-19-associated ARDS, with some groups suggesting that it is similar to non-COVID19 ARDS patients and others observing substantial differences. Moreover, while a hyperinflammatory phenotype associates with higher mortality in non-COVID19 ARDS, there is little information on the inflammatory landscape's association with mortality in COVID19 ARDS patients. Even though the circulating leukocytes' transcriptomic signature has been associated with distinct phenotypes and outcomes in critical illness including ARDS, it is unclear whether the mortality-associated inflammatory mediators from COVID19 patients are transcriptionally regulated in the leukocyte compartment. Here, we conducted a prospective cohort study of 41 mechanically ventilated patients with COVID19 infection using highly calibrated methods to define the levels of plasma cytokines/chemokines and their gene expressions in circulating leukocytes. Plasma IL1RA and IL8 were found positively associated with mortality while RANTES and EGF negatively associated with that outcome. However, the leukocyte gene expression of these proteins had no statistically significant correlation with mortality. These data suggest a unique inflammatory signature associated with severe COVID19.


*Findings:* The clinical information and laboratory tests of 166 COVID-19 patients were collected. Correlation analysis between KL-6 and other parameters was conducted. There were 17 (10.2%, 17/166) severe/critical and 149 (89.8%, 149/166) mild COVID-19 patients in our cohort. Serum KL-6 was significantly higher in severe/critical COVID-19 patients than in mild patients. KL-6 was next confirmed to be a sensitive and specific biomarker for distinguishing mild and severe/critical patients and correlate to computed tomography lung lesions areas. Serum KL-6 concentration during the follow-up period (>100 days post onset) was well correlated to those concentrations within 10 days post onset, indicating the prognostic value of KL-6 levels in predicting lung injury after discharge. Finally, elevated KL-6 was found to be significantly correlated to coagulation disorders, and T cells subsets dysfunctions. Serum KL-6 is a biomarker for assessing COVID-19 severity and predicting the prognosis of lung injury of discharged patients, and is also associated with lung lesions areas, coagulation disorders, and immune dysfunctions.


*Findings:* All ICU COVID-19 patients in Sweden until 27 May 2020 were matched to population controls on age and sex to assess the risk of ICU admission. We included 1981 patients and
7924 controls. Hypertension, type 2 diabetes mellitus, chronic renal failure, asthma, obesity, being a solid organ transplant recipient and immunosuppressant medications were independent risk factors of ICU admission and oral anticoagulants were protective. Stroke, asthma, chronic obstructive pulmonary disease and treatment with renin-angiotensin-aldosterone inhibitors (RAASi) were independent risk factors of ICU mortality in the pre-specified primary analyses; treatment with statins was protective. However, after adjusting for the use of continuous renal replacement therapy, RAASi were no longer an independent risk factor. In our cohort oral anticoagulants were protective of ICU admission and statins was protective of ICU death. Several comorbidities and ongoing RAASi treatment were independent risk factors of ICU admission and ICU mortality.

Findings: We conducted a multicenter cohort study between March 13 and June 19, 2020. We included all COVID-19 patients who underwent surgery in nine centres of the Province of Québec. Among the 44 COVID-19 patients, 31 surgeries (71%) were urgent and 16 (36%) were major. In these patients, pulmonary complications were frequent (25%) and 30-day mortality was high (15.9%). This mortality was higher in patients with symptoms (23.1%) compared to those without symptoms (5.6%), although not statistically significant (p = 0.118). Of the total 22,616 cases performed among participating centres during the study period, only 0.19% had COVID-19 at the time of surgery. Fewer procedures were performed during the study period compared to the same period in 2019 (44,486 cases). In this Canadian cohort study, postoperative 30-day mortality in COVID-19 patients undergoing surgery was high (15.9%). Although few surgeries were performed on COVID-19 patients, the pandemic impact on surgical activity volume was important.

Findings: A total of 38 articles, including 5699 patients with severity outcomes and 6033 patients with mortality outcomes, were included. The meta-analysis showed that severe and non-survivors of COVID-19 had higher on-admission NLR levels than non-severe and survivors. Regardless of the different NLR cut-off values, the pooled mortality RR in patients with elevated vs. normal NLR levels was 2.74. High NLR levels on admission were associated with severe COVID-19 and mortality. Further studies need to focus on determining the optimal cut-off value for NLR before clinical use.

Findings: Blood group A was associated with an increased odds of MACE (major adverse cardiovascular events), whereas blood group O was associated with a reduction in the odds of
MACE in patients with COVID-19. These findings may inform risk stratification of COVID-19 patients for cardiovascular complications. Additional studies are needed to validate our findings.


Findings: A total of 1062 patients were included in the analysis, with a median follow-up time of 62 days. The mean age of patients was 56.5 years, and 40.5% were women. At the end of the study, a total of 48 (4.5%) patients were readmitted within 30 days of discharge, and a median time to readmission was 5 days. The most common primary diagnosis of 30-day readmission was a hypoxic respiratory failure (68.8%) followed by thromboembolism (12.5%) and sepsis (6.3%). The patients with a peak serum creatinine level of ≥ 1.29 mg/dL during the index hospitalization, compared to those with a creatinine of < 1.29 mg/dL, had 2.4 times increased risk of 30-day readmission (adjusted odds ratio: 2.41; 95% CI: 1.23-4.74). The mortality rate during the readmission was 22.9%. With 4.5% of the thirty-day readmission rate, COVID-19 survivors were readmitted early after hospital discharge, mainly due to morbidities of COVID-19. One in five readmitted COVID-19 survivors died during their readmission.


Findings: 2,286 papers were screened resulting in 26 being included in the review. Most studies were from Europe, half from the UK, and one from Brazil; the median sample size was 242.5, median age 73.1 and 43.5% were female. 22/26 used the Clinical Frailty Scale; reported mortality ranged from 14 to 65%. Most, but not all studies showed an association between increasing frailty and a greater risk of dying. Two studies indicated a sub-additive relationship between frailty, COVID-19 and death, and two studies showed no association. Whilst the majority of studies have shown a positive association between COVID-19 related death and increasing frailty, some studies suggested a more nuanced understanding of frailty and outcomes in COVID-19 is needed. Clinicians should exert caution in placing too much emphasis on the influence of frailty alone when discussing likely prognosis in older people with COVID-19 illness.

**Survivorship & Rehabilitation**


Findings: At admission to sub-acute care in 2020, 236 COVID-19 patients were administered BRASS and classified into 3 levels of frailty risk. The Short Physical Performance Battery (SPPB) was also administered to measure physical function and disability. Differences between BRASS levels and associations between BRASS index and clinical parameters were analyzed. The
The median BRASS index was 14.0 denoting intermediate frailty. Significant differences emerged between the BRASS frailty classes regarding sex, comorbidities, history of cognitive deficits, previous mechanical ventilation support, and SPPB score. Patients with no comorbidities (14%) exhibited low frailty. Age ≥65 years, presence of comorbidities, cognitive deficit and SPPB % predicted <50% were significant predictors of high frailty. Most COVID-19 survivors exhibit substantial frailty and require continuing care after discharge from acute care. The BRASS index is a valuable tool for nurses to identify those patients most at risk of frailty, who require a program of rehabilitation and community reintegration.


Findings: At four weeks post-discharge, 39% of patients reported ongoing symptoms (325/837), and were assessed. Interstitial lung disease, predominantly organising pneumonia, with significant functional deficit was observed in 35/837 survivors (4.8%). Thirty of these patients received steroid treatment, resulting in a mean relative increase in transfer factor following treatment of 31.6%, and FVC of 9.6%, with significant symptomatic and radiological improvement. Following SARS-CoV-2 pneumonitis, a cohort of patients are left with both radiological inflammatory lung disease and persistent physiological and functional deficit. Early treatment with corticosteroids was well tolerated and associated with rapid and significant improvement. This preliminary data should inform further study into the natural history and potential treatment for patients with persistent inflammatory ILD following SARS-CoV2 infection.


Findings: Two hundred seventy seven patients recovered from mild (34.3%) or severe (65.7%) forms of SARS-CoV-2 infection were evaluated 77 days after disease onset. PCS was detected in 141 patients. Symptoms were mostly mild. Alterations in spirometry were noted in 25/269 (9.3%), while in radiographs in 51/277 (18.9%). No baseline clinical features behaved as independent predictors of PCS development. A Post-acute COVID-19 syndrome was detected in a half of COVID19 survivors. Radiological and spirometric changes were mild and observed in less than 25% of patients. No baseline clinical features behaved as independent predictors of Post-acute COVID-19 syndrome development.

Findings: A total of 23 subjects discharged after severe to critical COVID-19 infection underwent an individualized, multi-professional rehabilitation. At the start of post-acute rehabilitation, impairment of pulmonary function (87%), symptoms related to postintensive care syndrome, and neuropsychological dysfunction (85%) were frequently found, whereas cardiac function appeared to be largely unaffected. Of interest, multidisciplinary rehabilitation resulted in a significant improvement in lung function, as reflected by an increase of forced vital capacity (p=0.007) and forced expiratory volume in one second (p=0.014), total lung capacity (p=0.003), and diffusion capacity for carbon monoxide (p=0.002). Accordingly, physical performance status significantly improved as reflected by a mean increase of six-minute walking distance by 176 (SD ± 137) meters. Contrarily, a considerable proportion of patients still had limited diffusion capacity (83%) or neurological symptoms including peripheral neuropathy at the end of rehabilitation. Individuals discharged after a severe course of COVID-19 frequently present with persisting physical and cognitive dysfunctions after hospital discharge. Those patients significantly benefit from multi-disciplinary inpatient rehabilitation.


Findings: To our knowledge, our data represent the largest dataset to date on persistent skin signs and symptoms of COVID-19 and the duration for several distinct skin manifestations. Urticarial and morbilliform eruptions were relatively ephemeral, whereas papulosquamous eruptions, and particularly pernio, were longer-lasting. Our analysis revealed a previously unreported subset of patients who experience long-hauler symptoms in dermatology dominant COVID-19, raising questions about persistent inflammation even in patients who initially experienced relatively mild COVID-19.

**Therapeutics**


Findings: 639 non-severe patients with COVID-19 were enrolled. 45 patients received IVIg therapy and 594 received non-IVIg therapy. After PSM (1:2 ration), the baseline characteristics were well balanced between IVIg (n = 45) and control group (n = 90). No statistically significant differences were found between IVIg group and control group in the duration of fever (median, 3 vs 3 days, p = 0.667), virus clearance time (median, 11 vs 10 days, p = 0.288), length of hospital stay (median, 14 vs 13 days, p = 0.469), and the use of antibiotics (40% vs 38.9%, p = 0.901). Meanwhile, compared to IVIg group, no more patients progressed to severe cases (3.3% vs 6.6%, p = 0.376) and died (0 vs 2.2%, p = 0.156) in control group. In non-severe patients with COVID-19, no benefit was observed with IVIg therapy beyond standard therapy.
   
   Findings: In a retrospective study based on a U.S. national registry, we determined the anti–SARS-CoV-2 IgG antibody levels in convalescent plasma used to treat hospitalized adults with Covid-19. The primary outcome was death within 30 days after plasma transfusion. Of the 3082 patients included in this analysis, death within 30 days after plasma transfusion occurred in 115 of 515 patients (22.3%) in the high-titer group, 549 of 2006 patients (27.4%) in the medium-titer group, and 166 of 561 patients (29.6%) in the low-titer group. The association of anti–SARS-CoV-2 antibody levels with the risk of death from Covid-19 was moderated by mechanical ventilation status. A lower risk of death within 30 days in the high-titer group than in the low-titer group was observed among patients who had not received mechanical ventilation before transfusion, and no effect on the risk of death was observed among patients who had received mechanical ventilation. Among patients hospitalized with Covid-19 who were not receiving mechanical ventilation, transfusion of plasma with higher anti–SARS-CoV-2 IgG antibody levels was associated with a lower risk of death than transfusion of plasma with lower antibody levels.

**Transmission / Infection Control**

   
   Findings: Six patients were included in this small-scale study; three patients following the current standard of care for suctioning and oral hygiene and three receiving the new VAPCare and Lumen device protocol. With the new device protocol, the number of infected secretion interactions by a nurse was 50% lower, and nursing time spent on oral hygiene and secretion management 70% less than seen with the current standard of care. The number of disposable gloves used with VAPCare and Lumen was reduced by over 50%. All 10 nurses and six doctors gave positive feedback on device usage. The department recommended updating protocols to prioritize the use of the new secretion management system for patients with COVID19 and other highly contagious conditions. The findings are an early indication that using VAPCare for patients could help protect infected patients, other ICU patients, and health care workers.

   
   Findings: A prospective, international, quality improvement project was launched to collect information on HCWs involved in tracheal intubation of patients with suspected or confirmed COVID-19. From 3 March to 7 August 2020, 54 HCWs from 37 Canadian hospitals registered at least one tracheal intubation in a COVID-19 patient and subsequently recorded their own COVID-19 infection status. Overall, 136 tracheal intubations in COVID-19 patients were reported. Laboratory-confirmed COVID-19 was reported in one HCW five days after intubation (1/54 HCWs, 1.9%; one HCW/136 intubations, 0.7%).

Findings: Two tertiary care COVID-19 intensive care units treating 53 patients for 870 patient days were sampled after terminal cleaning and preparation for regular use to treat non-COVID-19 patients. A total of 176 swabs were sampled of defined locations covering both ICUs. No SARS-CoV-2 ribonucleic acid (RNA) was detected. Gram-negative bacterial contamination was mainly linked to sinks and siphons. Skin flora was isolated from most swabbed areas and Enterococcus faecium was detected on two keyboards. After basic cleaning with standard disinfection measures no remaining SARS-CoV-2 RNA was detected. Bacterial contamination was low and mainly localised in sinks and siphons.


Findings: This article gathers together and explores some of the most commonly held dogmas on airborne transmission in order to stimulate revision of the science in the light of current evidence. Six 'myths' are presented, explained, and ultimately refuted on the basis of recently published papers and expert opinion from previous work related to similar viruses. There is little doubt that SARS-CoV-2 is transmitted via a range of airborne particle sizes subject to all the usual ventilation parameters and human behaviour. Experts from specialties encompassing aerosol studies, ventilation, engineering, physics, virology and clinical medicine have joined together to present this review, in order to consolidate the evidence for airborne transmission mechanisms and offer justification for modern strategies for prevention and control of Covid-19 in healthcare and community.


Findings: We examined results of SARS-CoV-2 PCR and antibody tests in our south-west London laboratory, which serves four hospitals and a population of 1.3 million. We determined who had evidence of COVID-19 in the first wave of infections in the UK (February to July 2020, with a peak in early April), as shown either by a positive SARS-CoV-2 PCR or a positive antibody test, and determined their risk of having a positive SARS-CoV-2 PCR assay in the first five months of the second wave (August to December 2020), compared with patients who had a previous negative PCR or antibody test. We identified 66,001 patients who had a PCR and/or serological SARS-CoV-2 assay before the end of July, of whom 60% were female, with an average age of 50 years. It was not recorded which samples were from healthcare workers. 10,727 patients had evidence of COVID-19 in the first wave. Of these, eight had a positive PCR assay between 1st August and 30th December 2020, more than 90 days after their previous positive assay.
All eight reinfections were in female patients, and one (aged 71) was admitted to hospital. These results confirm other recent studies showing that patients who had COVID-19 in the first wave of infections have a significantly lower risk of a later positive PCR test. However, the emergence of a small number of reinfections in December, eight months after the first wave peak, is a cause for concern, suggesting that immunity may begin to wane in some patients around this time. Nonetheless, even with the limited number of reinfections, prior infection still confers a protective effect of 94% over the time of the study.


Findings: We investigated the effects of school reopening and easing of social distancing restrictions on the dynamics of SARS-CoV-2 infections in Israel, between March-July 2020. The incidence of SARS-CoV-2 infections gradually increased following school reopening in all age groups, with a significantly higher increase in adults compared to children. Higher relative ratios of sample positivity rates 21-27 days following school reopening relative to positivity rates prior to openings were found for the age groups 40-59 and 20-39 years, but not for children aged 0-9 and 10-19 years. No increase was observed in COVID-19 associated hospitalizations and deaths following school reopening. In contrast, permission of large-scale gatherings was accompanied by increases in incidence and positivity rates of samples for all age groups, and increased hospitalizations and mortality. This analysis does not support a major role of school reopening in the resurgence of the COVID-19 curve in Israel. Easing restrictions on large scale gatherings was the major influence on this resurgence.

Vaccine


Findings: In this multicenter, placebo-controlled, phase 1–2a trial, we randomly assigned healthy adults between the ages of 18 and 55 years (cohort 1) and those 65 years of age or older (cohort 3) to receive the Ad26.COV2.S vaccine at a dose of 5×1010 viral particles (low dose) or 1×1011 viral particles (high dose) per milliliter or placebo in a single-dose or two-dose schedule. Longer-term data comparing a single-dose regimen with a two-dose regimen are being collected in cohort 2; those results are not reported here. The primary end points were the safety and reactogenicity of each dose schedule. After the administration of the first vaccine dose in 805 participants in cohorts 1 and 3 and after the second dose in cohort 1, the most frequent solicited adverse events were fatigue, headache, myalgia, and injection-site pain. The most frequent systemic adverse event was fever. Systemic adverse events were less common in cohort 3 than in cohort 1 and in those who received the low vaccine dose than in those who received the high dose. Reactogenicity was lower after the second dose. Neutralizing-antibody titers against wild-type virus were detected in 90% or more of all participants on day 29 after the first vaccine dose and reached 100% by day 57 with a further
increase in titers, regardless of vaccine dose or age group. Titers remained stable until at least day 71. A second dose provided an increase in the titer by a factor of 2.6 to 2.9. Spike-binding antibody responses were similar to neutralizing-antibody responses. On day 14, CD4+ T-cell responses were detected in 76 to 83% of the participants in cohort 1 and in 60 to 67% of those in cohort 3, with a clear skewing toward type 1 helper T cells. CD8+ T-cell responses were robust overall but lower in cohort 3. The safety and immunogenicity profiles of Ad26.COV2.S support further development of this vaccine candidate.

**Women & Children**


Findings: The use of point-of-care antigen-based RDT for universal SARS-CoV-2 screening among asymptomatic parturients, was shown in the current study to have moderate sensitivity and high specificity. The potential benefits of a universal testing approach using RDT among women admitted for delivery may allow timely determination of COVID-19 status which will guide the utilization of proper protection measures and inform neonatal care.


Findings: In a large national cohort of US women hospitalized for childbirth, we found that absolute rates of death and adverse events in those diagnosed with COVID-19 were low, as might be expected in a young population in whom the disease may have been detected incidentally. Although the absolute risk differences were small, in-hospital death, VTE, and preeclampsia were considerably higher among women who gave birth with COVID-19 than in those without COVID-19. The present findings confirm previously reported mortality rates and indicate a higher risk of VTE in women diagnosed with COVID-19 in the setting of childbirth. The higher rates of preterm birth, preeclampsia, thrombotic events, and death in women giving birth with COVID-19 highlight the need for strategies to minimize risk. As studies investigating therapies for COVID-19 have largely excluded pregnant women, the data also underscore the importance of including this population in clinical trials of treatments and vaccines.


Findings: Reported weekly incidence of COVID-19 and percentage of positive test results among children, adolescents, and young adults increased during the review period, with spikes in early summer, followed by a decline and then steeply increased in October through December. In general, trends in incidence and percentage of positive test results among preschool-aged children (0–4 years) and school-aged children and adolescents (5–17 years) paralleled those
among adults throughout the summer and fall, including during the months that some schools were reopening or open for in-person education. In addition, reported incidence among children, adolescents, and young adults increased with age; among children aged 0–10 years, incidence and percentage of positive test results were consistently lower than they were among older age groups. Case data do not indicate that increases in incidence or percentage of positive test results among adults were preceded by increases among preschool- and school-aged children and adolescents. In contrast, incidence among young adults (aged 18–24 years) was higher than that in other age groups throughout the summer and fall, with peaks in mid-July and early September that preceded increases among other age groups, suggesting that young adults might contribute more to community transmission than do younger children.

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