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Daily COVID-19 Literature Surveillance Summary



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Coming soon:



COVID-19 Daily Literature Surveillance

COVID19LST



Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic



The Swab

Jasmine Rah



The untold stories of the coronavirus (COVID-19) pandemic.

April 24th, 2020

Executive Summary

Climate

- A literature review of 249 COVID-19 articles published between Dec 1st-Feb 6 found an that there was a lack of randomized controlled trials, cohort studies, and studies on clinical practice.
 - While this seems relatively unsurprising, they bring up a concerning implication - most guidance/guidelines developed by the WHO, US, CDC, ECDC and several Chinese Institutions did not fulfil the principles of evidence-based practice.
- And as we as a community begin developing drugs for treating COVID-19, there is also an urgent need to make sure that the production processes of those drugs are scalable, providing a unique opportunity for interprofessional work.

Epidemiology

- We are continuing to see a wide variety of symptoms and clinical presentation related to COVID-19
 - And there is continued speculation about [phylogenetic heterogeneity](#) in COVID-19 strains that may be contributing to the clinical spectrum of manifestations.

Understanding the Pathology

- The major finding of one observational study, adding to existing literature, was that patients with [severe obesity \(BMI \$\geq\$ 35 kg/m²\) had a higher requirement for invasive mechanical ventilation](#) when compared to patients who were not obese (81.8% vs 41.9%).
- In a study of 96 patients, the virus [survival duration was found to be highest in stool samples](#) and correlated with severity of the COVID-19 infection.

Transmission & Prevention

- Using an avian coronavirus as a surrogate, researchers found that [steaming N95 masks](#) over boiling water for 5 minutes inactivated the virus without causing significant loss of filtration.
- A main COVID-19 treatment center in Singapore of just over 10K hcp, found that stringent risk based ppe us helped keep the number of COVID-19 cases a at zero.

Management

- Adding to the growing literature regarding coagulopathies [in COVID-19 patients](#), a case-control study found significantly higher plasma fibrinogen and D-dimer in COVID-19 patients Leading to the recommendation to administer anticoagulant prophylaxis to diminish risk thromboembolic events
- A systematic review on [rehabilitation needs](#) patients found that
 - Early rehabilitation should be granted to inpatients with Covid-19
 - People with restricted mobility due to quarantine or lockdown should receive exercise programs to reduce the risk of frailty, sarcopenia, cognitive decline and depression
 - And, telerehabilitation may represent the first option for people at home

Adjusting Practice during COVID-19

- In New York, [15 kidney transplant patients](#) with COVID-19 were managed by discontinuation of their antimetabolites, addition of hydroxychloroquine, and reduction of immunosuppression therapies and found that their outcomes did not significantly differ from that of the general population.
- Pediatric allergy specialists recommend [continuation of allergy, asthma and immunodeficiency management as normal](#) with a proactive transition to telemedicine.

R&D: Diagnosis & Treatments

- A study of 21 severe or critical COVID-19 patients in China found [antinuclear antibodies](#) to be present in 50% of cases.
- [Remote telementored ultrasonography \(RTMUS\)](#) is being evaluated as a helpful method in working up patients with suspected COVID-19 while they are self-isolating to monitor the need for a higher level of care
- The in vitro efficacy of [dipyridamole](#) was found to have a potency below serum concentration of ~3 μM and a two-center randomized clinical trial in patients with severe or critical COVID-19 was found to have improved outcomes in the dipyridamole treatment group.
- Recent guidelines have also been published regarding the [preparation and transfusion of COVID-19 convalescent plasma](#)
- Another report outlines the [current knowledge and efficacy of several different therapeutic treatment options](#) for COVID-19
 - [NSAIDs](#): not recommended as “first line option for managing COVID-19”
 - [Chloroquine/Hydroxychloroquine](#): “Due to the excellent safety profile and vast experience, their use remains a pillar of current treatment protocols.”

Mental Health & Resilience

- Increased evidence of [psychological stress](#) being highest among COVID-19 front-line medical staff.
- In the field of research, recent changes including messages of support and unity, relaxed deadlines for grant proposals, and flexible working requests are leading to a shift towards a [kinder research culture](#) that may be here to stay.

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Current Diagnostics

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Developments in diagnostics

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[Rapid detection of COVID-19 coronavirus using a reverse transcriptional loop-mediated isothermal amplification \(RT-LAMP\) diagnostic platform.](#)

[Lung ultrasonography in a woman with COVID-19: This examination could be remote.](#)

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[Coronavirus Disease 2019: Reassembly Attack of Coronavirus](#)

Acknowledgements

Levels of Evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or n-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)*	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or n-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non-randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

* Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.

** As always, a systematic review is generally better than an individual study.

Credit: OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=5653>

Climate

[Reducing medical error during a pandemic.](#)

Hay-David AGC, Herron JBT, Gilling P, Miller A, Brennan PA

Br J Oral Maxillofac Surg.

Apr 11, 2020; PMID: 32312585

Level of Evidence: 5 - Expert Opinion

Type of Article: Opinion

BLUF: Practical suggestions on how to reduce medical error, including: 1) learning from other countries through webinars, social media, and podcasts, 2) creating a culture of assertive followership in all employees and caregivers, 3) practicing self care through debrief sessions with the clinical team, and 4) leaders promoting psychological safety, so that the team can feel like “family,” by self-monitoring and asking for open feedback.

Abstract: On 30 January 2020, the WHO declared the coronavirus disease 2019 (COVID-19) a public health emergency of international concern. By 11 March 2020, it was designated a pandemic owing to its rapid worldwide spread. In this short article we provide some information that might be useful and help equip colleagues to reduce medical error during a pandemic. **We advocate a systems-based approach, rather than an individual's sole responsibility, and, look at ways to provide safer healthcare.**

[Can Global Pharmaceutical Supply Chains Scale Up Sustainably for the COVID-19 Crisis?](#)

Yu DEC, Razon LF, Tan RR.

Resour Conserv Recycl

2020 Apr 17; PMID: 32313382

Level of Evidence: 5 - Expert opinion

Type of Article: Review

Summary: Potential hurdles in the scale-up of supply chains for COVID-19 drugs include predicting and compensating for potential bottlenecks in drug synthesis or production capacity, lack of scientific knowledge regarding COVID-19, disrupted global supply chains due the loss of labor and materials, shortages due to export restrictions, and environmental impacts. The authors identified five urgent research and development challenges for pharmaceutical supply chains based on these concerns. These challenges include “**decision-making under epistemic and stochastic uncertainty,**” “**optimal supply chain planning taking into account agility, resilience and sustainability,**” “**game theoretic analysis of conflicts of interests among agents in global value chains,**” “**life-cycle sustainability assessment of pharmaceutical product systems,**” and “**development of drug allocation strategies under resource or supply constraints.**”

Epidemiology

Global

Severe acute respiratory illness surveillance for coronavirus disease 2019, India, 2020.

Gupta N, Praharaj I, Bhatnagar T, Thangaraj JWV, Giri S, Chauhan H, Kulkarni S, Murhekar M, Singh S, Gangakhedkar RR, Bhargava B; ICMR COVID Team. Gupta N, et al.

Indian J Med Res

2020 Apr 9; PMID: 32317406

Level of Evidence: 4 - Epidemiology

Type of Article: Research

BLUF: An Indian sentinel surveillance study of 5,911 patients with severe acute respiratory illness (SARI), 104 (1.8%) were positive for COVID-19. These findings suggest the need to increase COVID-19 containment measures in targeted districts with known SARI patients.

Abstract:

Aims and background: Sentinel surveillance among severe acute respiratory illness (SARI) patients can help identify the spread and extent of transmission of coronavirus disease 2019 (COVID-19). SARI surveillance was initiated in the early phase of the COVID-19 outbreak in India. We describe here the positivity for COVID-19 among SARI patients and their characteristics.

Methods: SARI patients admitted at 41 sentinel sites from February 15, 2020 onwards were tested for COVID-19 by real-time reverse transcription-polymerase chain reaction, targeting E and RdRp genes of SARS-CoV-2. Data were extracted from Virus Research and Diagnostic Laboratory Network for analysis.

Results: **A total of 104 (1.8%) of the 5,911 SARI patients tested were positive for COVID-19.** These cases were reported from 52 districts in 20 States/Union Territories. **The COVID-19 positivity was higher among males and patients aged above 50 years.** In all, 40 (39.2%) COVID-19 cases did not report any history of contact with a known case or international travel.

Conclusions: **COVID-19 containment activities need to be targeted in districts reporting COVID-19 cases among SARI patients.** Intensifying sentinel surveillance for COVID-19 among SARI patients may be an efficient tool to effectively use resources towards containment and mitigation efforts.

Predicting turning point, duration and attack rate of COVID-19 outbreaks in major Western countries.

Zhang X, Ma R, Wang L. Zhang X, et al.

Chaos Solitons Fractals.

2020 Apr 20; PMID: 32313405

Level of Evidence: Statistical modeling

Type of Article: Research

BLUF: An epidemiological study used a segmented Poisson model to **predict the turning point, duration, and prevalence of COVID-19 in the G-7 countries with the following observations:** USA was predicted to have the most confirmed cases; France was predicted to have the highest prevalence; Canada was predicted to have the lowest confirmed cases and prevalence. If government interventions are left unchanged, the COVID-19 pandemic is **predicted to end around early June.**

Abstract:

In this paper, we employed a **segmented Poisson model** to analyze the available daily new cases data of the COVID-19 outbreaks in the six Western countries of the **Group of Seven, namely, Canada, France, Germany, Italy, UK and USA**. We incorporated the governments' interventions (stay-at-home advises/orders, lockdowns, quarantines and social distancing) against COVID-19 into consideration. Our analysis allowed us to make a **statistical prediction** on the **turning point** (the time that the daily new cases peak), **the duration** (the period that the outbreak lasts) and the **attack rate** (the percentage of the total population that will be infected over the course of the outbreak) for these countries.

Epidemiological trends of COVID-19 epidemic in Italy during March 2020. From 1,000 to 100,000 cases.

La Maestra S, Abbondandolo A, De Flora S. La Maestra S, et al.

J Med Virol.

2020 Apr 21; 2020.PMID: 32314804

Level of Evidence: 4- historical, observational

Type of Article: Research

BLUF: The authors of this study evaluate a data-set of 1,364 COVID-19 cases in Italy between February 29-March 31. There was a 100.9-fold increase in the cumulative number of cases and a 428.6-fold increase in the number of deaths in Italy. The comparison of cases and deaths in the Italian regions showed striking variations, particularly in the North. The authors surmise that this is because of the difference in the time of onset in each region before the implementation of national containment measures.

Abstract: Based on the Italian Ministry of Health data, we reconstructed the daily course of virus-positive cases and deaths during March 2020 for the whole Italy, 19 regions and 2 provinces. From February 29 to March 31 there was a 100.9-fold increase in the cumulative number of cases and a 428.6-fold increase in the number of deaths in Italy. When plotted on a semilogarithmic scale, the curves tended to diverge from linearity with 23%, 16%, and 7% average daily increases during the 3 decades of March. Similarly, the number of deaths decreased from an average daily growth of 19% during the 2nd decade to 10% during the 3rd decade. The correlation coefficients relating the days to cases or deaths during each one of the 3 decades approached the unity. As inferred from the equations of the regression lines relative to the 3 decades, the doubling times of cases were 3.4, 5.1 and 9.6 days, respectively. The doubling times of deaths during the 2nd and 3rd decades were 4.9 and 7.0 days, respectively. There was a broad geographic variability, with a striking gradient from North, where 40.8% of cases and 57.9% of deaths occurred in Lombardy, to South. On the whole, during March there was a trend to epidemic growth decline, but the time for the end of the epidemic will depend on a variety of factors and, at present, it is unpredictable.

Symptoms and Clinical Presentation

Clinical and Autoimmune Characteristics of Severe and Critical Cases with COVID-19.

Zhou Y, Han T, Chen J, Hou C, Hua L, He S, Guo Y, Zhang S, Wang Y, Yuan J, Zhao C, Zhang J, Jia Q, Zuo X, Li J, Wang L, Cao Q, Jia E.

Clin Transl Sci.

2020 Apr 21; PMID: 32315487

Level of Evidence: 3 – Local, non-random sample

Type of Article: Research

BLUF: Based on a study of 21 lab confirmed cases of COVID-19 from an ICU in Huangshi Central Hospital in China reports that the predominant presentation of severe COVID-19 is characterized by cough, fever, ground-glass opacity on chest CT, lymphocytopenia, and elevated CRP and IL-6. Anti-52 kDa SSA/Ro antibody, anti-60 kDa SSA/Ro antibody and antinuclear antibody were prevalent in 20%, 25%, and 50% of cases, respectively.

Abstract:

We aimed to **report the clinical and autoimmune characteristics of severe and critical novel coronavirus pneumonia caused by SARS-CoV-2**. The clinical, autoimmune, and laboratory characteristics of 21 patients who had laboratory-confirmed severe and critical cases of COVID-19 from the intensive care unit (ICU) ward of the Huangshi Central Hospital, Hubei Province, China were investigated. **A total of 21 patients** (13 males and eight females) including eight (38.1%) severe cases and 13 (61.9%) critical cases were enrolled. Cough (90.5%) and fever (81.0%) were the dominant symptoms, and most of them (76.2%) had at least one coexisting disorder on admission. The most common characteristics on chest CT were ground-glass opacity (100%) and bilateral patchy shadowing (76.2%). **The most common findings on laboratory measurements were lymphocytopenia (85.7%), elevated levels of C-reactive protein (94.7%), and Interleukin-6 (89.5%).** The prevalence of **anti-52 kDa SSA/Ro antibody, anti-60 kDa SSA/Ro antibody and antinuclear antibody in the cases was 20%, 25% and 50% respectively**. In the present work, we retrospectively analyzed the clinical and laboratory data from 21 severe and critical cases with COVID-19. Autoimmune phenomena exist in COVID-19 subjects, and the **results provide the rationale for a strategy of prevention of dysfunction of immune and optimal immunosuppressive therapy in the future.**

Unexpected Findings of Coronavirus Disease (COVID-19) at the Lung Bases on Abdominopelvic CT.

Dane B, Brusca-Augello G, Kim D, Katz DS.

AJR Am J Roentgenol

2020 Apr 22; PMID: 32319792

Level of Evidence: 4 - Cohort Study

Type of Article: Research

BLUF: A cohort study of 23 patients receiving an abdominal CT, 17 patients were found to have lower lung finding suggestive of COVID-19 and subsequently tested positive despite lacking respiratory symptoms.

Abstract:

Objective: The purpose of this study is to report **unanticipated lung base findings** on abdominal CT in 23 patients concerning for coronavirus disease (COVID-19). In these patients, who were not previously suspected of having COVID-19, **abdominal pain was the most common indication for CT** (n = 19), and 11 patients had no extrapulmonary findings. **Seventeen patients underwent polymerase chain reaction testing, which returned positive results for all 17.**

Conclusion: Unsuspected coronavirus disease may be strongly suggested on the basis of lung findings on abdominopelvic CT.

[Tracing New Clinical Manifestations in Patients with COVID-19 in Chile and Its Potential Relationship with the SARS-CoV-2 Divergence.](#)

Rodriguez-Morales AJ, Rodriguez-Morales AG, Méndez CA, Hernández-Botero S. Rodriguez-Morales AJ, et al.

Curr Trop Med Rep.

2020 Apr 18; PMID: 32313804

Level of Evidence: 5 - expert opinion

Type of Article: Review

BLUF: In Chile, out of 922 positive cases of COVID-19, 597 (64.8%) presented with headache as a cardinal symptom, while only 8.5% and 49.0% presented fever and cough. The **authors question whether phylogenetic heterogeneity among different strains of SARS-CoV-2 could be associated with the wide clinical spectrum of manifestations**, and the authors recommend updating the case definition of COVID-19.

Abstract:

Purpose of Review: In this review, we discuss the current implications of the changing genomic epidemiology of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), etiological agent of the Coronavirus Disease 2019 (COVID-19) and its potential relationship with the change of clinical manifestations in patients with confirmed infection.

Recent Findings: Over the course of the current pandemic, **the virus has been found more diverse in new countries**. Simultaneously, also **new clinical manifestations are observed, particularly more prominent gastrointestinal and neurological findings**.

Summary: SARS-CoV-2/COVID-19 is changing not only its epidemiology, but also its genomic diversity and clinical manifestations, both aspects coupled, needs to be considered in the study of this ongoing pandemic.

Table 1

Main clinical findings reported in the first 922 notified cases of COVID-19 in Chile, up to March 23, 2020

Symptoms	<i>n</i>	%
Headache	597	64.8
Dyspnea	498	54.0
Cough	452	49.0
Thorax pain	407	44.1
Sore throat	394	42.7
Fever	78	8.5
Abdominal pain	41	4.4
Myalgia	32	3.5

[The emergence of a novel coronavirus \(SARS-CoV-2\) disease and their neuroinvasive propensity may affect in COVID-19 patients.](#)

Yashavantha Rao HC, Jayabaskaran C.

J Med Virol.

2020 Apr 22; PMID: 32320066

Level of Evidence: 5 - Expert opinion

Type of Article: Review

BLUF: Prior coronavirus outbreaks such as SARS-CoV and SARS-CoV-2 have been demonstrated to have neuroinvasive propensity and COVID-19 may also have similar potential. Recently, a study of 214 COVID-19 infected patients found that around 88 % of severe patients showed neurological symptoms like acute cerebrovascular disease.

Abstract: An outbreak of a novel coronavirus (SARS-CoV-2) infection has recently emerged and rapidly spreading in humans causing a significant threat to international health and the economy. Rapid assessment and warning are crucial for an outbreak analysis in response to serious public health. SARS-CoV-2 shares highly homological sequences with SARS-CoVs causing highly lethal pneumonia with respiratory distress and clinical symptoms similar to those reported for SARS-CoV and MERS-CoV infections. Notably, some COVID-19 patients also expressed neurologic signs like nausea, headache, and vomiting. Several studies have reported that coronaviruses are not only causing respiratory illness but **also invade the central nervous system through a synapse-connected route**. SARS-CoV infections are reported in both patients and experimental animals' brains. Interestingly, some COVID-19 patients have shown the **presence of SARS-CoV-2 virus in their cerebrospinal fluid**. Considering the similarities between SARS-CoV and SARS-CoV-2 in various aspects, it remains to clarify whether the potent invasion of SARS-CoV-2 may affect in COVID-19 patients. All these indicate that more detailed criteria are needed for the treatment and the prevention of SARS-CoV-2 infected patients. In the absence of potential interventions for COVID-19, there is an urgent need for an alternative strategy to control the spread of this disease.

Pediatrics

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review.

Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, Rovida F, Baldanti F, Marseglia GL. Castagnoli R, et al.

JAMA Pediatr.

2020 Apr 22; PMID: 32320004

Level of Evidence: 1 - Systematic Review

Article Type: Research

BLUF: “In this systematic review of 18 studies with 1065 participants, most pediatric patients with SARS-CoV-2 infection presented with fever, dry cough, and fatigue or were asymptomatic; 1 infant presented with pneumonia, complicated by shock and kidney failure, and was successfully treated with intensive care. Most pediatric patients were hospitalized... received mainly supportive care; no deaths were reported in the age range of 0 to 9 years.”

Abstract:

Importance: The current rapid worldwide spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection justifies the global effort to identify effective preventive strategies and optimal medical management. While data are available for adult patients with coronavirus disease 2019 (COVID-19), limited reports have analyzed pediatric patients infected with SARS-CoV-2.

Objective: **To evaluate currently reported pediatric cases of SARS-CoV-2 infection.**

Evidence review: An extensive search strategy was designed to retrieve all articles published from December 1, 2019, to March 3, 2020, by combining the terms coronavirus and coronavirus infection in several electronic databases (PubMed, Cochrane Library, and CINAHL), and following the

Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. Retrospective cross-sectional and case-control studies, case series and case reports, bulletins, and national reports about the pediatric SARS-CoV-2 infection were included. The risk of bias for eligible observational studies was assessed according to the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline.

Findings: A total of 815 articles were identified. **Eighteen studies with 1065 participants (444 patients were younger than 10 years, and 553 were aged 10 to 19 years) with confirmed SARS-CoV-2 infection were included in the final analysis.** All articles reflected research performed in China, except for 1 clinical case in Singapore. **Children at any age were mostly reported to have mild respiratory symptoms, namely fever, dry cough, and fatigue, or were asymptomatic. Bronchial thickening and ground-glass opacities were the main radiologic features, and these findings were also reported in asymptomatic patients. Among the included articles, there was only 1 case of severe COVID-19 infection, which occurred in a 13-month-old infant. No deaths were reported in children aged 0 to 9 years.** Available data about therapies were limited.

Conclusions and relevance: To our knowledge, this is the first systematic review that assesses and summarizes clinical features and management of children with SARS-CoV-2 infection. The rapid spread of COVID-19 across the globe and the lack of European and US data on pediatric patients require further epidemiologic and clinical studies to identify possible preventive and therapeutic strategies.

Understanding the Pathology

Biomechanics

Cardiovascular Complications in Patients with COVID-19: Consequences of Viral Toxicities and Host Immune Response.

Zhu H, Rhee JW, Cheng P, Waliany S, Chang A, Witteles RM, Maecker H, Davis MM, Nguyen PK, Wu SM.

Curr Cardiol Rep.

2020 Apr 21; PMID: 32318865

Level of Evidence: 5 - Mechanism based reasoning

Type of Article: Research

BLUF: “Significant depletion and dysregulation of T lymphocytes may contribute to immune dysregulation and hyperactivity. Cardiac damage in the setting of cytokine storm may be analogous to that seen in cardiotoxicity from CAR-T therapy.”

Abstract:

Purpose of Review: Coronavirus disease of 2019 (COVID-19) is a cause of significant morbidity and mortality worldwide. While cardiac injury has been demonstrated in critically ill COVID-19 patients, the mechanism of injury remains unclear. Here, we review our current knowledge of the biology of SARS-CoV-2 and the potential mechanisms of myocardial injury due to viral toxicities and host immune responses.

Recent Findings: A number of studies have reported an epidemiological association between history of cardiac disease and worsened outcome during COVID infection. Development of new onset myocardial injury during COVID-19 also increases mortality. While limited data exist, potential mechanisms of cardiac injury include direct viral entry through the angiotensin converting enzyme 2 (ACE2) receptor and toxicity in host cells, hypoxia-related myocyte injury, and immune-mediated cytokine release syndrome. Potential treatments for reducing viral infection and excessive immune responses are also discussed.

Summary: COVID patients with cardiac disease history or acquire new cardiac injury are at an increased risk for in-hospital morbidity and mortality. More studies are needed to address the mechanism of cardiotoxicity and the treatments that can minimize permanent damage to the cardiovascular system.

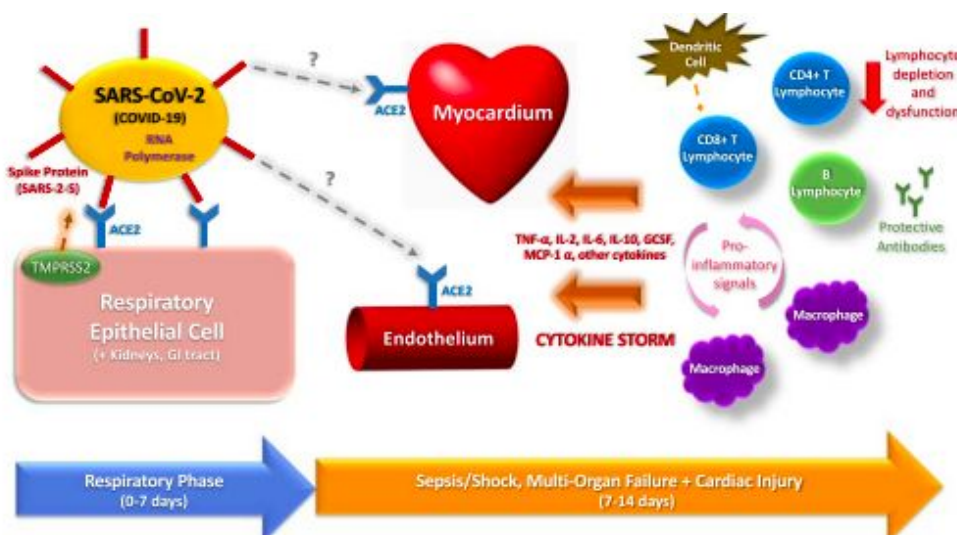


Image: Suggested hypothesis of SARS-CoV-2 pathogenesis and immune response.

[Age-related rhesus macaque models of COVID-19](#)

Yu P, Qi F, Xu Y, Li F, Liu P, Liu J, Bao L, Deng W, Gao H, Xiang Z, Xiao C, Lv Q, Gong S, Liu J, Song Z, Qu Y, Xue J, Wei Q, Liu M, Wang G, Wang S, Yu H, Liu X, Huang B, Wang W, Zhao L, Wang H, Ye F2, Zhou W, Zhen W, Han J, Wu G, Jin Q, Wang J, Tan W, Qin C.

Animal Model Exp Med

2020 Mar 30; PMID: 32318665

Level of Evidence: 5-Basic research

Type of Article: Short Communication

BLUF: Here, the authors compare SARS-CoV-2 infection in young versus old rhesus macaques. Although they only have five animals in total, they characterize the infection in these two animal groups quite extensively and find evidence of more severe disease in the older animals. They support the use of rhesus macaques as an animal model for COVID-19.

Abstract:

BACKGROUND: Since December 2019, an outbreak of the Corona Virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) in Wuhan, China, has become a public health emergency of international concern. The high fatality of aged cases caused by SARS-CoV-2 was a need to explore the possible age-related phenomena with non-human primate models. **METHODS:** Three 3-5 years old and two 15 years old rhesus macaques were intratracheally infected with SARS-CoV-2, and then analyzed by clinical signs, viral replication, chest X-ray, histopathological changes and immune response. **RESULTS:** Viral replication of nasopharyngeal swabs, anal swabs and lung in old monkeys was more active than that in young monkeys for 14 days after SARS-CoV-2 challenge. Monkeys developed typical interstitial pneumonia characterized by thickened alveolar septum accompanied with inflammation and edema, notably, old monkeys exhibited diffuse severe interstitial pneumonia. Viral antigens were detected mainly in alveolar epithelial cells and macrophages. **CONCLUSION: SARS-CoV-2 caused more severe interstitial pneumonia in old monkeys than that in young monkeys.** Rhesus macaque models infected with SARS-CoV-2 provided insight into the pathogenic mechanism and facilitated the development of vaccines and therapeutics against SARS-CoV-2 infection.

[Obesity is associated with severe forms of COVID-19.](#)

Caussy C, Wallet F, Laville M, Disse E.

Obesity (Silver Spring).

2020 Apr 21; PMID: 32314861

Level of Evidence: Level 4 - Cohort Study

Type of Article: Letter to the Editor

BLUF: Researchers report data on 291 COVID-19 patients admitted to Lyon University Hospital between February 27th and April 8th, 2020. The major finding of their study was that patients with severe obesity ($\text{BMI} \geq 35 \text{ kg/m}^2$) had a higher requirement for invasive mechanical ventilation when compared to lean patients (81.8% vs 41.9%).

Abstract: We have read with great interest the Brief Cutting Edge Report from Simonnet et al. which reports a high prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-Cov-2) requiring invasive mechanical ventilation. In the context of unprecedented health crisis due to the coronavirus disease 2019 (COVID-19) outbreak, these results are of a great importance and may have major implications in public health strategy especially in western countries affected by a high prevalence of obesity.

Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study

Zheng, S; Fan, J; Yu, F; Feng, B; Lou, B; Zou, Q; Xie, G; Lin, S; Wang, R; Yang, X; Chen, W; Wang, Q; Zhang, D; Liu, Y; Gong, R; Ma, Z; Lu, S; Xiao, Y; Gu, Y; Zhang, J; Yao, H; Xu, K; Lu, X; Wei, G; Zhou, J; Fang, Q; Cai, H; Qiu, Y; Sheng, J; Chen, Y; Liang, T
BMJ

2020 Apr 21; PMID: 32317267

Level of Evidence: 4 - Retrospective Cohort Analysis

Type of Article: Research

BLUF: After analyzing 3,497 stool, saliva, and serum samples for SARS-CoV-2 in 96 patients from Zhejiang province admitted for COVID-19, the virus survival duration was found to be highest in stool samples and correlated with severity of the COVID-19 infection.

Abstract:

Objective: To evaluate viral loads at different stages of disease progression in patients infected with the 2019 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during the first four months of the epidemic in Zhejiang province, China.

Design: Retrospective cohort study.

Setting: A designated hospital for patients with covid-19 in Zhejiang province, China.

Participants: 96 consecutively admitted patients with laboratory confirmed SARS-CoV-2 infection: 22 with mild disease and 74 with severe disease. Data were collected from 19 January 2020 to 20 March 2020.

Main outcome measures: Ribonucleic acid (RNA) viral load measured in respiratory, stool, serum, and urine samples. Cycle threshold values, a measure of nucleic acid concentration, were plotted onto the standard curve constructed on the basis of the standard product. Epidemiological, clinical, and laboratory characteristics and treatment and outcomes data were obtained through data collection forms from electronic medical records, and the relation between clinical data and disease severity was analysed.

Results: 3497 respiratory, stool, serum, and urine samples were collected from patients after admission and evaluated for SARS-CoV-2 RNA viral load. Infection was confirmed in all patients by testing sputum and saliva samples. RNA was detected in the stool of 55 (59%) patients and in the serum of 39 (41%) patients. The urine sample from one patient was positive for SARS-CoV-2. The median duration of virus in stool (22 days, interquartile range 17-31 days) was significantly longer than in respiratory (18 days, 13-29 days; $P=0.02$) and serum samples (16 days, 11-21 days; $P<0.001$). The median duration of virus in the respiratory samples of patients with severe disease (21 days, 14-30 days) was significantly longer than in patients with mild disease (14 days, 10-21 days; $P=0.04$). In the mild group, the viral loads peaked in respiratory samples in the second week from disease onset, whereas viral load continued to be high during the third week in the severe group. Virus duration was longer in patients older than 60 years and in male patients.

Conclusion: The duration of SARS-CoV-2 is significantly longer in stool samples than in respiratory and serum samples, highlighting the need to strengthen the management of stool samples in the prevention and control of the epidemic, and the virus persists longer with higher load and peaks later in the respiratory tissue of patients with severe disease.

IS COVID-19 a Proteiform Disease inducing Also Molecular Mimicry Phenomena?

Cappello, F.

Cell Stress Chaperones.

2020 Apr 20; PMID: 32314313

Level of Evidence: 6- Opinion

Type of Article: Editorial

BLUF: This author is of the opinion that the two common comorbidities (hypertension and diabetes) may specifically affect endothelial cells and predispose tissues to immune cross reactivity and cause autoimmunity.

Immune response

Two X-linked agammaglobulinemia patients develop pneumonia as COVID-19 manifestation but recover.

Soresina A, Moratto D, Chiarini M, Paolillo C, Baresi G, Foca E, Bezzi M, Baronio B, Giacomelli M, Badolato R.

Pediatr Allergy Immunol.

2020 Apr 22; PMID: 32319118

Level of Evidence: 5 – Case Report

Type of Article: Original

BLUF: Positive clinical outcomes in two COVID-19 patients with X linked agammaglobulinemia suggest **B cell response may be dispensable in the immune response against SARS-CoV-2 infection**, but these findings require validation from larger studies.

Abstract:

Background: The recent SARS-Cov2 pandemic, which has recently affected Italy since February 21, constitutes a threat for normal subjects, as the Coronavirus Disease 19 (COVID19) can manifest with a broad spectrum of clinical phenotypes ranging from asymptomatic cases to pneumonia or even death. There is evidence that older age and several comorbidities can affect the risk to develop severe pneumonia and possibly the need of mechanic (*sic*) ventilation in subjects infected with SARS-Cov2. Therefore, we **evaluated the outcome of SARS-Cov2 infection** in patients with inborn errors of immunity (IEI) such as **X linked agammaglobulinemia (XLA)**.

Methods: When the SARS-Cov2 epidemic has reached Italy, we have activated a surveillance protocol of patients with IEI, to perform SARS-Cov2 search by nasopharyngeal swab in patients presenting with symptoms which could be a manifestations of COVID-19, such as fever, cough, diarrhea or vomiting.

Results: We describe two patients with X-linked agammaglobulinemia (XLA) of 34 and 26 years of age with complete absence of B cells from peripheral blood who developed COVID-19, as diagnosed by SARS-Cov-2 detection by nasopharyngeal swab, while receiving immunoglobulin infusions. **Both patients developed interstitial pneumonia** characterized by fever, cough and anorexia and associated with elevation of CRP and ferritin, but have **never required oxygen ventilation or intensive care**.

Conclusion: Our report suggests that XLA patients might present high risk to develop pneumonia after SARS-Cov2 infection, but can recover from infection, suggesting that **B cell response might be important, but not strictly required to overcome the disease**. However, there is need of larger observational studies to extend these conclusions to other patients with similar genetic immune defects.

Transmission & Prevention

Developments in Transmission & Prevention

Decontamination of face masks with steam for mask reuse in fighting the pandemic COVID-19: experimental supports.

Ma QX, Shan H, Zhang CM, Zhang HL, Li GM, Yang RM, Chen JM
J Med Virol

2020 Apr 22; PMID: 32320083

Level of Evidence: 5 - Laboratory research

Type of Article: Research

BLUF: Using an avian coronavirus as a surrogate for SARS-CoV-2, researchers test N95 and medical masks' ability to filter aerosolized viral particles under laboratory conditions before and after a steam decontamination procedure and find no significant loss of filtration. They additionally present experimental evidence that avian coronavirus can be inactivated by steaming for 5 minutes over boiling water. The study concludes that steaming the masks in a sealed container over boiling water can be an effective and practical decontamination strategy that does not compromise later mask efficacy.

Abstract:

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 has claimed many lives worldwide. Wearing medical masks or N95 masks (namely N95 respirators) can slow the virus spread and reduce the infection risk. Reuse of these masks can minimize waste, protect the environment, and help to solve the current imminent shortage of masks. Disinfection of used masks is needed for reuse of them with safety, but improper decontamination can damage the blocking structure of masks. In this study, we demonstrated, using avian coronavirus of infectious bronchitis virus to mimic SARS-CoV-2, that medical masks and N95 masks remained their blocking efficacy after being steamed on boiling water even for 2 hours. We also demonstrated that three brands of medical masks blocked over 99% viruses in aerosols. The avian coronavirus was completely inactivated after being steamed for 5 minutes. Together, this study suggested that medical masks are adequate for use on most social occasions, and both medical masks and N95 masks can be reused for a few days with steam decontamination between use.

Potential of Live Pathogen Vaccines for Defeating the COVID-19 Pandemic: History and Mechanism.

Chen JW, Chen JM.

J Med Virol

2020 Apr 22; PMID: 32320059

Level of Evidence: 5 - Expert Opinion

Type of Article: Review

BLUF: This article advocates for research and development of a live pathogen vaccine for COVID-19. The authors argue that safe implementation of such a vaccine could be possible given COVID-19's relatively low pathogenicity as well as the potential for vaccine administration routes that bypass the respiratory tract, adjuvant use of antivirals with vaccine administration, and convalescent plasma treatment for people who become seriously ill after vaccine administration. Mass vaccination efforts could also be concentrated during hot seasons when concurrent infection risk is lower.

Summary: This article considers the potential for developing a live pathogen vaccine (LPV) for COVID-19. The authors review factors that could contribute to the safe use of a COVID-19 LPV. These include: 1) compared to viruses like HIV, rabies, and ebola, COVID-19 is not a highly pathogenic virus

in most cases, 2) oral administration of an LPV could allow the comparatively stronger immune function of the GI tract to defend against the virus and hopefully bypass infection of the respiratory tract, 3) antivirals that have demonstrated efficacy against COVID-19 could be administered early with an LPV to quickly minimize viral replication, 4) treatment with convalescent plasma could be used in patients who become ill after LPV use, and 5) targeting mass vaccination efforts with an LPV to hot seasons could help to minimize the risk of co-infection with pathogens common in colder seasons. The authors call for appropriate animal and clinical studies to test an LPV developed against COVID-19 and suggest that, with global collaboration, necessary studies could be completed in four months.

Prevention in the community

What do we know about the SARS-CoV-2 coronavirus in the environment?

Núñez-Delgado A

Sci Total Environ.

2020 Apr 16; PMID: 32315907

Level of Evidence: 6 - No data

Type of Article: Editorial

BLUF: SARS-CoV-2 may be spread through feces, indicating the need for wastewater and sewage sludge evaluation and treatment either using previously established programs like the “sewage epidemiology approach” or other methods. Consideration should also be given to viral mutations that may occur while the virus is out of living cells but still viable.

ABSTRACT: In view of the current situation regarding the Covid-19 disease, a discussion is proposed on the need for research focusing on the presence and evolution of the SARS-CoV-2 virus in water, soils and other environmental compartments, reached through wastewater and sewage sludge spreading. Also, the **evaluation of current treatments for wastewater and sewage sludge, as well as the eventual development of new specific techniques, based on sorption, nanotechnology, etc., would be of great interest** for controlling the environmental dissemination of these viruses in the current and eventual future outbreaks.

Who should wear a face mask? Experts weigh in on Canada's COVID-19 response.

Vogel L.

CMAJ

2020 Apr 20; PMID: 32312831

Level of Evidence: 5 – Expert Opinion

Type of Article: News Article

Summary: Two experts state that public masking may provide some degree of benefit, but in the context of limited supplies, delivery of masks should be prioritized to high-risk settings, such as hospitals and outpatient clinics. “It’s difficult to say what people in the community should wear... At some point, you’re going to get diminishing returns based on the risk of exposure being vanishingly small.”

Prevention in the hospital

Infection Risk in a Gastroenterological Ward During a Nosocomial COVID-19 Infection Event.

Tasuku Hara, Chie Yamamoto, Ryo Sawada, Tomoya Ohara, Kohei Oka, Naoto Iwai, et al.

J Med Virol.

2020 Apr 22; PMID: 32320062

Level of Evidence: 3 - Retrospective study

Type of Article: Research

BLUF: This retrospective study assessed SARS-Cov-2 infection among 87 patients gastrointestinal disorders in a gastroenterological ward in Kyoto, Japan between February 2020 to March 2020 and found that no patient with an underlying condition was infected with SARS-CoV-2. Therefore, appropriate implementation of contact and droplet transmission precautions appear to adequately minimize nosocomial spread of COVID-19.

Abstract: The coronavirus disease (COVID-19) first emerged in Wuhan, China, in December 2019 and rapidly infected a large number of individuals, and disease clusters have spread worldwide. A case of presumably nosocomial COVID-19 was detected in the gastroenterological ward; however, appropriate precautions against contact and droplet prevented a subsequent infection cluster.

Responding to the COVID-19 outbreak in Singapore: Staff Protection and Staff Temperature and Sickness Surveillance Systems.

Htun HL, Lim DW, Kyaw WM, Loh WJ, Lee LT, Ang B, Chow A

Clin Infect Dis

2020 Apr 21; PMID: 32315026

Level of Evidence: 4-Cohort study

Type of Article: Research

BLUF: A cohort study from Jan 23-Feb 23, 2020 was conducted at the main Covid-19 treatment center in Singapore with over 10,000 staff. The study assesses the efficacy of a staff protection system based on **risk based PPE use** (see table below), **staff surveillance for fever and other symptoms, and careful surveillance and follow up of ill staff**. They find that despite some illness and hospitalization among staff, **no staff members tested positive for COVID-19** during this period. The authors contend that the introduction of this system following SARS and **maintenance during the pre-pandemic period facilitated its adoption** and expansion during this crucial period.

Abstract

Background: Coronavirus disease 2019 (COVID-19) is an emerging infectious disease caused by novel coronavirus (SARS-CoV-2), and first reported in Wuhan, China, in December 2019. Since the severe acute respiratory syndrome (SARS) outbreak in 2003, Tan Tock Seng Hospital (TTSH) in Singapore has routinely fit-tested staff for high filtration N95 respirators, and established web-based staff surveillance systems. The routine systems were enhanced in response to Singapore's first imported COVID-19 case on January 23, 2020.

Methods: We conducted a cross-sectional study, from January 23, 2020 to February 23, 2020, among healthcare workers to evaluate the effectiveness of the staff protection and surveillance strategy in TTSH, a 1600-bed multidisciplinary acute-care hospital co-located with the 330-bed National Centre for Infectious Diseases (NCID). As of February 23, 2020, TTSH/NCID has managed 76% of confirmed COVID-19 cases in Singapore. The hospital adopted a multi-pronged approach to protect and monitor

staff with potential COVID-19 exposures: (1) Risk-based personal protective equipment, (2) Staff fever and sickness surveillance, and (3) Enhanced medical surveillance of unwell staff.

Results: A total of 10,583 staff were placed on hospital-wide fever and sickness surveillance, with 1,524 frontline staff working in COVID-19 areas under close surveillance. Among frontline staff, a median of eight staff illness episodes was seen per day, and almost 10% (n=29) resulted in hospitalization. None of the staff was found to be infected with COVID-19.

Conclusions: A robust staff protection and health surveillance system that is routinely implemented during non-outbreak periods and enhanced during the COVID-19 outbreak is effective in protecting frontline staff from the infection.

Table 1. Risk-based personal protective equipment (PPE) for healthcare staff

	Surgical mask	N95 respirator	Eye protection	Gown	Gloves
<i>High-risk areas (COVID-19 isolation rooms, TTSH ED Fever Zone, NCID SC, ID Clinic)</i>					
(i) Doctors and Nurses	..	✓	✓	✓	✓
(ii) Allied health professionals ^a	..	✓	✓	✓	✓
(iii) Ancillary staff ^b	..	✓	✓	✓	✓
(iv) Administrative staff	..	✓	✓	✓	✓
<i>Low-risk areas (Non-COVID-19 inpatient rooms, TTSH ED Non-Fever Zone, Non-ID Clinics, Other clinical areas)</i>					
(i) Doctors and Nurses	✓
(ii) Allied health professionals ^a	✓
(iii) Ancillary staff ^b	✓
(iv) Administrative staff	✓

Abbreviations: COVID-19, Coronavirus disease 2019; ED, Emergency Department; ID, infectious disease; NCID, National Centre for Infectious Diseases; SC, Screening Centre; TTSH, Tan Tock Seng Hospital. ^aAllied health professionals include pharmacists, occupational therapists, physiotherapists, phlebotomists, radiographers, and respiratory therapists. ^b Ancillary staff include health attendants, housekeepers, porters and security officers.

Put a lid on it: Are faecal bio-aerosols a route of transmission for SARS-CoV-2?

McDermott CV, Alicic RZ, Harden N, Cox EJ, Scanlan JM. McDermott CV, et al.

The Journal of Hospital Infection

2020 Apr 18, PMID: 32315667

Level of Evidence: 5 - Literature Cited

Type of Article: Expert Opinion

Summary: This article discussed the role of fecal shedding as a potential mode of transmission for COVID-19. They mention the outbreak of SARS-CoV-1, when it was learned post hoc that faecal shedding was a major contributor in Hong Kong. Thus, they encourage officials and hospitals to practice appropriate precautions or this mode of transmission as part of their directives for infection control.

Management

Acute care

Emergency Medicine

Cardiovascular complications in COVID-19.

Long B, Brady WJ, Koyfman A, Gottlieb M.

Am J Emerg Med

2020 Apr 18; PMID: 32317203

Level of Evidence: 5 - Expert Opinion

Type of Article: Research

BLUF: When treating patients with COVID-19, emergency physicians should be aware of the associated cardiovascular complications such as myocarditis, ACS, heart failure, dysrhythmias and VTE. They should also be aware of the interactions between the experimental antivirals and commonly used cardiovascular medications.

Abstract:

Background: The coronavirus disease of 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). While systemic inflammation and pulmonary complications can result in significant morbidity and mortality, cardiovascular complications may also occur.

Objective: This brief report evaluates cardiovascular complications in the setting of COVID-19 infection.

Discussion: The current COVID-19 pandemic has resulted in over one million infected worldwide and thousands of death [sic]. The virus binds and enters through angiotensin-converting enzyme 2 (ACE2). COVID-19 can result in systemic inflammation, multiorgan dysfunction, and critical illness. The cardiovascular system is also affected, with complications including myocardial injury, myocarditis, acute myocardial infarction, heart failure, dysrhythmias, and venous thromboembolic events. Current therapies for COVID-19 may interact with cardiovascular medications.

Conclusions: Emergency clinicians should be aware of these cardiovascular complications when evaluating and managing the patient with COVID-19.

Critical Care

Delivering extracorporeal membrane oxygenation for patients with COVID-19: what, who, when and how?

Zochios V, Brodie D, Charlesworth M, Parhar KK. Zochios V, et al.

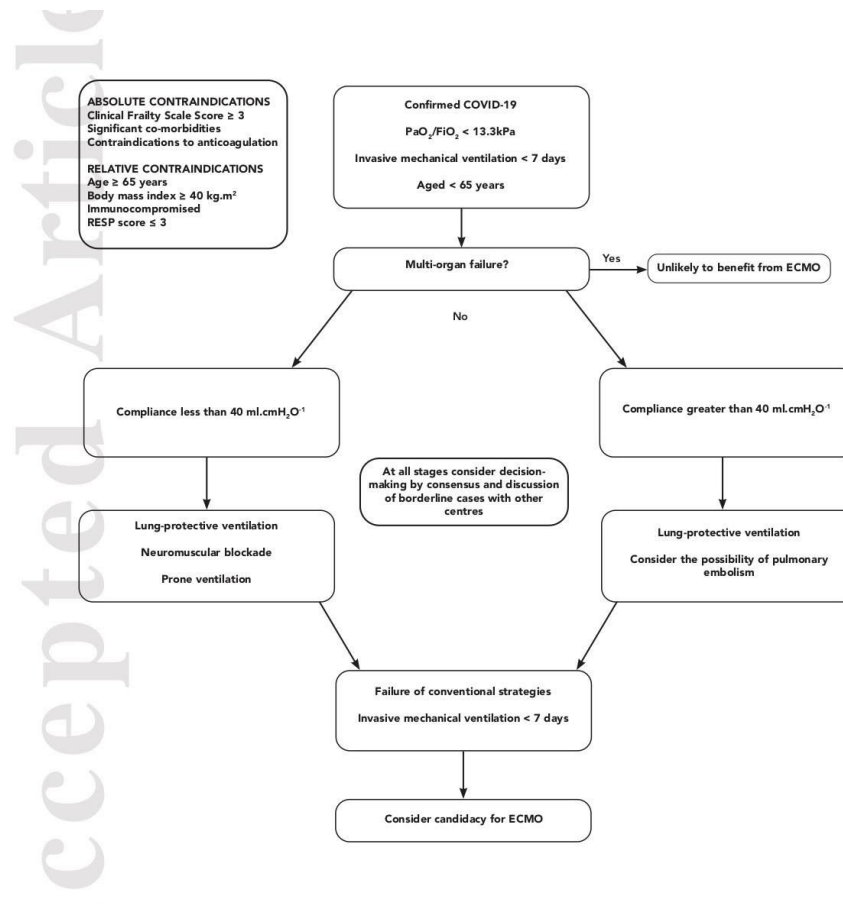
Anaesthesia. 2020 Apr 22; PMID: 32319081

Level of Evidence: 5 – Expert Opinion

Article Type: Letter to the Editor

BLUF: Experts discuss current best practices for ECMO used to treat covid patients.

Summary: Use of RESP, PRESET, and clinical frailty scores to determine whether a specific patient should be considered for ECMO are discussed. **ECMO should only be started after other options attempted. The patient's level of hypoxemia is associated with low or high respiratory failure and may affect the decision to initiate ECMO. Clinicians should always rule out PE in high-compliance hypoxaemia and respiratory failure.** They also report that “**patients who have severe respiratory failure, have been invasively ventilated for ≤ 7 days and meet general guidance criteria without extrapulmonary organ failure may be considered for ECMO**”. Finally, they present a decision making aid for patient's referred to ECMO centers is offered for consideration (below).



Internal Medicine

Clinical features and multidisciplinary treatment outcome of COVID-19 pneumonia: A report of three cases.

Liu, Chun; Wu, Changhui; Zheng, Xiangde; Zeng, Fanwei; Liu, Jinping; Wang, Pingxi; Zeng, Fanxin; Yuan, Lin; Zhu, Fangcheng; Gan, Xuemei; Huang, Yucheng
J Formos Med Assoc

2020 Apr 23; PMID: 32317205

Level of Evidence: 4 - Case Report

Type of Article: Research

BLUF: Successful treatment of three severe cases of COVID-19 in patients with multiple comorbidities through respiratory support, pharmacological intervention, traditional Chinese medicine therapy, psychological intervention, and aggressive control of comorbid conditions including chronic bronchitis and type-2 diabetes by pulmonologists and endocrinologists, respectively.

Abstract: The novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a pandemic threatening global public health. In the current paper, we describe our successful treatment of three COVID-19 pneumonia patients cases including severe cases and cases with mortality risk factors. One 32-year-old male COVID-19 patient was diagnosed with severe COVID-19 pneumonia and moderate ARDS. The second COVID-19 pneumonia patient had a history of diabetes and chronic bronchitis. The third case of COVID-19 pneumonia was an 82-year old female patient. All three cases had severe COVID pneumonia and therefore were aggressively managed with a multidisciplinary and personalized therapeutic approach

that included nutritional support, antiviral pharmacotherapy, active control of comorbidities, prevention of complication development and psychological intervention. **Our experience highlights the importance of the use of a multidisciplinary therapeutic approach that tailors to the specific condition of the patient in achieving a favorable clinical outcome.**

PediatricsMulticenter initial guidance on use of antivirals for children with COVID-19/SARS-CoV-2.

Chiotos K, Hayes M, Kimberlin DW, Jones SB, James SH, Pinninti SG, Yarbrough A, Abzug MJ, MacBrayne CE, Soma VL, Dulek DE, Vora SB, Waghmare A, Wolf J, Olivero R, Grapentine S, Wattier RL, Bio L, Cross SJ, Dillman NO, Downes KJ, Timberlake K, Young J, Orscheln RC, Tamma PD, Schwenk HT, Zachariah P, Aldrich M, Goldman DL, Groves HE, Lamb GS, Tribble AC, Hersh AL, Thorell EA, Denison MR, Ratner AJ, Newland JG, Nakamura MM.

J Pediatric Infect Dis Soc.

2020 Apr 22, PMID: 32318706

Level of Evidence: 5- Expert Opinion

Article Type: Literature Review

BLUF: In most cases of pediatric COVID-19 only supportive care is necessary. For critical cases, the decision needs to be made on an individual case basis if antivirals outweigh the risk of harm. If so, it is recommended to use Remdesivir or Hydroxychloroquine in those unable to receive Remdesivir.

Abstract:

Background: Although Coronavirus Disease 2019 (COVID-19) is mild in nearly all children, a small proportion of pediatric patients develops severe or critical illness. Guidance is therefore needed regarding use of agents with potential activity against severe acute respiratory syndrome coronavirus 2 in pediatrics.

Methods: A panel of pediatric infectious diseases physicians and pharmacists from 18 geographically diverse North American institutions was convened. Through a series of teleconferences and web-based surveys, a set of guidance statements was developed and refined based on review of best available evidence and expert opinion.

Results: Given the typically mild course of pediatric COVID-19, supportive care alone is suggested for the overwhelming majority of cases. The panel suggests a decision-making framework for antiviral therapy that weighs risks and benefits based on disease severity as indicated by respiratory support needs, with consideration on a case-by-case basis of potential pediatric risk factors for disease progression. If an antiviral is used, the panel suggests remdesivir as the preferred agent.

Hydroxychloroquine could be considered for patients who are not candidates for remdesivir or when remdesivir is not available. Antivirals should preferably be used as part of a clinical trial if available.

Conclusions: Antiviral therapy for COVID-19 is not necessary for the great majority of pediatric patients. For those rare children who develop severe or critical disease, this guidance offer an approach for decision-making regarding antivirals, informed by available data. As evidence continues to evolve rapidly, the need for updates to the guidance is anticipated.

PM&R

Systematic rapid "living" review on rehabilitation needs due to covid-19: update to march 31st 2020.

Ceravolo MG, De Sire A, Andrenelli E, Negrini F, Negrini S. Ceravolo MG, et al.
Eur J Phys Rehabil Med.

2020 Apr 22; PMID: 32316718

Level of Evidence: 4 - Systematic review of literature on expert recommendations

Type of Article: Research

BLUF: Here the authors conducted a systematic literature review of 2758 articles, with 9 included in the present review, with the aim of providing up-to-date recommendations for rehabilitation. Of the 9 articles meeting inclusion criteria, none were randomized control trials or based on direct observation of patients; the authors acknowledge this limitation and call for more research to establish legitimate guidelines for physical and rehabilitation medicine.

Summary of Guidelines:

- **In the hospital**, passive mobilization should be performed as early as possible, unnecessary maneuvers should be reduced, and checks should be made on ventilated patients in prolonged prone position.
- **Patients at home with restricted mobility or the elderly** should engage in a “rehabilitative program, including aerobic, resistance, balance, coordination and mobility training exercises, for 5-7 days/week, at moderate intensity.”
- **“tele-rehabilitation** approaches are welcome as they represent the first option for people capable of exercising at home under the guidance of rehabilitation professionals.”

Abstract:

Background: The outbreak of Covid-19 epidemics has challenged the provision of health care worldwide, highlighting the main flaws of some national health systems with respect to their capacity to cope with the needs of frail subjects. People experiencing disability due to Covid-19 express specific rehabilitation needs that deserve a systematic evidence-based approach.

Objectives: To provide the rehabilitation community with updates on the latest scientific literature on rehabilitation needs due to Covid-19. The first rapid “living” review will present the results of a systematic search performed up to March 31st, 2020.

Methods: A systematic search on PubMed, Pedro and Google Scholar was performed using the search terms: “Covid-19”, “Coronavirus”, “severe acute respiratory syndrome coronavirus 2”, “rehabilitation”, “physical therapy modalities”, “exercise”, “occupational therapy”, and “late complications”. Papers published up to March 31st, 2020, in English, were included.

Results: **Out of the 2758 articles retrieved, 9 were included in the present review.** Four of them are “calls for action”, 3 provide recommendations about rehabilitation interventions in the acute phase, 2 address the needs of people quarantined at home or with restricted mobility due to the lockdown, and 1 provides a Core Outcome Set to be used in clinical trials to test the efficacy of health strategies in managing Covid-19 patients.

Conclusions: All selected papers were based on previous literature and not on the current Covid-19 pandemic. **Main messages included: 1) early rehabilitation should be granted to inpatients with Covid-19; 2) people with restricted mobility due to quarantine or lockdown should receive exercise programs to reduce the risk of frailty, sarcopenia, cognitive decline and depression; 3) telerehabilitation may represent the first option for people at home.** Further updates are warranted in order to characterize the emerging disability in Covid-19 survivors and the adverse effects on the health of chronically disabled people.

Adjusting Practice during COVID-19

Internal Medicine

Cardiology

Society of Cardiovascular Computed Tomography guidance for use of cardiac computed tomography amidst the COVID-19 pandemic Endorsed by the American College of Cardiology.

Choi AD, Abbata S, Branch KR, Feuchtner GM, Ghoshhajra B, Nieman K, Pontone G, Villines TC, Williams MC, Blankstein R.

J Cardiovasc Comput Tomogr.

2020 Mar 21; PMID: 32317235

Level of Evidence: 5 - Expert opinion

Type of Article: Editorial

Summary: The authors outline guidelines for cardiac CT practitioners to decrease the risk of COVID-19 transmission, **which are presented in Table 1 below**. They also **recommend immediate scanning only in emergent scenarios**, such as acute chest pain with clinical suspicion of CAD, acute symptomatic prosthetic heart valve dysfunction, evaluation of left atrial appendage in acute atrial arrhythmia, patients requiring urgent structural intervention, and new cardiac masses suspected to be malignant.

Abstract: The world is currently suffering through a pandemic outbreak of severe respiratory syndrome coronavirus 2 (SARS-CoV-2) known as Coronavirus Disease 2019 (COVID-19). The United States (US) Centers for Disease Control and Prevention (CDC) currently advises medical facilities to "reschedule non-urgent outpatient visits as necessary". The European Centre for Disease Prevention and Control, the United Kingdom National Health Service and several other international agencies covering Asia, North America and most regions of the world have recommended similar "social distancing" measures. **The Society of Cardiovascular Computed Tomography (SCCT) offers guidance for cardiac CT (CCT) practitioners to help implement these international recommendations in order to decrease the risk of COVID-19 transmission in their facilities while deciding on the timing of outpatient and inpatient CCT exams.** This document also emphasizes SCCT's commitment to the health and well-being of CCT technologists, imagers, trainees, and research community, as well as the patients served by CCT.

Table 1

Guiding points to consider when deciding on the role and timing of CCT.

-
- The delivery of CCT services should be performed in a manner which will be safe to technologists and imagers, as well as patients.
 - Consider deferring CCT exams which can be safely postponed in order to minimize risk of exposure to patients and staff.
 - CCT may be preferred to transesophageal echocardiography (TEE) in order to rule-out left atrial appendage and intracardiac thrombus prior to cardioversion in order to reduce coughing and aerosolization related to TEE.
 - The ability of CCT to decisively exclude coronary disease or high risk anatomy may prevent the need for inpatient admissions and resource use.
 - Consider that elderly patients, those with co-morbidities, and those who may be immunosuppressed are at greater risk of morbidity/mortality from COVID-19, and the benefit and risk of cardiac CT should be evaluated on a case by case basis.
 - In patients under investigation (PUI) and with confirmed COVID-19, the benefit of CCT in most clinical scenarios will likely be lower than the risk of exposure and infection to healthcare personnel. These cases should be considered on a case-by-case basis.
-

Surgery

Transplants

Early Description of Coronavirus 2019 Disease in Kidney Transplant Recipients in New York.

S Ali Husain, Jae H Chang, David J Cohen, R John Crew, Geoffrey K Dube, Hilda E Fernandez, Heather K Morris, Justin G Aaron, Benjamin A Miko, Marcus R Pereira, Mark A Hardy, Kasi R McCune, Lloyd E Ratner, P Rodrigo Sandoval, Joshua Weiner, Demetra Tsapepas, Sumit Mohan
J Am Soc Nephrol

2020 April 21; PMID: 32317402

Level of Evidence: 4 - Case Series

Type of Article: Research

BLUF: The 15 kidney transplant recipients included in this case series with COVID-19 overall presented similarly to the general population. The treatment plan for each individual was catered to the Columbia University COVID-19 protocol that includes withdrawing antimetabolite, introducing hydroxychloroquine, and reducing immunosuppression.

Abstract:

Background: The novel SARS-CoV-2 virus has caused a global pandemic of coronavirus disease 2019 (COVID-19). Although immunosuppressed individuals are thought to be at an increased risk of severe disease, little is known about their clinical presentation, disease course, or outcomes.

Methods: We report 15 kidney transplant recipients from the Columbia University kidney transplant program who required hospitalization for confirmed COVID-19, and describe their management, clinical course, and outcomes.

Results: Patients presented most often with a **fever (87%) and/or cough (67%)**. Initial chest x-ray most commonly showed bilateral infiltrates, but 33% had no acute radiographic findings. **Patients were managed with immunosuppression reduction and the addition of hydroxychloroquine and azithromycin.** Although **27% of our patients needed mechanical ventilation, over half were discharged home by the end of follow-up.**

Conclusions: Kidney transplant recipients with COVID-19 have presentations that are similar to that of the general population. Our current treatment protocol appears to be associated with favorable outcomes, but longer follow-up of a larger cohort of patients is needed.

Pediatrics

Managing childhood allergies and immunodeficiencies during respiratory virus epidemics - the 2020 COVID-19 pandemic.

Brough HA, Kalayci O, Sediva A, Untersmayr E, Munblit D, Rodriguez Del Rio P, Vazquez-Ortiz M, Arasi S, Alvaro-Lozano M, Tsabouri S, Galli E, Beken B, Eigenmann PA. Brough HA, et al.

Pediatr Allergy Immunol.

2020 Apr 22; PMID: 32319129

Level of Evidence: 5 - Expert opinion

Type of Article: Review

BLUF: Based on general knowledge and a survey of literature, which the author acknowledges is limited, this review recommends **continued allergy, asthma, and immunodeficiency management based on established guidelines** with a **proactive transition to telemedicine** under quarantine conditions so higher risk pediatric patients have no disruption to care.

Abstract:

While the world is facing an unprecedented pandemic with COVID-19, patients with chronic diseases need special attention and if warranted adaptation of their regular treatment plan. In children, allergy and asthma are among the most prevalent non-communicable chronic diseases, and health care providers taking care of these patients need guidance. At the current stage of knowledge, **children have less severe symptoms of COVID-19, and severe asthma and immunodeficiency are classified as risk factors.** In addition, there is **no evidence that currently available asthma and allergy treatments, including antihistamines, corticosteroids, bronchodilators increase the risk of severe disease** from COVID-19. Most countries affected by COVID-19 have opted for nationwide confinement, which means that **communication with the primary clinician is often performed by telemedicine.** **Optimal disease control of allergic, asthmatic and immunodeficient children should be sought according to usual treatment guidelines.** This statement of the EAACI Section on Pediatrics puts forward six recommendations for the management of childhood allergies and immunodeficiencies based on six underlying facts and existing evidence

R&D: Diagnosis & Treatments

Current Diagnostics

Comparison of nasopharyngeal and oropharyngeal swabs for SARS-CoV-2 detection in 353 patients received tests with both specimens simultaneously.

Wang X, Tan L, Wang X, Liu W, Lu Y, Cheng L, Sun Z. Wang X.

International Journal of Infectious Disease

2020 April 18; PMID: 32315809

Level of Evidence: 3 Cohort Study

Type of Article: Research

BLUF: 353 medical records were reviewed from February 16, 2020 - March 2, 2020 comparing the performance between nasopharyngeal and oropharyngeal swabs in SARS-CoV-2 detection simultaneously. The study reveals nasopharyngeal swabs had a higher positive rate compared to oropharyngeal swabs and suggests nasopharyngeal swabs may be a more suitable test during this time of COVID-19 outbreak.

Abstract:

Background: Since the outbreak of coronavirus disease (COVID-19) in Wuhan in December 2019, by March 10, 2020, a total of 80,932 confirmed cases have been reported in China. **Two consecutively negative RT-PCR test results in respiratory tract specimens is required for the evaluation of discharge from hospital**, and oropharyngeal swabs were the most common sample. However, **false negative results occurred in the late stage of hospitalization, and avoiding false negative result is critical essential.**

Methods: We reviewed the medical record of 353 patients who received tests with both specimens simultaneously, and compared the performance between nasopharyngeal and oropharyngeal swabs.

Results: Of the 353 patients (outpatients, 192; inpatients, 161) studied, the median age was 54 years, and 177 (50.1%) were women. **Higher positive rate (positive tests/total tests) was observed in nasopharyngeal swabs than oropharyngeal swabs**, especially in inpatients.

Nasopharyngeal swabs from inpatients showed higher positive rate than outpatients. Nasopharyngeal swabs from male showed higher positive rate than female, especially in outpatients. Detection with both specimens slightly increased the positive rate than nasopharyngeal swab only. **Moreover, the consistency between from nasopharyngeal and oropharyngeal swabs were poor (Kappa=0.308).**

Conclusion: In conclusion, our study suggests that nasopharyngeal swabs may be more suitable than oropharyngeal swab at this stage of COVID-19 outbreak.

Developments in diagnostics

Evaluation of the Auxiliary Diagnostic Value of Antibody Assays for the Detection of Novel Coronavirus (SARS-CoV-2)

Gao Yong, Yuan Yi, Li Tuantuan, Wang Xiaowu, Li Xiuyong, Li Ang, Han Mingfeng

J Med Virol.

2020 Apr 20; PMID: 32320064

Level of Evidence: 3 - Retrospective study

Type of Article: Research

BLUF: It was found that 13% of throat swabs were positive for SARS-CoV-2 in the later phase (≥ 15 days) of infection. The sensitivities of IgM and IgG against SARS-CoV-2 were 52.2% and 91.3%, respectively. Combining the antibody assay with nucleic acid detection greatly improved the sensitivity of diagnosis of SARS-CoV-2 infection. When viral RNA is not detectable in throat swabs at the early stage of illness, IgM/IgG may become seropositive after 7 days, indicating an auxiliary diagnostic potential of the antibody assays.

Abstract: The spread of SARS-CoV-2 has taken on pandemic proportions, affecting over 100 countries in a matter of weeks. The goal of this study was to assess the diagnostic values of different methods of detecting and estimating the SARS-CoV-2 infection, and the auxiliary diagnostic potential of antibody assays. By **retrospectively analyzing the data of viral RNAs and serum IgM-IgG antibodies against SARS-CoV-2 from 38 cases with confirmed COVID-19** in the Second People's Hospital of Fuyang, we found that, in the early phase of the illness, the viral RNA was most abundant in the sputum specimens, followed by that in the throat swabs, while the antibody assays identified fewer positive cases at this stage. However, the sensitivity of the antibody assays overtook that of RNA test from the eighth day of disease onset. Simultaneous use of antibody assay and RT-qPCR improved the sensitivity of the diagnoses. Moreover, we found that most of these cases with no detectable viral RNA load during the early stages were able to be seropositive after 7 days. Our findings indicate that the antibody detection could be used as an effective supplementary indicator of SARS-CoV-2 infection in suspected cases with no detectable viral RNA, and in conjunction with nucleic acid detection in confirming the infection. This article is protected by copyright. All rights reserved.

Rapid detection of COVID-19 coronavirus using a reverse transcriptional loop-mediated isothermal amplification (RT-LAMP) diagnostic platform.

Yu L, Wu S, Hao X, Dong X, Mao L, Pelechano V, Chen WH, Yin X, Yu L, et al.

Clin Chem.

2020 Apr 21; PMID: 32315390

Level of Evidence: 4 - Single Cohort Design

Type of Article: Research

Summary:

A loop-mediated isothermal amplification combined with reverse transcription (LAMP-RT) protocol named iLACO (isothermal LAMP based method for COVID-19) was developed and optimized to detect COVID-19. The RT-primers were optimized by comparisons with nine corona and two influenza sequences. The bedside test uses 1.5 mL tubes incubated at 65°C, requires 20 minutes incubation time, and reports results with a pH color change. **The test's sensitivity was 89.9% (223/248) on confirmed COVID-19 patients from Shenyang province, China. The 25 false negatives were attributed to low viral load.**

Lung ultrasonography in a woman with COVID-19: This examination could be remote.

Kirkpatrick AW, McKee JL

CMAJ

2020 Apr 20; PMID: 32312827

Level of Evidence: 5 - Expert opinion

Type of Article: Comment

BLUF: Remote telementored ultrasonography (RTMUS) is being evaluated as a helpful method in working up patients with suspected COVID-19 while they are self-isolating, so they can access a higher level of care if needed.

Summary: Remote telementored ultrasonography (RTMUS) can provide helpful anatomic and physiologic information that can be remotely interpreted and can serve as a valuable tool in the workup of patients with suspected COVID-19. Reported lung ultrasound findings in COVID-19 include multifocal B-lines, pleural thickening and subpleural consolidation, which are similar results to computed tomography of the chest. Both CT and ultrasound may show findings before polymerase chain reaction results. The authors propose that RTMUS could help screen self-isolating adults at risk of or with COVID-19, by guiding a family member or the patient to examine their lung fields as an early warning of COVID-19 progression, allowing for timely escalation of care for patients who deteriorate during isolation.

Developments in Treatments

Potential therapeutic effects of dipyridamole in the severely ill patients with COVID-19

Liu X, Li Z, Liu S, Sun J, Chen Z, et al.

Acta Pharm Sin B

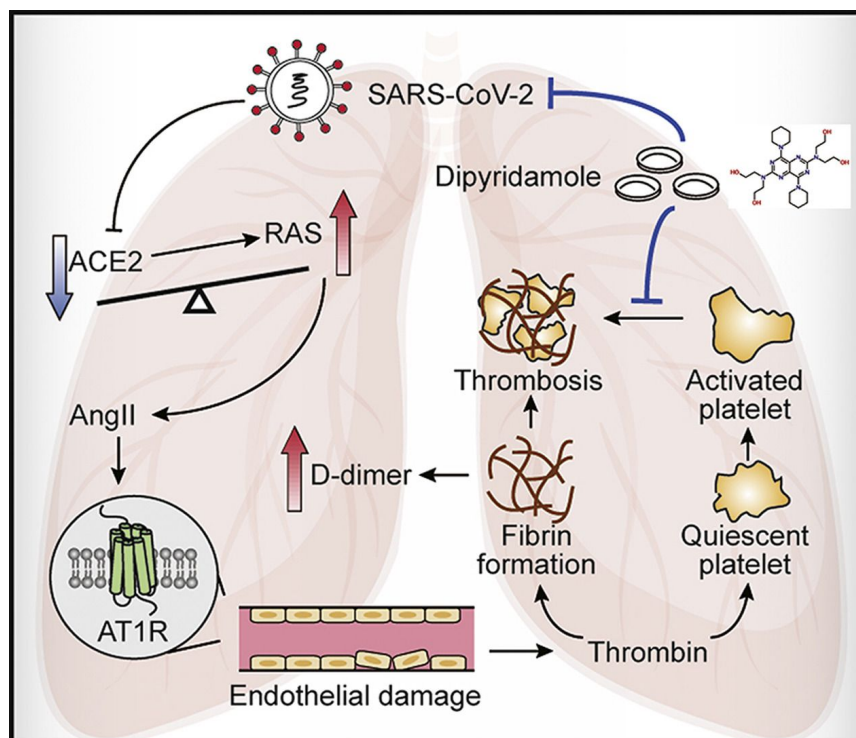
2020 Apr 20; PMID: 32318327

Level of Evidence: 2 – Randomized Controlled Trial

Type of Article: Research

BLUF: This study investigates the *in vitro* and clinical efficacy of dipyridamole, DIP, an FDA-approved anticoagulant drug that was selected for study using *in silico* screening methods against the SARS-CoV-2 spike protein. DIP effects on inhibition of viral replication were **first validated in vitro** in SARS-CoV-2-susceptible Vero E6 cells ($IC_{50} = 530 \pm nM$), with a **potency below serum concentrations $\sim 3 \mu M$** for standard use (50mg PO TID). The authors followed up with DIP administration a **two-center randomized control trial** ($n = 31$) of patients with clearly-defined severe or critical COVID-19, which correlates with increased D-dimers and thrombocytopenia. The authors report **improved outcomes in the DIP treatment group**, though they acknowledge the **need for a higher-powered study**.

Abstract: Severe acute respiratory syndrome coronavirus 2 (**SARS-CoV-2**) **infection** can cause acute respiratory distress syndrome, **hypercoagulability**, hypertension, and multiorgan dysfunction. Effective antivirals with safe clinical profile are urgently needed to improve the overall prognosis. In an analysis of a randomly collected cohort of 124 patients with Corona Virus Disease 2019 (COVID-19), we found that **hypercoagulability** as indicated by elevated concentrations of D-dimers was **associated with disease severity**. By virtual screening of a U.S. Food and Drug Administration (FDA) approved drug library, we identified an **anticoagulation agent dipyridamole (DIP) in silico**, which **suppressed SARS-CoV-2 replication in vitro**. In a **proof-of-concept trial involving 31 patients with COVID-19**, DIP supplementation was associated with significantly **decreased** concentrations of **D-dimers** ($P < 0.05$), **increased lymphocyte and platelet recovery** in the circulation, and markedly improved clinical outcomes in comparison to the control patients. In particular, **all 8 of the DIP-treated severely ill patients showed remarkable improvement**: 7 patients (87.5%) achieved clinical cure and were discharged from the hospitals while the remaining 1 patient (12.5%) was in clinical remission.



Graphical Abstract: Dipyridamole bound to the SARS-CoV-2 protease Mpro after identified via the virtual screening and bioassay validation, and thus suppressed viral replication in vitro. As a result, dipyridamole supplementation was associated with significantly decreased concentrations of D-dimers, increased lymphocyte and platelet recovery in the circulation, and markedly improved clinical outcomes in comparison to the control patients.

[Fast Identification of Possible Drug Treatment of Coronavirus Disease -19 \(COVID-19\) Through Computational Drug Repurposing Study](#)

Wang, Junmei

J Chem Inf Model

2020 Apr 21; PMID: 32315171

Level of Evidence: 5 – Expert Opinion

Type of Article: Correspondence

BLUF: With the help of the recently released crystal structure of SARS-Cov-2 main protease in complex with a covalently-bonded inhibitor, virtual docking screening of drug candidates in clinical trials was conducted, in the hopes of facilitating drug design targeting the SARS-Cov-2 main protease.

Abstract:

The recent outbreak of novel coronavirus disease -19 (COVID-19) calls for and welcomes possible treatment strategies using drugs on the market. It is very **efficient to apply computer-aided drug design techniques to quickly identify promising drug repurposing candidates, especially after the detailed 3D-structures of key viroic proteins are resolved.** The virus causing COVID-19 is SARS-Cov-2. Taking the advantage of a recently released crystal structure of SARS-Cov-2 main protease in complex with a covalently-bonded inhibitor, N_{3,1} I conducted virtual **docking screening of approved drugs and drug candidates in clinical trials.** For the top docking hits, I then performed **molecular dynamics simulations followed by binding free energy calculations using an endpoint method called MM-PBSA-WSAS** (Molecular Mechanics-Poisson Boltzmann Surface Area-Weighted Solvent-Accessible Surface Area).²⁻⁴ Several

promising known drugs stand out as potential inhibitors of SARS-Cov-2 main protease, including Carfilzomib, Eravacycline, Valrubicin, Lopinavir and Elbasvir. Carfilzomib, an approved anti-cancer drug acting as a proteasome inhibitor, has the best MM-PBSA-WSAS binding free energy, -13.8 kcal/mol. The second-best repurposing drug candidate, eravacycline, is synthetic halogenated tetracycline class antibiotic. Streptomycin, another antibiotic and a charged molecule, also demonstrates some inhibitory effect, even though the predicted binding free energy of the charged form (-3.8 kcal/mol) is not nearly as low as that of the neutral form (-7.9 kcal/mol). One bioactive, PubChem 23727975, has a binding free energy of -12.9 kcal/mol. Detailed receptor-ligand interactions were analyzed and hot spots for the receptor-ligand binding were identified. I found that one hotspot residue HIS41, is a conserved residue across many viruses including SARS-Cov, SARS-Cov-2, MERS-Cov, and HCV. **The findings of this study can facilitate rational drug design targeting the SARS-Cov-2 main protease.**

D3Targets-2019-nCoV: a webserver for predicting drug targets and for multi-target and multi-site based virtual screening against COVID-19.

Shi Y, Zhang X, Mu K, Peng C, Zhu Z, Wang X, Yang Y, Xu Z, Zhu W.

Acta Pharm Sin B

2020 Apr 20; PMID: 32318328

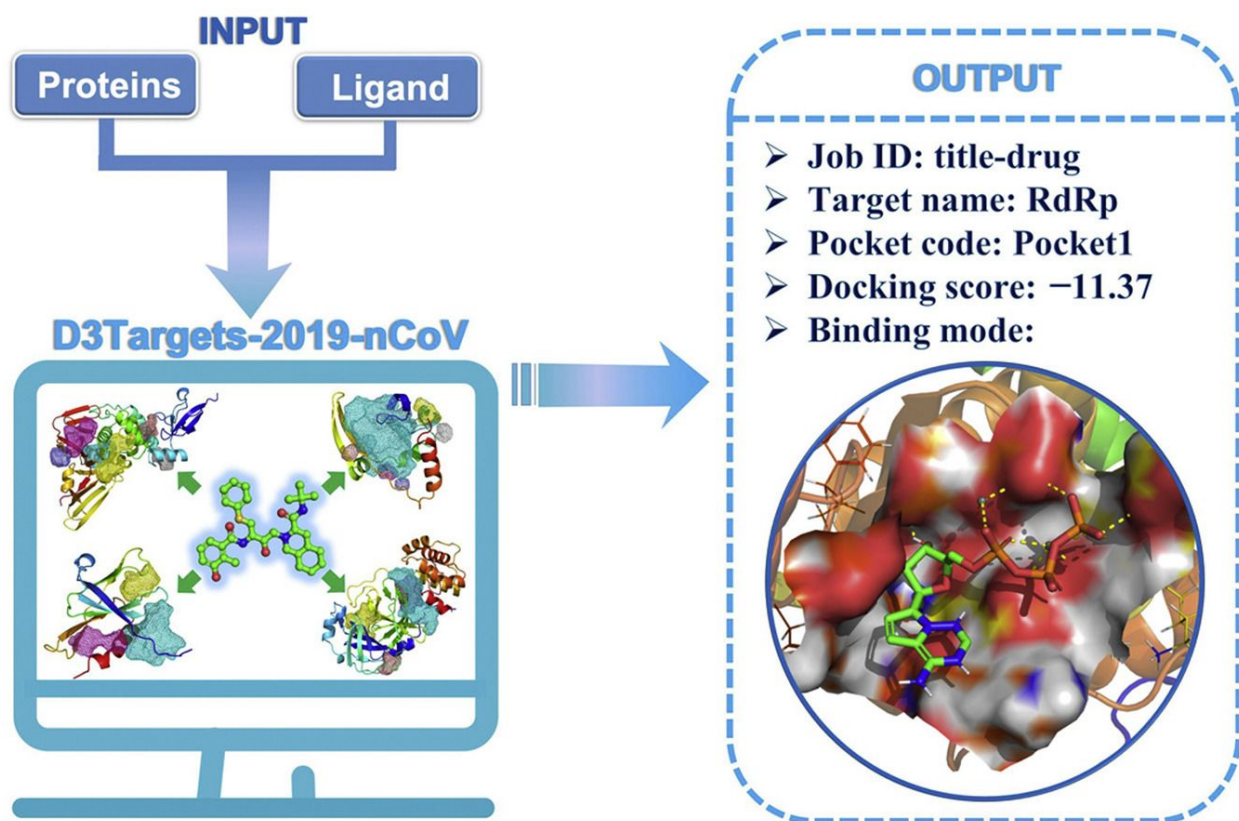
Level of Evidence: 5 - Mechanism- based

Type of Article: Research

BLUF: The authors of this article developed a molecular docking based webserver (D3Targets-2019-nCoV) that is free for public use that can predict both human and viral targets for the development of drugs to be used in treatment of COVID-19. The reliability of this webserver was supported by successful testing (high docking score) of 6 active compounds/drugs found by literature review to be active in treatment of COVID-19.

Abstract:

A highly effective medicine is urgently required to cure coronavirus disease 2019 (COVID-19). For the purpose, **we developed a molecular docking based webserver**, namely D3Targets-2019-nCoV, **with two functions, one is for predicting drug targets for drugs or active compounds observed from clinic or in vitro/in vivo studies, the other is for identifying lead compounds against potential drug targets via docking.** This server has its unique features, (1) the potential target proteins and their different conformations involving in the whole process from virus infection to replication and release were included as many as possible; (2) all the potential ligand-binding sites with volume larger than 200 Å³ on a protein structure were identified for docking; (3) correlation information among some conformations or binding sites was annotated; (4) it is easily to be updated, and is accessible freely to public (<https://www.d3pharma.com/D3Targets-2019-nCoV/index.php>). Currently, the webserver contains 42 proteins [20 severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) encoded proteins and 22 human proteins involved in virus infection, replication and release] with 69 different conformations/structures and 557 potential ligand-binding pockets in total. With 6 examples, **we demonstrated that the webserver should be useful to medicinal chemists, pharmacologists and clinicians for efficiently discovering or developing effective drugs against the SARS-CoV-2 to cure COVID-19.**



Prediction of the SARS-CoV-2 (2019-nCoV) 3C-like protease (3CL^{pro}) structure: virtual screening reveals velpatasvir, ledipasvir, and other drug repurposing candidates.

Chen, Yu Wai; Yiu, Chin-Pang Benu; Wong, Kwok-Yin

F1000 Research

2020 Apr 09; PMID: 32194944

Level of Evidence: 5 - Mechanism Based Reasoning

Type of Article: Research

BLUF: This article strived to build a molecular model of the 3-chymotrypsin-like protease which is considered to be a promising drug target in COVID-19. Virtual screening was carried out to explore possible readily available therapeutics, yielding 16 candidates that are further evaluated for their actions, targets, and side effects, with the antivirals ledipasvir and velpatasvir demonstrating promise.

Abstract: We prepared the three-dimensional model of the SARS-CoV-2 (aka 2019-nCoV) 3C-like protease (3CL^{pro}) using the crystal structure of the highly similar (96% identity) ortholog from the SARS-CoV. All residues involved in the catalysis, substrate binding and dimerisation are 100% conserved. Comparison of the polyprotein PP1AB sequences showed 86% identity. The 3C-like cleavage sites on the coronaviral polyproteins are highly conserved. Based on the near-identical substrate specificities and high sequence identities, we are of the opinion that some of the previous progress of **specific inhibitors development for the SARS-CoV enzyme can be conferred on its SARS-CoV-2 counterpart**. With the 3CL^{pro} molecular model, we performed virtual screening for purchasable drugs and proposed **16 candidates** for consideration. Among these, the **antivirals ledipasvir or velpatasvir** are particularly attractive as therapeutics to combat the new coronavirus with **minimal side effects**, commonly fatigue and headache. The drugs **Epclusa**

(velpatasvir/sofosbuvir) and Harvoni (ledipasvir/sofosbuvir) could be very effective owing to their dual inhibitory actions on two viral enzymes.

Table 3. The results of virtual screening of drugs on the active sites of SARS-CoV-2 3CL^{pro} model. The left and right columns are the results of A and B chains, respectively. The top scorers are listed first, then the equivalent top scorers of the other chain listed at the lower half. 'M.W.': molecular weight in g mol⁻¹. 'B.E.': AutoDock Vina binding energy in kcal mol⁻¹. The 'Hits' column is the number of times a compound appears as top scorers (representing different stereoisomers) out of the total number of stereoisomers of that compound in the library; only the binding energy of the top-ranking hit was shown. Etoposide and its phosphate are listed separately in the screens. 'n.f.' = not found. Approved and pre-approved drugs are shown in green and orange, respectively. Except dihydroergocristine and ditercalinium, all approved drugs have undergone post-market surveillance, i.e. Phase 4. The mean score of each screen (1500 results), scores of lopinavir and ritonavir are included at the bottom for reference.

A Chain				B Chain			
A Top scorers	M.W.	B.E.	Hits	B Top scorers	M.W.	B.E.	Hits
diosmin	609	-10.1	1/1	etoposide	669	-8.7	1/32
hesperidin	611	-10.1	8/38	R428	507	-8.6	2/2
MK-3207	558	-10.1	1/4	MK-3207	558	-8.6	1/4
venetoclax	868	-10.0	1/1	teniposide	657	-8.5	2/34
dihydroergocristine	612	-9.8	1/6	UK-432097	778	-8.5	1/2
bolazine	-9.8	-9.8	1/1	eluxadoline	570	-8.4	1/1
R428	507	-9.8	2/2	venetoclax	868	-8.4	1/1
ditercalinium	719	-9.8	1/1	ledipasvir	889	-8.4	1/1
etoposide-phosphate	669	-9.8	1/21	irinotecan	587	-8.4	1/1
				lumacaftor	452	-8.4	1/1
				velpatasvir	883	-8.4	1/5
(B Top scorers)				(A Top scorers)			
		-9.7		hesperidin		-8.3	
		-9.7		etoposide-phosphate		-8.3	
		-9.6		bolazine		-8.3	
		-9.5		dihydroergocristine		-8.1	
		-8.9		diosmin		-7.9	
		-8.5		ditercalinium		-7.7	
		-8.0					
		n.f.					
(Reference)				(Reference)			
Mean of 1500		-8.2		Mean of 1500		-7.1	
lopinavir		-8.0		lopinavir		-6.8	
ritonavir		-7.9		ritonavir		-6.9	

Points to consider in the preparation and transfusion of COVID-19 convalescent plasma.

Epstein J, Burnouf T

Vox Sang

2020 Apr 22; PMID: 32319102

Level of Evidence: 5- Expert opinion

Type of Article: Guideline

BLUF: Detailed guidelines on acquisition and use of convalescent plasma in the treatment of COVID-19. Highlights of the guidelines include:

- **Confirm donor eligibility**
 - history of laboratory confirmed Covid-19
 - full recovery >14 days prior to donation with 2 confirmed negative tests, or 28 days prior without confirmatory negative tests
 - consider avoiding donors who have previously been pregnant to reduce TRALI risk
- **Plasma donation should follow standard guidelines**
 - Use officially designated locations and personnel
 - screen for blood-borne illness
 - viral/pathogen inactivation after donation is recommended
 - restrict donation volume and repeat donation timeline
- **Facilitate future research**
 - collect details of donor covid illness history
 - analyze donated plasma for antibody titers
 - store a sample of plasma for future research
 - blood samples of the recipient prior to and after transfusion should be stored
- **Follow standard plasma transfusion guidelines**
 - consider transfusing from 2 separate donors for increased antibody diversity
 - consider transfusing an initial 200ml followed by additional treatments

Abstract:

This document prepared and endorsed by the Working Party on Global Blood Safety of the International Society of Blood Transfusion presents elements, as of April 2020, to take into consideration in the preparation and transfusion of COVID-19 convalescent plasma as a possible treatment approach of COVID-19. The document covers the following important factors to have in mind when considering this treatment: (a) eligibility criteria of convalescent COVID-19 patients to donate whole blood or plasma, (b) pre-screening and pre-donation testing of convalescent COVID-19 donors; (c) criteria for collection of COVID-19 plasma; (d) post-donation treatment of plasma; and (e) it offers recommendations for plasma transfusion.

Depriving Iron Supply to the Virus Represents a Promising Adjuvant Therapeutic Against Viral Survival

Liu W, Zhang S, Nekhai S, Liu S, Liu W, et al.

Curr Clin Microbiol Rep

2020 Apr 20; PMID: 32318324

Level of Evidence: 5 – Mechanism-based Reasoning

Type of Article: Review

BLUF: This review discusses the **potential benefits of iron chelation therapy**, which would **reduce** the amount of this **essential trace ion** available for **host replicative machinery that viruses depend on**. Citing *in vitro* and clinical studies of indirect and direct deprivation of iron

from other hosts infected with viruses, namely HIV-1, the authors posit that **iron and other trace metals might be sequestered *in vivo* to reduce viral replication**, though they acknowledge that iron chelation **also results in reduced host cell proliferation**, a likely contributor to hindered viral proliferation.

Abstract:

Purpose of the review: The ongoing outbreak of novel coronavirus pneumonia (COVID-19) caused by the 2019 novel coronavirus (SARS-CoV-2) in China is lifting widespread concerns. Thus, therapeutic options are urgently needed, and will be discussed in this review.

Recent findings: **Iron-containing enzymes are required for viruses** most likely including coronaviruses (CoVs) to complete their **replication process**. Moreover, **poor prognosis** occurred in the conditions of **iron overload** for patients upon **infections of viruses**. Thus, **limiting iron** represents a **promising adjuvant strategy** in treating viral infection through oral uptake or venous injection of iron chelators, or through the manipulation of the key iron regulators. For example, treatment with **iron chelator deferiprone** has been shown to **prolong the survival of** acquired immunodeficiency syndrome (**AIDS**) patients. Increasing intracellular **iron efflux** via increasing iron exporter ferroportin expression also exhibits **antiviral effect** on human immunodeficiency virus (**HIV**). The implications of other metals besides iron are also briefly discussed.

Summary: For even though we know little about iron regulation in COVID-19 patients thus far, it could be deduced from other viral infections that iron chelation might be an alternative beneficial adjuvant in treating COVID-19.

The anti-viral facet of anti-rheumatic drugs: Lessons from COVID-19.

Perricone C, Triggianese P, Bartoloni E, Cafaro G, Bonifacio AF, Bursi R, Perricone R, Gerli R.
Journal of Autoimmunity

2020 Apr 17; PMID: 32317220

Level of Evidence: 5 - Literature review

Type of Article: Literature Review

BLUF: This article details the current knowledge and efficacy of several different therapeutic treatment options for COVID-19. Table 2 provides a more in depth review of the drugs mentioned below:

- Glucocorticoids: No current evidence supporting benefits.
- NSAIDs: not recommended as “first line option for managing COVID-19”
- Chloroquine/Hydroxychloroquine: “Due to the excellent safety profile and vast experience, their use remains a pillar of current treatment protocols.”
- Leflunomide: “Its usage in COVID-19 treatment is doubtful.”
- Mycophenolate mofetil: Inconclusive data but hypothetically is a good potential support drug.
- Methotrexate: “Its usage as an anti-viral drug and as a therapeutic weapon against COVID-19 may not be suitable.”
- Colchicine: Based on studies in Italy, seems like a suitable and cheap option for COVID-19 patients.
- Anti-interleukin 1: “may be helpful.”
- Tumor necrosis factor alpha inhibitors: Potentially helpful in critical patients.
- Tocilizumab: Hypothetically good therapeutic option. Not enough data.
- Intravenous immunoglobulins: Hypothetically good therapeutic option. Not enough data.
- Janus kinases inhibitors: High risk option and “their usage should be carefully evaluated”
- Granulocyte-monocyte colony stimulating factor: Unknown but currently under research.

Abstract: The outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has posed the world at a pandemic risk. Coronavirus-19 disease (COVID-19) is an infectious disease caused by SARS-CoV-2, which causes pneumonia, requires intensive care unit hospitalization in about 10% of cases and can lead to a fatal outcome. Several efforts are currently made to find a treatment for COVID-19 patients. So far, several anti-viral and immunosuppressive or immunomodulating drugs have demonstrated some efficacy on COVID-19 both in vitro and in animal models as well as in cases series. In COVID-19 patients a pro-inflammatory status with high levels of interleukin (IL)-1B, IL-1 receptor (R)A and tumor necrosis factor (TNF)- α has been demonstrated. Moreover, high levels of IL-6 and TNF- α have been observed in patients requiring intensive-care-unit hospitalization. This provided rationale for the use of anti-rheumatic drugs as potential treatments for this severe viral infection. Other agents, such as hydroxychloroquine and chloroquine might have a direct anti-viral effect. The anti-viral aspect of immunosuppressants towards a variety of viruses has been known since long time and it is herein discussed in the view of searching for a potential treatment for SARS-CoV-2 infection.

Table 2
Ongoing Clinical Trials on rheumatologic drugs in COVID-19 (last updated on the April 1, 2020).

Compound	Approved indications for clinical practice in Rheumatology	Potential target viruses	Anti-viral mechanism of action
<i>Glucocorticoids</i>	Several including rheumatoid arthritis, systemic lupus erythematosus, vasculitis	H1N1	Controversy. Low dose for short time (10 days) may improve acute respiratory distress syndrome.
<i>Nonsteroidal anti-inflammatory drugs</i>	Several	CMV, HCV, Flaviviridae, H7N9, H3N2, SARS-CoV	COX-2 inhibition impairs viral replication Spike protein of SARS-CoV inhibited by COX-2 via ERK/NF- κ B and PI3K/JNK pathways Ibuprofen effect ACE2 receptor
<i>Chloroquine</i> <i>Hydroxychloroquine</i>	Rheumatoid arthritis Juvenile idiopathic arthritis Discoid lupus erythematosus	HIV, HAV, Influenza, HCoV-OC43, HPV, HCoV-229E, SARS-CoV, SARS-CoV-2	Increases pH of host cell organelles, impairing enzymatic activity for virus antigen-binding, replication and pro-inflammatory cytokine production and secretion
<i>Leflunomide (and teriflunomide)</i>	Systemic lupus erythematosus Rheumatoid arthritis Psoriatic arthritis	CMV, HSV-1, HSV-2, EBV (teriflunomide), HIV-1, Argentinian mammarenavirus, FMDV, EBOV, Influenza A, Polyomavirus, NDV, EV-A71, RSV	Tyrosine kinase inhibition Inhibition of pyrimidine de novo synthesis through the blockade of dihydroorotate dehydrogenase Possible reduction of IL-6 <i>in vitro</i>
<i>Mycophenolate Mofetil</i>	Severe Autoimmune disease (Systemic lupus erythematosus)	Influenza, ZIKV, West Nile-virus, Chikungunya, smallpox virus, FMDV, PPRV, Junin virus, norovirus, Lassa's hemorrhagic fever, reovirus, rotavirus, HCV, MERS-CoV	Inhibition IMPDH and conversion of inosine monophosphate to guanosine monophosphate hampering lymphocyte proliferation Increased IFN-stimulated gene expression Synergizes the anti-viral effects penciclovir, lobocavir, 37-fluorodeoxyguanosine, diaminopurine dioxolane of through the depletion of the endogenous GTP pools Inhibition of dihydrofolate reductase
<i>Methotrexate</i> <i>Colchicine</i>	Gout treatment and prevention Acute and recurrent pericarditis Familial Mediterranean fever	ZIKV Flaviviridae, RSA59, M – CoV, RSV	Alters cytoskeleton organization via microtubules assembly inhibition Inhibition of the inflammasome Reduction of IL-1 and IL-6 Anti-neutrophilic action
<i>Anakinra</i> <i>Canakinumab</i> <i>Rilonacept</i>	Rheumatoid arthritis Cryopirrin Associated Periodic Syndromes Systemic Juvenile Idiopathic arthritis Adult onset Still's disease Rheumatoid arthritis	No evidence of direct anti-viral activity Indirect evidence on reduction of inflammatory response in infections by arthritogenic alphavirus and parainfluenza	IL-1 receptor inhibitor (Anakinra), IL-1 β inhibitor (Canakinumab), IL-1 α /IL-1 β inhibitor (Rilonacept), inhibition of the inflammasome
<i>TNFα inhibitors</i>	Juvenile idiopathic arthritis Non-radiographic axial spondyloarthritis Ankylosing spondylitis Psoriasis	Rotavirus and indirect evidence on reduction of inflammatory response in infections by influenza viruses	Reduction of inflammatory response
<i>Tocilizumab</i>	Psoriatic arthritis Rheumatoid arthritis Juvenile idiopathic arthritis	No evidence of direct anti-viral activity. Indirect evidence on reduction of inflammatory response in COVID-19	IL-6 inhibition, inhibition of the cytokine storm?
<i>IVIg</i>	Primary immunodeficiency syndromes with impaired antibody production Hypogammaglobulinemia Primary immune thrombocytopenia (ITP)	HAV, HSV, CMV, VZV, EBV, measles, mumps, rubella, parvovirus B19, CMV, hMPV, ADV, RSV, HSV 2, Flaviviridae, HIV, Ebola, SARS-CoV	Direct action both on innate immune components (complement, monocytes, macrophages, natural killer cells), and on adaptive immune cells (CD4 T-cells and B-cells) Saturate FcR
<i>JAK inhibitors</i>	Kawasaki disease Rheumatoid arthritis Psoriatic arthritis Ulcerative colitis	No evidence of direct anti-viral activity SARS-CoV-2? Potential reduction of inflammatory response in ALL	Inhibition of JAK/STAT pathway, reduction of pro-inflammatory cytokines Potential inhibition of AP2-associated protein kinase 1 (AAK1) by baricitinib that SARS-CoV-2 uses to infect lung cells through binding with ACE2
<i>GM-CSFα</i>	Rheumatoid arthritis	Potential reduction of inflammatory response in ALL	GM-CSF neutralization effective in reducing the severity of inflammation

Mental Health & Resilience Needs

COVID-19's impact on healthcare workforce

Psychological stress of medical staffs during outbreak of COVID-19 and adjustment strategy.

Wenzhi Wu Yan Zhang Pu Wang Li Zhang Guixiang Wang Guanghui Lei Qiang Xiao Xiaochen Cao Yueran Bian Simiao Xie Fei Huang Na Luo Jingyuan Zhang Mingyan Luo
J Med Virol.

2020 Apr 15; PMID: 32314806

Level of Evidence: 4 - Case series

Type of Article: Research

BLUF: The differences in psychological stress, measured through a questionnaire survey, was studied between college students, front-line medical staff in Wuhan, and medical staff outside of Wuhan. Psychological stress was highest among COVID-19 front-line medical staff.

Abstract: COVID-19 has a significant impact on public health and poses a challenge to medical staffs, especially to front-line medical staffs who are exposed to direct contact with patients. To understand the psychological stress status of medical staffs during the outbreak of COVID-19. Random sample questionnaire survey was conducted among 2110 medical staffs and 2158 college students in all provinces of China through a questionnaire which was compiled and completed through the Questionnaire Star platform relying on Wechat, QQ and other social software. The differences in psychological stress status of different groups were compared through the analysis of the questionnaire. Results revealed that in all provinces of China, medical staffs scored significantly higher on all items of psychological stress than college students($P < 0.001$). In Wuhan, medical staff scored significantly higher than college students in all items of psychological stress($P < 0.001$). While for medical staff, the group in Wuhan area scored significantly higher than the group outside Wuhan on "Thought of being in danger", "The possibility of self-illness", "Worrying about family infection"($P < 0.05$), "Poor sleep quality", "Needing psychological guidance" and "Worrying about being infected"($P < 0.01$) items in the psychological stress questionnaire, and in the item of "Confidence in the victory of the epidemic", the group in Wuhan area scored significantly lower than the group in the area outside Wuhan($P < 0.05$). **The emotion, cognition, physical and mental response of front-line medical staff showed obvious "exposure effect", and psychological crisis intervention strategy can be helpful.**

Silver Linings

How COVID-19 lockdowns could lead to a kinder research culture.

Derrick, Gemma

Nature

2020 Apr 22; PMID: 32313158

Level of Evidence: 6 - No Data Cited

Type of Article: Column

Summary: The author shares their experiences since the start of the COVID-19 pandemic that have shown how it is changing research culture for the better. Science is an ultra-competitive field but through recent changes, including messages of support and unity from colleagues, relaxed deadlines for grant proposals, and flexible working requests, a shift to a kinder research culture is underway; this momentum should be used to extend this change beyond a temporary situation.

Resources

Coronavirus disease (COVID-19): a scoping review.

Lv M, Luo X, Estill J, Liu Y, Ren M, Wang J, Wang Q, Zhao S, Wang X, Yang S, Feng X, Li W, Liu E, Zhang X, Wang L, Zhou Q, Meng W, Qi X, Xun Y, Yu X, Chen Y, On Behalf Of The Covid-Evidence And Recommendations Working Group.

Euro Surveill

2020 Apr; PMID: 32317050

Level of Evidence: 1 - Scoping Review

Type of Article: Review

BLUF: This review of all literature related to COVID-19 published in English and Chinese between Dec. 1, 2019 and Feb. 6, 2020 identified research gaps including a lack of randomized controlled trials, cohort studies, and studies on clinical practice. Additionally, the authors found that most of the guidance/guidelines developed by the WHO, US, CDC, ECDC and several Chinese Institutions did not fulfil the principles of evidence-based practice.

Abstract:

Background: In December 2019, a pneumonia caused by a novel coronavirus (SARS-CoV-2) emerged in Wuhan, China and has rapidly spread around the world since then.

Aim: This study aims to understand the research gaps related to COVID-19 and propose recommendations for future research.

Methods: We undertook a scoping review of COVID-19, comprehensively searching databases and other sources to identify literature on COVID-19 between 1 December 2019 and 6 February 2020. We analysed the sources, publication date, type and topic of the retrieved articles/studies.

Results: We included 249 articles in this scoping review. More than half (59.0%) were conducted in China. Guidance/guidelines and consensus statements (n = 56; 22.5%) were the most common. Most (n = 192; 77.1%) articles were published in peer-reviewed journals, 35 (14.1%) on preprint servers and 22 (8.8%) posted online. Ten genetic studies (4.0%) focused on the origin of SARS-CoV-2 while the topics of molecular studies varied. Nine of 22 epidemiological studies focused on estimating the basic reproduction number of COVID-19 infection (Ro). Of all identified guidance/guidelines (n = 35), only ten fulfilled the strict principles of evidence-based practice. The number of articles published per day increased rapidly until the end of January.

Conclusion: The number of articles on COVID-19 steadily increased before 6 February 2020. However, they lack diversity and are almost non-existent in some study fields, such as clinical research. The findings suggest that evidence for the development of clinical practice guidelines and public health policies will be improved when more results from clinical research becomes [sic] available.

Coronavirus Disease 2019: Reassembly Attack of Coronavirus

Yang, Chenglei; Qiu, Xue; Fan, Haoran; Jiang, Mei; Lao, Xiaojie; Zeng, Yukeng; Zhan, Zhiming
Int J Environ Health Res

2020 Apr 21; PMID: 32316751

Level of Evidence: 5 - Literature Review

Type of Article: Research

BLUF: Authors summarize the epidemiological characteristics of COVID-19 and current prevention and control measures from the pandemic.

Abstract:

There have been three major global outbreaks of acute respiratory disease caused by coronavirus in the last two decades. The ongoing Coronavirus Disease 2019 (COVID-19) first emerged in Wuhan,

China, is the most dangerous, which spread to 163 countries and 6 continents and caused a major public health emergency worldwide. The outbreak is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) originated from bats, which spreads rapidly from human to human. As of 17 March 2020, there have been 179,112 confirmed cases and 7426 deaths worldwide, with a mortality rate of 4.1%. There is currently no effective treatment or approved vaccine, so isolating the source of infection and blocking the routes of transmission is important. In this article, **we summarized the worldwide epidemic trend of COVID-19 and discussed its epidemiological characteristics, prevention and control measures. We hope this article could provide experience and help for global epidemic prevention and control.**

Acknowledgements

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