

COVID-19

Sep 10 - 16, 2020



RESEARCH PUBLICATIONS

Publication Date: Sep 16, 2020

Impact of interleukin-6 blockade with tocilizumab on SARS-CoV-2 viral kinetics and antibody responses in patients with COVID-19: A prospective cohort study

Abstract

Background: The virological and immunological effects of the immunomodulatory drugs used for COVID-19 remain unknown. We evaluated the impact of interleukin (IL)-6 blockade with tocilizumab on SARS-CoV-2 viral kinetics and the antibody response in patients with COVID-19.

Methods: Prospective cohort study in patients admitted with COVID-19. Serial nasopharyngeal and plasma samples were measured for SARS-CoV-2 RNA and S-IgG/N-IgG titers, respectively.

Findings: 138 patients with confirmed infection were included; 76 (55%) underwent IL-6 blockade. Median initial SOFA ($p = 0.016$) and SARS-CoV-2 viral load ($p < 0.001$, Mann-Whitney-Wilcoxon test) were significantly higher among anti-IL-6 users. Patients under IL-6 blockade showed delayed viral clearance in the Kaplan-Meier curves (HR 0.35 [95%CI] [0.15–0.81], log-rank $p = 0.014$), but an adjusted propensity score matching model did not demonstrate a significant relationship of IL-6 blockade with viral clearance (HR 1.63 [0.35–7.7]). Cox regression showed an inverse association between SARS-CoV-2 RNA clearance and the initial viral load (HR 0.35 [0.11–0.89]). Patients under the IL-6 blocker showed shorter median time to seropositivity, higher peak antibody titers, and higher cumulative proportion of seropositivity in the Kaplan Meier curves (HR 3.1 [1.9–5] for S-IgG; and HR 3.0 [1.9–4.9] for N-IgG; log-rank $p < 0.001$ for both).

However, no significant differences between groups were found in either S-IgG (HR 1.56 [0.41–6.0]) nor N-IgG (HR 0.96 [0.26–3.5]) responses in an adjusted propensity score analysis.

Interpretation: Results suggest that in patients infected with SARS-CoV-2, IL-6 blockade does not impair the viral specific antibody responses. Although a delayed viral clearance was observed, it was driven by a higher initial viral load. The study supports the safety of this therapy in patients with COVID-19.

Reference

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(20\)30375-3/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(20)30375-3/fulltext)

Publication Date: Sep 15, 2020

Convalescent plasma treatment of severe COVID-19: a propensity score–matched control study

Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a new human disease with few effective treatment. Convalescent plasma, donated by persons who have recovered from COVID-19, is the acellular component of blood that contains antibodies, including those that specifically recognize SARS-CoV-2. These antibodies, when transfused into patients infected with SARS-CoV-2, are thought to exert an antiviral effect, suppressing virus replication before patients have mounted their own humoral immune responses. Virus-specific antibodies from recovered persons are often the first available therapy for an emerging infectious disease, a stopgap treatment while new antivirals and vaccines are being developed. This retrospective, propensity score–matched case–control study assessed the effectiveness of convalescent plasma therapy in 39 patients with severe or life-threatening COVID-19 at The Mount Sinai Hospital in New York City. Oxygen requirements on day 14 after transfusion worsened in 17.9% of plasma recipients versus 28.2% of propensity score–matched controls who were hospitalized with COVID-19 (adjusted odds ratio (OR), 0.86; 95% confidence interval (CI), 0.75–0.98; chi-square test P value = 0.025). Survival also improved in plasma recipients (adjusted hazard ratio

(HR), 0.34; 95% CI, 0.13–0.89; chi-square test $P = 0.027$). Convalescent plasma is potentially effective against COVID-19, but adequately powered, randomized controlled trials are needed.

Reference

<https://www.nature.com/articles/s41591-020-1088-9>

SARS-CoV-2 viral load predicts mortality in patients with and without cancer who are hospitalized with COVID-19

Abstract

Patients with cancer may be at increased risk of severe coronavirus disease 2019 (COVID-19), but the role of viral load on this risk is unknown. We measured SARS-CoV-2 viral load using cycle threshold (CT) values from reverse transcription-polymerase chain reaction assays applied to nasopharyngeal swab specimens in 100 patients with cancer and 2914 without cancer who were admitted to three New York City hospitals. Overall, the in-hospital mortality rate was 38.8% among patients with a high viral load, 24.1% among patients with a medium viral load, and 15.3% among patients with a low viral load ($P < 0.001$). Similar findings were observed in patients with cancer (high, 45.2% mortality; medium, 28.0%; low, 12.1%; $P = 0.008$). Patients with hematologic malignancies had higher median viral loads (CT=25.0) than patients without cancer (CT=29.2; $P = 0.0039$). SARS-CoV-2 viral load results may offer vital prognostic information for patients with and without cancer who are hospitalized with COVID-19.

Reference

[Westblade, Lars F., Gagandeep Brar, Laura Pinheiro, Demetrios Paidoussis, Mangala Rajan, Peter Martin, Parag Goyal *et al.* "SARS-CoV-2 Viral Load Predicts Mortality in Patients with and Without Cancer Who are Hospitalized with Coronavirus Disease 2019."](#)

COVID-19 risk and outcomes in patients with substance use disorders: Analyses from electronic health records in the United States

Abstract

The global pandemic of COVID-19 is colliding with the epidemic of opioid use disorders (OUD) and other substance use disorders (SUD) in the United States (US). Currently, there is limited data on risks, disparity, and outcomes for COVID-19 in individuals suffering from SUD. This is a retrospective case-control study of electronic health records (EHRs) data of 73,099,850 unique patients, of whom 12,030 had a diagnosis of COVID-19. Patients with a recent diagnosis of SUD (within past year) were at significantly increased risk for COVID-19 (adjusted odds ratio or AOR = 8.699 [8.411–8.997], $P < 10^{-30}$), an effect that was strongest for individuals with OUD (AOR = 10.244 [9.107–11.524], $P < 10^{-30}$), followed by individuals with tobacco use disorder (TUD) (AOR = 8.222 [7.925–8.530], $P < 10^{-30}$). Compared to patients without SUD, patients with SUD had significantly higher prevalence of chronic kidney, liver, lung diseases, cardiovascular diseases, type 2 diabetes, obesity and cancer. Among patients with recent diagnosis of SUD, African Americans had significantly higher risk of COVID-19 than Caucasians (AOR = 2.173 [2.01–2.349], $P < 10^{-30}$), with strongest effect for OUD (AOR = 4.162 [3.13–5.533], $P < 10^{-25}$). COVID-19 patients with SUD had significantly worse outcomes (death: 9.6%, hospitalization: 41.0%) than general COVID-19 patients (death: 6.6%, hospitalization: 30.1%) and African Americans with COVID-19 and SUD had worse outcomes (death: 13.0%, hospitalization: 50.7%) than Caucasians (death: 8.6%, hospitalization: 35.2%). These findings identify individuals with SUD, especially individuals with OUD and African Americans, as having increased risk for COVID-19 and its adverse outcomes, highlighting the need to screen and treat individuals with SUD as part of the strategy to control the pandemic while ensuring no disparities in access to healthcare support.

Reference

<https://www.nature.com/articles/s41380-020-00880-7>

Associations of procalcitonin, C-reaction protein and neutrophil-to-lymphocyte ratio with mortality in hospitalized COVID-19 patients in China

Abstract

Coronavirus disease 2019 (COVID-19) is an important and urgent threat to global health. Inflammation factors are important for COVID-19 mortality, and we aim to explore whether the baseline levels of procalcitonin (PCT), C-reaction protein (CRP) and neutrophil-to-lymphocyte ratio (NLR) are associated with an increased risk of mortality in patients with COVID-19. A retrospective study was conducted and a total of 76 patients with confirmed COVID-19 were included between January 17, 2020 to March 2, 2020, of these cases, 17 patients were dead. After adjusting covariates, PCT (≥ 0.10 ng/mL) and CRP (≥ 52.14 mg/L) exhibited independent increasing risks of mortality were used hazard ratio (HR) of 52.68 (95% confidence interval [CI]: 1.77–1571.66) and 5.47 (95% CI: 1.04–28.72), respectively. However, NLR (≥ 3.59) was not found to be an independent risk factor for death in our study. Furthermore, the elevated PCT levels were still associated with increasing risk of mortality in the old age group (age ≥ 60 y), and in the critically severe and severe patients after adjustment for complications. Thus Baseline levels of PCT and CRP have been addressed as independent predictors of mortality in patients with COVID-19.

Reference

<https://www.nature.com/articles/s41598-020-72164-7>

Changes in network centrality of psychopathology symptoms between the COVID-19 outbreak and after peak

Abstract

The current study investigated the mechanism and changes in psychopathology symptoms throughout the COVID-19 outbreak and after peak. Two studies were conducted separately in China during outbreak and the after peak stages, with 2540 participants were recruited from February 6 to 16, 2020, and 2543 participants were recruited from April 25 to May 5, 2020. The network models were created to explore the relationship between psychopathology symptoms both within and across anxiety and

depression, with anxiety measured by the Generalized Anxiety Disorder-7 and depression measured by the Patient Health Questionnaire-9. Symptom network analysis was conducted to evaluate network and bridge centrality, and the network properties were compared between the outbreak and after peak. Noticeably, psychomotor symptoms such as impaired motor skills, restlessness, and inability to relax exhibited high centrality during the outbreak, which still relatively high but showed substantial remission during after peak stage (in terms of strength, betweenness, or bridge centrality). Meanwhile, symptoms of irritability (strength, betweenness, or bridge centrality) and loss of energy (bridge centrality) played an important role in the network after the peak of the pandemic. This study provides novel insights into the changes in central features during the different COVID-19 stages and highlights motor-related symptoms as bridge symptoms, which could activate the connection between anxiety and depression. The results revealed that restrictions on movement were associated with worsen in psychomotor symptoms, indicating that future psychological interventions should target motor-related symptoms as priority.

Reference

<https://www.nature.com/articles/s41380-020-00881-6>

Type I IFN deficiency: An immunological characteristic of severe COVID-19 patients

Abstract

Severe COVID-19 is clinically characterized by two-phase disease progression. A secondary respiratory worsening 9–12 days after the first onset of symptoms can occur early in the disease. Among the respiratory failure patients, young adults (aged 50 years and lower) with previously mild comorbidities have relatively high rates. The respiratory failure is concomitant with characteristic CT scan, lymphocytopenia, high prothrombin time, and D-dimer levels. This biphasic evolution suggests a dysregulated inflammatory host response driven by virus resulting in an imbalance between pro- and anti-inflammatory mediators. However, the immunological features and mechanisms involved in COVID-19 severity are unclear. In order to test whether the severity disease can be caused by SARS-CoV-2 viral infection and hyperinflammation, Hadjadj *et al.*

conducted a comprehensive immune analysis of grouped 50 COVID-19 patients with different disease severity. Studies identified an impaired type I IFN response, characterized by no IFN- β and low IFN- α production and activity, should be a hallmark of severe COVID-19. Clinically, type I IFN deficiency is associated with hyperinflammation driven by NF- κ B and lower viral clearance. The authors indicated that IFN response is possible to incorporate as an indication to assess early severe COVID-19. The application of IFN administration and targeted anti-inflammatory therapies may aid in the development of improved treatments to overcome SARS-CoV-2 infection.

Reference

<https://www.nature.com/articles/s41392-020-00306-4>

Tracing asymptomatic SARS-CoV-2 carriers among 3674 hospital staff: A cross-sectional survey

Abstract

Background: Asymptomatic carriers were positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) without developing symptoms, which might be a potential source of infection outbreak. Here, we aim to clarify the epidemiologic and influencing factors of asymptomatic carriers in the general population.

Methods: In our hospital, all hospital staff have received throat swab RT-PCR test, plasma COVID-19 IgM/IgG antibodies test and chest CT examination. We analyzed the correlation between infection rates and gender, age, job position, work place and COVID-19 knowledge training of the staff. After that, all asymptomatic staff were re-examined weekly for 3 weeks.

Findings: A total of 3764 hospital staff were included in this single-center cross-sectional study. Among them, 126 hospital staff had abnormal findings, and the proportion of asymptomatic infection accounted for 0.76% (28/3674). There were 26 staff with IgM+, 73 with IgG+, and 40 with ground glass shadow of chest CT. Of all staff with abnormal findings, the older they are, the more likely they are to be the staff with abnormal results, regardless of their gender. Of 3674 hospital staff, the positive rate of labor staff

is obviously higher than that of health care workers (HCWs) and administrative staff ($P < 0.05$). In the course of participating in the treatment of COVID-19, there was no statistically significant difference in positive rates between high-risk departments and low-risk departments ($P > 0.05$). The positive rate of HCWs who participated in the COVID-19 knowledge training was lower than those did not participate in early training ($P < 0.01$). Importantly, it was found that there was no statistical difference between the titers of IgM antibody of asymptomatic infections and confirmed patients with COVID-19 in recovery period ($P > 0.05$). During 3 weeks follow-up, all asymptomatic patients did not present the development of clinical symptoms or radiographic abnormalities after active intervention in isolation point.

Interpretation: To ensure the safety of resumption of work, institutions should conduct COVID-19 prevention training for staff and screening for asymptomatic patients, and take quarantine measures as soon as possible in areas with high density of population.

Reference

Zhou, Fuling, Jingfeng Li, Mengxin Lu, Xiaobin Zhu, Chao Hu, Xiaoyan Liu, Yunbao Pan *et al.* "Tracing Asymptomatic SARS-CoV-2 Carriers Among 3674 Hospital Staff." *EClinicalMedicine* (2020).

Molecular architecture of the SARS-CoV-2 virus

Abstract

SARS-CoV-2 is an enveloped virus responsible for the COVID-19 pandemic. Despite recent advances in the structural elucidation of SARS-CoV-2 proteins, detailed architecture of the intact virus remains to be unveiled. Here we report the molecular assembly of the authentic SARS-CoV-2 virus using cryo-electron tomography (cryo-ET) and subtomogram averaging (STA). Native structures of the S proteins in both pre- and postfusion conformations were determined to average resolutions of 8.7-11 Å. Compositions of the N-linked glycans from the native spikes were analyzed by mass-spectrometry, which revealed highly similar overall processing states of the native glycans to that of the recombinant glycoprotein glycans. The native conformation of the ribonucleoproteins (RNP) and its higher-order assemblies were revealed. Overall, these characterizations have revealed the architecture of the SARS-CoV-2 virus in

exceptional detail, and shed lights on how the virus packs its ~30 kb long single-segmented RNA in the ~80 nm diameter lumen.

Reference

Yao, Hangping, Yutong Song, Yong Chen, Nanping Wu, Jialu Xu, Chujie Sun, Jiaying Zhang *et. al.* "Molecular architecture of the SARS-CoV-2 virus." *Cell* (2020).

Publication Date: Sep 13, 2020

Obesity is a potential risk factor contributing to clinical manifestations of COVID-19

Abstract

Background: Since December 2019, novel coronavirus (SARS-CoV-2)-induced pneumonia (COVID-19) occurred in Wuhan, and rapidly spread throughout China. COVID-19 patients demonstrated significantly different outcomes in clinic. We aimed to figure out whether obesity is a risk factor influencing the progression and prognosis of COVID-19.

Methods: 95 Patients with COVID-19 were divided into obesity group and non-obesity group according to their body mass index (BMI). The demographic data, clinical characteristics, laboratory examination, and chest computed tomography (CT) were collected, analyzed and compared between two groups.

Results: Our data showed that COVID-19 patients with obesity had more underlying diseases and higher mortality rate compared to those without obesity. Furthermore, patients with obesity also demonstrated more severe pathological change in lung and higher blood lymphocytes, triglycerides, IL-6, CRP, cystatin C, alanine aminotransferase (ALT), erythrocyte sedimentation rate (ESR), which may greatly influence disease progression and poor prognosis of COVID-19.

Conclusions: It suggest that obesity contributes to clinical manifestations and may influence the progression and prognosis of COVID-19 and it is considered as a potential risk factor of the prognosis of COVID-19. Special medical care and appropriate intervention should be performed in obesity patients with COVID-19 during

hospitalization and later clinical follow-up, especially for those with additional other comorbidities.

Reference

<https://www.nature.com/articles/s41366-020-00677-2>

Publication Date: Sep 11, 2020

Intranasal Bifidobacterium longum protects against viral-induced lung inflammation and injury in a murine model of lethal influenza infection

Background: Prophylactic strategies are urgently needed for prevention of severe inflammatory responses to respiratory viral infections. Bacterial-host interactions may modify the immune response to viral infections.

Methods: It was examined the contribution of Intranasal administration of two different Bifidobacterium longum strains or its isolated cell wall in controlling viral induced inflammation using a murine model of influenza infection. It was monitored mortality and morbidity over a 10-day period and viral load, differential broncho alveolar lavage (BAL) fluid inflammatory cell counts, Lung tissue histology, BAL and serum cytokines, markers of vascular damage and cell death were quantified.

Findings: Intranasal administration of Bifidobacterium longum 35624® or its isolated cell wall prior to virus inoculation significantly reduced viral load within the lungs and significantly improved survival. Reduced viral load was associated with reduced lung injury as suggested by cell death and vascular leakage markers, a shift from neutrophil to macrophage recruitment, reduced inflammatory cytokine levels (including IL-6), reduced type 1 and 2 interferon levels, but increased levels of interferon- λ and surfactant protein D. These protective effects were maintained when the bifidobacterial cell wall preparation was administered 24 h after viral inoculation. The protective effects were also observed for the Bifidobacterium longum PB-VIR™ strain.

Interpretation: Exposure to these bifidobacterial strains protect against the inflammatory sequelae and damage associated with uncontrolled viral replication within the lung.

Reference

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(20\)30357-1/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(20)30357-1/fulltext)

Publication Date: Sep 10, 2020

Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: A large-scale retrospective temporal modelling study

Abstract

Background: There is growing evidence of vaccine delays or refusals due to a lack of trust in the importance, safety, or effectiveness of vaccines, alongside persisting access issues. Although immunisation coverage is reported administratively across the world, no similarly robust monitoring system exists for vaccine confidence. In this study, vaccine confidence was mapped across 149 countries between 2015 and 2019.

Methods: In this large-scale retrospective data-driven analysis, we examined global trends in vaccine confidence using data from 290 surveys done between September, 2015, and December, 2019, across 149 countries, and including 284 381 individuals. We used a Bayesian multinomial logit Gaussian process model to produce estimates of public perceptions towards the safety, importance, and effectiveness of vaccines. Associations between vaccine uptake and a large range of putative drivers of uptake, including vaccine confidence, socioeconomic status, and sources of trust, were determined using univariate Bayesian logistic regressions. Gibbs sampling was used for Bayesian model inference, with 95% Bayesian highest posterior density intervals used to capture uncertainty.

Findings: Between November, 2015, and December, 2019, we estimate that confidence in the importance, safety, and effectiveness of vaccines fell in Afghanistan, Indonesia, Pakistan, the Philippines, and South Korea. We found significant increases in respondents strongly disagreeing that vaccines are safe between 2015 and 2019 in six countries: Afghanistan, Azerbaijan, Indonesia, Nigeria, Pakistan, and Serbia. We find signs that confidence has improved between 2018 and 2019 in some EU member states, including Finland, France, Ireland, and Italy, with recent losses detected in Poland. Confidence in the importance of vaccines (rather than in their safety or effectiveness) had the strongest univariate association with vaccine uptake compared

with other determinants considered. When a link was found between individuals' religious beliefs and uptake, findings indicated that minority religious groups tended to have lower probabilities of uptake.

Interpretation: To our knowledge, this is the largest study of global vaccine confidence to date, allowing for cross-country comparisons and changes over time. Our findings highlight the importance of regular monitoring to detect emerging trends to prompt interventions to build and sustain vaccine confidence.

Reference

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31558-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31558-0/fulltext)

The emergence of SARS-CoV-2 in Europe and North America

Abstract

Accurate understanding of the global spread of emerging viruses is critically important for public health responses and for anticipating and preventing future outbreaks. Here, we elucidate when, where and how the earliest sustained SARS-CoV-2 transmission networks became established in Europe and North America. Our results suggest that rapid early interventions successfully prevented early introductions of the virus into Germany and the US from taking hold. Other, later introductions of the virus from China to both Italy and to Washington State founded the earliest sustained European and North America transmission networks. Our analyses demonstrate the effectiveness of public health measures in preventing onward transmission and show that intensive testing and contact tracing could have prevented SARS-CoV-2 from becoming established.

Reference

<https://science.sciencemag.org/content/early/2020/09/11/science.abc8169>

NEWS LETTER

Publication Date: Sep 15, 2020

COVID research updates: Immunity to common-cold coronaviruses is short-lived

Nature wades through the literature on the new coronavirus — and summarizes key papers as they appear.

A groundbreaking guide to making ‘cocktails’ to treat COVID-19 (15 September 2020):

A new method pinpoints every mutation that a crucial SARS-CoV-2 protein could use to evade an attacking antibody. The results could inform the development of antibody treatments for COVID-19. The immune system produces molecules called antibodies to fend off invaders. Antibodies that bind to an important region of the SARS-CoV-2 spike protein can inactivate the viral particles, making such antibodies attractive as therapies. But over time, viruses can accumulate mutations — and some can interfere with antibody binding and allow viral particles to ‘escape’ immune forces. James Crowe at the Vanderbilt University Medical Center in Nashville, Tennessee, Jesse Bloom at the Fred Hutchinson Cancer Center in Seattle, Washington, and their colleagues created the most detailed map so far of the spike-protein mutations that could prevent binding by ten human antibodies (A. J. Greaney *et al.* Preprint at bioRxiv <https://doi.org/d8zm>; 2020). The team then used that information to design three antibody cocktails, each consisting of two antibodies. In laboratory tests of the cocktails against SARS-CoV-2, the virus did not develop mutations that could escape antibody binding. The findings have not yet been peer reviewed.

Nearly half of coronavirus transmission is from people not yet feeling ill (11 Sep 2020):

Some three-quarters of incidents of SARS-CoV-2 transmission occur in the few days before or after the onset of symptoms in the person who passes on the virus. Luca Ferretti at the University of Oxford, UK, and colleagues studied 191 cases of SARS-CoV-2 transmission from an infected person to an uninfected person. The team analysed the timing of the transmitting person’s initial infection and onset of symptoms, and when that person spread the infection to someone else (L. Ferretti *et al.* Preprint at medRxiv <https://doi.org/d8ms>; 2020). They found that roughly 40% of transmission events occurred before the onset of symptoms, and around 35% took place on the day

that symptoms appeared or on the following day. The researchers say their findings underscore the importance of mass testing, contact tracing and physical distancing to prevent transmission from pre-symptomatic people, as well as self-isolation for at least two days at the first sign of symptoms such as cough, fever, fatigue and loss of smell — however mild.

Surprise! A host of tantalizing new SARS-CoV-2 proteins is unveiled (10 September 2020):

Researchers have discovered nearly two dozen previously unknown proteins encoded by SARS-CoV-2 — and their role during infection is mostly mysterious. Until now, SARS-CoV-2's RNA genome was known to hold the instructions for making 29 proteins, such as the spike protein that helps viral particles to infect cells, and a variety of viral proteins that become active inside cells. But scientists were uncertain whether the virus had more than those 29. To identify further proteins, Noam Stern-Ginossar at the Weizmann Institute of Science in Rehovot, Israel, and her colleagues sequenced SARS-CoV-2 RNA bound to protein-making machines called ribosomes inside infected cells (Y. Finkel et al. Nature <https://doi.org/d8pb>; 2020). This scan turned up 23 previously unknown proteins, including some that are entirely new and others that are shortened or extended versions of known proteins. Some of the newfound proteins might control production of known viral molecules, but the role of many is unknown.

Reference

<https://www.nature.com/articles/d41586-020-00502-w>

CORRESPONDANCE

Publication Date: Sep 15, 2020

Associations between phone mobility data and COVID-19 cases

Understanding factors that affect the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is crucial for mitigating the impacts of COVID-19. Hamada Badr and colleagues¹ found a strong correlation between phone mobility data and decreased COVID-19 case growth rates, making the explicit assumption that phone mobility data serves as a proxy for social distancing. Thus, if true, concomitant increases in mobility will be correlated with an increased number of cases. We did a similar analysis using three social distancing metrics created from phone mobility data provided by the Unacast Social Distancing Scorecard.² The first metric—the daily distance difference—is analogous to the mobility ratio metric calculated by Badr and colleagues. The mobility ratio metric quantifies changes in behaviour relative to a baseline period before widespread transmission of COVID-19. The other two Unacast metrics measure changes in visits to non-essential places and encounter density, which were noted as limitations in the study by Badr and colleagues.

Using the daily distance difference metric, we identified a strong correlation between decreased mobility and reduced COVID-19 case growth between March 27 and April 20, 2020 (appendix). The other two metrics showed similarly strong correlations (data not shown). However, when we extended the analysis to later time periods (April 21 to May 24, 2020, and May 25 to July 22, 2020) only a weak correlation between daily distance difference and COVID-19 case growth was identified (appendix). In the first time period, when each metric was decreasing, the correlation across all counties was around 0.6. However, as the metrics increased in later time periods, consistent with reductions in social distancing, the correlation decreased to 0.11 or less for all three metrics. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30725-8/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30725-8/fulltext)

Intention to vaccinate against COVID-19 in Australia

As the COVID-19 pandemic continues, we eagerly await the arrival of safe and effective COVID-19 vaccines. However, the success of any vaccination programme depends on high vaccine acceptance and uptake. Previously, Rachael Dodd and colleagues reported that 4.9% of adults in Australia would refuse a vaccine, which is low compared with estimates in the USA (20%) and France (27%). The Australian data were collected in April, 2020, 4 weeks after lockdown measures commenced, which was at a time when community transmission was perceived to be high.

As part of the Royal Children's Hospital National Child Health Poll, we did an intention-to-vaccinate analysis in a nationally representative sample of Australian parents (n=2018) during June 15–23, 2020, and collected data via an online survey. At this time, restrictions had been eased throughout Australia and there was minimal community transmission. Compared with the earlier Australian estimates, the weighted proportion of people in our study indicating that they were unsure or unwilling to accept a COVID-19 vaccine had increased by 10.0% (14.2% in April¹ to a weighted proportion of 24.2% in June [95% CI 7.9–12.1]; $p < 0.0001$). Among parents who were unsure (320 [16.7%]) or unwilling (138 [7.6%]) to accept a COVID-19 vaccine, 379 (82.8%) were concerned about vaccine efficacy and safety, and 123 (26.9%) believed that a COVID-19 vaccine was unnecessary. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30724-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30724-6/fulltext)

PERSPECTIVE

Publication Date: Sep 11, 2020

Shining light on the COVID-19 pandemic: A Vitamin D receptor checkpoint in defense of unregulated wound healing

SARS-CoV-2 pneumonitis can quickly strike to incapacitate the lung, leading to severe disease and sometimes death. In this perspective, it was suggested that vitamin D deficiency and the failure to activate the vitamin D receptor (VDR) can aggravate this respiratory syndrome by igniting a wounding response in stellate cells of the lung. The FDA-approved injectable vitamin D analog, paricalcitol, suppresses stellate cell-derived murine hepatic and pancreatic pro-inflammatory and pro-fibrotic changes. Therefore, a possible parallel program was suggested in the pulmonary stellate cells of COVID-19 patients and propose repurposing paricalcitol infusion therapy to restrain the COVID-19 cytokine storm. This proposed therapy could prove important to people of color who have higher COVID-19 mortality rates and lower vitamin D levels. For more details, read the link given below.

Reference

[https://www.cell.com/cell-metabolism/fulltext/S1550-4131\(20\)30485-X](https://www.cell.com/cell-metabolism/fulltext/S1550-4131(20)30485-X)

Coronavirus dons a new crown

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), belongs to the positive-strand RNA [(+)RNA] viruses, a large class of viruses that includes Zika, hepatitis C, and chikungunya viruses. (+)RNA viruses package their genomes in infectious virions as messenger-sense RNA and reproduce these genomes solely through RNA intermediates in replication complexes (RCs) formed by rearranging intracellular membranes. RNA replication is a major target of antiviral drugs, including remdesivir, which shows promise for treating COVID-19 patients. RCs of coronaviruses and some other (+)RNA viruses are ~250- to 300-nm-diameter double-membrane vesicles (DMVs) that contain viral double-stranded RNA (dsRNA) replication intermediates. On page 1395 of this issue, Wolff *et al.* identify a crown-like double-membrane–spanning molecular pore on

SARS-CoV-2 and other coronavirus DMVs that likely solves the longstanding problem of how progeny (+)RNA genomes are released from DMVs. Like other (+)RNA viruses, most (~70%) of the SARS-CoV-2 genome encodes functions for RNA replication, underscoring the importance of this process for understanding and controlling these viruses. RCs support genome replication by organizing viral RNA replication proteins, viral RNA templates, specific host factors required for RNA replication, and successive reproductive steps. The RC-bounding membranes sequester RNA replication templates and intermediates from translation, virion assembly, RNA decay, and host defenses such as RNA interference and interferon-stimulated antiviral responses. Although infection by coronaviruses induces several types of membrane rearrangements, multiple lines of evidence identified the dsRNA-containing DMVs as the viral RNA synthesis sites. However, because DMVs lacked known openings, it was unclear how new (+)RNA genomes copied from dsRNA templates in the DMV interior could transit to the cytoplasm to be translated, packaged into virions, and potentially form new RCs. For more details, read the link given below.

Reference

<https://science.sciencemag.org/content/369/6509/1306>

REPORT

Publication Date: Sep 10, 2020

Estimating the binding of Sars-CoV-2 peptides to HLA class I in human subpopulations using artificial neural networks

Epidemiological studies show that SARS-CoV-2 infection leads to severe symptoms only in a fraction of patients, but the determinants of individual susceptibility to the virus are still unknown. The major histocompatibility complex (MHC) class I exposes viral peptides in all nucleated cells and is involved in the susceptibility to many human diseases. Here, we use artificial neural networks to analyze the binding of SARS-CoV-2 peptides with polymorphic human MHC class I molecules. In this way, we identify two sets of haplotypes present in specific human populations: the first displays weak binding with SARS-CoV-2 peptides, while the second shows strong binding and T cell propensity. Our work offers a useful support to identify the individual susceptibility to COVID-19 and illustrates a mechanism underlying variations in the immune response to SARS-CoV-2. A record of this paper's transparent peer review process is included in the Supplemental Information.

Reference

[https://www.cell.com/cell-systems/fulltext/S2405-4712\(20\)30295-7](https://www.cell.com/cell-systems/fulltext/S2405-4712(20)30295-7)

Cryptic transmission of SARS-CoV-2 in Washington state

Following its emergence in Wuhan, China, in late November or early December 2019, the SARS-CoV-2 virus has rapidly spread globally. Genome sequencing of SARS-CoV-2 allows reconstruction of its transmission history, although this is contingent on sampling. We have analyzed 453 SARS-CoV-2 genomes collected between 20 February and 15 March 2020 from infected patients in Washington State, USA. We find that most SARS-CoV-2 infections sampled during this time derive from a single introduction in late January or early February 2020 which subsequently spread locally before active community surveillance was implemented. For more details, read the link given below.

Reference

<https://science.sciencemag.org/content/early/2020/09/09/science.abc0523>

EDITORIAL

Publication Date: Sep 11, 2020

Responses of pediatric palliative care to the COVID-19 pandemic in China

The widespread outbreak of the coronavirus disease 2019 (COVID-19) has been a significant global concern. As of July 23, 2020, 15,012,731 COVID-19 cases have been confirmed, resulting in 619,150 deaths globally. A systematic review reported that children have accounted for 1–5% of diagnosed cases. A basic principle of pediatric palliative care (PPC) is to improve the quality of life for seriously ill children and their families, whether they are suffering from severe COVID-19 or another disease. Providing effective palliative care is especially vital but difficult in the context of a pandemic. Palliative care has never been so important; however, palliative care is underemphasized in the World Health Organization's essential health services' guidance. This paper aims to describe the impacts of the COVID-19 pandemic on PPC in China and the response of PPC to the pandemic based on the experience of a tertiary children's hospital in Beijing, China. For more details, read the link given below.

Reference

<https://www.nature.com/articles/s41390-020-01137-3>

Curing COVID-19

As the COVID-19 pandemic moves into its 10th month, greater patient survival suggests that treatment of severe disease has improved. How much of this improvement is due to better supportive care and how much to pharmaceuticals is a matter of debate. Given the huge effort that the biomedical community has put into finding drugs to treat COVID-19, with thousands of trials completed and ongoing, it's worth taking stock of the evidence for what has worked and what has not.

The hunt for COVID-19 treatments has become extraordinarily politicised, and no more so than with the aminoquinoline drugs chloroquine and hydroxychloroquine. Early observational studies suggested a beneficial effect of treatment with these cheap drugs, leading to acclamation by US President Trump. However, randomised controlled trials

(RCTs) in hospitalised patients have shown no effect of hydroxychloroquine in reducing mortality. One RCT hinted at an effect when used as post-exposure prophylaxis, but this was not statistically significant. Unless new, high-quality evidence emerges, the aminoquinolines appear to have no future in the management of COVID-19. Remdesivir, an antiviral, was also the subject of White House fanfare. The US Government has attempted to corner the market for this costly drug but results of clinical trials are ambiguous. One review concluded that remdesivir may reduce time to clinical improvement and decrease mortality but had no effect on need for invasive ventilation or length of hospital stay. A subsequent RCT found no effect on mortality. Although approved to treat COVID-19 in the USA and Europe, conclusive evidence to support remdesivir is lacking. For other antivirals, there is no good evidence for efficacy of favipiravir, although it has been approved in Russia, and the lopinavir/ritonavir combination showed no clinical benefit in the UK RECOVERY RCT. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30706-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30706-4/fulltext)

COMMENT

Publication Date: Sep 16, 2020

Sensor-aided continuous care and self-management: Implications for the post-COVID era

As the COVID-19 pandemic sweeps across the world, there has been a rapid adoption of telemedicine in the care of patients. Although telehealth has been around for a few years, the previously slow uptick of this technology has markedly accelerated over the last few months. One of the biggest barriers in the USA, low reimbursement, was eliminated on April 30, 2020, when the Centers for Medicare & Medicaid Services expanded its reimbursement to cover nearly 250 categories of telehealth. Savings in time and cost by the avoidance of travel, adherence to physical distancing, and the elimination of exposure to infectious agents in a congested outpatient waiting room made for easy adoption by most patients.

It is widely believed that in the post-COVID era, a substantial proportion of outpatient visits will continue to be virtual. This change could lower overall health-care expenditure by way of reduced need for staff and space. The economic benefits of increased virtual visits are also indirectly exemplified by e-consults, a form of digital medicine that involve asynchronous electronic consultations between providers for straightforward clinical questions. E-consults expedite clinical decisions by reducing unnecessary outpatient specialty visits, ancillary testing and imaging, and restrict rising health-care costs. However, despite the positive downstream influence of increasing access, digital modalities involving the exchange of information with patients, unlike e-consults between providers, might intensify health-care disparities because not all patients have reliable access to technology or internet. For more details, read the link given below.

Reference

[https://www.thelancet.com/journals/landig/article/PIIS2589-7500\(20\)30220-X/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30220-X/fulltext)

Artificial intelligence, drug repurposing and peer review

Artificial intelligence, drug repurposing and peer review

The COVID-19 pandemic has transformed the way scientific and clinical results are shared and disseminated. According to a recent analysis, an average of 367 COVID-19 papers are being published every week, with a median time from submission to acceptance of just 6 days (compared with 84 days for non-COVID-19 content). These unprecedented peer review turnaround times — and in some cases relaxed editorial standards — are justifiable in a context where new information may accelerate knowledge and solutions to the emerging global medico-socio-economic disaster, but they also risk the release of preliminary or flawed publications that can mislead research and development efforts, compromise clinical practice and misinform policy makers. What can be done to compensate for inadequate peer review in the context of a pandemic? Here, we propose a strategy whereby rigorous community and peer review is coupled to the use of artificial intelligence to prioritize research and therapeutic alternatives described in the literature, enabling the community to focus resources on treatments that have undergone appropriate and thorough clinical testing. For more details, read the link given below.

Reference

<https://www.nature.com/articles/s41587-020-0686-x>