May 1, 2020
Daily COVID-19 Literature Surveillance Summary

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NOW LIVE!

COVID-19 Daily Literature Surveillance

COVID19LST

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

Coming soon:

The Swab

Jasmine Rah

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

May 1st, 2020
Executive Summary

Climate
- Critical illness in health care workers with COVID-19 has not been explored so a national data repository is suggested to aggregate data to facilitate research.
- There is curiosity and call for research on how sexual activity and state of relationships have been affected during the pandemic.

Epidemiology
- A case series in California of 100 hospitalized COVID-19 patients found that 13% exhibited coinfection with other respiratory viruses, highlighting that a positive test for another pathogen should not exclude COVID-19 from the differential.
- There are a number of case reports highlighting atypical presentations of patients subsequently found to be COVID-19 positive, most notably:
    - A patient presented complaining of otalgia and tinnitus only was found to have positive COVID-19 RT-PCR as well as lung involvement in CT.

Understanding the Pathology
- An in vitro test of hydroxychloroquine and azithromycin at lower concentrations (5μM/L and 5/10μM/L, respectively) than previous studies shows effective inhibition of viral replication 60hrs post-infection. Further clinical research is recommended as doses have poor external validity.
- Based on in-silico studies, there is postulation that the SARS-CoV-2 virus could epigenetically affect metabolism.
- Adding to the conversation of androgen associations to COVID-19, researchers hypothesize that benign prostatic hyperplasia treatments, specifically 5α-reductase inhibitors, may contribute to the higher mortality observed in men by causing increased lung concentrations of androgens, which can have anti-regenerative effects in damaged lung tissue.

Transmission & Prevention
- Korean officials attribute the country's success in containing the pandemic to rapid, early diagnosis and isolation, effective triage of patients, contingency plans for enhancing critical care capacity, and continuous communication between local authorities and the department of health.
- An observational study of over 10,000 residents of Hong Kong found that 95% of people wore masks in public; however, 13% were wearing them incorrectly highlighting both the high adherence to mask wearing in Hong Kong and the importance of education on proper PPE use.

Management
- Thus far, current commonly recommended treatment for COVID-19 includes hydroxychloroquine and azithromycin, remdesivir, IL-6 antagonists, and convalescent plasma with consensus growing that ACE inhibitors and ARBS should not be discontinued during management.
- Contrast enhanced sonography (CEUS) is an effective bedside tool to quickly rule out organ infarction in COVID-19 patients.

Adjusting Practice during COVID-19
- Guidelines and recommendations for today include:
    - Neuraxial anesthesia and peripheral nerve blocks during the pandemic.
    - Proton beam radiotherapy.
    - Management of hemodialysis patients and considerations for peritoneal dialysis during the pandemic.
    - Care of patients in labor and delivery units.
    - Virtual orthopedic examinations.
- Canadian cardiologists suggest that cardiac rehabilitation during the pandemic should transition to a technology-based model utilizing smart phones, mobile apps, and wearable sensors.
- Surgeons in the US encourage the utilization of telehealth and provide guidelines for preoperative evaluations and postoperative visits when possible to minimize COVID-19 transmission risk.

R&D: Diagnosis & Treatments
- In comparison to radiologists, the artificial intelligence program COVID-19 Reporting and Data System (CO-RADS) yielded a high discriminatory power in detecting pulmonary involvement in moderate and severe COVID-19 patients.
- A retrospective case-control study with 81 non-ICU COVID-19 patients in China found that Umifenovir is not associated with accelerated clearance of SARS-CoV-2.

Mental Health & Resilience
- To prevent burnout, there is a call for mental health provisions for our healthcare workers during this pandemic.
    - This is further stressed by another article which highlights that critical care nurses on the front-lines of the COVID-19 pandemic may be at high risk for compassion fatigue and burnout
- In order to shape professional identities of medical students during this health crisis, one US medical school rewired its curriculum to promote aspects of wellness.

Silver Linings
- In a cross-sectional study comparing 12 weeks from 2020 to the same in 2019, researchers found a statistically significant reduction in the number of influenza strains, positivity rate, and severe influenza cases.

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Contributors and Associate Contributors

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

We have added Level 6 to denote papers that do not cite any sources or provide any supporting evidence.

Climate

Global

COVID-19 and malaria: A symptom screening challenge for malaria endemic countries.
Chanda-Kapata P, Kapata N, Zumla A.
Int J Infect Dis
2020 Apr 25, PMID: 32344326
Level of Evidence: 5 - Expert opinion
Type of Article: Editorial
BLUF: In Africa, diagnostic suspicion should not ignore malaria in this time of increased alertness for COVID-19. Malaria is endemic to many areas of Africa and shares many symptoms with COVID-19. Key resources should still be allocated for this illness in the time of pandemic.

Summarizing excerpt: "COVID-19 currently imposes an additional burden to the already overstretched, resource strapped health services [in Africa] which are grappling to bring under control the high burden of existing infectious and non-infectious diseases, including TB, HIV, and malaria." Malaria and COVID-19 share similar symptoms, an emphasis on travel history, and are localized to similar geographical regions. Currently in Africa, a "high index of suspicion is skewed towards COVID-19 given the alertness at community, health centre, country, regional and global level," which may lead to underdiagnosis and lack of treatment for malaria. The authors recommend rapid testing for malaria while screening for COVID-19 and moving malaria supplies to COVID-19 testing sites to address these concerns.

Is Coronavirus Disease 2019 (COVID-19) seen less in countries more exposed to Malaria?
Sargin G, Yavaşoğlu Sİ, Yavasoglu I.
Med Hypotheses.
2020 Apr 22, PMID: 32344306
Level of Evidence: 5 - Expert Opinion
Article Type: Letter to the Editor
BLUF: Authors suggest further research should be done in countries with high rates of malarial treatment to determine if they have lower rates of COVID-19 due to chloroquine and hydroxychloroquine use.

Summary: Researchers have been studying the use of chloroquine and hydroxychloroquine for treatment of COVID-19. Chloroquine and hydroxychloroquine is currently used in the prophylaxis and treatment of malaria. Countries with high prevalence of malaria have experienced lower rates of confirmed COVID-19 cases. The authors suggest that further research be conducted in these areas to learn if the lower rates are due to their exposure to malarial treatments.

Covid-19 lock down: People psychology due to law enforcement
Varalakshmi R, Swetha R.Varalakshmi R, et al.
Asian J Psychiatr.
2020 Apr 17;PMID: 32344332
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
Summary: This letter discusses how India's government is managing the COVID-19 outbreak by enacting laws of enforcement. These are normally deemed unconstitutional but during a time of crisis are allowed. The lockdown in India has caused panic in the general public. Some strategies utilized by the government to reduce fear among the public include: declaring insurance for healthcare workers, Reserve Bank of India reducing loan rates or withdrawal fees, and the government instructing wages to be paid to employees during lockdown, concluding that the spread of the virus can only be controlled if the public cooperates.

Restructured society and environment: A review on potential technological strategies to control the COVID-19 pandemic.
Madurai Elavarasan, Rajvikram; Pugazhendhi, Rishi
Sci Total Environ
2020 Apr 23; PMID: 32336562
Level of Evidence: 5 - Expert Opinion & Mechanism-based Reasoning
Type of Article: Research
BLUF: This study provides a critical investigation and evaluation of various technology-based strategies that are being utilized to assist the healthcare systems, government, and public during the COVID-19 pandemic. Furthermore, prospective technologies such as applications of artificial intelligence, machine learning, internet of things, drone technology, and robotics are discussed for their benefits and potential impact in this pandemic; while these technologies hold promise, they need extensive testing before being implemented in a practical environment.

Abstract
The emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in China at December 2019 had led to a global outbreak of coronavirus disease 2019 (COVID-19) and the disease started to spread all over the world and became an international public health issue. The entire humanity has to fight in this war against the unexpected and each and every individual role is important. Healthcare system is doing exceptional work and the government is taking various measures that help the society to control the spread. Public, on the other hand, coordinates with the policies and act accordingly in most state of affairs. But the role of technologies in assisting different social bodies to fight against the pandemic remains hidden. The intention of our study is to uncover the hidden roles of technologies that ultimately help for controlling the pandemic. On investigating, it is found that the strategies utilizing potential technologies would yield better benefits and these technological strategies can be framed either to control the pandemic or to support the confinement of the society during pandemic which in turn aids in controlling the spreading of infection. This study enlightens the various implemented technologies that assists the healthcare systems, government and public in diverse aspects for fighting against COVID-19. Furthermore, the technological swift that happened during the pandemic and their influence in the environment and society is discussed. Besides the implemented technologies, this work also deals with untapped potential technologies that have prospective applications in controlling the pandemic circumstances. Alongside the various discussion, our suggested solution for certain situational issues is also presented. *[sic]*

Table 2
Reported AI and ML technologies utilized for COVID-19.

S.·no	Company/Authors	Application Category	Description	Outcome	Reference
1	BlueDot	Prediction	AI powered infection-surveillance system which scans more than 100,000 online articles across the globe in 65 languages for every 15 min	Predicted the outbreak of unknown disease which is later identified as COVID-19	(MIT Technology Review, 2020a)
2	Constantinos Siettos et al.	Prediction	Used Susceptible-Infected-Recovered-Dead (SIRD) model to calibrate the data and forecasted the outbreak in Hubei, China	Forecasted a minimum of 45,000 infected cases and 2700 deaths by 29 February 2020. The actual data was 67,000 infected case and 2800 deaths.	(ITN, 2020a)
3	Mingli Yuan et al.	Prediction	Associating CT scan scores with mortality of the patients infected with COVID-19	The average score of patients who died was 30 and the patients who recovered was 12.	(Yuan et al., 2020)
4	Xiangao Jiang et al.	Prediction	Data-Driven Prediction of Coronavirus Clinical Severity	Predictive models that learned the patient's data from Wenzhou, Zhejiang hospitals in China achieved 70% to 80% accuracy in predicting severe cases.	(Jiang et al., 2020)
5	Lishi Wang et al.	Prediction	Patient Information Based Algorithm (PIBA) to estimate and predict the mortality rate of COVID-19 in Hubei, China	The real death number was in the predicted range	(Wang et al., 2020a)
6	Shuai Wang et al.	Diagnosis	Using deep-learning method to extract the COVID-19 radiographical changes in CT scan images to provide diagnosis	The internal validation showed 89.5% accuracy and the external validation achieved an accuracy of 79.3%	(Wang et al., 2020b)
7	Delft Imaging and Thirona	Diagnosis	CAD4COVID was developed on the same high-quality standard as CAD4TB, which has contributed to screening 6 million people worldwide across 40 countries.	Developed CAD4COVID AI software triages COVID-19 suspects from chest X-rays images and indicates the affected lung tissue.	(ITN, 2020b)
8	Stratifyd	Social media	Scans posts on social media and cross-references the same with description of diseases from validated sources	False information can be reduced and the information quality is enhanced	(MIT Technology Review, 2020a)
9	Ramesh Raskar and team	App	Users can see if they had come contact with an infected individual without knowing who it might be only if the infected person has shared that information.	Track infected people with many other features	(MIT Technology Review, 2020b)
10	White House Office of Science and Technology Policy (OSTP)	Database	Covid-19 Open Research Dataset (CORD-19) that includes over 24,000 research papers covering all COVID-19 related topics	Extensive collection of scientific literature related to COVID-19 and further updation as more research is published	(MIT Technology Review, 2020c)

Affecting the Healthcare Workforce

Impact of the COVID-19 pandemic on endoscopy practice: results of a cross-sectional survey from the New York metropolitan area.
Mahadev S, Aroniadis OS, Barraza L, Agarunov E, Goodman AJ, Benias PC, Buscaglia JM, Gross SA, Kasmin FE, Cohen JJ, Carr-Locke DL, Greenwald DA, Mendelsohn RB, Sethi A, Gonda TA; NYSGE research committee.
Gastrointest Endosc.
2020 Apr 24; PMID: 32339595
Level of Evidence: 4 – Cross Sectional Study
Type of Article: Letter to the Editor

Summary: The authors compared endoscopic case volumes and PPE use in the New York metropolitan area before and after the onset of COVID-19, from a survey of 69 endoscopists. They found that since the onset of COVID-19, case volume was markedly reduced, with 71% of gastroenterologists no longer regularly performing endoscopy at all, and 62% reporting zero cases over the preceding seven days. This data provides insight into the negative impacts of COVID-19 pandemic on GI practices.

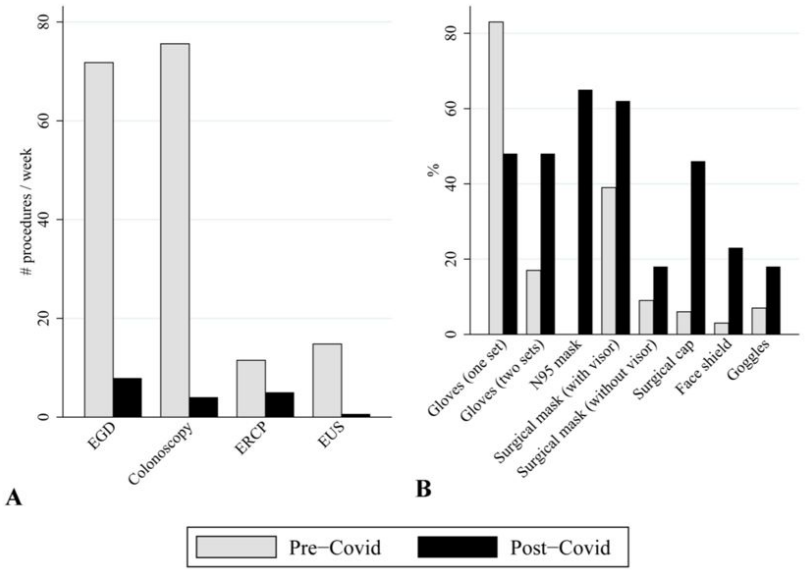

Figure 1. Average weekly endoscopy unit volume and universal personal protective equipment (PPE) use before and since the onset of the COVID-19 pandemic.

Risk factors for serious/critical COVID-19 illness in health care workers: Too many unknowns.
Wander PL, Orlov M, Merel SE, Enquobahrie DA
Infect Control Hosp Epidemiol
2020 Apr 27; PMID: 32336303
Level of Evidence: 5- Expert opinion
Type or Article: Letter

Summary: A call for more research into the factors leading to serious/critical illness in health care workers with COVID-19, with particular concern for the possibility of spread via stool. The authors **suggest the creation of a national data repository of de-identified healthcare worker information to facilitate research** in this area.

Disparities
Stories regarding how different populations are disproportionally affected

From the Editor of *Sexuality and Disability*: The Impact of COVID-19 on Sexuality and Disability-Are We Closer or More Isolated?
Hough, Sigmund
Sex Disabil
2020 Apr 24; PMID: 32336835
Level of Evidence: 6 - No data cited
Type of Article: Editorial
Summary: This editorial discusses the purpose of the journal, *Sexuality and Disability*, and shares the opportunity that is available to investigate the impact of this pandemic on sex and sexual activity, dating and relationships, social media, and social distancing. The author extends an invitation to readers to help contribute to these research efforts.

Epidemiology

Methodological challenges in studying the COVID-19 pandemic crisis.
Knottnerus JA, Tugwell P
J Clin Epidemiol
2020 May; PMID: 32336471
Level of Evidence:5 - Expert opinion
Type of Article: Editorial
SUMMARY: Authors discuss methodological challenges and potential areas of possible research in studying the COVID-19 pandemic, including:

- The need for high speed scoping reviews of potential useful prior knowledge and experience from similar previous events.
- Surveillance to monitor the current pandemic threat and how to model this spread, as well as real-time studies of the occurrence of COVID-19.
- Evaluation of diagnostic testing for active and past COVID-19 infection, and evaluation of potential antiviral agents and vaccines.
- Evaluation of pandemic-specific interventions, standards for research and reporting, and methods for evaluating strength of recommendation for public health and healthcare practice.
- Evaluation of decision making under uncertainty.
- Methods to support establishing, monitoring, and evaluating post-pandemic COVID-19 measures as well as methods to retrospectively evaluate COVID-19 occurrence over time and its determinants.
- Improvement of the methodology of studying prevention and early detection, anticipation and monitoring strategies, and modeling and prediction.

Modeling
Pretty self explanatory- modeling to predict/trend the prevalence of disease and anticipating needs in the future

On the Global Trends and Spread of the COVID-19 Outbreak: Preliminary Assessment of the Potential Relation Between Location-Specific Temperature and UV Index.
Gunthe, S. S., Swain, B., Patra, S. S., & Amte, A.
Z Gesundh Wiss.
2020 Apr 24; PMID: 32337151
Level of Evidence: Modeling
Type of Article: Research
BLUF: Analysis of region-specific data for the spread of COVID-19 has shown that the virus is sensitive to meteorological parameters. Understanding the optimal temperature and UV index affecting the transmission of the virus can better inform management and evaluation strategies going forward.

Abstract:
The novel coronavirus, since its first outbreak in December, has, up till now, affected approximately 114,542 people across 115 countries. Many international agencies are devoting efforts to enhance the understanding of the evolving COVID-19 outbreak on an international level, its influences, and preparedness. At present, COVID-19 appears to affect individuals through person-to-person means, like other commonly found cold or influenza viruses. It is widely known and acknowledged that viruses causing influenza peak during cold temperatures and gradually subside in the warmer temperature, owing to their seasonality. Thus, COVID-19, due to its regular flu-like symptoms, is also expected to show similar seasonality and subside as the global temperatures rise in the northern hemisphere with the onset of spring. Despite these speculations, however, the systematic analysis in the global perspective of the relation between COVID-19 spread and meteorological parameters is unavailable. Here, by analyzing the region- and city-specific affected global data and corresponding meteorological parameters, we show that **there is an optimum range of temperature and UV index strongly affecting the spread and survival of the virus, whereas precipitation, relative humidity, cloud cover, etc. have no effect on the virus.** Unavailability of pharmaceutical interventions would require greater preparedness and alert for the effective control of COVID-19. Under these conditions, the information provided here could be very helpful for the global community struggling to fight this global crisis. It is, however, important to note that the **information presented here clearly lacks any physiological evidences, which may merit further investigation.** Thus, any attempt for management, implementation, and evaluation strategies responding to the crisis arising due to the COVID-19 outbreak must not consider the evaluation presented here as the foremost factor.

The effect of uncontrolled travelers and social distancing on the spread of novel coronavirus disease (COVID-19) in Colombia.
Gómez-Ríos D, Ramirez-Malule D, Ramirez-Malule H.Gómez-Ríos D, et al.
Travel Med Infect Dis.
2020 Apr 25; PMID: 32344113
Level of Evidence: 5 - Expert Opinion Modeling
Type of Article: Letter
Summary: This letter advocated for continued tight control of distancing and essential workers in Colombia through May 2020. Initially, a relaxed control of travellers, mobility, and distancing led to many COVID-19 cases. Since the tightened control in March, the first 30 days saw a predictable SEIR (susceptible - exposed - infectious - recovered) as in Wuhan, but the letter emphasized how lifting restrictions in April could lead to an increased incidence with many delayed cases detected (see figure below).

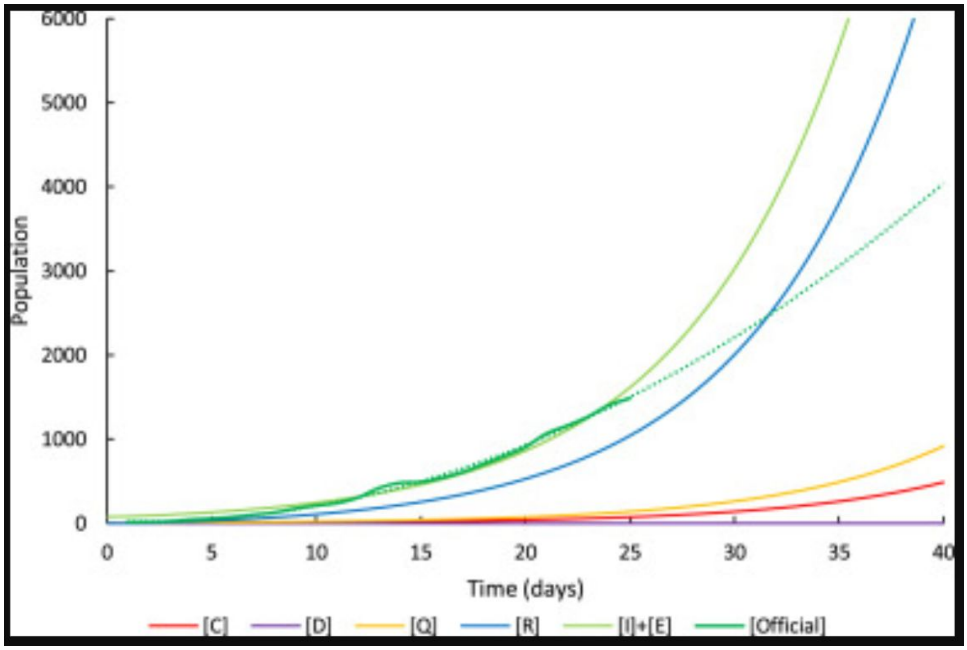

Figure. 1. Simulation of exposed and infective [I] + [E], recovered [R], quarantined [Q] critical [C] and dead [D] people caused by COVID-19 in Colombia in a non-social distancing scenario. Dashed green line is the current projection of the infection curve. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

The Data set for Patient Information Based Algorithm to Predict Mortality Cause by COVID-19.

Li, Jing; Wang, Lishi; Guo, Sumin; Xie, Ning; Yao, Lan; Cao, Yanhong; Day, Sara W; Howard, Scott C; Graff, J Carolyn; Gu, Tianshu; Ji, Jiafu; Gu, Weikuan; Sun, Dianjun

Data Brief

2020 Apr 24; PMID: 32337324

Level of Evidence: Modeling

Type of Article: Research

BLUF: This group used a Patient Information Based Algorithm to process collected data, including 33 deaths in Wuhan in Hubei province during the early outbreak of COVID-19, as well as further confirmed COVID-19 cases and resulting deaths in other areas in China and South Korea. This enabled them to generate a death rate that was updated in real-time. This methodology was used to predict and compare death rates in regions of China and South Korea and can be utilized for future epidemics.

Abstract:

The data of COVID-19 disease in China and then in South Korea were collected daily from several different official websites. The collected data included **33 death cases in Wuhan city of Hubei province** during early outbreak as well as **confirmed cases and death toll in some specific regions**, which were chosen as representatives from the perspective of the coronavirus outbreak in China. Data were copied and pasted onto Excel spreadsheets to perform data analysis. A new methodology, **Patient Information Based Algorithm (PIBA)** [1], has been adapted to process the data and used to **estimate the death rate of COVID-19 in real-time**. Assumption is that the number of days from inpatients to death fall into a pattern of normal distribution and the scores in normal distribution can be obtained by observing 33 death cases and analysing the data [2]. We selected 5 scores in normal distribution of these durations as lagging days, which will be used in the following estimation of death rate. We calculated each death rate on accumulative confirmed cases with each lagging day from the current data and then weighted every death rate with its corresponding possibility to obtain the total death rate on each day. While the **trendline of these death rate curves meet the curve of current ratio between accumulative death cases and confirmed cases at some points in the near future**, we considered that these intersections are within the range of real death rates. Six tables were presented to illustrate the PIBA method using data from China and South Korea. One figure on estimated rate of infection and patients in serious condition and retrospective estimation of initially occurring time of CORID-19 *[sic]* based on PIBA.

Table 6. Deaths prediction by PIBA and actual death data in South Korea.

Date	3/22/2020	3/21/2020	3/20/2020	3/19/2020	3/18/2020	3/17/2020	3/16/2020
7 lagging day	1	1	1	3	0	2	3
13 lagging day	2	3	5	3	7	5	9
19 lagging day	9	6	6	9	6	5	3
Date	**3/22/2020**	**3/21/2020**	**3/20/2020**	**3/19/2020**	**3/18/2020**	**3/17/2020**	**3/16/2020**
Min	1	1	1	3	0	2	3
Max	9	6	6	9	7	5	9
Actual deaths	2	8	3	7	3	6	0

Symptoms and Clinical Presentation

Adults

Characteristics of Emergency Department Patients With COVID-19 at a Single Site in Northern California: Clinical Observations and Public Health Implications.

Duanmu Y, Brown IP, Gibb WR, Singh J, Matheson LW, Blomkalns AL, Govindarajan P
Acad Emerg Med
2020 Apr 28; PMID: 32344458
Level of Evidence: 4 - Case series
Type or Article: Research Letter

Summary: This article presents a case series of 100 patients who tested positive for COVID-19 (RT-PCR) between March 4-23 at a single California hospital. The researchers briefly examine a wide range of clinical and demographic data including medical history, radiologic findings, lab results, and hospitalization/ICU use. Highlights of their findings include common coinfections with other respiratory viruses (13%), immunosuppression in 18%, and an overall mortality rate of 1%.

New type of corona virus *[sic]* induced acute otitis media in adult.

Fidan V.
Am J Otolaryngol.
2020 Apr 16, PMID: 32336572
Level of Evidence: 4 - Case Report
Article Type: Research

BLUF: The authors report a 35-year-old female patient presenting with otalgia and tinnitus with no classical COVID-19 symptoms. She tested positive after RT-PCR and chest x-ray showed bilateral lung involvement. After 13 days she had a complete recovery. Authors recommend performing complete physical exams on patients even without classic symptoms of COVID-19 as it can have different manifestations.

Abstract:
Since late December 2019, a new type of coronavirus (COVID-19) causing a cluster of respiratory infections was first identified in Wuhan-China. And it disseminated to all countries. Generally, COVID-19 cases have fever, cough, respiratory distress findings (dyspnoea, intercostal retraction, cyanosis etc.). In this paper, we have presented an adult otitis media case whom *[sic]* infected with COVID-19, but she have *[sic]* not any classical COVID-19 symptoms.

COVID-19 outbreak impact in Spain: A role for tobacco smoking?

Vázquez JC, Redolar-Ripoll D.Vázquez JC, et al.
Tob Induc Dis.
2020 Apr 6; PMID: 32336968
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

Summary: Men (51%) and women (49%) are getting infected by COVID-19 at similar rates, but men have been dying from COVID-19 at a significantly higher rate (4.4%) than women (2.5%), and the sex differences regarding vulnerability in those with COVID-19 and preexisting CVD seem to be again reflected in men (35%) and women (26%). The authors hypothesize that these gendered differences could be attributed to differences in patterns of tobacco smoking and recommend that public health efforts to mitigate the effects of COVID-19 should also encourage smoking cessation.

Understanding the Pathology

Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19.
Liu F, Li L, Xu M, Wu J, Luo D, Zhu Y, Li B, Song X, Zhou X
J Clin Virol
2020 Apr 14; PMID: 32344321
Level of Evidence: 3 - Retrospective cohort study
Type or Article: Research

BLUF: A retrospective cohort study of 140 COVID-19 positive (per RT-PCR) patients at a single Chinese hospital between Jan 18-Mar 12 finds that elevated levels of IL-6 and C-reactive protein (CRP) are associated with an increased risk of severe disease. Further analysis finds the optimal cutoff values to be IL-6 > 32.1 pg/mL and CRP >41.8 mg/L. The sample of patients with elevated procalcitonin (n=8) was too low to draw meaningful conclusions.

Abstract:
Background: The inflammatory response plays a critical role in coronavirus disease 2019 (COVID-19), and inflammatory cytokine storm increases the severity of COVID-19.
Objective: To investigate the ability of interleukin-6 (IL-6), C-reactive protein (CRP), and procalcitonin (PCT) to predict mild and severe cases of COVID-19.
Study design: This retrospective cohort study included 140 patients diagnosed with COVID-19 from January 18, 2020, to March 12, 2020. The study population was divided into two groups according to disease severity: a mild group (MG) (n = 107) and a severe group (SG) (n = 33). Data on demographic characteristics, baseline clinical characteristics, and the levels of IL-6, CRP, and PCT on admission were collected.
Results: Among the 140 patients, the levels of IL-6, CRP, and PCT increased in 95 (67.9 %), 91 (65.0 %), and 8 (5.7 %) patients on admission, respectively. The proportion of patients with increased IL-6, CRP, and PCT levels was significantly higher in the SG than in the MG. Cox proportional hazard model showed that IL-6 and CRP could be used as independent factors to predict the severity of COVID-19. Furthermore, patients with IL-6 > 32.1 pg/mL or CRP > 41.8 mg/L were more likely to have severe complications.
Conclusion: The serum levels of IL-6 and CRP can effectively assess disease severity and predict outcome in patients with COVID-19.

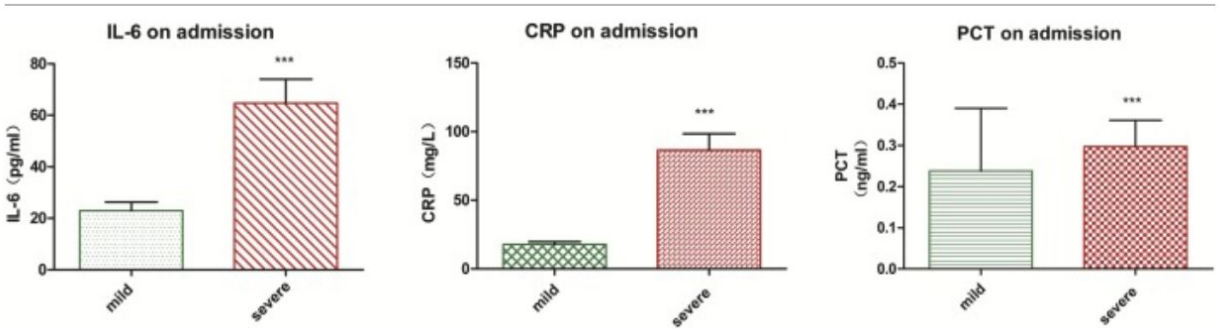

Fig. 1. Serum levels of IL-6, CRP, and PCT in patients with COVID-2019 ***P<0.0001.

Variables	Assessment of validity							
	AUC	Optimal cut-off value	Sensitivity	Specificity	Predictive value		Likelihood ratio	
					Positive	Negative	Positive	Negative
IL-6	0.808	32.1 pg/mL	85.19 %	66.67 %	57.89 %	89.21 %	2.55	0.22
CRP	0.858	41.8 mg/L	88.89 %	72.73 %	66.67 %	91.35 %	3.25	0.15
PCT	0.812	0.07 ng/mL	73.15 %	84.85 %	49.12 %	93.98 %	4.82	0.31

AUC, area under the curve.

Table 3. Area under the receiver operating characteristic curve and optimal cut-off values of IL-6, CRP, and PCT.

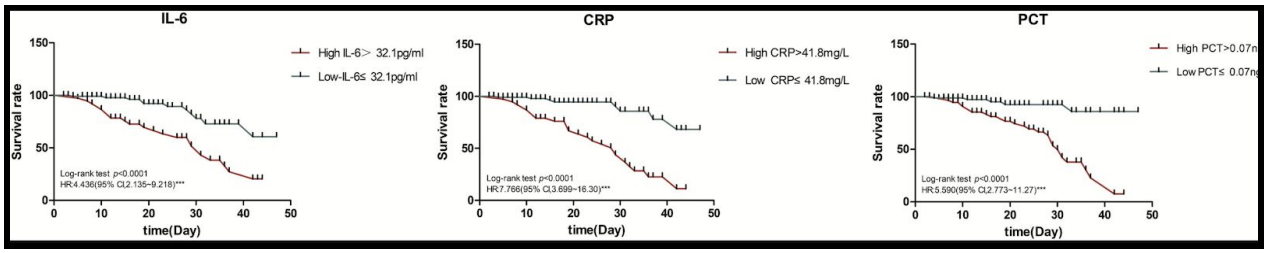

Fig. 3. Survival according to the levels of interleukin-6 (IL-6),C-reactive protein (CRP), and procalcitonin (PCT).

COVID-19: Possible Impact of the Genetic Background in IFNL Genes on Disease Outcomes.
Mihm, Sabine
J Innate Immun
2020 Apr 28; PMID: 32344401
Level of Evidence: 5 - Mechanism-based Reasoning
Type of Article: Letter to the Editor
BLUF: Based on variations in interferon lamda (INFL) genes, different populations and individuals within those populations, may not have the same risk of susceptibility to COVID-19 infection beyond the known risk differences associated with age and sex.

Summary: This letter includes discussion of the IFNL4 gene (IFN = interferon) which is suggested to be a possible variation in the type III IFN (IFN-λ1–4) gene locus and has been associated with the host's ability to cope with an infection induced by hepatitis C virus, also a positive sense, enveloped ssRNA virus like SARS-CoV-2. The type III IFN gene locus is induced by TLR7 (Toll-like recepetor 7) and has been shown to exhibit sex differences in response, a feature that is also associated with COVID-19.

The Role of the Renin-Angiotensin System in Severe Acute Respiratory Syndrome-CoV-2 Infection.
Alfano G, Guaraldi G, Fontana F, Ferrari A, Magistroni R, Mussini C, Cappelli G.
Modena Covid-19 Working Group
2020 Apr 28; PMID: 32344395
Level of Evidence: 5 –Review
Type of Article: Letter
BLUF: This letter assesses the potential role of ace inhibitors and angiotensin II (Ang II)-receptor blockers with the COVID-19 outbreak, as ACE2 is the host receptor required for cellular entry of severe acute respiratory syndrome (SARS)-CoV-2, the etiological agent of the current SARS. Ultimately, the authors review the current evidence and state that there is no scientific data supporting an aggravation of lung injury in patients treated with renin-angiotensin system (RAS) blockers who develop pneumonia.

Summarizing Excerpt: "We believe that multiple factors are implicated in the battle of the host against SARS-Cov-2 including immune response, comorbidities, early respiratory support, and modulation of inflammation. Regarding this latter variable, understanding the physiological regulation of the ACE2 pathway can help physicians for the management of SARS-CoV-2 infection. Variability of RAS activation in patient subgroups might explain the enormous variability in clinical manifestations... In summary, there is no scientific evidence supporting an aggravation of lung injury in patients treated with RAS blockers who develop pneumonia. The apparent beneficial effect of RAS modulation and the use of ace inhibitor and Ang II-receptor blockers in these patients warrant the conduction of further clinical trials, to elucidate the underlying pathophysiological mechanism of this concerning infectious disease and provide information on its best management."

May Patients Receiving 5-alpha-reductase Inhibitors Be in Higher Risk of COVID-19 Complications?
Adamowicz J, Juszczak K, Drewa T
Med Hypotheses
2020 Apr 22; PMID: 32344304
Level of Evidence: 5 – Mechanism-based Reasoning
Type of Article: Review
BLUF: The authors **hypothesize** that benign prostatic hyperplasia treatments, namely **5α-reductase inhibitors**, might contribute to the **higher COVID-19 mortality observed in men**. They reason that **decreased lung 5α-reductase activity** allows **increased lung concentrations of androgens**, which have been observed to have **anti-regenerative effects** in damaged lung tissue.

Abstract:
COVID-19 pandemic is a major challenge for global and national healthcare providers. Number (*sic*) of new cases is continuously increasing with an emerging trend showing **worse prognosis in males** in comparison to females. Based on this observation, our proposed hypothesis is that **5-alpha-reductase inhibitors**, that are commonly used for BPH treatment, may be one of the factors **contributing to poorer prognosis** in males.

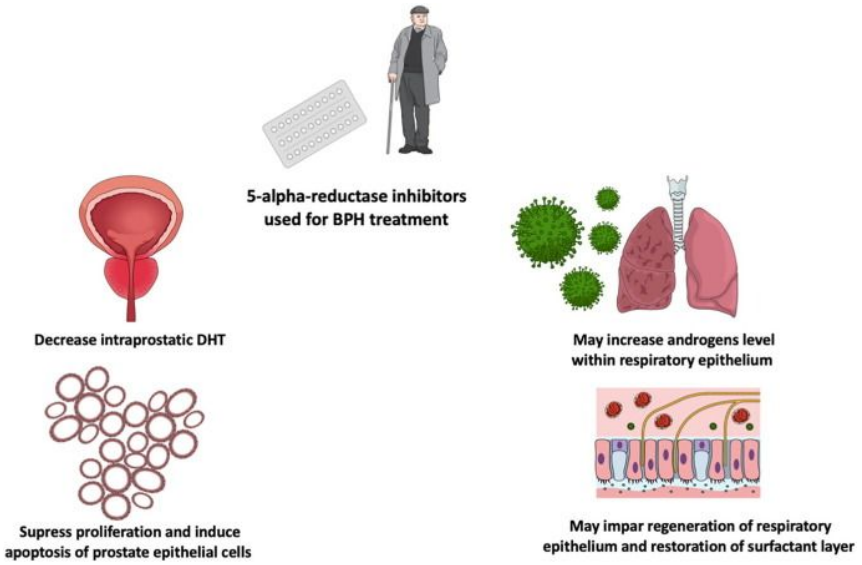

Figure 1. 5-alpha-reductase inhibitors therapy due to BPH may increase the risk of COVID-19 infection unfavorable outcome.

2019-nCoV-SARS-CoV-2 (COVID-19) infection: Cruciality of Furin and relevance with cancer.
Usul Afsar C
Med Hypotheses
2020 Apr 22; PMID: 32344311
Level of Evidence: 5- Expert opinion
Type or Article: Hypothesis
Summary: Recent research showing SARS-CoV-2 has a furin like cleavage site combined with past research suggesting the furin may be pro-oncogenic in certain cancers leads the authors to hypothesize that SARS-CoV-2 could potentially be carcinogenic. The authors also note evidence of differential furin expression and death rates in China and Italy to hypothesize that furin could be involved in determining the severity of COVID-19.

COVID-19 type III hypersensitivity reaction.
Mutar Mahdi B.
Med Hypotheses
2020 Apr 23; PMID: 32344307
Level of Evidence: 5 - Mechanism based reasoning
Type of Article: Editorial
BLUF: The author describes the type III hypersensitivity reaction proposed as a pathologic feature of COVID-19 infection noting that antigen-antibody complexes deposit in the lung at the site of infection and activate the complement system through the classical pathway leading to neutrophil infiltration and aggregation at the infection site causing severe tissue damage.

Summary: SARS-CoV-2 infects lung alveolar epithelial cells using receptor-mediated endocytosis through coronavirus S-protein, which contains a ligand binding domain with angiotensin-converting enzyme II. After viral entry, it is recognized by pathogen associated molecular patterns, which leads to a downstream signaling cascade that induces expression of type I IFN and other pro-inflammatory cytokines. The virus may directly infect macrophages, which present viral antigenic peptide to T-lymphocytes, ultimately differentiating into CD4, CD8+ T-lymphocytes. SARS-CoV-2 viral antigens stimulate antibody formation of IgM in the acute phase, and IgG in the chronic phase. **Antigen-antibody immune complexes deposit in the lungs and activate the complement system through the classical pathway.** Vasoactive amines release from mast cells and basophils, and platelets aggregate in the coronary vasculature, which can lead to microthrombus formation. **Neutrophil infiltration and aggregation at the site of infection in alveoli leads to severe tissue damage and a type III hypersensitivity reaction.** Immune complexes may induce cytokine release, which precipitates the cytokine store syndrome observed in some patients.

Eosinophil Responses During COVID-19 Infections and Coronavirus Vaccination.
Lindsley AW, Schwartz JT, Rothenberg ME.
J Allergy Clin Immunol
2020 Apr 25; PMID: 32344056
Level of Evidence: 5 – Mechanism-based reasoning
Type of Article: Review
BLUF: The authors argue that there is little supportive evidence to suggest that patients with eosinophil-associated diseases have an altered course of COVID-19. There is no evidence that patients with eosinopenia induced by anti-eosinophil therapeutics have increased susceptibility to infection, and pulmonary eosinophilia is not part of the lung pathology attributed to COVID-19.

Abstract:
Eosinophils are circulating and tissue-resident leukocytes that have potent pro-inflammatory effects in a number of diseases. Recently, eosinophils have been shown to have a variety of other functions, including immunoregulation and antiviral activity. Eosinophil levels vary dramatically in a number of clinical settings, especially following eosinophil-targeted therapy, which is now available to selectively deplete these cells. There are key COVID-19-related questions concerning eosinophils whose answers affect recommended prevention and care. **First, do patients with eosinophilia-associated diseases have an altered course of COVID-19? Second, do patients with eosinopenia (now intentionally induced by biological drugs) have unique COVID-19 susceptibility and/or disease course?** This is a particularly relevant question as eosinopenia is associated with acute respiratory deterioration during infection with the Severe Acute Respiratory Syndrome (SARS)-Corona Virus

(CoV)-2, the causative agent of COVID-19. **Third, do eosinophils contribute to the lung pathology induced during COVID-19 and will they contribute to immunopotentiation potentially associated with emerging COVID-19 vaccines?** Herein, we address these timely questions and project considerations during the emerging COVID-19 pandemic.

In silico

A data-driven hypothesis on the epigenetic dysregulation of host metabolism by SARS coronaviral infection: Potential implications for the SARS-CoV-2 modus operandi.

Vavougios GD.
Med Hypotheses.
2020 Apr 23; PMID: 32344305
Level of Evidence: 5 - Mechanism-based Reasoning
Type of Article: Review

BLUF: The study hypothesizes that **SARS-CoV-2 has the potential to epigenetically affect human metabolism.** The hypothesis is based on *in silico* and genomic studies. The literature has discussed how SARS-CoV-2 can induce diabetes through pancreatic ACE2-dependent uptake. It has been proposed that lipid lowering drugs may be useful against SARS-CoV-2.

Abstract:
COVID-19, the disease caused by the novel SARS-CoV-2, a betacoronavirus structurally similar to SARS-CoV. Based on both structural and syndromic similarities with SARS-CoV, a hypothesis is formed on SARS-CoV-2 potential to affect the host's metabolism as part of its lifecycle. This hypothesis is evaluated by (a) exploratory analysis of SARS-CoV/human transcriptomic interaction data and gene set enrichment analysis (b) a confirmatory, focused review of the literature based on the findings by (a). A STRING Viruses (available search for human - SARS-CoV (NCBI taxonomy Id: 9606 vs. NCBI taxonomy Id: 694009) genomic interactions reveals ten human proteins, interacting with SARS-CoV: SGTA, FGL2, SPECC1, STAT3, PHB, BCL2L1, PPP1CA, CAV1, JUN, XPO1. Gene set enrichment analyses (GSEA) with STRING on this network revealed their role as a putative protein - protein interaction network (PPI; Enrichment p-value = 0.0296) mediating, viral parasitism, interleukin as well as insulin signaling, diabetes and triglyceride catabolism. In the literature, SARS-CoV has been known to cause de novo diabetes by ACE2-dependent uptake on pancreatic isle *[sic]* cells, and furthermore dysregulate lipid autophagy in favor of the viral lifecycle *[sic]*. Conversely, currently there are *[sic]* only non-causative, observational evidence of worse outcomes for COVID-19 patients with comorbid diabetes or hyperglycemia. No study has reported on the lipid profiles of COVID-19 patients; however, lipid-targeting molecules have been proposed as agents against SARS-CoV-2. Future studies, reporting on lipid and glucose metabolism of COVID-19 patients could help elucidate the disease's seculae *[sic]* and aid drug design.

Combination of Biodata Mining and Computational Modelling in Identification and Characterization of ORF1ab Polyprotein of SARS-CoV-2 Isolated From Oronasopharynx of an Iranian Patient

Emameh RZ, Nosrati H, Taheri RA
Biol Proced Online
2020 Apr 21; PMID: 32336957
Level of Evidence: 5 – Mechanism-based Reasoning
Type of Article: Research

BLUF: The authors studied a **SARS-CoV-2 sample** from an Iranian patient with 100% coding sequence identity to that of a Wuhan isolate, and further, **model ORF1ab**, encoding a polyprotein that generates **nonstructural proteins**. *In silico* modelling predicted structure based on an **83% similar protein from SARS-CoV**, suggesting an **key ancestral role in virulence and viral replication**. The authors identified **2 domains with predicted high antigenicity** as potential vaccine targets.

Abstract:
Background: Coronavirus disease 2019 (COVID-19) is an emerging zoonotic viral infection, which was started in Wuhan, China, in December 2019 and transmitted to other countries worldwide as a pandemic outbreak. Iran is one of the top ranked countries in the tables of COVID-19-infected and -mortality cases that make the Iranian patients as the potential targets for diversity of studies including epidemiology, biomedical, biodata, and viral proteins computational modelling studies.
Results: In this study, we applied bioinformatic biodata mining methods to **detect CDS and protein sequences of ORF1ab polyprotein of SARS-CoV-2** isolated from oronasopharynx of an Iranian patient. Then through the computational modelling and antigenicity prediction approaches, the identified polyprotein sequence was analyzed. The results revealed that the identified **ORF1ab polyprotein** belongs to a **part of nonstructural protein** 1 (nsp1) with the **high antigenicity residues** in a glycine-proline or hydrophobic amino acid rich domain.
Conclusions: The results revealed that nsp1 as a **virulence factor and crucial agent in spreading of the COVID-19** among the society can be a potential target for the future epidemiology, drug, and vaccine studies.

In vitro

In vitro testing of combined hydroxychloroquine and azithromycin on SARS-CoV-2 shows synergistic effect.

Julien Andreania, Marion Le Bideaua, Isabelle Duflota, Priscilla Jardota, Clara Rollanda, Manon Boxbergera, Nathalie Wurtza, Jean-Marc Rolaina, Philippe Colsona, Bernard La Scolaa, Didier Raoult
Microb Pathog.
2020 Apr 25; PMID: 32344177
Level of Evidence: 5 – Bench Research
Article Type: Research report

Summary: SARS-CoV-2 IHUMI-3 strain was tested *in vitro* with Vero E6 cells in 13 control wells and against various concentrations of hydroxychloroquine (1, 2, or 5 μM/L) and azithromycin (5 or 10 μM/L). Viral replication/cytopathology was noted in all 13 control wells. Hydroxychloroquine at 5 μM/L concentration with azithromycin at 5 and 10 μM/L were effective at inhibiting viral replication 60 hours post-infection. HCQ at lower concentrations did not demonstrate statistically significant results. The authors note that prior *in vitro* studies used concentrations of HCQ that were too high, and therefore unrealistic for treating human patients. This tested HCQ/azithromycin concentrations that have been observed in pulmonary tissue and serum. Authors recommend clinical investigation of early intervention to determine whether this combination of medication prevents respiratory distress or cytokine storm.

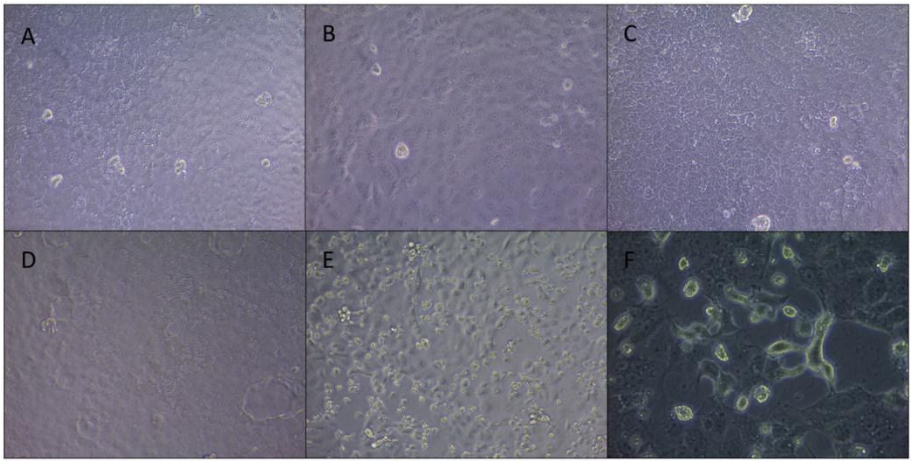

Fig. 1: Observations of infected cells resistant or not to viral replication after inoculation of SARS-CoV 2 strain IHUMI-3 at multiplicity of infection (MOI) 0.25.

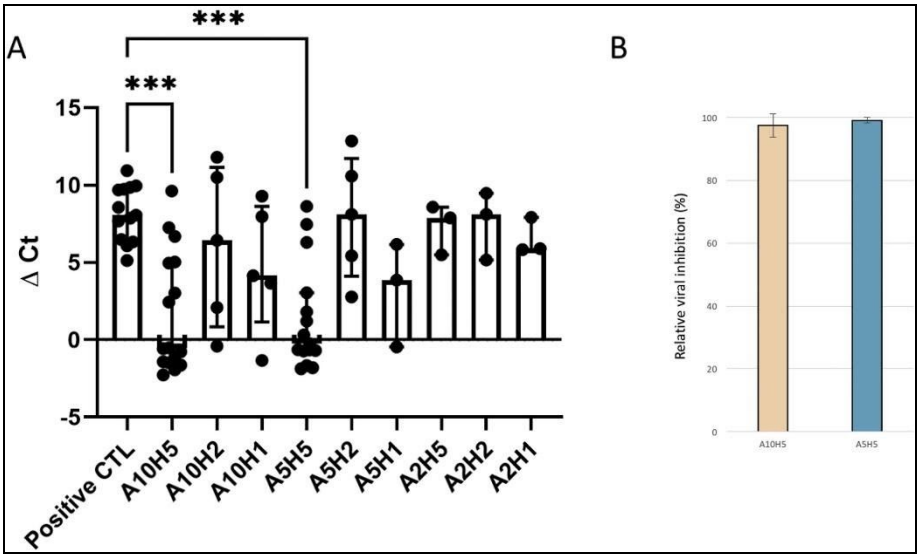

Fig. 2: Effect of hydroxychloroquine and azithromycin association on SARS-CoV 2 replication. **2A**: Delta Ct between 0 and 60 h post infection. Ordered axis represents the variation of delta cycle-thresholds obtained by RT-PCR between H0 and H60for each condition. Each point represents data obtained for one well. Number of replicates was indicated for each conditions are A10H5 n = 16,A10H2 n = 5, A10H1 n = 5, A5H5 n = 15, A5H2n = 5, A5H1 n = 3, A2H5 n = 3, A2H2 n = 3, A2H1n = 3 and n = 13 for the positive control. Median and interquartile range were indicated for each condition. *** represent significant results under p < 0,0005. Others are not significant compared to the control. **2B**: Percentage of inhibition as compared to control by the combinations of 5µM of hydroxychloroquine associated with 5 or 10µM for azithromycin. Data represent the mean ± SD, re-presenting three independent experiments conducted at least in triplicate.

Transmission & Prevention

Prevention in the Community

A reality check on the use of face masks during the COVID-19 outbreak in Hong Kong.
Victor CWT, Shing YT, Wai KP, Helen KWL, Shara WYL.
EClinicalMedicine
2020 Apr 24, PMID: 32337502
Level of Evidence: 4 - Observational study
Type of Article: Preliminary report
Summary: This observational study of 10,211 residents in Hong Kong found that 94.8% of participants wore masks in public with 13% of individuals incorrectly wearing masks. Another study currently in progress "explor[ing] local citizens' views on wearing face masks" found that 94.1% of them "believed mass masking reduces the chance of infection and community outbreak" and 76.3% of participants reused their masks. The authors recommend that infection control experts should "formulate rational guidelines and devise methods for safe handling and storage of face masks for reuse" and that community-wide mass masking is an effective transmission control measure.

Does a Crying Child Enhance the Risk for COVID-19 Transmission?
Sivabalan S, Srinath MV.
Indian Pediatr
2020 Apr 26, PMID: 32336688
Level of Evidence: Article is not able to be accessed to be verified.
Type of Article: Article is not able to be accessed to be verified.
Summary: Article is not able to be accessed to be verified.

Prevention in the Hospital

Reply to: Personal Protective Equipment Recommendations Based on COVID-19 Route of Transmission.
Cavanagh G, Wambier C.Cavanagh G, et al.
J Am Acad Dermatol.
2020 Apr 25; PMID: 32344068
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary: In response to current research, more specifically regarding handwashing, the authors agree that alcohol sanitizers are safe, practical, and potentially more effective in neutralizing COVID-19. However, hexachlorophene and nitazoxanide, moreover, because open wound transmission could still be a risk as plasma shedding has been observed, caution should be used with hand washing.

Early diagnosis and rapid isolation: response to COVID-19 outbreak in Korea.
Peck KR.Peck KR.
Clin Microbiol Infect.
2020 Apr 25; PMID: 32344168
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence
BLUF: The author discusses what he believes are key factors (summarized below) in reducing COVID-19 incidence in Korea from a peak of 813 cases on 2/29/2020 to less than 100 cases by 3/15/2020.

Summary: The author discusses Korea's response to COVID-19, highlighting the factors he believes were most important in 'overcoming' the COVID-19 pandemic.

1. **"…rapid diagnosis and rapid isolation is the key for prevention of transmission."** The Korea CDC partnered with commercial companies to make a RT-PCR assay for SARS-CoV-2 widely available. By early March, Korea was running upto 20,000 tests/day and had run 433, 211 by 4/3/2020.
2. **"…patient triage and prioritization of medical resources are essential for the preparation of surge**[sic]**…facilities [were prepared] for patients with variable severity."** Additionally, known contacts were tested and triaged immediately to either hospital care or quarantine at "isolation-and-care facilities" to prevent transmission to household contacts.
3. **"…[a] contingency plan should be prepared to enhance the capacity for critical care."** Korea mobilized additional health care workers including volunteer nurses and doctors, military personnel, and EMT/EMS. Wards and whole hospitals were dedicated solely to COVID-19 care and patients were transferred out of the outbreak epicenter when needed.
4. **Continuous communication between health and local authorities** was essential

Management of healthcare areas for the prevention of COVID-19 emergency in an Italian teaching hospital (Pisa, Tuscany): A hospital renovation plan.
Baggiani A, Briani S, Luchini G, Giraldi M, Martino MC, Porretta A, Totaro M, Privitera G
Infect Control Hosp Epidemiol
2020 Apr 27; PMID: 32336306
Level of Evidence: 5- Expert opinion
Type or Article: Letter
Summary: A description of the renovations and structural changes made in a hospital in Pisa, Italy in an effort to curb COVID-19 spread.

- Physical division into COVID and non-COVID zones
- Recruitment of extra beds from old hospitals and cancelled procedures
- Workers did not move between zones
- Differential PPE use depending on zone
- Negative pressure and HEPA15 filtration systems installed in COVID-19 ICU rooms

Management

Acute care

Emergency Medicine

Asymptomatic COVID-19 infection in a patient evaluated for ureteric colic: Radiological findings and impact on management.

Pang KH, Osman NI.

Urology.

2020 Apr 24; PMID: 32339558

Level of Evidence: 4 – Case Study

Type of Article: Letter to the Editor

Summary: The authors present the case of a 31 year-old female who presented with isolated flank pain and was assessed as a non-suspected COVID-19 case given the lack of respiratory symptoms and fever. CT revealed a distal right ureteral stone causing hydronephrosis, as well as incidental findings of multifocal ground glass opacities at the base of the right lung. Subsequent nasopharyngeal swab test was positive for COVID-19. This case highlights the need for timely recognition of asymptomatic COVID-19 patients presenting with other pathology, so that surgical and aesthetic approaches can be modified to mitigate risk to patients and the healthcare team.

Pharmacotherapy in COVID-19; A narrative review for emergency providers.

Mehta N, Mazer-Amirshahi M, Alkindi N, Ali Pourmand.Mehta N

Am J Emerg Med

2020 Apr 15; PMID:32336586

Level of Evidence: 5 - Literature Review

Type of Article: Research

BLUF: Though there are no proven therapies to treat COVID-19 infection, several drugs have been recognized at potential treatments and are included in the following recommendations:

- Hydroxychloroquine and azithromycin are recommended in patients with moderate severity disease.
- Remdesivir and convalescent plasma may be used in critical patients with respiratory failure .
- IL-6 antagonists may be used in patients exhibiting cytokine storm
- Corticosteroids should be avoided except in situations where they are strongly indicated such as refractory septic shock or acute respiratory distress syndrome.
- ACE inhibitors and ARBs should **not** be discontinued at this time.
- Ibuprofen may be used for fever.

Abstract:

Introduction: The COVID-19 pandemic has been particularly challenging due to a lack of established therapies and treatment guidelines. With the rapid transmission of disease, even the off-label use of available therapies has been impeded by limited availability. Several antivirals, antimalarials, and biologics are being considered for treatment at this time. **The purpose of this literature review is to synthesize the available information regarding treatment options** for COVID-19 and serve as a resource for health care professionals.

Objectives: This narrative review was conducted to summarize the effectiveness of current therapy options for COVID-19 and address the controversial use of **non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs)**. PubMed and SCOPUS were queried using a combination of the keywords "COVID 19," "SARS-CoV-2," and "treatment." All types of studies were evaluated including systematic reviews, case-studies, and clinical guidelines.

Discussion: There are currently no therapeutic drugs available that are directly active against SARS-CoV-2; however, several antivirals (remdesivir, favipiravir) and antimalarials (chloroquine, hydroxychloroquine) have emerged as potential therapies**. Current guidelines recommend combination treatment with hydroxychloroquine/azithromycin or chloroquine**, if hydroxychloroquine is unavailable, in patients with moderate disease, although these recommendations are based on limited evidence. **Remdesivir and convalescent plasma may be considered in critical patients with respiratory failur**e; however, access to these therapies may be limited. I**nterleukin-6 (IL-6) antagonists may be used in patients who develop evidence of cytokine release syndrome** (CRS). **Corticosteroids** should be avoided unless there is evidence of **refractory septic shock**, acute respiratory distress syndrome (**ARDS**), or another compelling indication for their use. **ACE inhibitors and ARBs should not be discontinued at this time and ibuprofen may be used for fever.**

Conclusion: There are several ongoing clinical trials that are testing the efficacy of single and combination treatments with the drugs mentioned in this review and new agents are under development. Until the results of these trials become available, we must use the best available evidence for the prevention and treatment of COVID-19. Additionally, we can learn from the experiences of healthcare providers around the world to combat this pandemic.

Table 2
Pharmacologic therapies considered for treatment of COVID-19.

	Mechanism of action	Adverse effects	Current recommendations
Antivirals			
Remdesivir	Nucleotide analog that is incorporated into the viral RNA chain and results in premature chain termination [4]	- Gastrointestinal distress - Elevated transaminases - Infusion site reactions	Consider for patients with severe disease and respiratory failure [8].
Favipiravir	Nucleoside analog which inhibits viral RNA polymerase [1]	- Abnormal transaminases - Psychiatric symptoms - Gastrointestinal discomfort - Elevated serum uric acid [11]	Not recommended at this time [8].
Ribavirin	Guanosine analog that interferes with viral replication [1]	- Hemolytic anemia	Not recommended at this time [8].
Lopinavir/ritonavir	Protease inhibitors that prevent the production of active viral peptides [1]	- Gastrointestinal distress - QT prolongation - Drug-drug interactions (ritonavir)	Not recommended at this time [19].
Antimalarials			
Chloroquine	Elevates endosomal pH and inhibits pH dependent steps in the viral replication process [21]	- Electrolyte imbalance - Fatal dysrhythmias (Torsades de Pointes)	May be used as an alternative when hydroxychloroquine is unavailable.
Hydroxychloroquine	Elevates endosomal pH and inhibits pH dependent steps in the viral replication process [21]	- Electrolyte imbalance - Fatal dysrhythmias (Torsades de Pointes)	Combination treatment with azithromycin recommended for patients with moderate to severe disease [20,25].
CorticosteroidsCorticosteroids			
Corticosteroids	Binds to cytoplasmic receptors to change the transcription of mRNA and reduce production of inflammatory mediators	- Avascular necrosis - Psychosis - Hyperglycemia - Adrenal suppression	Only indicated for patients with refractory septic shock or severe ARDS. Not recommended for routine use [19,20].
Biologics			
Tocilizumab Sarilumab	Monoclonal antibody against the IL-6 receptor	- Abnormal transaminases - GI perforation - Neutropenia - Infusion reactions	May be considered in patients with evidence of CRS and worsening respiratory function [8].
Convalescent plasma	Passive immunization using plasma from recovered patients	- Hypersensitivity reactions - Serum sickness	Recommendations are controversial. May be considered in patients with worsening clinical conditions refractory to other treatment [14].
NSAIDS			
Ibuprofen	Block COX 1 and 2, inhibiting production of prostaglandins	- Gastrointestinal ulcers/bleeding - May upregulate ACE2	No evidence to support that its use is contraindicated. May be used for its anti-inflammatory and anti-pyretic effects [39].
Indomethacin	Block COX 1 and 2, inhibiting production of prostaglandins	- Gastrointestinal ulcers/bleeding - May upregulate ACE2	No evidence of its antiviral effects against SARS-CoV-2 in humans [40]. May be used for its anti-inflammatory and anti-pyretic effects.
RAAS antagonists			
ACE Inhibitors	Inhibits conversion of angiotensin I to angiotensin II	- Cough - Upregulation of ACE2 (may increase risk for severe COVID-19)	These medications should not be routinely discontinued. Consider clinical condition of individual patients before changing anti-hypertensive treatment regimens [41].
ARBs	Prevents angiotensin II from binding to its receptor	- Cough - Upregulation of ACE2 (may increase risk for severe COVID-19)	

Diagnostic radiology

Contrast enhanced ultrasonography (CEUS) to detect abdominal microcirculatory disorders in severe cases of COVID-19 infection: First experience.

Jung EM, Stroszczynski C, Jung F.
Clin Hemorheol Microcirc.
2020 Apr 23, PMID: 32333581
Level of Evidence: 4- Case series
Article Type: Research

BLUF: Authors conducted (contrast enhanced sonography) CEUS abdominal examinations on five male patients with severe COVID-19 cases and early abdominal microvascular disorders and determined it to be an effective bedside instrument to quickly rule out organ infarction in COVID-19 patients. However, set-up takes up to 60 minutes and requires an experienced examiner.

Abstract:
In the hands of experienced examiners, the contrast enhanced sonography (CEUS) offers the possibility to analyze dynamic microcirculatory disturbances in real time dynamically without any risk for kidneys and thyroid gland even in severe progressing disease bedside. Based on severe COVID-19 infections, first experiences with abdominal CEUS examinations are presented. In the stage of an imminent organ failure with significantly reduced kidney and liver function, **CEUS can be used to show a narrowing of the organ-supplying arteries,** as well as a delayed capillary filling of vessels near the capsule, a regional reduced parenchymal perfusion or an inflammatory hyperemia with capillary hypercirculation. **It is possible to quickly rule out organ infarction** and to dynamically record the mesenteric arterial and venous blood flow.

Sedating ventilated COVID-19 patients with inhalational anesthetic drugs.

Orser BA, Wang DS, Lu WY.Orser BA, et al.
EBioMedicine.
2020 Apr 21; PMID: 32344199
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

Summary: Inhalational anesthetics should be considered for COVID-19 patients requiring ventilation. These include isoflurane and sevoflurane. Inhaled anesthetics enable for close and reversible sedation control. They are widely available, not cost-prohibitive and may decrease pulmonary

inflammation leading to improved oxygen delivery and likely a decrease in mortality. With many operating rooms empty due to surgery restrictions, gas delivery systems may be more widely available in critical care units than before, mitigating any drug delivery system concerns for feasibility. The authors recommend consulting trained anesthesiologists before starting this regimen.

Critical Care

Respiratory conditions in coronavirus disease 2019 (COVID-19): Important considerations regarding novel treatment strategies to reduce mortality.

Geier MR, Geier DA
Med Hypotheses
2020 Apr 22; PMID: 32344310
Level of Evidence: 5 - Expert Opinion
Type of Article: Research

BLUF: The current management of acute respiratory distress syndrome (ARDS) caused by COVID-19 is to increase respiratory and ventilator support; however, current standard treatments are associated with high mortality rates. As a result, alternative treatment strategies are being recommended to increase oxygenation of tissues: hyperbaric oxygen therapy (HBOT), packed red blood cell (pRBC) transfusions, or erythropoiesis-stimulating agent (ESA) therapy.

Abstract:
A novel virus named 2019 novel coronavirus (2019-nCoV/SARS-CoV-2) causes symptoms that are classified as coronavirus disease (COVID-19). Respiratory conditions are extensively described among more serious cases of COVID-19, and the onset of acute respiratory distress syndrome (ARDS) is one of the hallmark features of critical COVID-19 cases. ARDS can be directly life-threatening because it is associated with low blood oxygenation levels and can result in organ failure. There are no generally recognized effective treatments for COVID-19, but treatments are urgently needed. Anti-viral medications and vaccines are in the early developmental stages and may take many months or even years to fully develop. **At present, management of COVID-19 with respiratory and ventilator support are standard therapeutic treatments, but unfortunately such treatments are associated with high mortality rates.** Therefore, it is imperative to consider novel new therapeutic interventions to treat/ameliorate respiratory conditions associated with COVID-19. Alternate treatment strategies utilizing clinically available treatments such as **hyperbaric oxygen therapy (HBOT), packed red blood cell (pRBC) transfusions, or erthropoiesis-stimulating agent (ESA) therapy were hypothesized to increase oxygenation of tissues by alternative means** than standard respiratory and ventilator treatments. It was also revealed that alternative treatments currently being considered for COVID-19 such as **chloroquine and hydroxychloroquine by increasing hemoglobin production and increasing hemoglobin availability for oxygen binding** and acetazolamine (for the treatment of altitude sickness) by causing hyperventilation with associated increasing levels of oxygen and decreasing levels of carbon dioxide in the blood may significantly ameliorate COVID-19 respiratory symptoms. **In conclusion, is recommend, given HBOT, pRBC, and ESA therapies are currently available and routinely utilized in the treatment of other conditions, that such therapies be tried among COVID-19 patients with serious respiratory conditions and that future controlled-clinical trials explore the potential usefulness of such treatments among COVID-19 patients with respiratory conditions.**

SARS-CoV-2 (COVID-19) and intravascular volume management strategies in the critically ill.

Kazory A, Ronco C, McCullough PA.Kazory A, et al.
Proc (Bayl Univ Med Cent).
2020 Apr 16; PMID: 32336959
Level of Evidence: 5 – Expert Opinion
Article Type: Editorial

Summary: COVID-19 causes critical illness, and the authors note a paradigm of assumed hypo-perfusion and microcirculatory dysfunction that could drive treatment of critical COVID-19 towards over-resuscitation. It is noted that aggressive resuscitation to maintain atrial preload can contribute to pulmonary edema and even ARDS, and that it is possible to monitor for or prevent AKI even with a restrictive fluid strategy. They comment on the value of timing fluid resuscitation with stages of shock, and on active fluid removal.

Summary Statement: "Constantly reminding ourselves of the currently available evidence on fluid resuscitation strategies, and judiciously applying those principles to the specific features of this disease as we learn them (e.g., high percentage of heart failure, volume overload, and circulatory failure), is likely to help optimize the care of these patients."

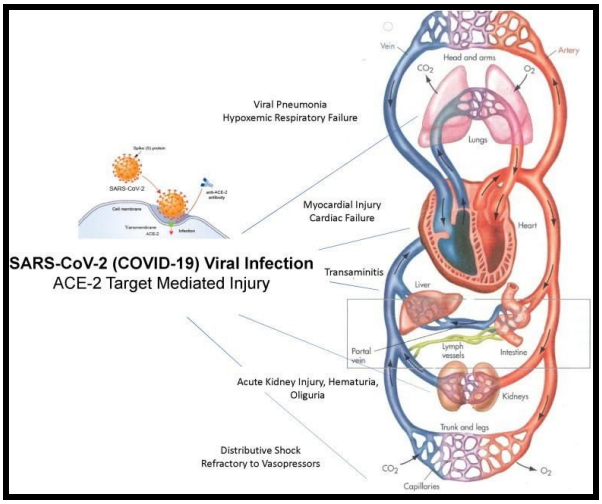

Figure 1. SARS-CoV-2 (COVID-19)–mediated organ injury in critically ill patients mediated by viral entry and target mediated destruction of the angiotensin converting enzyme II (ACE-2) receptor enzyme.

Optimizing provision of extracorporeal life support during the COVID-19 pandemic: practical considerations for Canadian jurisdictions.
Parhar KKS, Lequier L, Blackwood J, Murthy DJZ, Singh G.Parhar KKS, et al.
CMAJ
2020 Mar 26; PMID: 32336679
Level of Evidence: 5 – Expert Opinion
Article Type: Editorial
Summary: To maximize extracorporeal membrane oxygenation/life support (ECMO/ECLS) in the COVID-19 pandemic, authors recommend a consultant on call 24/7, presence of pre-established referral criteria, and a tracking system to determine resource availability (they use a green-yellow-red board corresponding to maximum availability, limited resources requiring rationing, and critically low supplies likely to limit cardiac surgery and critical care). To maximize benefit for resources, authors also recommend deciding on and following "entry" and "exit" criteria for these limited resources.
"**KEY POINTS**

- COVID-19 pandemic preparation requires a multidisciplinary, stakeholder-guided approach, given that about 14% of people with COVID-19 develop severe disease, which may include acute respiratory distress syndrome.
- World Health Organization guidelines suggest that patients with COVID-19 with refractory hypoxemia despite lung protective ventilation be considered for extracorporeal life support (ECLS), which is a scarce resource that may require rationing in a pandemic situation.
- An accurate and easily understood strategy to communicate ECLS capacity is essential; in Alberta, we have developed a red-yellow-green dashboard to indicate capacity and readiness.
- For large geographic areas, as in many of Canada's provinces and territories, clearly delineating the referral process for each feeder centre is important, and adult and pediatric ECLS centres may need to support one another.
- In the case of an overwhelming demand for critical care resources, ECLS services would need to be suspended in order to redirect all available critical care resources according to need."

Medical subspecialties

What do monitoring platelet counts in COVID-19 teach us?
Thachil J
J Thromb Haemost.
2020 Apr 28.PMID: 32344467
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
BLUF: Thrombocytopenia (in the range of 43 – 129 x 109/L) has been shown to be associated with greater mortality in COVID-19 patients. It is hypothesized that platelets are being consumed to form microthrombi. Patients recovering from COVID-19 are observed to have an increase in platelet count, which further highlights the utility of monitoring platelet count to track disease progression.

Abstract:
Yang and colleagues published the relevance of thrombocytopenia in COVID-19 patients and its association with mortality in this condition in the Journal of Thrombosis and Haemostasis. The authors are to be applauded for the largest so-far analysis in the epidemiology of thrombocytopenia in patients with COVID-19. In addition to the association with mortality, there may be several other findings in this interesting paper which deserves mention. First of all, the study confirms that COVID-19 is not associated with significant thrombocytopenia (only 20.7% had counts less than 125 x 109/L, the lower range in this study). The 'higher' platelet counts for an illness as severe as COVID-19 is unusual and likely points towards liver activation and thrombopoietin release.

Debate on Drugs That May Aggravate COVID-19.
Giavina-Bianchi P, Aun MV, Agondi RC, Kalil J.
J Allergy Clin Immunol Pract.
2020 Apr 25; PMID: 32344190
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter to the Editor
Summary: The withdrawal of ACE inhibitors may contribute to aggravation of cardiomyopathy, hypertension and diabetes, which are well-recognized risk factors for worse outcome of COVID-19. "At present, there is no evidence to generate even a weak recommendation to discontinue these medications during the pandemic. Patients' care must be personalized, and ACE inhibitors and/or NSAIDs may be used if indicated, after weighing the benefits and risks."

Generating Randomized Trial Evidence to Optimize Treatment in the COVID-19 Pandemic
Cheng, M; Lee, TCL; Tan, DHS; Murthy, S
CMAJ
2020 Apr 14; PMID: 32336678
Level of evidence: 5 - Expert Opinion
Type of Article: Comment
Summarizing Excerpt: "In the COVID-19 pandemic, experimental medications that are not currently approved for any indication in any country have already been widely used outside of clinical trial protocols. **But there is a strong ethical and clinical argument for replacing such "random" care with randomized care, in which patients are routinely randomly assigned to the most promising available option(s) or to control arm(s), so that evidence regarding the safest, most effective therapies may be generated in the shortest possible time.** This means that although earlier patients may receive our best-guess treatments, subsequent patients can receive evidence-based therapies and be spared from harm."

Dermatology
Calm before the storm: understanding the role of JAK inhibitors in COVID-19.
Peterson D, Damsky W, King B.

J Am Acad Dermatol.
2020 Apr 25; PMID: 32344070
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
Summarizing excerpt: "In summary, we believe there is insufficient evidence to recommend that JAK inhibitors be continued in all patients taking these medications who are acutely infected with SARS-CoV-2. While JAK inhibitors may prove useful in the treatment of SARS-CoV-2-associated [cytokine release syndrome], this is a separate consideration of a relatively uncommon manifestation of this viral infection that occurs late in disease course. "

Hematology and Oncology
Thrombosis management in times of COVID-19 epidemy; a Dutch perspective.
Ten Cate H
Thromb J
2020 Apr 20; PMID: 32336956
Level of Evidence: Level 5 - Expert opinion
Type of Article: Editorial
BLUF: The current triage process during the COVID-19 epidemic leaves room for pulmonary emboli to go undiagnosed, especially since D-dimer levels can be elevated in patients with COVID-19. In all patients taking Vitamin K Antagonists, switching to direct oral anticoagulants (DOAC) may be prudent to avoid the excessive contact necessary to monitor PT/INR.

DIC in COVID-19: Implications for Prognosis and Treatment?
Seitz R, Schramm W
J Thromb Haemost
2020 Apr 28; PMID: 32344469
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary
Disseminated intravascular coagulation (DIC) is frequent in COVID-19 patients with serious respiratory failure, particularly in non-survivors (71.4 %) versus survivors (0.6%). It is possible that DIC also contributes to circulatory and organ failure in COVID-19 patients, particularly pulmonary damage in cases with acute respiratory distress syndrome (ARDS). The authors suggest that establishing the diagnosis of DIC might be a useful prognostic parameter, and encourage research into the pathophysiology and clinical impact of DIC in severe COVID-19.
Oncology
COVID-19 in lung cancer patients receiving ALK/ROS1 inhibitors.
Leonetti A, Facchinetti F, Zielli T, Brianti E, Tiseo M.
Eur J Cancer.
2020 Apr 23; PMID: 32344292
Level of Evidence: 4 – Case Series
Type of Article: Letter to the Editor
Summary: The authors present two cases that suggest tyrosine-kinase inhibitors (TKI) may be maintained during COVID-19 pneumonia, especially when not severe, in patients with oncogene-driven non-small cell lung cancer (NSCLC) in order to avoid potentially dangerous withdrawal of effective anticancer drugs (see figures below). The decision to maintain TKI therapy was made because the severity of COVID-19 in both cases was mild. Large scale studies are urgently needed to further inform this decision.

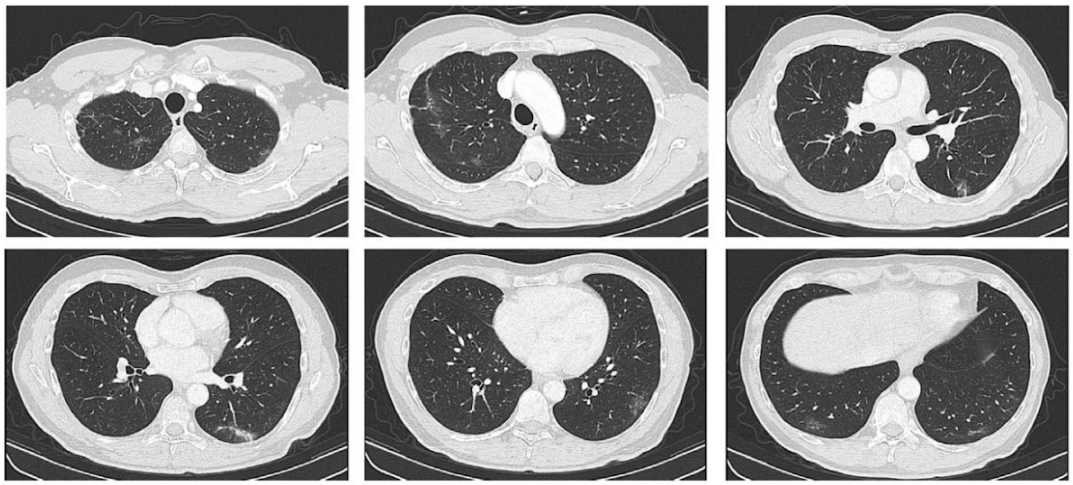

Fig. 1. CT scan of Case 1 (alectinib for *ALK*-positive NSCLC) showed the onset of multiple bilateral subpleuric ground glass opacities in upper and lower lobes, suspicious for SARS-CoV-2 pneumonia.

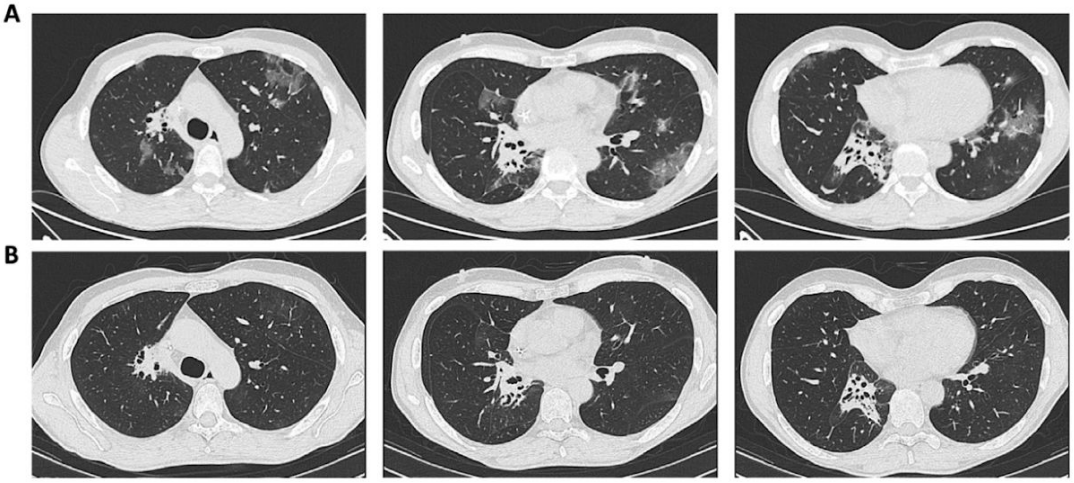

Fig. 2. **A**) CT scan of Case 2 (lorlatinib for *ROS1*-positive NSCLC) performed on March 12th documented multiple bilateral subpleuric ground-glass opacities in a crazy paving pattern, highly suggestive for SARS-CoV-2 pneumonia; **B**) CT scan after recovery of symptoms (April 9th) showed complete resolution of interstitial pneumonia.

Surgical Subspecialties

General Surgery

Covid-19 patients and surgery: Guidelines and checklist proposal.

Grelat M, Pommier B, Portet S, Amelot A, Barrey C, Leroy HA, Madkouri R.
World Neurosurg.
2020 Apr 25; PMID: 32344143
Level of Evidence: 5 – Expert Opinion
Type of Article: Recommendations

Summary: The authors offer recommendations to help professionals in the establishment of protocols for the management of patients with COVID-19, as well as offer a checklist that can be used in the operating room (see figure below).

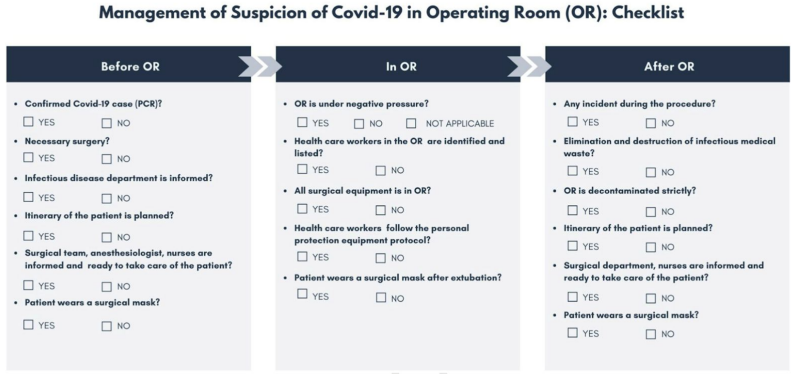

Figure 3. Management of suspicion of coronavirus 2019 (COVID-19) in the operating room: safety checklist of mandatory points to limit the surgical staff exposure and the spread of the disease.

Neurosurgery

Lessons from China when Performing Neurosurgical Procedures During the COVID-19 Pandemic.

Wen J, Qi X, Lyon KA, Liang B, Wang X, Feng D, Huang JH.
World Neurosurg.
2020 Apr 25; PMID: 32344132
Level of Evidence: 4 – Case Study
Type of Article: Letter

Summary: The authors share the case of a patient who presented to a hospital in Guangzhou with headache followed by loss of consciousness. Head CT revealed subarachnoid hemorrhage and left frontal lobe hematoma. A suspected COVID-19 diagnosis was made given recent travel history and fever. The patient underwent surgical repair and the nasopharyngeal test for COVID-19 returned to be negative. The patient was discharged home on post-op day 14 with intact neurological function. This case demonstrates that emergent neurosurgical procedures can be safely performed for critical patients with appropriate precautions during the COVID-19 pandemic.

Adjusting Practice During COVID-19

Acute care

Diagnostic radiology

Radiology department strategies to protect radiologic technologists against COVID19: Experience from Wuhan.

Zhao Y, Xiang C, Wang S, Peng C, Zou Q, Hu J.
Eur J Radiol
2020 Apr 20; PMID: 32344294
Level of Evidence: 5 - Expert Opinion
Type of Article: Review

BLUF: This article details the strategies used in Tongji hospital in Wuhan, P.R. China to protect radiologic technologists from COVID-19. These strategies include:

- Personnel education, health monitoring, and surge scheduling
- PPE protocols requiring each radiology technician to wear a cap, surgical mask, respirator, protective glass, isolation gown, gloves, shoe covers, and disposable gown with operators performing mobile scans also requiring a face shield.
- Designating a CT scanner and hallways leading to and from the scanner specifically for COVID-19 positive patients.
- Protocols to perform CT scans without the technician entering the scanner room with the patient.
- Specific protocols for donning and doffing PPE
- Disinfection through air filters, alcohol wipes, and UV lamps.

Abstract:
The outbreak of Coronavirus Disease 2019 (COVID-19) is a huge threat to global public health security. In the absence of specific antiviral medicines to prevent or treat COVID-19, it is essential to detect the infected patients at an early stage and immediately isolate them from the healthy population. In view of the advantages of sensitivity and high spatial resolution, CT imaging has played an important role in screening and diagnosing of COVID-19 in China. The radiologic technologists performing CT scans for the infected patients become high-risk medical care personnel. It is critical for the radiology department to ensure the personal safety of radiologic technologists and avoid cross-infection. **In this review article, we describe the systematic strategies to combat COVID-19 from the radiology department in Tongji hospital in Wuhan, P.R. China, including personnel arrangements, environmental modification, protection levels and configurations, radiological imaging (CT and radiography), and disinfection methods.** It can provide guidance to other radiology departments faced with COVID-19 to reduce infection risk for radiologic technologists.

Anaesthesia

Neuraxial anaesthesia and peripheral nerve blocks during the COVID-19 pandemic: a literature review and practice recommendations

Uppal, V; Sondekoppam, RV; Landau, R; El-Boghdadly, K; Narouze, S; Kalagara, HKP
Anaesthesia
2020 Apr 28; PMID: 32344456
Level of Evidence: 5 - Expert Opinion
Type of Article: Guidelines

BLUF: Authors review current literature and provide anesthesia recommendations, such as increased usage of regional anesthesia more to reduce the need to perform intubations or tracheostomies. Other recommendations below:

- Neuraxial anesthesia and peripheral nerve blocks as first line for COVID-19 patients when possible
- Reduce overall surgical volume so institutions can plan for a surge and stock up on personal protective equipment (PPE)
- Consider possibly performing entire surgeries under regional anesthesia
- Screen all surgical patients for COVID-19, presume positive if no testing is available
- Use operating rooms or other negative pressure rooms when possible
- For PPE: when performing regional anesthesia, use droplet precautions at a minimum
- For patient oxygen needs, use masks whenever possible.

Abstract:
Coronavirus disease 2019 (COVID-19) has had a significant impact on global healthcare services. In an attempt to limit the spread of infection and to preserve healthcare resources, one commonly used strategy has been to postpone elective surgery, whilst maintaining the provision of anaesthetic care for urgent and emergency surgery. General anaesthesia with airway intervention leads to aerosol generation, which increases the risk of COVID-19 contamination in operating rooms and significantly exposes the healthcare teams to COVID-19 infection during both tracheal intubation and extubation. Therefore, the provision of regional anaesthesia may be key during this pandemic, as it may reduce the need for general anaesthesia and the associated risk from aerosol-generating procedures. **However, guidelines on the safe performance of regional anaesthesia in light of the COVID-19 pandemic are limited. The goal of this review is to provide up-to-date, evidence-based recommendations, or expert opinion when evidence is limited, for performing regional anaesthesia procedures in patients with suspected or confirmed COVID-19 infection.** These recommendations focus on seven specific domains including: (1) planning of resources and staffing; (2) modifying the clinical environment; (3) preparing equipment, supplies and drugs; (4) selecting appropriate personal protective equipment; (5) providing adequate oxygen therapy; (6) assessing for and safely performing regional anaesthesia procedures; and (7) monitoring during the conduct of anaesthesia and post-anaesthetic care. Implicit in these recommendations is preserving patient safety whilst protecting healthcare providers from possible exposure.

Critical Care

Contingency plan for the intensive care services for the COVID-19 pandemic.

Authors: Rascado S, Ballesteros M, Bodí S, Carrasco Rodríguez-Rey L, Castellanos O, Catalán González M, López C, Díaz Santos E, Escriba Barcena A, et al.
Med Intensiva.
2020 Apr 23; PMID: 32336551
Level of Evidence: 5 - Expert Opinion
Type of Article: Guidelines

BLUF: Two major societies of critical care medicine in Spain provide a "contingency plan" as a tool to use the lessons learned from the COVID-19 crisis in Spain to provide strategies for preparing and responding to COVID-19 surges and minimize the overwhelming of resources in intensive care units. These include:

- Phases of response and recommended actions for each stage
- Expansion plans
- Human and technical support (communication and follow-up with patients/family)
- Optimizing resources (Personal Protective Equipment (PPE), respiratory support devices, staff workforce)
- Clinical indications for ICU admission (Table 1)

Abstract:
In January 2020, the Chinese authorities identified a new virus of the Coronaviridae family as the cause of several cases of pneumonia of unknown aetiology. The outbreak was initially confined to Wuhan City, but then spread outside Chinese borders. On 31 January 2020, the first case was declared in Spain. On 11 March 2020, The World Health Organization (WHO) declared the coronavirus outbreak a pandemic. On 16 March 2020, there were 139 countries affected. In this situation, the Scientific Societies SEMICYUC and SEEIUC have decided to draw up this Contingency Plan to guide the response of the Intensive Care Services. The objectives of this plan are to estimate the magnitude of the problem and **identify the necessary human and material resources**. This is to provide the Spanish Intensive Medicine Services with a **tool to programme optimal response strategies.**

Table 1

Major and minor criteria for admission to the intensive care unit (ICU)

Major criteria
Septic shock with the need for vasoactive amines
Respiratory failure requiring mechanical ventilation
Minor criteria
Respiratory rate> 30 rpm with conventional oxygen therapy
PaO_2 / FiO_2 <250 with conventional oxygen therapy
Bilateral infiltrates
Altered level of consciousness
Elevation of urea (> 20 mg / dl)
Leukocytopenia (<4,000 cells / ml) and lymphocytopenia
Thrombocytopenia (<100,000 / ml)
Hypothermia (<36 ° C)
Hypotension requiring aggressive resuscitation with
D-Dimer fluids > 1 µg / l

Cardiology

COVID-19: A Time for Alternate Models in Cardiac Rehabilitation to Take Center Stage

Babu, A. S., Arena, R., Ozemek, C., & Lavie, C. J.
Can J Cardiol
2020 Apr 25; PMID: 32344000
Level of Evidence: 5 – Expert Opinion
Type of Article: Editorial

Summary: The authors believe that the traditional cardiac rehabilitation model should be replaced by a technology-based rehabilitation model during the COVID-19 pandemic. This new model would include the utilization of smartphones, mobile apps, internet, messaging, websites, and the use of wearable sensors. This would help to increase accessibility for patients with cardiovascular disease (CVD) so that they can continue to get the benefits from this program.

Hematology and Oncology

Practice considerations for proton beam radiotherapy of uveal melanoma during the COVID-19 pandemic: PTCOG Ocular experience.

Mishra KK, Afshar A, Thariat J, Shih HA, Scholey JE, Daftari IK, Kacperek A, Pica A, Hrbacek J, Dendale R, Mazal A, Heufelder J, Char DH, Sauerwein W, Weber DC, Damato BE.
Adv Radiat Oncol.
2020 Apr 23; PMID: 32337386
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

BLUF: In light of the COVID-19 pandemic, practice considerations for proton beam radiotherapy include applying infection precautions, clean immobilization head mask and frame thoroughly, limit physical aperture adjustments, and organizing clinical flow.

Abstract:
"Uveal melanoma (UM) is a rare but life-threatening cancer of the eye. In light of the COVID-19 pandemic, hospitals and proton eye therapy facilities must analyze several factors to ensure appropriate treatment protocols for patients and provider teams. Practice considerations to limit COVID-19 transmission in the proton ocular treatment setting for UM are necessary. The Particle Therapy Co-Operative Group (PTCOG) is the largest international community of particle/proton therapy providers. Participating experts are/were affiliated with the member institutions of the PTCOG Ocular subcommittee with long-standing high-volume proton ocular programs. The practices reviewed in this document must be taken in conjunction with local hospital procedures, multidisciplinary recommendations, and regional/national guidelines, as each community may have its unique needs, supplies, and protocols. Importantly, as the pandemic evolves, so will the strategies and recommendations. Given the unique circumstances for UM patients, along with indications of potential ophthalmologic transmission as a result of healthcare providers working in close proximity to patients and intrinsic

infectious risk from eyelashes, tears and hair, practice strategies may be adapted to reduce the risk of viral transmission. Certainly, providers and health care systems will continue to examine and provide as safe and effective care as possible for patients in the current environment"

Coronavirus outbreak: Reorganising the breast unit during a pandemic.
Joseph AO, Joseph JP, Pereira B, Gahir J.
Eur J Surg Oncol.
2020 Apr 21; PMID: 32336625
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summarizing excerpt: "For our breast surgery unit in a district general hospital [the COVID-19 pnademic] has led to multiple changes to our work practices. These include physical re-organisation of the breast consultations spaces; changes to staffing; stricter criteria for one stop clinic referrals; embracing telemedicine for routine follow-up; identifying essential imaging; virtual MDTs; a straight-to-surgery policy inoperable tumours; and creation of a "clean" hospital site for breast cancer surgery. Time will tell which of these changes are here to stay."

Nephrology
Peritoneal Dialysis During the Coronavirus 2019 (COVID-19) Pandemic: Acute Inpatient and Maintenance Outpatient Experiences.
El Shamy O, Sharma S, Winston J, Uribarri J.
Kidney Med.
2020 Apr 23; PMID: 32337505
Level of Evidence: 5 –Review
Type of Article: Editorial
BLUF: This editorial highlights experiences of caring for hemodialysis patients during the COVID-19 crisis in the outpatient setting. Additionally, the authors review procedures to use acute peritoneal dialysis to combat the inexorable rise in the number of admitted patients requiring kidney replacement therapy (KRT) in the inpatient setting. The primary focus was to transition hospitalized patients with new dialysis needs to peritoneal dialysis. View decision tree below.

Summarizing Excerpt: "The COVID-19 pandemic has presented healthcare professionals with extraordinary challenges. As of April 13, 2020, there are ~555,000 confirmed cases in the United States and ~22,000 deaths; almost half of the deaths to date are in the state of New York. In New York City, with a population density of 26,430 people per square mile, the densest of any American municipality with a population above 100,000[1], social distancing may mitigate the strain on existing health care systems. Furthermore, the absence of widely available testing has resulted in additional use of already limited resources, including hospital beds, personal protective equipment and staff. As nephrologists, we see our primary goals as twofold: 1) keeping our existing patients safe both at home and in their dialysis units, and 2) meeting the needs of patients who do require hospitalization, both COVID related and unrelated."

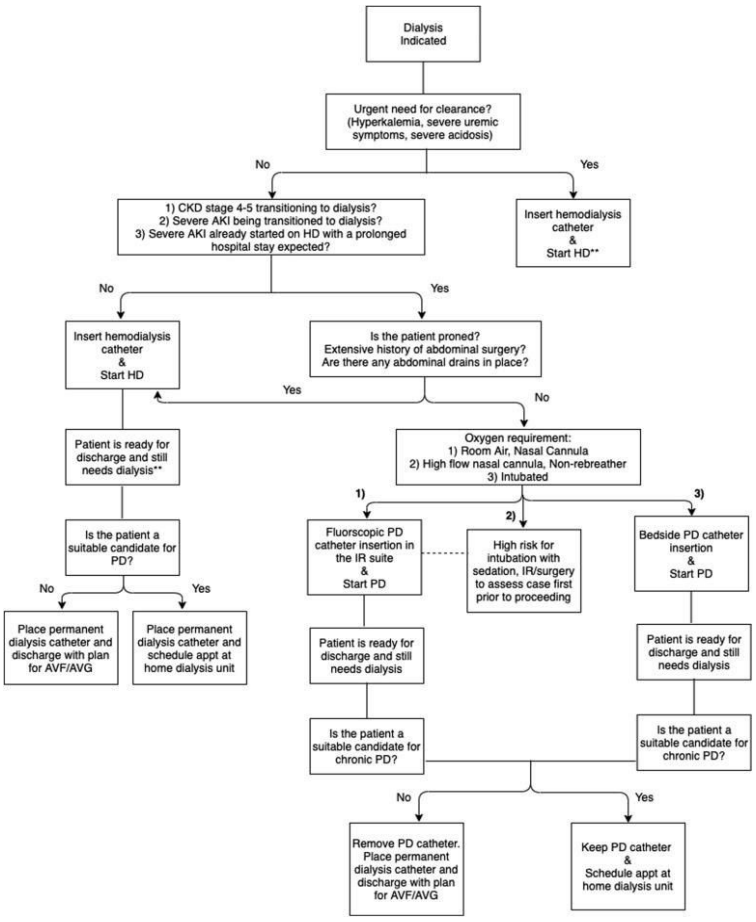

Figure 1. Dialysis Decision Tree

Surgical Subspecialties

Suggestions on surgical treatment during coronavirus disease 2019 (COVID-19) pandemic.

Zhao Z, Li M, Liu R
Biosci Trends
2020 Apr 27; PMID: 32336725
Level of Evidence: 5 - Expert Opinion
Type of Article: Communication

BLUF: Surgeons at a hospital in China created a list of suggestions on surgical issues during the COVID-19 pandemic, including:

- **Emergency surgery considerations:**
  - Screening of symptoms and exposure should be followed by nasopharyngeal swab testing.
  - For infected or suspected patients, the highest level of PPE should be implemented, a separate transport path should be pre-designated, and a dedicated negative-pressure operating room (OR) and experienced surgeons are recommended.
  - Application of laparoscopy and energy devices should be carefully evaluated for aerosolization risk, and traditional surgery may be replaced by alternative treatments such as percutaneous transhepatic-gallbladder drainage with postponed cholecystectomy for acute cholecystitis.
  - Caesarean section is recommended in infected pregnant women.
- **Elective surgery considerations:**
  - Elective surgery should be postponed for infected patients or non-infected patients with non-time-sensitive surgeries, and telemedicine is suggested for follow-up and assessment of benign diseases.
  - Surgery can be performed when a severe complication occurs due to malignant diseases, but extra caution should be taken with cancer patients and alternative therapies or surgical postponement may be recommended.
  - Robot-assisted surgery minimizes the number of exposed surgeons and staff.
- **Anesthesia considerations:**
  - Non-essential staff should not enter the OR during intubation and extubation.
  - Epidural anesthesia and local anesthesia may be recommended in place of general anesthesia.
- **Patient transport:**
  - A surgical mask is suggested for a non-intubated patient, a face mask over surgical mask is recommended for a non-intubated patient with an oxygen requirement, and a dedicated ventilator is recommended for an intubated patient.
  - Disinfection measures must be taken immediately if contamination occurs during transport.

ABSTRACT:
Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 virus, is now generating a global epidemic, leading to a severe public health emergency. Until April 12, 2020 around 1,700,954 confirmed cases and 105,633 deaths have been reported all over the world. The World Health Organization (WHO) has declared COVID-19 as a Public Health Emergency of International Concern. Under this circumstance, **surgical activities should be carefully evaluated to avoid excessive occupation of limited medical resources, and to reduce the possibility of hospital infection**. China has achieved an inspiring achievement on epidemic control. Here, we reviewed available studies on surgical activities during the outbreak, in combination with our current experience, with the **aim of providing feasible suggestions on surgical issues during the COVID-19 pandemic**.

Implications for the Use of Telehealth in Surgical Patients During the COVID-19 Pandemic

Hakim AA, Kellish AS, Atabek U, Spitz FR, Hong YK
Am J Surg
2020 Apr 21; PMID: 32336519
Level of Evidence: 5 – Expert Opinion
Type of Article: Editorial

BLUF: This editorial summarizes the function of **telemedicine in surgical specialties** during the **COVID-19 pandemic** in the United States. The authors conclude that telemedicine may play a valuable role during certain **preoperative evaluations, postoperative visits, and surgical consults** while still maintaining HIPAA compliance.

Abstract:
The COVID-19 pandemic has brought rapid changes to the way care must be delivered to keep patients and providers safe while simultaneously managing limited resources. **Multiple fields have used telemedicine** to continue care while maintaining social distancing and quarantine practices in the pandemic. Presented in this paper is a **review describing the application of telemedicine in caring for surgical patients**, and **methods for potential implications of telehealthcare for surgical patients during the COVID-19 pandemic**. A review of the PubMed Central and Medline provides articles examining the role of **telemedicine for preoperative, postoperative, and follow up evaluation of surgical patients encompassing the past two decades**. Additionally, articles examining the **financial and legal considerations of telemedicine, and the effect COVID-19 has had on the current legislature** were included. We report the summarized findings of these studies, the financial and HIPAA considerations of using telemedicine, potential benefits, pitfalls and strategies for the utilization of telemedicine into the clinical practice of general surgery and its subspecialties during the COVID-19 pandemic.

Vascular Surgery

Vascular Surgery in the COVID-19 Pandemic

Ünal EU, Mavioğlu HL, İscan HZ
J Vasc Surg
2020 Apr 25, PMID: 32344111
Level of Evidence: 5 – Expert opinion
Type of Article: Guidelines

Summary: The authors propose **vascular surgery guidelines in a Turkish "pandemic" hospital that services primarily COVID-19 patients**, with goals to reduce infectious risk while continuing to provide emergent care for vascular and endovascular procedures.

- **Shifts**
  - One vascular surgeon on duty at all times
  - Endovascular surgical team (two senior and four junior surgeons) on at all times for endovascular procedures
- **Deferred elective operations**

- **"Level of Priority" (LoP) classification** of cases which determines whether to defer a vascular surgical procedure (Table 1), with LoP I patients being subject to deferral
- **Additional PPE** for suspected/confirmed COVID-19 positive patient
    - Use of a face shield over goggles and mask
    - Surgical coat
    - Double gloves fixed with adhesive drapes to surgical coat

LoP I - Elective Surgery (routine admission for operation)
Aneurysmal vascular disease (AVD) • Unruptured and hemodynamically stable patients Peripheral arterial disease (PAD) • Patients with intermittent claudication • Chronic limb ischemia with rest pain or tissue loss • Asymptomatic by-pass graft/stent restenosis AV access for hemodialysis • Fistulas Revision for malfunction/steal • AV fistula and graft placement for dialysis Venous diseases (VD) • Varicose veins, ablations • Inferior vena cava filter removal • Venous stenting for asymptomatic patients
LoP II - Urgent Surgery (patients who have not been electively admitted for operation but who require intervention or surgery on the current admission for medical reasons. These patients cannot be discharged without a definitive procedure)
AVD • TAAA/AAA with acute contained rupture with hemodynamically stable patients • Rapid progression of the aneurysmal diameter and large diameter (TAAA/AAA > 6- 6.5 cm) • Symptomatic peripheral artery aneurysm • Pseudoaneurysm (not suitable for thrombin injection and US-guided compression) PAD • In the absence of neurological deficit, revascularization is indicated within hours after initial imaging in a case-by-case decision • Infected arterial prosthesis without overt sepsis hemorrhagic shock, or impending rupture • Surgical drainage and debridement (including minor amputation if needed) and commence antibiotic treatment in all patients with suspected chronic limb-threatening ischemia who present with deep space foot infection or wet gangrene • Amputations for infection/necrosis and non-salvageable limb • Symptomatic acute mesenteric ischemia AV access for hemodialysis • Thrombosed or non-functional dialysis access • Infected access • AV fistulas revision for ulceration • Tunneled catheter
LoP III - Emergency (operation before the beginning of the next working day after decision to operate)
AVD • TAAA/AAA and peripheral aneurysm with rupture with hemodynamically unstable patients PAD • Acute limb ischemia (neurological deficit in the limb, particularly involving motor loss (Rutherford IIb)) • Patients with acute limb ischemia secondary to acute aortic occlusion • Fasciotomy (to treat post-ischemic compartment syndrome) Dissection of aorta • Type A Aortic Dissection • Complicated Type B Aortic Dissection Traumatic injury with hemorrhage VD • Acute iliofemoral deep venous thrombosis with extensive involvement with high-risk of pulmonary embolism
LOP IV - Salvage (patients requiring cardiopulmonary resuscitation en route to the operating theatre or prior to induction of anesthesia)

Table 1: Definition of Level of Priority (LoP) for Vascular Surgery (modified from Mavioglu et al).

Urology

Risk of SARS-CoV-2 Diffusion When Performing Minimally Invasive Surgery During the COVID-19 Pandemic

Novara G, Giannarini G, De Nunzio C, Porpiglia F, Ficarra V
Eur Urol
2020 Apr 13, PMID: 32336644
Level of Evidence: 5 – Expert opinion
Type of Article: Letter to the Editor

Summary: In light of possible evidence that SARS-CoV-2 may be concentrated in surgical smoke as well as stool, authors propose **urological surgery guidelines in an Italian hospital**, with goals to alleviate infectious risk while continuing to provide minimally invasive care for various urologic pathologies. In essence, the authors recommend that **personal protective equipment (PPE) must be reinforced**, **patients should be tested** for SARS-CoV-2 via nasopharyngeal swab, **smoke formation** during procedures using cautery and ultrasonic scalpels **must be reduced, and immediate removal of any generated smoke.**

Oral Maxillofacial Surgery and Dentistry

Rapid detection of SARS-CoV-2 in saliva: Can an endodontist take the lead in point-of-care COVID-19 testing?

Sharma S, Kumar V, Chawla A, Logani A.
Int Endod J
2020 Apr 28; PMID: 32344452
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter To Editor

BLUF: Endodontists needed for endodontic emergencies during COVID-19 are at a high risk of infection and therefore need a rapid point-of-care (POC) COVID-19 diagnostic tool to use before starting a procedure.

Summary: A study found that most dental emergencies in Wuhan, China during COVID-19 were endodontic emergencies. Endodontists are needed to address these endodontic emergencies and are at a greater risk of COVID-19 than other healthcare workers since most of their work involves aerosol generation. The authors argue for a rapid, sensitive, POC COVID-19 diagnostic tool that can be used routinely by endodontists utilizing saliva as a specimen before starting an emergency procedure. Some proposed diagnostic tools include loop-mediated isothermal amplification (LAMP) tests, antibody testing, and microfluidic RT-PCR devices (lab-on-a-chip).

OBGYN

General Guidelines in the Management of an Obstetrical Patient on the Labor and Delivery Unit during the COVID-19 Pandemic.

Stephens AJ, Barton JR, Bentum NA, Blackwell SC, Sibai BM.
Am J Perinatol
2020 Apr 28; PMID: 32344441
Level of Evidence: 5 - Guidelines
Type of Article: Clinical Opinion

Summary: The authors of this study present a series of guidelines for care of patients on labor and delivery units, with the goal of optimizing patient and healthcare worker safety as well as obstetric outcomes. The recommendations were developed based on input from experts in the United States and a review of current literature. The guidelines include:

- **Admission to L&D:** Screen patients and visitors upon presentation to labor and delivery and limit the number of allowed visitors.
- **General Precautions:** Droplet and contact precautions should be used during all clinical encounters.
- **Delivery Considerations:** Patients with suspected or known COVID-19 infection should deliver in rooms with negative pressure capabilities. Scheduled cesareans should continue as planned. For patients with severe COVID-19, stabilizing the patients prior to delivery should be prioritized, though some indications could necessitate delivery to improve resuscitative efforts.
- **Intrapartum Management:** Limit the number of room visits and cervical exams during delivery.
- **Drug Considerations:** Corticosteroid use to promote fetal lung development should be minimized with decisions to be made in patients with suspected or known COVID-19 on a case-by-case basis. Judicious use of magnesium sulfate is advised. Data on NSAIDs' effect on COVID-19 is equivocal, so continued use according to clinical indications is advised. Consider VTE prophylaxis in patients with suspected or known COVID-19 infection.

Abstract: Novel coronavirus disease 2019 (COVID-19) is a respiratory tract infection that was first identified in China. Since its emergence in December 2019, the virus has rapidly spread, transcending geographic barriers. The World Health Organization and the Centers for Disease Control and Prevention have declared COVID-19 as a public health crisis. Data regarding COVID-19 in pregnancy is limited, consisting of case reports and small cohort studies. However, obstetric patients are not immune from the current COVID-19 pandemic, and obstetric care will inevitably be impacted by the current epidemic. As such, clinical protocols and practice on labor and delivery units must adapt to optimize the safety of patients and health care workers and to better conserve health care resources. In this commentary, we provide suggestions to meet these goals without impacting maternal or neonatal outcomes.

Point of view of the Dutch Society for Gynaecological Endoscopy (WGE) on surgery during the COVID-19 crisis.

Radder C, de Leeuw R, Coppus S.
J Minim Invasive Gynecol
2020 Apr 25; PMID: 32344025
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

Summary: This article presents the Dutch Society for Gynaecological Endoscopy's opinions on how to safely resume elective surgeries during the pandemic. They propose the following recommendations, specific to patients who tested positive for COVID-19:

- Delay elective surgery for two weeks, then retest and proceed with surgery if results are negative.
- Laparoscopic surgery personal protective equipment (PPE) should include eye protection, gown, and a type IIR surgical mask at minimum.
- Perform laparoscopies according to standard indications.
- No limitations to vaginal or hysteroscopic surgeries are needed beyond appropriate PPE use.
- Low pressure operating rooms (ORs) are advised to minimize risk to healthcare providers and OR air should be refreshed between surgeries.

How Brazil is dealing with COVID-19 pandemic arrival regarding elective gynecological surgeries.
Brito LGO, Ribeiro PA, Silva-Filho AL; FEBRASGO Brazilian Gynecological Surgery Group for COVID-19
J Minim Invasive Gynecol.
2020 Apr 25; PMID: 32344034
Level of Evidence: 5- Expert opinion
Type of Article: Brief Guidelines
BLUF: Due to a lack of resources, Brazil faces many obstacles in its effort to flatten the curve. To combat this, the Brazilian Federation of Association of Gynecology and Obstetrics has encouraged the postponement of elective surgeries and emphasized the importance of appropriate personal protective equipment (PPE), among other recommendations (bullets below).

Summary: Brazil faces many obstacles during the current pandemic, including a "lack of massive testing for patients, either asymptomatic or symptomatic, disparities between the number of COVID-19 patients interned in public intensive care units (ICUs) versus private ICUs (and also number of available ICUs throughout the country)[...] and most importantly, not all facilities have sufficient personal protective equipment (PPE)." Attempting to flatten the curve, Brazil has implemented several guidelines regarding gynecological surgeries:

- Joint decisions should be made between the surgeon and patient regarding the postponement of elective surgeries
- COVID-19 risk factors should be addressed with the patients
- Testing is highly encouraged prior to surgery
- N-95 masks and face shields (in addition to other appropriate PPE) should be worn by all members of the surgical team for abdominal and vaginal surgeries
- The number of members on the surgical team should be restricted
- Smoke dispersion should be avoided
- Care should be taken to avoid pneumoperitoneum escape during laparoscopic procedures

Orthopedics

Telemedicine in the Era of COVID-19: The Virtual Orthopaedic Examination.
Tanaka MJ, Oh LS, Martin SD, Berkson EM
J Bone Joint Surg Am
2020 Apr 24; PMID: 32341311
Level of Evidence: 5 - Expert Opinion
Type of Article: Guideline
BLUF: Due to the COVID-19 pandemic promoting increased utilization of tele-medicine, the authors offer guidelines to improve the quality and efficiency of virtual orthopaedic physical examinations. Using web-based goniometry (Figure 1), which has been validated in previous studies, they offer guidance on virtual musculoskeletal exam maneuvers of the knee, hip, shoulder, and elbow joints to assess for common pathology.

Abstract:
With the onset of the COVID-19 pandemic, the shifting of clinical care to telemedicine visits has been hastened. Because of current limitations in resources, many elective surgeons have been forced to venture into utilizing telemedicine, in which the standards for orthopaedic examinations have not previously been fully developed. We report our experience with protocols and methods to standardize these visits to maximize the benefit and efficiency of the virtual orthopaedic examination. At the time of scheduling, patients are asked to prepare for their virtual visit and are given a checklist. In addition to confirming audiovisual capabilities prior to the visit, patients are given specific instructions on camera positioning, body positioning, setting, and attire to improve the efficiency of the visit. During the examination, digital tools can be utilized as needed. In the setting of outpatient injury evaluations, a systematic virtual examination can aid in triaging and managing common musculoskeletal conditions. With the rapid incorporation of telehealth visits, as well as the unknown future with regard to the pandemic, the utilization and capabilities of telemedicine will continue to expand. Future directions include the development of validated, modified examination techniques and new technology that will allow for improved interactive physical examinations, as we rapidly move forward into the realm of telemedicine due to unexpected necessity.

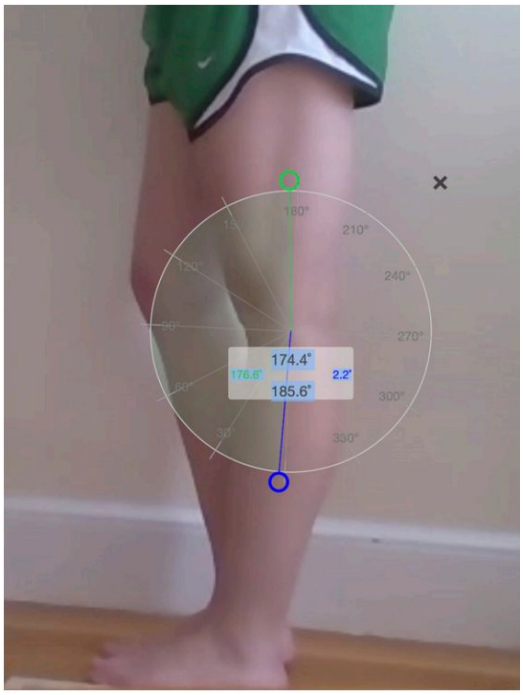

Figure 1: During the virtual examination, hyperextension of the knee is assessed by having the patient stand on the affected leg while pushing the knee posteriorly. A virtual goniometer can be utilized on most web-based platforms; in this case, it indicates hyperextension of 2.2.

Pediatrics

Pediatric laryngoscopy and bronchoscopy during the COVID-19 pandemic: A four-center collaborative protocol to improve safety with perioperative management strategies and creation of a surgical tent with disposable drapes

Francom, CR; Javia, LR; Wolter, NE; Lee, GS; Wine, T; Morrissey, T; Papsin, BC; Peyton, JM; Matava, CT; Volk, MS; Prager, JD; Propst, EJ
Int J Pediatr Otorhinolaryngol
2020 Apr 21; PMID: 32339971
Level of Evidence: 5 - Expert Opinion
Type of Article: Guideline

BLUF: Authors of this article present a protocol for pediatric laryngoscopy and bronchoscopy that they propose will reduce aerozilation. The authors intend for this protocol to be translatable to other aerosolized procedures, especially for COVID-19 patients. Methods used include:

- Use non-contrast computerized tomography to confirm foreign body presence to better ensure the bronchoscopy is necessary.
- Use surgical drapes to cover the patient from head to toe, usually completed with three drapes with one forming a tent over the patient's head.
- Limit procedure to essential personnel only.
- Use an ultrafiltrate smoke evacuator on the opening of the surgical drape tent.

Abstract:
Aerosolization procedures during the COVID-19 pandemic place all operating room personnel at risk for exposure. We offer detailed perioperative management strategies and present a specific protocol designed to improve safety during pediatric laryngoscopy and bronchoscopy. **Several methods of using disposable drapes for various procedures are described, with the goal of constructing a tent around the patient to decrease widespread contamination of dispersed droplets and generated aerosol.** The concepts presented herein are translatable to future situations where aerosol generating procedures increase risk for any pathogenic exposure. This protocol is a collaborative effort based on knowledge gleaned from clinical and simulation experience from Children's Hospital Colorado, Children's Hospital of Philadelphia, The Hospital for Sick Children in Toronto, and Boston Children's Hospital.

Psychiatry

Eating disorders in the time of COVID-19.

Touyz S, Lacey H, Hay P
J Eat Disord.
2020 Apr 20; PMID: 32337045
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

BLUF: This editorial calls attention to the unique difficulties faced by individuals with eating disorders during the COVID-19 pandemic. Patients with compromised physical health due to very low weight and emaciation may be more susceptible to the virus. Individuals with rigid and inflexible eating habits may not have access to their typical foods due to food insecurity and panic buying, leading to weight loss. With stay-at-home orders in effect, patients with bulimia nervosa and binge-eating disorder have no escape from food at home as well as limited opportunity to buy food. The authors conclude by calling for a rapid increase in research regarding the impact of COVID-19 on eating disorders.

Summarizing statement: "A former Australian of the Year and leading Psychiatrist, Professor McGorry, has made a call for the Australian government to urgently establish a national mental health response to address the increased need of the community at large [10]. We would go further and say an international response is needed to a virus which does not think nationally. **Both the short-term and long -term consequences of having both an eating disorder and COVID-19 simultaneously are unknown and with time this is likely to become more apparent. It**

is therefore important that we rapidly develop a repository of comments, protocols, case histories, pertinent literature reviews as well as empirical papers on this topic. To expedite this, the Journal of Eating Disorders is running a special issue on this topic. There are, without doubt, many more important aspects warranting our immediate attention. **We hope that this brief editorial will spur you, readers and researchers, into action**."

A smartphone based e-Consult in addiction medicine: An initiative in COVID lockdown.
Ganesh A, Sahu P, Nair S, Chand P.Ganesh A, et al.
Asian J Psychiatr.
2020 Apr 22; PMID: 32344333
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary: The authors highlight the importance of e-consults in the realm of addiction medicine in India. With a complete lockdown, many people cannot access care for treatments like buprenorphine treatment, anti-craving drugs, and withdrawal management. They offer E-consults as a solution to this problem, which can serve as a rapid, direct, and documented communication between healthcare providers and specialists. Currently, with telemedicine guidelines doctors are not allowed to prescribe narcotic and psychotropic drugs to the patient. E-consults can mitigate this and have the ability to enable cost effective and convenient care to patients during this pandemic.

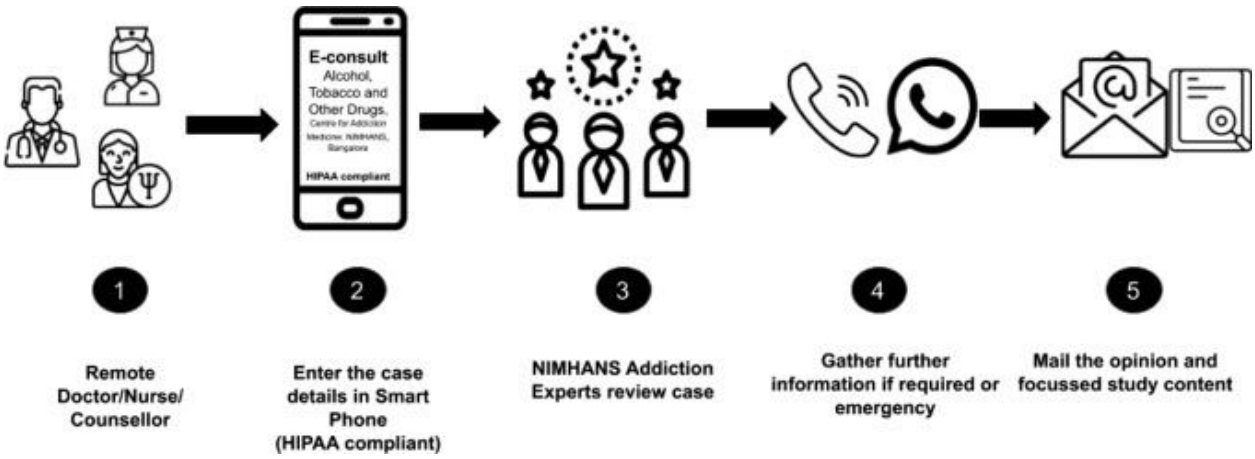

Fig. 1. Flow of events in e-consult.

R&D: Diagnosis & Treatments

COVID-19: An Update on Diagnostic and Therapeutic Approaches

Iyer, M; Jayaramayya, K; Subramaniam, MD; Lee, SB; Dayem, AA; Cho, SG; Vellingiri, B

BMB

2020 Apr; PMID: 32336317

Level of evidence: 5 - Expert Opinion

Type of Article: Research

BLUF: Authors provide a review of current treatment considerations for COVID-19 and testing modalities. They also provide the following clinical recommendations.

- Governing bodies should maintain strict adherence to current recommended policies for COVID-19
- Hydroxychloroquine should be approved as soon as possible for COVID-19 use
- State hospitals should take the charge to conduct clinical trials for convalescent plasma therapy
- Social strategies such as quarantining and social distancing are crucial to this pandemic

Abstract:

The unexpected pandemic set off by the novel coronavirus 2019 (COVID-19) has caused severe panic among people worldwide. COVID-19 has created havoc, and scientists and physicians are urged to test the efficiency and safety of drugs used to treat this disease. In such a pandemic situation, various steps have been taken by the government to control and prevent the Severe Acute Respiratory Syndrome coronavirus 2 (SARSCoV- 2). This pandemic situation has forced scientists to rework strategies to combat infectious diseases through drugs, treatment, and control measures. COVID-19 treatment requires both limiting viral multiplication and neutralizing tissue damage induced by an inappropriate immune reaction. Currently, various diagnostic kits to test for COVID-19 are available, and repurposing therapeutics for COVID-19 has shown to be clinically effective. As the global demand for diagnostics and therapeutics continues to rise, it is essential to rapidly develop various algorithms to successfully identify and contain the virus. **This review discusses the updates on specimens/samples, recent efficient diagnostics, and therapeutic approaches to control the disease and repurposed drugs mainly focusing on chloroquine/hydroxychloroquine and convalescent plasma (CP).** More research is required for further understanding of the influence of diagnostics and therapeutic approaches to develop vaccines and drugs for COVID-19.

Current Diagnostics

COVID-19 diagnostic process in mainland China: the math beyond pneumonia.

Wu F, Huang W.Wu F, et al.

J Allergy Clin Immunol.

2020 Apr 25; PMID: 32344058

Level of Evidence: 5 - Expert Opinion

Article Type: Editorial

Summary: The authors provide a clear explanation and flowchart to depict the COVID-19 diagnostic process developed and implemented in mainland China. Cases with any COVID-19 symptoms and/or a documented contact history with confirmed COVID-19 cases had CT scanning and RT-PCR testing. Based on the findings from testing and imaging, patients were either excluded from being a reported case, reported as an asymptomatic case, or reported as a confirmed COVID-19 case.

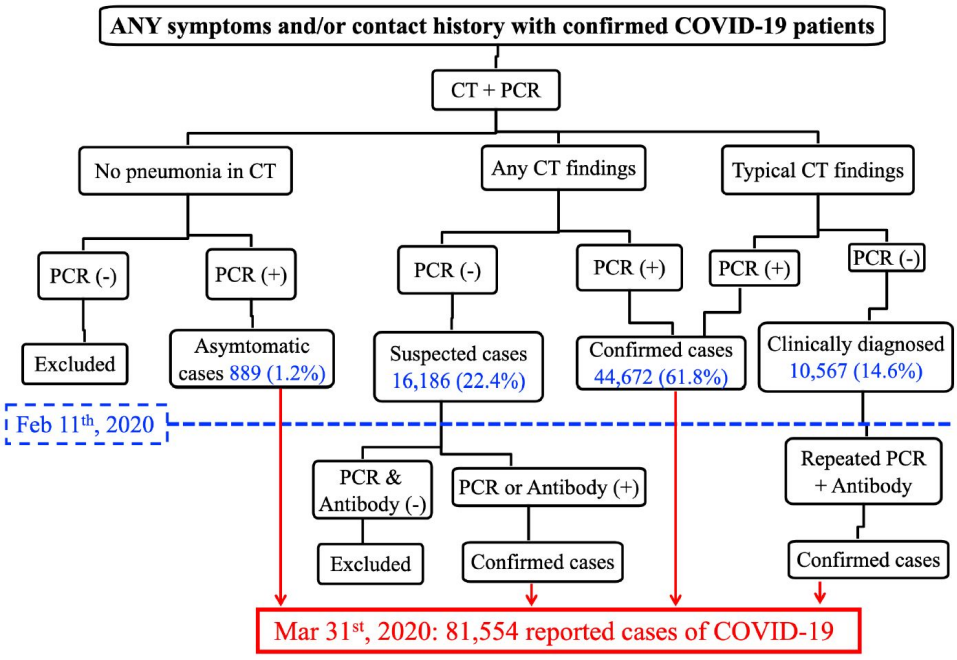

Figure 1: Scheme of COVID-19 diagnostic process in mainland China

Developments in Diagnostics

CO-RADS - A categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation

Prokop, M; van Everdingen, W; van Rees Vellinga, T; Quarles van Ufford, J; Stöger, L; Beenen, L; Geurts, B; Gietema, H; Krdzalic, J; Schaefer-Prokop, C; van Ginneken, B; Brink, M; "COVID-19 Standardized Reporting" Working Group of the Dutch Radiological Society

Radiology
2020 Apr 27; PMID: 32339082
Level of Evidence: 4 - Case Series
Type of Article: Research
BLUF: Authors tested an artificial intelligence (AI) program, called the COVID-19 Reporting and Data System (CO-RADS), with eight radiologists to detect COVID-19 on non-contrast chest computed tomography in patients with moderate to severe COVID-19. CO-RADS had a high discriminatory power for detecting pulmonary involvement in COVID-19 patients, with an overall Fleiss' kappa of 0.47 for agreement among observers. Radiologist performance in detecting COVID-19 pneumonia was improved with AI use.

Abstract:
Purpose To introduce the COVID-19 Reporting and Data System (CO-RADS) for standardized assessment of pulmonary involvement of COVID-19 on non-enhanced chest CT and report its initial interobserver agreement and performance.
Methods The Dutch Radiological Society (NVvR) developed CO-RADS based on other efforts for standardization, such as Lung-RADS or BI-RADS. CO-RADS assesses the suspicion for pulmonary involvement of COVID-19 on a scale from 1 (very low) to 5 (very high). The system is meant to be used in patients presenting with moderate to severe symptoms of COVID-19. The system was evaluated using 105 chest CTs of patients admitted to the hospital with clinical suspicion of COVID-19 in whom RT-PCR was performed (62 +/- 16 years, 61 men, 53 with positive RT-PCR). Eight observers assessed the scans using CO-RADS. Fleiss' kappa was calculated, and scores of individual observers were compared to the median of the remaining seven observers. The resulting area under the receiver operating characteristics curve (AUC) was compared to results from RT-PCR and clinical diagnosis of COVID-19.
Results There was absolute agreement among observers in 573 (68.2%) of 840 observations. Fleiss' kappa was 0.47 (95% confidence interval (CI) 0.45-0.47), with the highest kappa for CO-RADS categories 1 (0.58, 95% CI 0.54-0.62) and 5 (0.68, 95% CI 0.65-0.72). The average AUC was 0.91 (95% CI 0.85-0.97) for predicting RT-PCR outcome and 0.95 (95% CI 0.91-0.99) for clinical diagnosis. The false negative rate for CO-RADS 1 was 9/161 (5.6%, 95% CI 1.0-10%), and the false positive rate for CO-RADS 5 was 1/286 (0.3%, 95% CI 0-1.0%).
Conclusions CO-RADS is a categorical assessment scheme for pulmonary involvement of COVID-19 on non-enhanced chest CT providing very good performance for predicting COVID-19 in patients with moderate to severe symptoms and has a substantial interobserver agreement, especially for categories 1 and 5.

SEPAR-AEER Consensus Recommendations on the Usefulness of the Thoracic Ultrasound in the Management of the Patient with Suspected or Confirmed Infection with COVID-19.
Pérez Pallarés J, Flandes Aldeyturriaga J, Cases Viedma E, Cordovilla Pérez R.
Arch Bronconeumol
2020 Apr 2; PMID: 32336564
Level of Evidence: Level 5 - Expert opinion
Type of Article: Guidelines
BLUF: The Sociedad Española de Neumología y Cirugía Torácica (SEPAR) and the Asociación Española de Endoscopia Respiratoria y Neumología Intervencionista (AEER) in Spain propose the use of thoracic ultrasound for early diagnosis and daily evaluation of the progression of COVID-19 disease process. **They propose a systematic ultrasound examination which divides the thorax into quadrants and looks for : A lines, B lines, parenchymal condensation, pleural lines and pleural effusion**.

Developments in Treatments

Umifenovir treatment is not associated with improved outcomes in patients with coronavirus disease 2019: A retrospective study.
Lian N, Xie H, Lin S, Huang J, Zhao J, Lin Q
Clin Microbiol Infect
2020 Apr 25; PMID: 32344167
Level of Evidence: 3 - Retrospective case control study
Type of Article: Research
BLUF: In this retrospective study, the authors reviewed a total of 81 non-ICU COVID-19 positive patients at Jinyintan Hospital (China) from 2/2/20 to 3/20/20 comparing those that received Umifenovir 200mg TID (n=45) to those that did not (n=36). Using RT-PCR nasopharyngeal swabs every other day, they found that 73.3% of the Umifenovir group and 77.8% of the control group tested negative for SARS-CoV-2 within seven days of admission with a median time of symptom onset to negative RT-PCR testing of 18 days in the Umifenovir group and 16 days in the control group to conclude that Umifenovir may not accelerate clearance of SARS-CoV-2.

Abstract:
Objectives: Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Umifenovir (Arbidol®) is an antiviral drug being used to treat influenza in Russia and China. This study aimed to investigate the effectiveness and safety of umifenovir for COVID-19.
Methods: A retrospective study was performed in non-ICU Ward in Jinyintan Hospital from February 2, 2020 to March 20, 2020. COVID-19 was confirmed by real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay for pharyngeal swab specimens. The confirmed patients were divided into umifenovir group and control group according to the use of umifenovir. The main outcomes were the negative rate of pharyngeal swab's test for SARS-CoV-2 within 1 week after admission, as well as the duration for virus turning negative. The negativity time of SARS-CoV-2 was defined as the first day of a negative test if the nucleid *[sic]* acid of SARS-CoV-2 was negative for 2 consecutive tests.
Results: A total of 81 COVID-19 patients were included, with 45 in *[sic]* umifenovir group and 36 in *[sic]* control group. Baseline clinical, laboratory characteristics were comparable between two groups. 33/45 (73.3%) patients in *[sic]* umifenovir group were tested negative in SARS-CoV-2 within 7 days after admission, the number was 28/36 (77.8%) in *[sic]* control group (p=0.19). The median time from onset of symtoms *[sic]* to SARS-CoV-2 turning negative were 18 days (interquartile range [IQR] 12-21) in umifenovir group and 16 days (IQR, 11-21) in *[sic]* control group (p= 0.42). Patients in *[sic]* umifenovir group had longer hospital stay than patients in *[sic]* control group (13 days [IQR, 9-17] vs 11 days [IQR, 9-14], p=0.04). No deaths or severe adverse reaction *[sic]* were found in both groups.
Conclusions: Umifenovir might not improve the prognosis or accelerate the SARS-CoV-2 clearance in non-ICU patients. A randomized control clinical trial is needed to assess the efficacy of umifenovir.

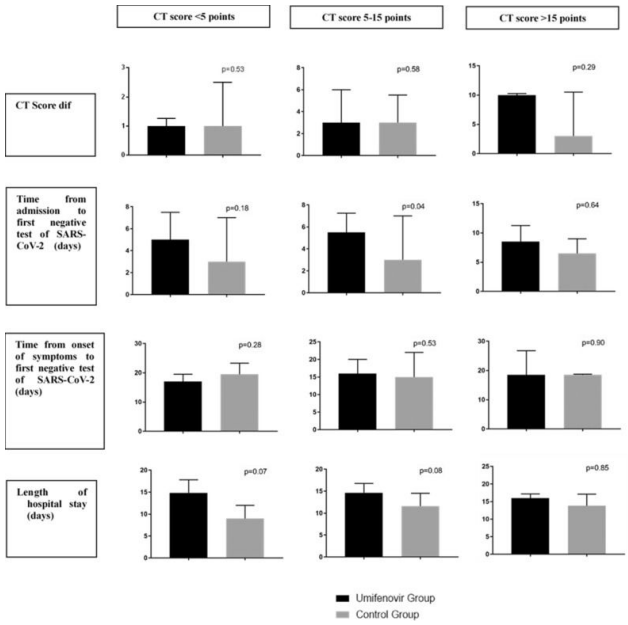

Figure 1. Effectiveness of umifenovir in patients with COVID-19, a subgroup analysis based on CT scores. Data were presented as median (IQR). Abbreviations: COVID-19, coronavirus disease 2019; CT Score dif= CT Score (within 2 days of admission)- CT Score (at the 7th day after hospitalization); SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Treatment of SARS-CoV-2: How Far Have We Reached?
Ahsan W, Javed S, Al Bratty M, Alhazmi HA, Najmi A
Drug Discov Ther
2020 Apr 25; PMID: 32336723
Level of Evidence: 5 – Literature Review
Type of Article: Review
BLUF: This article reviews studies of COVID-19 treatments enrolled in clinical trials across the world, highlighting the need for therapeutics as we await the vaccine development pipeline. Key findings are summarized below:

- Fujifilm's **favipiravir**, an RNA-dependent RNA polymerase inhibitor, has shown promise in **reducing viral load** in **non-critical patients** in 2 clinical trials
- Abbott Laboratories' Kaletra (**lopinavir/ritonavir**), a dual protease inhibitor combo, has **not been shown to improve clinical outcomes**
- Johnson & Johnson's **darunavir**, a protease inhibitor, has **not been shown to improve clinical outcomes**
- **Chloroquine and Hydroxychloroquine** have shown success in **reducing viral load**, though numerous **studies have been halted** due to **increased risk of cardiac death**.
- **Convalescent plasma** from recovered patients **might treat severe disease**, though **more trials are necessary**.

Abstract:
The virus severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is currently affecting more than 200 countries and territories worldwide. It has been declared as pandemic by (*sic)* World Health Organization (WHO) and the whole world is suffering from corona virus [*sic*] disease 2019 (COVID-19). Currently, **no treatment for SARS-CoV-2 are approved** [*sic*] because of lack of evidence, but a **number of clinical trials are in process** [*sic*] and we are expecting fruitful results very soon. This review focuses on **various approaches of treatment** and few [*sic*] of the most recent clinical trials carried out in this field.

Innate Immunity in COVID-19 Patients Mediated by NKG2A Receptors, and Potential Treatment Using Monalizumab, Cholroquine (*sic*), and Antiviral Agents.
Yaqinuddin, A., & Kashir, J.
Med Hypotheses.
2020 Apr 22; PMID: 32344314
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence
BLUF: The authors hypothesize that patients with severe COVID-19 who show overexpression of Natural Killer group 2 member A (NKG2A) receptor, which hampers immune response, can be treated with Monalizumab, chloroquine, or other antivirals that can inhibit NKG2A.

Abstract:
Following the outbreak of a novel coronavirus (SARS-CoV-2), studies suggest that the resultant disease (COVID-19) is more severe in individuals with a weakened immune system. Cytotoxic T-cells (CTLs) and Natural Killer (NK) cells are required to generate an effective immune response against viruses, functional exhaustion of which enables disease progression. **Patients with severe COVID-19 present significantly lower lymphocyte, and higher neutrophil, counts in blood.** Specifically, CD8+ lymphocytes and NK cells were significantly reduced in cases of severe infection compared to patients with mild infection and healthy individuals. The NK group 2 member A (NKG2A) receptor transduces inhibitory signalling, suppressing NK cytokine secretion and cytotoxicity. **Overexpression of NKG2A has been observed on CD8+ and NK cells of COVID-19 infected patients** compared to healthy controls, while NKG2A overexpression also functionally exhausts CD8+ cells and NK cells, resulting in a severely compromised innate immune response. Blocking NKG2A on CD8+ cells and NK cells in cancers modulated tumor growth, restoring CD8+ T and NK cell function. A recently proposed mechanism via which SARS-CoV-2 overrides innate immune response of the host is by over-expressing NKG2A on CD+ T and NK

cells, culminating in functional exhaustion of the immune response against the viral pathogen**. Monalizumab is an inhibiting antibody against NKG2A which can restore the function of CD8 + T and NK cells** in cancers, successfully ceasing tumor progression with no significant side effects in Phase 2 clinical trials. We hypothesize that patients with severe COVID-19 have a severely compromised innate immune response and could be treated via the use of Monalizumab, interferon α, chloroquine, and other antiviral agents.

Finding the dose for hydroxychloroquine prophylaxis for COVID-19; the desperate search for effectiveness.
Al-Kofahi M, Jacobson P, Boulware DR, Matas A, Kandaswamy R, Jaber MM, Rajasingham R, Young JH, Nicol MR.Al-Kofahi M, et al.
Clin Pharmacol Ther.
2020 Apr 28; PMID: 32344449
Level of Evidence: 5 - Mechanism-based reasoning
Type of Article: Research
BLUF: The authors examined different dosing strategies for hydroxychloroquine use in COVID-19 pre-exposure and post-exposure prophylaxis by comparing predicted plasma exposures to *in vitro* efficacy targets in a simulation. To maintain weekly trough levels over the half maximal effective concentration (EC50) in >50% subjects at steady state for pre-exposure prophylaxis, an 800 mg loading dose followed by 400 mg 2-3x/week is required. Likewise, for post-exposure prophylaxis, an 800 mg loading dose followed in 6 hours by 600 mg, then 600 mg daily for 4 more days achieved daily troughs above EC50 in >50% subjects.

Abstract: Hydroxychloroquine is an antimalarial drug being tested as a potential treatment for the novel coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2((SARS-CoV-2. Although the efficacy of hydroxychloroquine for COVID-19 remains uncertain, it may serve as a potential prophylactic agent especially in those at high risk, such as healthcare workers, household contacts of infected patients, and the immunocompromised. Our aim was to identify possible hydroxychloroquine dosing regimens through simulation in those at high risk of infections by optimizing exposures above the in vitro generated half maximal effective concentration (EC50) and to help guide researchers in dose-selection for COVID-19 prophylactic studies. **To maintain weekly troughs above EC50 in >50% of subjects at steady state in a pre-exposure prophylaxis setting, an 800 mg loading dose followed by 400 mg twice or three times weekly is required.** In an exposure driven post-exposure prophylaxis setting, 800 mg loading dose followed in 6 hours by 600 mg, then 600 mg daily for 4 more days achieved daily troughs above EC50 in >50% subjects. These doses are higher than recommended for malaria chemoprophylaxis, and clinical trials are needed to establish safety and efficacy.

COVID-19 Tragic Pandemic: Concerns over Unintentional "Directed Accelerated Evolution" of Novel Coronavirus (SARS-CoV-2) and Introducing a Modified Treatment Method for ARDS.
Ghadimi-Moghadam A, Haghani M, Bevelacqua J, Kaveh-Ahangar A, Mortazavi S.
J Biomed Phys Eng.
2020 Apr 23; PMID: 32337192
Level of Evidence: 5- Mechanism-Based Research
Type of Article: Research
BLUF: An international group of researchers apply the theoretical concept of "**selective pressure and directed acceleration**" (Figure 2), whereby medical intervention unintentionally selects for more treatment-resistant organisms, to the SARS-CoV-2 virus. Additionally, the authors propose an alternative treatment method for COVID-19 pneumonia that utilizes **low dose radiation (LDR)** to modulate production of proinflammatory cytokines implicated in the pathogenesis of **lymphopenia** and **cytokine storm** in severe COVID-19. This is **largely theoretical**, although limited proof of concept data does exist on the biological effects of LDR.

Abstract:
Global health authorities are trying to work out the current status of the novel coronavirus (COVID-19) outbreak and explore methods to reduce the rate of its transmission to healthy individuals. In this viewpoint we provide insights concerning how health care professionals can unintentionally shift the novel coronavirus type to more drug-resistant forms. It is worth noting that viruses usually have different sensitivities to physical and chemical damaging agents *[sic]* such antiviral drugs, UV and heat ranging from extremely sensitive (ES) to extremely resistant (ER) based on a bell-shaped curve. Given this consideration, the widespread infection of people with such ER viruses would be a real disaster. Here, we introduce a modified treatment method for COVID-19-associated pneumonia. In this proposed method, COVID-19 patients will receive a single dose of 100, 180 or 250 mSv X-ray radiation that is less than the maximum annual radiation dose of the residents of high background radiation areas of Ramsar that is up to 260 mSv. In contrast with antiviral drugs, a single dose of either 100, 180 or 250 mSv of low LET X-rays cannot exert a significant selective pressure on the novel coronavirus (SARS-CoV-2) and hence does not lead to directed accelerated evolution of these viruses. Moreover, Low Dose Radiation (LDR) has the capacity of modulating **excessive inflammatory responses, regulating lymphocyte counts, and controlling bacterial co-infections in patients with COVID-19.** excessive inflammatory responses, regulating lymphocyte counts, and controlling bacterial co-infections in patients with COVID-19.

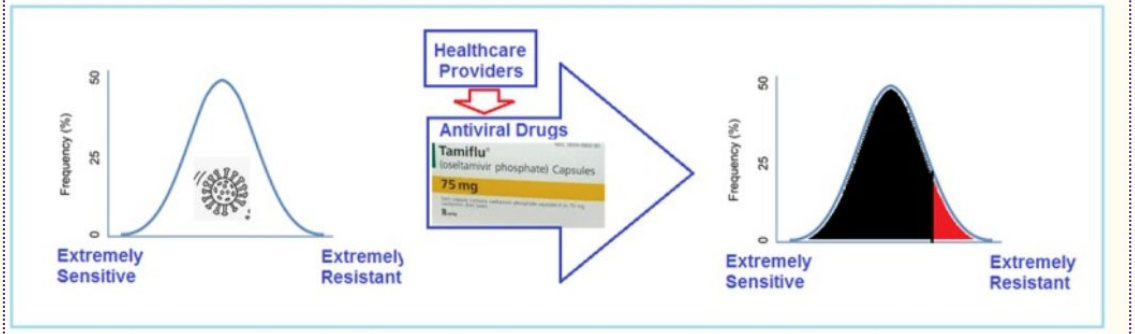

Figure 2

How the two phenomena of selective pressure and directed evolution can shift the population of viruses to extremely resistant ones.

Can pioglitazone be potentially useful therapeutically in treating patients with covid-19?
Carboni E, Carta AR, Carboni E.
Med Hypotheses.
2020 Apr 22; PMID: 32344313
Level of Evidence: 5 - Expert Opinion
Type of Article: Research
BLUF: The diabetic drug pioglitazone, from the drug family thiazolidinediones (TZD), is hypothesized to be useful in attenuating COVID-19 in patients with diabetes, hypertension, and cardiovascular comorbidities. The reasoning is that TZDs mitigate inflammatory cytokines and have been shown in *in vivo* studies to reduce lung injury.

Abstract:
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a pandemic disease (COVID-19) that has spread globally causing more than 30,000 deaths. Despite the immense and ongoing global effort, no efficacious drugs to fight this plague have been identified and patients admitted to the intensive care units (ICU), for respiratory distress, are managed mostly by means of supportive care based on oxygen maintenance. Several authors have reported that the prevalence of hypertension, diabetes, cardiovascular and cerebrovascular diseases comorbidities were indeed frequent among patients with COVID-19, which suggests that these conditions are likely to aggravate and complicate the prognosis. What the aforementioned diseases have in common is a latent chronic inflammatory state that may be associated with the alteration of laboratory parameters that are typical of the metabolic syndrome and insulin resistance. **In severe COVID-19 patients laboratory markers of inflammation such as C-reactive protein, IL-6, D-dimer, serum ferritin and lactate dehydrogenase are elevated in many patients**; assessed since the 4th-6th day of illness onset, such increases seem to be predictive of an adverse prognosis. Our hypothesis is that drugs belonging to the **family of thiazolidinediones (TZD) such as pioglitazone or rosiglitazone, approved for treating the condition of insulin resistance and the accompanying inflammation, could ameliorate the prognosis of those COVID-19 patients with diabetes, hypertension and cardiovascular disorders comorbidities.** TZD are PPARγ agonists that act on nuclear receptors, thereby triggering certain transcription factors. TZD were widely used for type-2 diabetes in the first decade of this century and although concerns have been raised for possible side effects associated with long-term treatment, their use has been recently revaluated for their anti-inflammatory properties in numerous medical conditions.

Impact of immune enhancement on Covid-19 polyclonal hyperimmune globulin therapy and vaccine development.
de Alwis R, Chen S, Gan ES, Ooj EE.
EBioMedicine
2020 Apr 16; PMID: 32344202
Level of Evidence: 5 – Mechanism-based reasoning
Type of Article: Review
BLUF: The author argues that the risk of antibody-mediated COVID-19 exacerbation due to hyperimmune globulin treatment or a highly efficacious vaccine is low.

Abstract:
The pandemic spread of a novel coronavirus - SARS coronavirus-2 (SARS-CoV-2) as a cause of acute respiratory illness, named Covid-19, is placing the healthcare systems of many countries under unprecedented stress. Global economies are also spiraling towards a recession in fear of this new life-threatening disease. Vaccines that prevent SARS-CoV-2 infection and therapeutics that reduces the risk of severe Covid-19 are thus urgently needed. A rapid method to derive antiviral treatment for Covid-19 is the use of convalescent plasma derived hyperimmune globulin. **However, both hyperimmune globulin and vaccine development face a common hurdle - the risk of antibody-mediated disease enhancement.** The goal of this review is to examine the body of evidence supporting the hypothesis of immune enhancement that could be pertinent to Covid-19. We also discuss how this risk could be mitigated so that both hyperimmune globulin and vaccines could be rapidly translated to overcome the current global health crisis.

Dapsone, Colchicine and Olanzapine as Treatment Adjuncts to Prevent COVID-19 Associated Adult Respiratory Distress Syndrome (ARDS).
Eric L Altschuler, Richard E Kast
Med Hypotheses.

2020 Apr 23, PMID: 32344275
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
Summary: The authors summarize that the elevated IL-8 for neutrophil chemotaxis seen in patients with acute respiratory distress syndrome (ARDS) can be therapeutically managed by dapsone and colchicine. The reported elevated IL-6 seen in patients with COVID-19 can be targeted by olanzapine. The authors recommend a trial of dapsone 100 mg every 12 h, colchicine 0.4 mg daily and olanzapine 10 mg daily in hospitalized but not yet ventilated patients.

Oxytocin as a potential defence against Covid-19?
Soumier A, Sirigu A.
Med Hypotheses
2020 Apr 23; PMID: 32344303
Level of Evidence: 5 - Mechanism Based Reasoning
Type of Article: Letter
Summary: The authors of this article propose oxytocin as a potential agent for COVID-19 treatment, especially in higher risk patients. They argue that oxytocin has been shown to improve immune defense and simultaneously suppress overactive innate immune responses, and note that animal models suggest that exposure to oxytocin may reduce inflammatory protein expression after acute lung injury.

Mental Health & Resilience Needs

COVID-19's Impact on Healthcare Workforce

Effective health communication - a key factor in fighting the COVID-19 pandemic.
Finset A, Bosworth H, Butow P, Gulbrandsen P, Hulsman RL, Pieterse AH, et al.
Patient Educ Couns.
2020 May; PMID: 32336348
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
Summary: The authors discuss ways to handle the massive increase in health information from COVID-19. To handle uncertainty and fear, they first suggest open and honest discussion with fact-based information only. Second, they suggest information to be specific and consistent. Third, they push for strong leadership. And last, they highlight the importance of acknowledging emotions like anxiety, depression, and distress. Together, the authors hope effective communication will aid in fighting the COVID-19 pandemic.

The potential for COVID-19 to contribute to compassion fatigue in critical care nurses.
Alharbi J, Jackson D, Usher K
J Clin Nurs.
2020 Apr 28; PMID: 32344460
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
BLUF: This editorial highlights that critical care nurses on the front-lines of the COVID-19 pandemic may be at high risk for compassion fatigue and burnout due to increased patient numbers with higher acuity and limited access to necessary equipment. To reduce this risk, the authors suggest that a clear set of guidelines for self-care and psychological well-being of critical care nurses during public health crises be developed and implemented through collaboration with other stakeholders.

Summarizing statement: "In conclusion, **large-scale public health events such as the COVID-19 pandemic require a dedicated and highly-demanding response from critical care nurses**. To support these nurses, the broader response to COVID-19 must include multiple stakeholders including, but not limited to, senior nursing staff, government policy makers, technology designers, hospital administrations, as well as members of the broader community. **The decision and actions of stakeholders can play a central role in assisting nurses to manage the competing care demands caused by increased acuity, increased patient numbers, clinical uncertainty and limited access to necessary equipment**. Hence, in addition to critical care nurses doing all they can to protect their own and their colleagues' wellbeing, they need to work with other stakeholders to mobilise beneficial partnership and collaborate on developing creative solutions. Only through a collaborative effort can any risks associated with CF and burnout in the critical care nurse workforce be identified and mitigated."

Professional Identity Formation in Disorienting Times.
Stetson GV, Kryzhanovskaya IV, Lomen-Hoerth C, Hauer KE
Med Educ.
2020 Apr 28; PMID: 32344447
Level of Evidence: 5 - Expert Opinion
Type of Article: Correspondence
Summary: The University of California San Francisco School of Medicine documents how they have transformed their curriculum during the COVID-19 pandemic to help shape their medical students' professional identities. The medical school offered students virtual activities to promote wellbeing which include 1) physical exercise, 2) mindfulness, 3) small-group reflections to process emotions, and 4) increased contact with established faculty coaches and peers through group "check-ins." Implementing these aspects into medical student education during a healthcare crisis may help students process emotions such as anxiety and fear, combat social isolation, and ultimately positively impact how they view their professional identity.

Impact on Public Mental Health

Loss and Grief amidst COVID-19: A Path to Adaptation and Resilience.
Zhai Y, Du X.Zhai Y, et al.
Brain Behav Immun.
2020 Apr 23; PMID: 32335197
Level of Evidence: 5- Expert Opinion
Type of Article: Letter
BLUF: The authors discuss the implications of coronavirus in regards to loss and grief. They urge recognizing the uniqueness of each individual's loss and grief to provide opportunities to develop tailored strategies that facilitate mental wellbeing.

Abstract: The COVID-19 pandemic has posed an extreme threat to global health and become a leading cause of death worldwide. Loss, as a more encompassing theme, interweaves many aspects of people's life in this challenging time. Failure to address the pressing needs of those experiencing loss and grief may result in poor mental and physical health. Recognizing the uniqueness of each individual and their loss and grief will provide opportunities to develop tailored strategies that facilitate functional adaptation to loss and promote mental health and wellbeing in this crisis.

Pakistanis' mental health during the COVID-19.
Mukhtar S.
Asian J Psychiatr.
2020 Apr 23; PMID: 32344330
Level of Evidence: 5 - Expert opinion
Article Type: Commentary
Summary: The author argues that Pakistan should incorporate psychological interventions as part of the healthcare system to mitigate the psychosocial and mental health impact of COVID-19. She proposes that individuals "adopt behavior modification" to adapt to the current consequences of COVID-19. Strategies include: "mindfulness of hand-washing, healthy diet, physical activity; practicing introspection, meditation and minimalism; learning new

skills...; acquiring new languages; procuring knowledge of books, and podcasts; accumulating influential videos, series, movies, games, and music; and expressing gratitude through introspection and mindfulness...".

Silver Linings

Collateral Benefit of COVID-19 Control Measures on Influenza Activity, Taiwan.
Kuo SC, Shih SM, Chien LH, Hsiung CA.
Emerg Infect Dis.
2020 Apr 27. PMID: 32339091
Level of Evidence: 4 - Cross Sectional
Type of Article: Research
BLUF: The study hypothesized that the strict infection control for the COVID-19 pandemic would have a collateral benefit of reducing influenza transmission. Comparing 12 weeks from 2020 with the same weeks from 2019, the researchers found that there was a **statistically significant decrease in the number of influenza strains, positivity rate, and severe influenza cases.** The study did not find a significant difference when analyzing varicella transmission.

Abstract:
Taiwan has strictly followed infection control measures to prevent spread of coronavirus disease. Meanwhile, nationwide surveillance data revealed drastic decreases in influenza diagnosis in outpatient departments, positivity rates of clinical specimens, and confirmed severe cases during the first 12 weeks of 2020 compared with the same period of 2019.

Resources

COVID-19 pandemic - A focused review for clinicians.
Cevik M, Bamford C, Ho A.Cevik M, et al.
Clin Microbiol Infect.
2020 Apr 25; PMID: 32344166
Level of Evidence: 5 - Literature Review
Type of Article: Review
BLUF: Authors review many unknowns about COVID-19, including the importance of understanding the risks that asymptomatic patients pose, the populations most at risk, and effectiveness of social distancing. They also provide a condensed overview of virology, clinical presentation, and testing. They emphasize that many questions still exist involving the accuracy of common COVID-19 testing modalities (including serology, RT-PCR and radiological testing) and the efficacy of current treatment options.

Abstract:
Background: The COVID-19 pandemic caused by SARS-CoV-2 remains a significant issue for global health, economics and society. A wealth of data has been generated since its emergence in December 2019 and it is vital for clinicians to keep up with this data from across the world at a time of uncertainty and constantly evolving guidelines and clinical practice.
Objectives: Here we provide an update for clinicians on the recent developments about virology, diagnostics, clinical presentation, viral shedding, and treatment options for COVID-19 based on current literature.
Sources: We considered published peer-reviewed papers and non-peer-reviewed pre-print manuscripts on COVID19 and related aspects with an emphasis on clinical management aspects.
Content: We describe the virological characteristics of SARS-CoV-2 and clinical course of COVID-19 with an emphasis on diagnostic challenges, duration of viral shedding, severity markers and current treatment options.
Implications: The key challenge in managing COVID-19 remains the patient density. However, accurate diagnoses as well as early identification and management of high-risk severe cases are important for many clinicians. **For improved management of cases, there is a need to understand test probability of serology, qRT-PCR and radiological testing, and the efficacy of available treatment options** that could be used in severe cases with a high risk of mortality.

COVID-19: Disease, management, treatment, and social impact.
Ali I, Alharbi OML.Ali I, et al.
Sci Total Environ.
2020 Apr 22; PMID: 32344226
Level of Evidence: 5 - Expert opinion
Type of Article: Review
Summary: A **general summation of previously available knowledge** on COVID-19 transmission, symptoms, prevention, and management. The treatment references several allopathic medical trials and notes **many used chloroquine with some evidence of benefit**. **The discussion of alternative medicine**; Unani, Ayurvedic, and homeopathic remedies is **a novel contribution. Particularly, *Glycyrrhiza glabra's* antiviral activity against previous SARS-related coronavirus**.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): Emergence, History, Basic and Clinical Aspects.
Al-Qahtani AA.
Saudi J Biol Sci.
2020 Apr 23; PMID: 32336927
Level of Evidence: 5 - Expert opinion
Type of Article: Review
BLUF: This review article examines how the COVID-19 pandemic came to light and reviews its epidemiology, genomic structures, transmission, pathogenesis, and emerging treatment strategies. The similarity of genomic sequences between COVID-19 and the prior coronavirus outbreaks including SARS-CoV and MERS might help with developing treatments.

Abstract: In late December 2019, the world woke to a reality of a pandemic of Coronavirus Disease (COVID-19), elicited by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which belongs to a group of β-coronavirus. The potential to cause life-threatening respiratory failure and rapid transmission puts COVID-19 in the list of Public Health Emergency of International Concern (PHEIC). In the last two decades, this is the 3rd deadliest Coronavirus pandemic, following SARS which lasted between 2002 and 2003 and Middle East Respiratory Syndrome (MERS) from 2012 till date. Globally and as of April 1st 2020, COVID-19 has affected 924,688 individuals in over 200 countries, causing 46,368 fatalities. While the SARS-CoV-2 originated in China with over 82,724 confirmed cases and more than 3000 deaths as at the time of writing this review, the rapid transmission of SARS-CoV-2 has resulted in exponential increase in the number of cases outside of China to about 10 times the report case and death in mainland China. SARS-CoV-2 is suspected to be zoonotic in nature as genetic studies have shown sequence similarity to viruses originating from bats. Extreme precautionary measures, such as curfew, shutting of borders and quarantining of individuals suspected to be infected have been instituted with immediate effect; however, due to individuals that are asymptomatic, uncontrolled human-to-human transmission has resulted in exponential infection rate and numerous loss of lives even with this lockdown measures. This review article **summarizes the developing situation surrounding the SARS-CoV-2 pandemic with respect to its epidemiology, unique genomic structure, possible origins, transmission, pathogenesis, comparison with other deadly species of Coronaviruses (CoV) and emerging treatment strategies** built on informed literature.

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