

April 22, 2020
Daily COVID-19 Literature Surveillance Summary



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Coming soon:



COVID-19 Daily Literature Surveillance

COVID19LST



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



The Swab

Jasmine Rah



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

April 22, 2020

Executive Summary

Climate

- Efforts to “[flatten the curve](#)” correlate with reduced fatality rates in a study of 65 countries.
- The pandemic is also drawing attention to racial, ethnic, and socioeconomic disparities in society:
 - A [disproportionate number](#) of COVID-19 cases and deaths are African American
 - The brunt of the effects [fall on already vulnerable populations](#).

Epidemiology

- Data driven models predict that an additional 60 days of lockdown in Italy would achieve a [35% decrease in COVID-19 cases and a 66% increase in those recovered](#).
- Emerging findings reveal that [mutated, distinct clades of SARS-CoV-2](#) with varying virulence may be an additional factor at play during this pandemic and could explain the difference in the severity of the infections seen on the west and east coast of the United States.
 - These multiple strains could complicate vaccine development.
- An analysis of 30 provincial capital cities in China found that [increases in ambient temperature and diurnal temperature range](#) were correlated with a decline in daily case counts, similar to what has been observed with influenza
- Emerging trends in symptomatology:
 - American Academy of Otolaryngology recommend that [smell dysfunction with or without taste dysfunction](#) be a primary screening symptom for COVID-19
 - There are growing reports of a [varicella-like rash](#) and [coagulopathies](#) in COVID-19 patients.
- Current literature estimates [Ro for COVID-19 to be between 2.44-4.2](#)

Pathology

- A meta-analysis of 28 studies found that [elevated cardiac injury biomarkers](#) and acute cardiac injury are more common in severe to fatal cases.
- One comprehensive *in silico* analysis showed that certain [HLA alleles](#) may be associated with increased disease severity and may be one explanation for the spectrum of symptoms we see in patients with COVID-19
- Continued reports of [coagulopathies](#), [endothelial activation](#), and [cytokine storm](#) in COVID-19 patients
- Men consistently appear to have worse clinical outcomes than women, potentially due to androgens

Transmission & Prevention

- Loose-fitting surgical masks [will not prevent inhalation](#) of airborne viral particles.

Management

- One Chinese case series of 20 patients found that patients in critical condition with COVID-19 pneumonia are more likely to survive if they are [intubated before their blood gas becomes abnormal](#).

Adjusting Practice During COVID-19

- There are continued concerns over the use of [ACE inhibitors and increased risk of COVID-19](#) infection
 - and the use of [aerosol mitigation intubation boxes](#) given no conclusive evidence that it provides increased safety to personnel.
- A study found [46 of 48 late-term pregnant women](#) with COVID-19 underwent an elective cesarean despite no conclusive evidence of vertical transmission.

- Strategies for health care professionals
 - A band-aid and hydrocolloid dressing over existing [pressure sores](#) from continuous mask use
 - Other [management strategies](#) for adverse skin reactions from respirators, gowns and goggles

R&D Diagnosis and treatment

- Potential therapies/prophylaxis based on mechanism:
 - [interferon lambda](#), [azithromycin](#), [ibrutinib](#), and [convalescent plasma](#)
- A cohort study found that by setting empiric cutoffs for [AST and LDH from routine blood tests](#), they were able to confirm COVID-19 positive or negative patients, suggesting a use for routine labs in settings where PCR is not readily available
- Another study found that their version of the [reverse transcription loop-mediated isothermal amplification \(RT-LAMP\) assay](#) shows promise due to its ease of use and quick turnaround time.

Guidelines

- [Extubation guidelines](#) have been aimed at minimizing staff exposure.
- A summary of guidelines for managing patients with [IBS](#) during COVID-19 as well as the usage of a barrier box to [reduce transmission risk](#) during endoscopic retrograde cholangiopancreatography procedures.
- [Adapting Emergency Department decontamination rooms](#) for airway management.
- The [European ADHD Guidelines Group](#) published guidance about the ADHD management during this pandemic, which includes families using behavioral parenting strategies and avoiding increasing medication doses or drug “holidays” along with other recommendations.
- Guidelines have been published by the American College of Cardiology, American College of Emergency Physicians, and the Society for Cardiovascular Angiography and Interventions on [management of acute myocardial infarction](#) during the COVID-19 pandemic.

Table of Contents

Coming soon:

April 22, 2020

Executive Summary

Table of Contents

Levels of Evidence

Climate

Healthcare

Flooded by the torrent: the COVID-19 drug pipeline.

Global

The Socio-Economic Implications of the Coronavirus and COVID-19 Pandemic: A Review.

Disparities

COVID-19 and Racial Disparities.

COVID-19 exacerbating inequalities in the US.

Education

The Use of UV Fluorescent Powder for COVID-19 Airway Management Simulation Training

Epidemiology

Global

Regulation and trust: COVID-19 mortality in 25 European countries.

Flattening-the-curve Associated With Reduced COVID-19 Case Fatality Rates- An Ecological Analysis of 65 Countries

Estimation of basic reproduction number for COVID-19 and the reasons for its differences.

Modelling the epidemic spread of COVID-19 virus infection in Northern African countries.

COVID-19 virus outbreak forecasting of registered and recovered cases after sixty day lockdown in Italy: A data driven model approach.

Assessing Nitrogen Dioxide (NO₂) Levels as a Contributing Factor to Coronavirus (COVID-19) Fatality

The Second Worldwide Wave of Interest in Coronavirus since the COVID-19 Outbreaks in South Korea, Italy and Iran: A Google Trends Study.

Association of the COVID-19 Pandemic With Internet Search Volumes: A Google TrendsTM Analysis

Distinct Viral Clades of SARS-CoV-2: Implications for Modeling of Viral Spread.

Supporting pandemic response using genomics and bioinformatics: a case study on the emergent SARS-CoV-2 outbreak.

Symptoms and Severity

[The Impact of 2019 Novel Coronavirus on Heart Injury: A Systemic Review and Meta-analysis.](#)

[Smell and taste dysfunction in patients with COVID-19.](#)

[Symptom Screening at Illness Onset of Health Care Personnel With SARS-CoV-2 Infection in King County, Washington](#)

[Multicenter analysis of clinical characteristics and outcome of COVID-19 patients with liver injury.](#)

[Clinical characteristics of 80 hospitalized frontline medical workers infected with COVID-19 in Wuhan, China.](#)

[Diarrhea is associated with prolonged symptoms and viral carriage in COVID-19.](#)

Abstract:

[Risk factors of fatal outcome in hospitalized subjects with coronavirus disease 2019 from a nationwide analysis in China.](#)

[Risk factors for severe COVID-19: evidence from 167 hospitalized patients in Anhui, China.](#)

[Wei YY, Wang RR, Zhang DW, Tu YH, Chen CS, Ji S, Li CX, Li XY, Zhou MX, Cao WS, Han MF, Fei GH.](#)

[J Infect.](#)

[2020 Apr 16; PMID: 32305487](#)

[Level of Evidence: 4 – Case series](#)

[Type of Article: Letter to Editor](#)

[Risk Factors Associated With Disease Severity and Length of Hospital Stay in COVID-19 Patients](#)

[Liu, Xiaofan; Zhou, Hong; Zhou, Yilu; Wu, Xiaojun; Zhao, Yang; Lu, Yang; Tan, Weijun; Yuan, Mingli; Ding, Xuhong; Zou, Jinjing Zou; Li, Ruiyun; Liu, Hailing; Ewing, Rob M; Hu, Yi; Nie, Hanxiang; Wang, Yihua](#)

[J Infect](#)

[2020 Apr 16; PMID: 32305490](#)

[Level of Evidence: 3 - Cohort Study](#)

[Type of Article: Letter to the Editor, Research](#)

[Cardiac Involvement in COVID-19 Patients: Risk Factors, Predictors, and Complications: A Review](#)

[Diabetic patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcome.](#)

Disparities

[The impact of nutrition on COVID-19 susceptibility and long-term consequences.](#)

Women's Health

[Pregnant Versus Non-Pregnant SARS-CoV-2 and COVID-19 Hospital Admissions: The First 4 Weeks in New York.](#)

Pediatrics

[Coronavirus Infections in Children Including COVID-19: An Overview of the Epidemiology, Clinical Features, Diagnosis, Treatment and Prevention Options in Children.](#)

[Flash survey on severe acute respiratory syndrome coronavirus-2 infections in paediatric patients on anticancer treatment.](#)

Understanding the Pathology

Pathology

[COVID-19 Associated Hepatitis Complicating Recent Living Donor Liver Transplantation.](#)

[The Potential Role of Th17 Immune Responses in Coronavirus Immunopathology and Vaccine-induced Immune Enhancement](#)

[Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1, MERS-CoV and lessons from the past.](#)

Severe COVID-19 Infection Associated With Endothelial Activation

Escher, Robert; Breakey, Neal; Lämmle, Bernhard

Thromb Res

2020 Apr 15; PMID: 32305740

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Letter

Biomechanics

[Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19.](#)

[Clinical Implications of SARS-CoV2 Interaction with Renin Angiotensin System](#)

[Causes of hypogeusia/hyposmia in SARS-CoV2 infected patients.](#)

Immune response

[Human Leukocyte Antigen Susceptibility Map for SARS-CoV-2.](#)

[Comparative Computational Analysis of SARS-CoV-2 Nucleocapsid Protein Epitopes in Taxonomically Related Coronaviruses](#)

[Androgen hazards with COVID-19.](#)

[SARS-CoV-2: A new aetiology for atypical lymphocytes.](#)

[SARS-CoV-2 and viral sepsis: observations and hypotheses.](#)

Abstract: Since the outbreak of coronavirus disease 2019 (COVID-19), clinicians have tried every effort to understand the disease, and a brief portrait of its clinical features have been identified. In clinical practice, we noticed that many severe or critically ill COVID-19 patients developed typical clinical manifestations of shock, including cold extremities and weak peripheral pulses, even in the absence of overt hypotension. Understanding the mechanism of viral sepsis in COVID-19 is warranted for exploring better clinical care for these patients. With evidence collected from autopsy studies on COVID-19 and basic science research on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and SARS-CoV, we have put forward several hypotheses about SARS-CoV-2 pathogenesis after multiple rounds of discussion among basic science researchers, pathologists, and clinicians working on COVID-19. We hypothesise that a process called viral sepsis is crucial to the disease mechanism of COVID-19. Although these ideas might be proven imperfect or even wrong later, we believe they can provide inputs and guide directions for basic research at this moment.

[Miller Fisher Syndrome and Polyneuritis Cranialis in COVID-19](#)

Transmission & Prevention

Developments in Transmission & Prevention

[Impact of meteorological factors on the COVID-19 transmission: A multi-city study in China.](#)

[Re-emergence of SARS-CoV2 in a discharged COVID-19 case.](#)

[Airborne Transmission of Severe Acute Respiratory Syndrome coronavirus-2 to Healthcare Workers: A Narrative Review](#)

[Preterm Delivery in Pregnant Woman With Critical COVID-19 Pneumonia and Vertical Transmission.](#)

Prevention in the community

[Sustaining containment of COVID-19 in China.](#)

[Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China.](#)

[Preparedness for COVID-19 infection prevention in Korea: Single-center experience.](#)

[Recommendations for protecting against and mitigating the COVID-19 pandemic in long-term care facilities.](#)

[The immunological case for staying active during the COVID-19 pandemic.](#)

[Primary and Secondary Prevention of Cardiovascular Disease in the Era of the Coronavirus Pandemic.](#)

[COVID-19 Mobile Positioning Surveillance and Contact Tracing, and Patient Privacy](#)

[COVID-19: Health prevention and control in non-healthcare settings.](#)

Prevention in the hospital

[PPE and possible routes of airborne spread during the COVID-19 pandemic.](#)

[Inactivation of severe acute respiratory syndrome coronavirus 2 in plasma and platelet products using a riboflavin and ultraviolet light-based photochemical treatment.](#)

[COVID-19 putting patients at risk of unplanned extubation and airway providers at increased risk of contamination](#)

PPE & Decontamination Methods

[Challenges and solutions for addressing critical shortage of supply chain for personal and protective equipment \(PPE\) arising from Coronavirus disease \(COVID19\) pandemic - Case study from the Republic of Ireland.](#)

[SARS-CoV-2 RNA detection of hospital isolation wards hygiene monitoring during the Coronavirus Disease 2019 outbreak in a Chinese hospital.](#)

[Adaption of the Emergency Department Decontamination Room for Airway Management During COVID-19](#)

Management

Healthcare workforce injuries from COVID-19 related changes

[Covid-19: Countermeasure for N95 mask-induced pressure sore.](#)

[Skin Reactions to Non-glove Personal Protective Equipment: An Emerging Issue in the COVID-19 Pandemic.](#)

Acute care

[Thromboembolic events and apparent heparin resistance in patients infected with SARS-CoV-2.](#)

Emergency Medicine

[Summary of 20 tracheal intubation by anesthesiologists for patients with severe COVID-19 pneumonia: retrospective case series.](#)

[Coronavirus Outbreak: Is Radiology Ready? Mass Casualty Incident Planning. Which intravascular access should we use in patients with suspected/confirmed COVID-19?](#)

[Smereka J, Szarpak L, Filipiak KJ, Jaguszewski M, Ladny JR. Resuscitation.](#)

[Publication Date: April 15, 2020; PMID: 32304800.](#)

[Level of Evidence: 3 - Literature review](#)

[Comparing Rapid Scoring Systems in Mortality Prediction of Critical Ill \(sic\) Patients With Novel Coronavirus Disease](#)

Critical Care

[Blood transfusion strategies and ECMO during the COVID-19 pandemic.](#)

[Hypercoagulability of COVID-19 patients in Intensive Care Unit. A Report of Thromboelastography Findings and other Parameters of Hemostasis.](#)

[Chinese Expert Consensus on Diagnosis and Treatment of Coagulation Dysfunction in COVID-19](#)

[First Successful Treatment of COVID-19 Induced Refractory Cardiogenic Plus Vasoplegic Shock by Combination of pVAD and ECMO - A Case Report](#)

[A process for daily checks when using anaesthetic machines to ventilate the lungs of COVID-19 patients: the 'domino switch' technique.](#)

Radiology

[Contributory Role of Positron Emission Tomography in a Left Ventricular Assist Device Recipient at the time of COVID-19 pandemic.](#)

[Review of Artificial Intelligence Techniques in Imaging Data Acquisition, Segmentation and Diagnosis for COVID-19.](#)

Anesthesiology

[Extubation of patients with COVID-19.](#)

Internal Medicine

[Acute pulmonary embolism in a patient with COVID-19 pneumonia.](#)

[Pulmonary embolism in patients with COVID-19: Time to change the paradigm of computed tomography.](#)

[D-dimer Levels on Admission to Predict In-Hospital Mortality in Patients With Covid-19](#)

[ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection.](#)

Dermatology

[Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients.](#)

Cardiology

[Considerations for Drug Interactions on QTc in Exploratory COVID-19 \(Coronavirus Disease 2019\) Treatment.](#)

[Management of Acute Myocardial Infarction During the COVID-19 Pandemic.](#)

Neurology

[Meningoencephalitis without Respiratory Failure in a Young Female Patient with COVID-19 Infection in Downtown Los Angeles, Early April 2020.](#)

[Letter: COVID-19 Infection Affects Surgical Outcome of Chronic Subdural Hematoma.](#)

Immunology

[COVID-19 in patients with HIV: clinical case series.](#)

[Thromboinflammation and the hypercoagulability of COVID-19.](#)

Oncology

[Rapid Detection of Asymptomatic COVID-19 by CT Image-Guidance for Stereotactic Ablative Radiotherapy.](#)

Surgery

Vascular

[Venous thrombosis and arteriosclerosis obliterans of lower extremities in a very severe patient with 2019 novel coronavirus disease: a case report.](#)

Neurosurgery

[A COVID-19 Patient Who Underwent Endonasal Endoscopic Pituitary Adenoma Resection: A Case Report.](#)

Pediatric surgery

[Pediatric Endoscopy in the Era of Coronavirus Disease 2019: A North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Position Paper.](#)

Pediatrics

[Neonatal COVID-19: Little Evidence and the Need for More Information](#)

[Managing COVID-19-Positive Maternal-Infant Dyads: An Italian Experience.](#)

Adjusting Practice during COVID-19

Acute care

Emergency Medicine

[Practical diagnosis and treatment of suspected venous thromboembolism during COVID-19 Pandemic.](#)

Internal Medicine

Dermatology

[Overzealous hand hygiene during COVID 19 pandemic causing increased incidence of hand eczema among general population](#)

[Recommendations for Treatment of Cutaneous Lymphomas During the COVID-19 Pandemic.](#)

[Phototherapeutic approach to dermatological patients during the 2019 Coronavirus pandemic: Real-life Data from the Italian Red Zone.](#)

Cardiology

['COVID-19 Pandemic' Anxiety induced Tako-tsubo Cardiomyopathy.](#)

[Adapting to a Novel Disruptive Threat: Nuclear Cardiology Service in the Time of the Coronavirus \(COVID-19\) Outbreak 2020 \(SARS REBOOT\).](#)

Neurology

[Cerebrovascular disease is associated with an increased disease severity in patients with Coronavirus Disease 2019 \(COVID-19\): A pooled analysis of published literature.](#)

[EXPRESS: COVID-19 and Stroke - A Global World Stroke Organization perspective.](#)

[Multiple sclerosis and the risk of infection: considerations in the threat of the novel coronavirus, COVID-19/SARS-CoV-2.](#)

[Parkinson's disease and COVID-19: Perceptions and implications in patients and caregivers.](#)

Gastroenterology

[Plexiglass barrier box to improve ERCP safety during the COVID-19 pandemic.](#)

[ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic.](#)

[Covid-19 and immunomodulation in IBD.](#)

Abstract: The current coronavirus pandemic is an ongoing global health crisis due to covid-19, caused by severe acute respiratory syndrome coronavirus 2. Although covid-19 leads to little or mild flu-like symptoms in the majority of affected patients, the disease may cause severe, frequently lethal complications such as progressive pneumonia, acute respiratory distress syndrome and organ failure driven by hyperinflammation and a cytokine storm syndrome. This situation causes various major challenges for gastroenterology. In the context of IBD, several key questions arise. For instance, it is an important question to understand whether patients with IBD (eg, due to intestinal ACE2 expression) might be particularly susceptible to covid-19 and the cytokine release syndrome associated with lung injury and fatal outcomes. Another highly relevant question is how to deal with immunosuppression and immunomodulation during the current pandemic in patients with IBD and whether immunosuppression affects the progress of covid-19. Here, the current understanding of the pathophysiology of covid-19 is reviewed with special reference to immune cell activation. Moreover, the potential implications of these new insights for immunomodulation and biological therapy in IBD are discussed.

[British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic.](#)

[Prevention of COVID-19 in patients with inflammatory bowel disease in Wuhan, China.](#)

[Potential implications of COVID-19 in non-alcoholic fatty liver disease.](#)

Endocrinology

[Managing New-Onset Type 1 Diabetes During the COVID-19 Pandemic: Challenges and Opportunities.](#)

[2020 Apr 17; PMID: 32302499](#)

[Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic.](#)

[Diabetes self-management amid COVID-19 pandemic.](#)

Rheumatology

[Should SARS-CoV-2 influence immunosuppressive therapy for autoimmune blistering diseases?](#)

[2020 Apr 17; PMID: 32302437](#)

Hematology

[American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group Position Statement on Pharmacy Practice Management and Clinical Management for COVID-19 in Hematopoietic Cell Transplant and Cellular Therapy Patients in the United States.](#)

Oncology

[Strategies for patient with cancer during COVID-19 pandemic.](#)

Surgery

[ENT/otolaryngology](#)

Cardiothoracic

[Cardiovascular Surgery in the COVID-19 Pandemic](#)

[Vascular](#)

Urology

[Endourological Stone Management in the Era of the COVID-19.](#)

OBGYN

[COVID19 during pregnancy: a systematic review of reported cases.](#)

[No-Test Medication Abortion: A Sample Protocol for Increasing Access During a Pandemic and Beyond.](#)

Pediatrics

[Rapid Development of Telehealth Capabilities within Pediatric Patient Portal Infrastructure for COVID-19 Care: Barriers, Solutions, Results.](#)

[Paediatric Anaesthetic implications of COVID-19 - A Review of Current Literature.](#)

Abstract: Paediatric anaesthetists have an important role to play in the management of patients suspected or confirmed to have COVID-19. In many institutions, the COVID-19 intubation teams are staffed with anaesthetists as the proceduralists working throughout the hospitals also in the ICU and Emergency Departments. As practitioners who perform aerosol generating procedures involving the airway, we are at high risk of exposure to the virus SARS-CoV-2 and need to ensure we are well-prepared and trained to manage such cases. This article reviews the relevant paediatric literature surrounding COVID-19 and summarises the key recommendations for anaesthetists involved in the care of children during this pandemic.

Transplant medicine

[Pharmacologic treatment of transplant recipients infected with SARS-CoV-2: considerations regarding therapeutic drug monitoring and drug-drug interactions.](#)

Palliative Care

[Emergency Palliative Care Planning and Support in a COVID-19 Pandemic.](#)

R&D: Diagnosis & Treatments

Current Diagnostics

[Detection and analysis of nucleic acid in various biological samples of COVID-19 patients.](#)

[A report of three COVID-19 cases with prolonged viral RNA detection in anal swabs.](#)

[Testing for SARS-CoV-2: Can We Stop at Two?](#)

[SARS-CoV-2: What Can Saliva Tell Us?](#)

[Detection of SARS-CoV-2 RNA and Antibodies in Diverse Samples: Protocol to Validate the Sufficiency of Provider-Observed Home-Collected Blood, Saliva and Oropharyngeal Samples](#)

[The Appropriate Use of Testing for COVID-19.](#)

Developments in Diagnostics

[CRISPR-Cas12-based Detection of SARS-CoV-2](#)

[Routine Blood Tests as a Potential Diagnostic Tool for COVID-19](#)

[The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients](#)

[Antibody Detection and Dynamic Characteristics in Patients with COVID-19.](#)

Developments in Treatments

[Comparative Pathogenesis of COVID-19, MERS, and SARS in a Nonhuman Primate Model](#)
[A Detectable Serum SARS-CoV-2 Viral Load \(RNAemia\) Is Closely Correlated With Drastically Elevated Interleukin 6 \(IL-6\) Level in Critically Ill COVID-19 Patients](#)

[Weak Induction of Interferon Expression by SARS-CoV-2 Supports Clinical Trials of Interferon Lambda to Treat Early COVID-19](#)

[Clinical Pharmacology Perspectives on the Antiviral Activity of Azithromycin and Use in COVID-19.](#)

[Novel 2019 Coronavirus Structure, Mechanism of Action, Antiviral drug promises and rule out against its treatment.](#)

[The BTK-inhibitor ibrutinib may protect against pulmonary injury in COVID-19 infected patients.](#)

[Coronavirus drugs: Using plasma from recovered patients as a treatment for COVID-19](#)

Abstract

[The ongoing COVID-19 pandemic has infected nearly 400,000 individuals with 17000 deaths since it was first identified in human populations in December 2019, in Wuhan, China. No antiviral therapies or vaccines are available for their treatment or prevention. Passive immunization PI through broadly neutralizing antibodies that bind to the specific antigens of SARS-CoV 2 might be a potential solution to address the immediate health threat of COVID-19 pandemic while vaccines are being developed. The PI approach in treating COVID-19 is discussed herein, including a summary of its historical applications to confront epidemics.](#)

[Peptide-like and Small-Molecule Inhibitors Against COVID-19](#)

Mental Health & Resilience Needs

[ADHD management during the COVID-19 pandemic: guidance from the European ADHD Guidelines Group.](#)

[Public Health Approach of Ayurveda and Yoga for COVID-19 Prophylaxis.](#)

Silver Linings

[World Leaders' Usage of Twitter in Response to the COVID-19 Pandemic: A Content Analysis](#)

Resources

[Epidemiology and clinical features of COVID-19: A review of current literature.](#)

Acknowledgements

Levels of Evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

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

Climate

Healthcare

Flooded by the torrent: the COVID-19 drug pipeline.

Mullard A.

Lancet

2020 Apr 18, PMID: 32305088

Level of Evidence: 5 - Expert Opinion

Article Type: Commentary

Summary: Researchers are working on clinical trials for treatment options and outcomes of COVID-19. They recommend investigators to search for the Solidarity trial, a WHO sanctioned study of four therapeutic approaches for hospitalised patients with confirmed COVID-19, when creating their own trial to learn what is currently known or being investigated.

Global

Following Data as it Crosses Borders During the COVID-19 Pandemic.

Plasek JM, Tang C, Zhu Y, Huang Y, Bates DW. Plasek JM, et al.

J Am Med Inform Assoc

2020 Apr 20; PMID: 32311047

Level of Evidence: 5 - Expert opinion

Type of Article: Perspective

BLUF: The dissemination of global data on disease trajectories can assist governments, policymakers, public health and healthcare systems, and the public to coordinate pandemic responses, implement prevention and mitigation strategies, epidemiological tracing, and allocate healthcare resources. Other benefits of data sharing include greater research efforts, increased drug and equipment development, and population travel and disease surveillance.

Abstract:

Data changes the game in terms of how we respond to pandemics. Global data on disease trajectories and the **effectiveness and economic impact of different social distancing measures are essential to facilitate effective local responses to pandemics**. COVID-19 data flowing across geographic borders are extremely useful to public health professionals for many purposes such as **accelerating the pharmaceutical development pipeline, and for making vital decisions about intensive care unit rooms, where to build temporary hospitals, or where to boost supplies of personal protection equipment, ventilators, or diagnostic tests**. Sharing data enables **quicker dissemination and validation of pharmaceutical innovations**, as well as **improved knowledge of what prevention and mitigation measures work**. Even if physical borders around the globe are closed, it is crucial that data continues to transparently flow across borders to enable a data economy to thrive which will promote global public health through global cooperation and solidarity.

The Socio-Economic Implications of the Coronavirus and COVID-19 Pandemic: A Review.

Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, Agha M, Agha R.

Int J Surg.

2020 Apr 16; PMID: 32305533

Level of Evidence:5 - Mechanism Based Reasoning

Type of Article: Economic Review

BLUF: The following is an economic review of the global impact of the COVID-19 pandemic. Central banks globally commit to a 'Whatever it takes' approach in an attempt to save the global economy. Europe pledges a €1.7tn rescue package. The road to economic recovery is predicted to be a long one, with a period of economic inactivity for years to come.

Abstract: The COVID-19 pandemic has resulted in over 1.4 million confirmed cases and over 83,000 deaths globally. It has also sparked fears of an impending economic crisis and recession. Social distancing, self-isolation and travel restrictions forced a decrease in the workforce across all economic sectors and caused many jobs to be lost. Schools have closed down, and the need of commodities and manufactured products has decreased. In contrast, the need for medical supplies has significantly increased. The food sector has also seen a great demand due to panic-buying and stockpiling of food products. In response to this global outbreak, we summarise the socio-economic effects of COVID-19 on individual aspects of the world economy.

Disparities

COVID-19 and Racial Disparities.

Shah M, Sachdeva M, Dodiuk-Gad RP.

Dermatol

2020 Apr 16; PMID: 32305444

Level of Evidence: 5 – Expert Opinion

Type of Article: Letter

Summary: The author's **initial review of data** from several cities in the United States suggests that a disproportionate number of COVID-19 cases and deaths are affecting African Americans. A higher comorbidity burden, lower socio-economic status (leading to closer contact with others and decreased access to health care resources), and a higher likelihood of working as part of the essential workforce may contribute to this disparity. They call for measures to ensure equitable access to healthcare resources and more research on racial differences in COVID-19 prevalence and outcomes.

COVID-19 exacerbating inequalities in the US.

Dorn AV, Cooney RE, Sabin ML

Lancet

2020 Apr 18; PMID: 32305087

Level of Evidence: 6- No data cited

Type of Article: World Report

Summary excerpt: "Emerging morbidity and mortality data have already clearly demonstrated what many have feared: a pandemic in which the brunt of the effects fall on already vulnerable US populations, and in which the deeply rooted social, racial, and economic health disparities in the country have been laid bare."

Education

The Use of UV Fluorescent Powder for COVID-19 Airway Management Simulation Training

Gardiner, Casey; Veall, J; Lockhart, Steven

Anaesthesia

2020 Apr 16; PMID: 32298467

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Correspondence

BLUF: Authors specify a training simulation for intubation using UV fluorescent powder to represent the risk of the aerosolization of COVID-19 during endotracheal intubations.

Abstract:

The COVID-19 pandemic has made it imperative to rapidly implement changes to typical medical practice in order to minimise spread of the SARS-CoV-2 virus. Many of these changes are non-intuitive or differ significantly from normal practice. For this reason, we read with great appreciation the timely article by Fregene et al. [1], which describes translational simulation leading to increased preparedness at their institution. With the recognition that aerosol generating procedures are of particular importance to practice due to their high risk of virus transmission, we offer an additional tool for COVID-19 airway simulation training that helped consolidate learning and motivate change to practice in hospitals across Vancouver.

Epidemiology

Global

Regulation and trust: COVID-19 mortality in 25 European countries.

Oksanen A, Kaakinen M, Latikka R, Savolainen I, Savela N, Koivula A. Oksanen A, et al.

JMIR Public Health Surveill.

2020 Apr 16; PMID: 32301734

Level of Evidence: 3 - Cross-Sectional Study

Article Type: Research

BLUF: This study examines the role of societal and socio-psychological factors that drive the spread of COVID-19 by assessing social risk factors, restrictions, control measures and institutional trust. They found that institutional trust was inversely correlated with higher mean and daily mortality, while perceived sociability was positively correlated with COVID-19 mortality (Figure 2). Curfews were also associated with increased COVID-19 mortality (Model 2, table 2). Interestingly, there were no significant differences in daily mortality based on institutional trust. This, however, became significant in daily mortality 3 weeks following the onset of the outbreak (Figure 4).

Abstract:

Background: The outbreak of COVID-19 has dramatically changed societies in 2020. Since the end of February, Europe has been hit particularly hard by COVID-19, but there are major country differences in both the spread of the virus and measures taken to stop the virus. Social psychological factors such as institutional trust could be important in understanding the development of the epidemic.

Objective: The aim of our study was to examine country-variation in COVID-19 mortality in Europe by analyzing 1) social risk factors explaining the spread of the disease, 2) restrictions and control measures and 3) institutional trust.

Methods: The present study was based on a background analysis of European Social Survey data on 25 European countries ($N = 47,802$). Multilevel mixed effects linear regression models focused on 84 days of the COVID-19 epidemic (January 22 - April 14, 2020) and modelled the daily COVID-19 mortality. Analysis focused on the impact of social relations, restrictions and institutional trust within each country.

Results: The spread of the COVID-19 epidemic has been fast everywhere, but our findings reveal significant differences between countries in COVID-19 mortality. Perceived sociability predicted higher COVID-19 mortality. Major differences between the 25 countries were found in reaction times to the crisis. Late reaction to the crisis predicted later mortality figures. Institutional trust was associated with lower COVID-19 mortality. Increase in mortality was more rapid in countries that reacted late during the 21-day follow-up.

Conclusions: The analyses demonstrated the importance of societal and social psychological factors in the spread of the COVID-19 epidemic. By considering multiple perspectives, our study showed that country differences in Europe are major and this will have an impact on how countries will cope with the ongoing crisis in the following months. Our results indicate the importance of timely restrictions and cooperation with people.

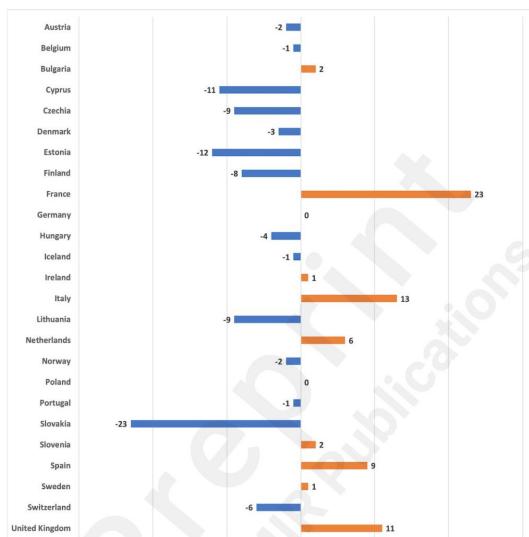


Figure 1. First national restrictions placed before (-) or after (+) the first COVID-19 death (days).

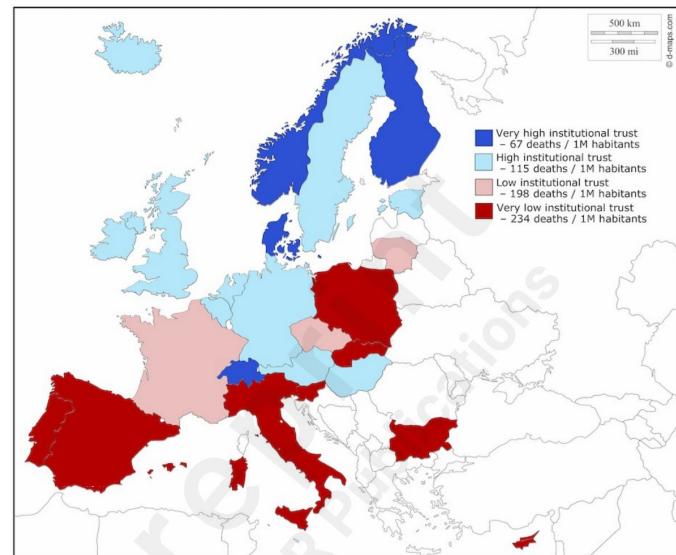


Figure 2. Mean deaths per million habitants by countries' level of institutional trust.

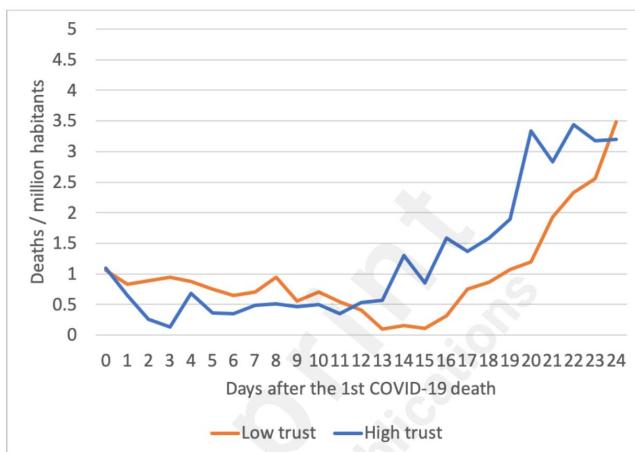


Figure 3. Deaths per day after first COVID-19 death in low and high trust countries.

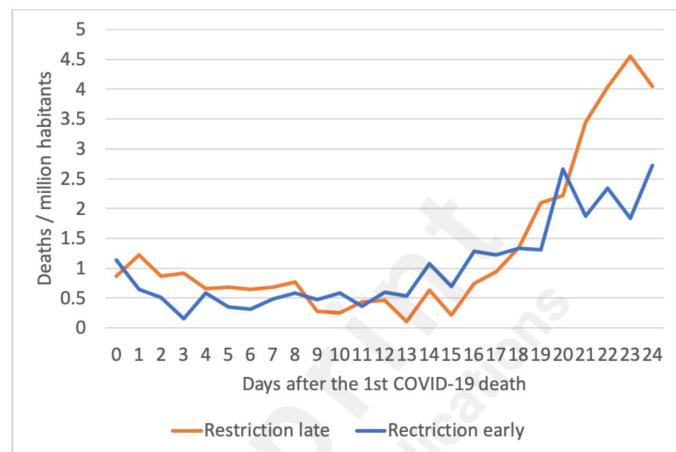


Figure 4. Deaths per day after first COVID-19 death in countries reacting late and early.

Table 3. Multilevel mixed effects linear regression models predicting daily COVID-19 mortality in 25 European countries

Fixed part	Model 1			Model 2			Model 3		
	B	95% CI	p value	B	95% CI	p value	B	95% CI	p value
Constant	6.81	[4.05–9.56]	<0.001	5.75	[3.15–8.34]	<0.001	5.29	[2.67–7.90]	<0.001
Within country effects									
Time	0.16	[0.11–0.22]	<0.001	0.16	[0.10–0.22]	<0.001	0.16	[0.10–0.22]	<0.001
Between country effects									
Perceived sociality	7.04	[0.25–13.83]	0.042						
National restrictions after first death				2.55	[1.08–4.02]	0.001			
Institutional trust							-0.42	[-0.65–0.19]	<0.001
Population	0.02	[-0.03–0.08]	0.422	0.02	[-0.03–0.07]	0.392	-0.02	[-0.08–0.05]	0.600
Population density	0.00	[0.00–0.01]	0.043	0.00	[0.00–0.01]	0.199	0.00	[0.00–0.01]	0.048
Old-age dependency ratio	-0.04	[-0.29–0.20]	0.729	0.03	[-0.20–0.26]	0.801	-0.04	[-0.26–0.18]	0.732
Country household size average	0.96	[-1.00–2.92]	0.336	0.98	[-0.94–2.91]	0.315	-0.55	[-2.45–1.35]	0.569
Life expectancy at birth	0.27	[-0.01–0.54]	0.058	0.37	[0.14–0.59]	0.002	0.29	[0.05–0.52]	0.015
Health care expenditure per inhabitant	-0.60	[-1.28–0.07]	0.080	-0.25	[-0.59–0.08]	0.142	0.46	[0.03–0.88]	0.034
High tourist arrival	0.65	[-0.62–1.93]	0.317	1.11	[-0.10–2.33]	0.072	2.12	[0.40–3.83]	0.016
The length of follow-up period	0.13	[0.06–0.20]	0.001	0.12	[0.05–0.19]	0.001	0.19	[0.12–0.26]	<0.001
Random part	SD	95% CI		SD	95% CI		SD	95% CI	
Time	0.10	[0.07–0.15]		0.10	[0.07–0.15]		0.11	[0.07–0.15]	
Const	3.58	[2.55–5.00]		3.60	[2.61–4.97]		3.59	[2.59–4.97]	

Flattening-the-curve Associated With Reduced COVID-19 Case Fatality Rates- An Ecological Analysis of 65 Countries

Kenyon C

J Infect

2020 Apr 16; PMID: 32305488

Level of Evidence: 5 - Expert opinion

Type of Article: Research

BLUF: The author provides **some statistical support for the “flattening-the-curve” model of COVID-19 fatality rate reduction by correlating rough numbers for fatality rates for 65 countries to number of tests and number of cases**, taking care to account for some confounding variables like per capita healthcare expenditure and WHO region.

Abstract:

- COVID-19 incidence is an independent predictor of the COVID-19 case fatality rate.
- These findings support ongoing efforts to flatten-the-curve.
- Flattening-the-curve likely reduces the probability of hospitals being overrun and therefore delivering suboptimal care.

Estimation of basic reproduction number for COVID-19 and the reasons for its differences.

Najafimehr H, Mohamed Ali K, Safari S, Yousefifard M, Hosseini M.

Int J Clin Pract.

2020 Apr 16; PMID: 32301199

Level of Evidence: 5 - Expert opinion

Type of Article: Letter to the Editor

Summary: A review of current data **estimates the R_0 for COVID-19 to be between 2.44-4.2.** Studies from China give a wide range of R_0 , from 1.4 to 7.23. In Italy, it was estimated as 4.2. The

WHO range is 1.4-2.5. Differences in the authors' estimated R_0 values are primarily due to the different methods of calculation (mathematical, statistical, or stochastic). Another explanation for the variance is due to the contact rate varying wildly by geographical location, as well as the varied accuracy of the reported data used in these studies.

Modelling the epidemic spread of COVID-19 virus infection in Northern African countries.

Daw MA, El-Bouzedi AH.

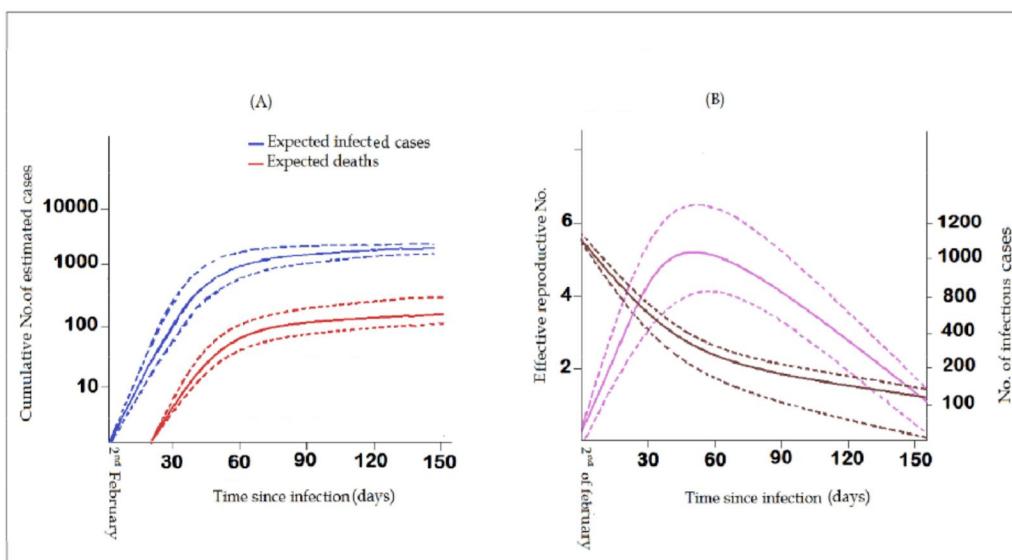
Travel Med Infect Dis.

2020 Apr 15; PMID: 32304743

Level of Evidence: 5 -

Type of Article: Letter to the Editor

Summary: Response to the ongoing COVID-19 pandemic remains challenging in Northern African countries that suffer from poor infrastructure, political instability, and lack of experience in combatting epidemics. Herein, the transmissibility of COVID-19 in Northern Africa was evaluated using the serial interval equal to that of COVID-19 in Wuhan, China, with a mean of 7.5 days and a standard deviation of 3.4 days. The number of **infected individuals is expected to peak in early May 2020** (80 days since initiation) with a **peak population size of 795 (750-1,200)** infectious individuals in Northern Africa. Promotion of face mask use and reduction of travel are measures that should be promoted in these regions to slow the ongoing spread.



COVID-19 virus outbreak forecasting of registered and recovered cases after sixty day lockdown in Italy: A data driven model approach.

Chintalapudi N, Battineni G, Amenta F

J Microbiol Immunol Infect.

2020 Apr 13; PMID: 32305271

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Research

BLUF: An autoregressive integrated moving average (ARIMA) model predicts a 35% decrease in COVID-19 cases and 66% increase in recovered cases if Italy remains locked down for 60 more days.

ABSTRACT:

Background: Till 31 March 2020, 105,792 COVID-19 cases were confirmed in Italy including 15,726 deaths which explains how worst the epidemic has affected the country. After the announcement of lockdown in Italy on 9 March 2020, situation [sic] was becoming stable since last [sic] days of March. In view of this, it is important to forecast the COVID-19 evaluation of Italy condition and the possible effects, **if this lock down could continue for another 60 days.**

Methods: COVID-19 infected patient data has extracted [sic] from the Italian Health Ministry website includes **registered and recovered cases from mid February to end March**. Adoption of seasonal ARIMA forecasting package with R statistical model was done.

Results: Predictions were done with 93.75% of accuracy for registered case models and 84.4% of accuracy for recovered case models. The forecasting of **infected patients could be reach [sic] the value of 182,757**, and **recovered cases could be registered value of [sic] 81,635** at end of May.

Conclusions: This study highlights the **importance of country lockdown and self isolation** in control [sic] the disease transmissibility among Italian population through data driven model analysis. Our findings suggest that nearly 35% decrease of registered cases and 66% growth of recovered cases will be possible.

[**Assessing Nitrogen Dioxide \(NO₂\) Levels as a Contributing Factor to Coronavirus \(COVID-19\) Fatality**](#)

Ogen Y

Sci Total Environ

2020 Apr 11; PMID: 32302812

Level of Evidence: 5 – Mechanism-based Reasoning

Type of Article: Research

BLUF: Nitrogen dioxide is an ambient gas and pollutant that has been associated with various morbidities, including hypertension and COPD. This study explores **COVID-19 fatality rates as a function of local atmospheric nitrogen dioxide** concentration. The authors report the **highest fatality rates colocalizing** to the same five regions across Spain, France, Germany, and Italy with the **highest concentrations of nitrogen dioxide**.

Abstract:

Nitrogen dioxide (NO₂) is an ambient trace-gas result of both natural and anthropogenic processes. Long-term exposure to NO₂ may cause a wide spectrum of severe health problems such as hypertension, diabetes, heart and cardiovascular diseases and even death. The objective of this study is to **examine the relationship between long-term exposure to NO₂ and coronavirus fatality**. The Sentinel-5P is used for mapping the tropospheric NO₂ distribution and the NCEP/NCAR reanalysis for evaluating the atmospheric capability to disperse the pollution. The spatial analysis has been conducted on a regional scale and combined with the number of death cases taken from 66 administrative regions in Italy, Spain, France and Germany. Results show that out of the 4443 fatality cases, **3487 (78%) were in five regions located in north Italy and central Spain**. Additionally, the **same five regions** show the **highest NO₂ concentrations** combined with downwards airflow which prevent an efficient dispersion of air pollution. These results indicate that the **long-term exposure** to this pollutant **may be one of the most important contributors to fatality** caused by the COVID-19 virus in these regions and maybe across the whole world.

The Second Worldwide Wave of Interest in Coronavirus since the COVID-19 Outbreaks in South Korea, Italy and Iran: A Google Trends Study.

Strzelecki A.

Brain Behav Immun

2020 Apr 17; PMID: 32311493

Level of Evidence: 5 - Predictive modeling

Type of Article: Letter to the Editor

BLUF: The author reports that google trend data on ‘coronavirus’ queries preceded the regional and global increase in disease incidence in COVID-19, potentially as a result of symptomatic persons seeking validation. The authors warn of second peak as the number of queries peaked once again globally on **April 5, 2020**.

Summary: The authors conducted an analysis of global and regional interest in COVID-19 using google trend data and compared this to WHO data on new COVID-19 cases. **Queries using the search term “coronavirus” were used as the marker of interest in the virus** and they analyzed google trend data from China, South Korea, Italy, Iran, and world wide between 1/15/2020 and 4/11/2020. The analysis showed **peaks in search queries occurred prior to global and regional peaks in new cases in these areas**. They also noted that this **pattern was duplicated in the worldwide data set prior to a “second wave of cases” with a new peak in searches on April 5, 2020 after an initial decrease in interest in the beginning of February**.

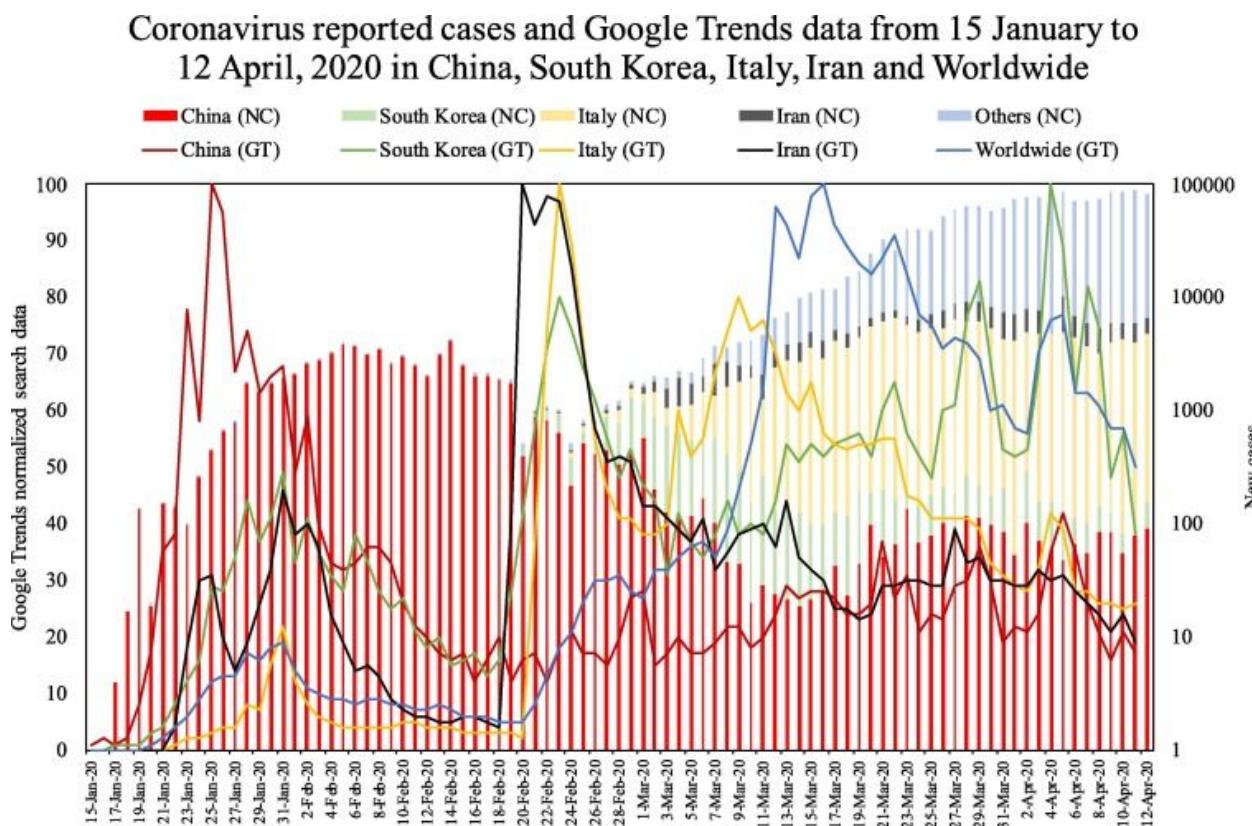


Figure 1. This figure shows the number of new cases as vertical bars and the google search queries as line charts for the time period of the data analysis and visually represents the peaks in each.

Association of the COVID-19 Pandemic With Internet Search Volumes: A Google Trends™ Analysis

Effenberger M, Kronbichler A, Shin JI, Mayer G, Tilg H, Perco P.

Int J Infect Dis.

2020 Apr 16; PMID: 32305520

Level of Evidence: 5 – Mechanism Based Reasoning

Type of Article: Research

Summary: This article presents an “infodemiology” analysis of relative internet search volumes (RSV) to determine if a correlation exists between public interest in COVID-19 (as measured by RSV determined from Google Trends™ data worldwide) and the incidence of COVID-19. The analysis found many countries saw a peak in public interest an average about 11.5 days before a peak in new cases was observed. The authors speculate the correlation partially be a result of searches performed to look up symptoms and propose potential applications for an infodemiology approach to predict peaks in COVID-19 cases.

Abstract:

Objectives: To assess the association of public interest in coronavirus infections with the actual number of infected cases for selected countries across the globe.

Methods: We performed a Google TrendsTM search for "Coronavirus" and compared Relative Search Volumes (RSV) indices to the number of reported COVID-19 cases by the European Center for Disease Control (ECDC) using time-lag correlation analysis.

Results: Worldwide public interest in Coronavirus reached its first peak end of January when numbers of newly infected patients started to increase exponentially in China. The worldwide Google TrendsTM index reached its peak on the 12th of March 2020 at a time when numbers of infected patients started to increase in Europe and COVID-19 was declared a pandemic. At this time the general interest in China but also the Republic of Korea has already significantly decreased as compared to the end of January. Correlations between RSV indices and number of new COVID-19 cases were observed across all investigated countries with highest correlations observed with a time lag of -11.5 days, i.e. highest interest in coronavirus observed 11.5 days before the peak of newly infected cases. This pattern was very consistent across European countries but also holds true for the US. In Brazil and Australia, highest correlations were observed with a time lag of -7 days. In Egypt the highest correlation is given with a time lag of 0, potentially indicating that in this country, numbers of newly infected patients will increase exponentially within the course of April.

Conclusions: Public interest indicated by RSV indices can help to monitor the progression of an outbreak such as the current COVID-19 pandemic. Public interest is on average highest 11.5 days before the peak of newly infected cases.

Distinct Viral Clades of SARS-CoV-2: Implications for Modeling of Viral Spread.

Brufsky A. Brufsky A.

J Med Virol.

2020 Apr 20; PMID: 32311094

Level of Evidence: 5 - Expert Opinion

Type of Article: Commentary

BLUF: A commentary hypothesizing varied virulence in SARS-CoV-2 from mutated/distinct clades of viral strains that may be an additional factor at play during this pandemic.

Abstract: Distinct viral clades have a likely impact on COVID-19 pathogenesis and spread. Sequence analysis from 2310 viral isolates from Nexstrain reveals that residue at 614 of the viral spike protein is changed from a putative ancestral aspartic acid (D) to a glycine (G) between two viral clades. The G strain is predominantly on the East Coast of the United States, and the D strain is predominantly on the West Coast. This mutation of the SARS-CoV-2 S protein spike is conserved in coronaviruses. Point mutations in a murine coronavirus spike protein can result in increased virulence through instability of the viral machinery and altered viral to cell membrane fusion. This observation may partially explain the discrepancy in predicted deaths from COVID-19 between the East Coast and West Coast, and possibly explain that other factors aside from social distance, such as competition between two strains of differing virulence, may be at play.

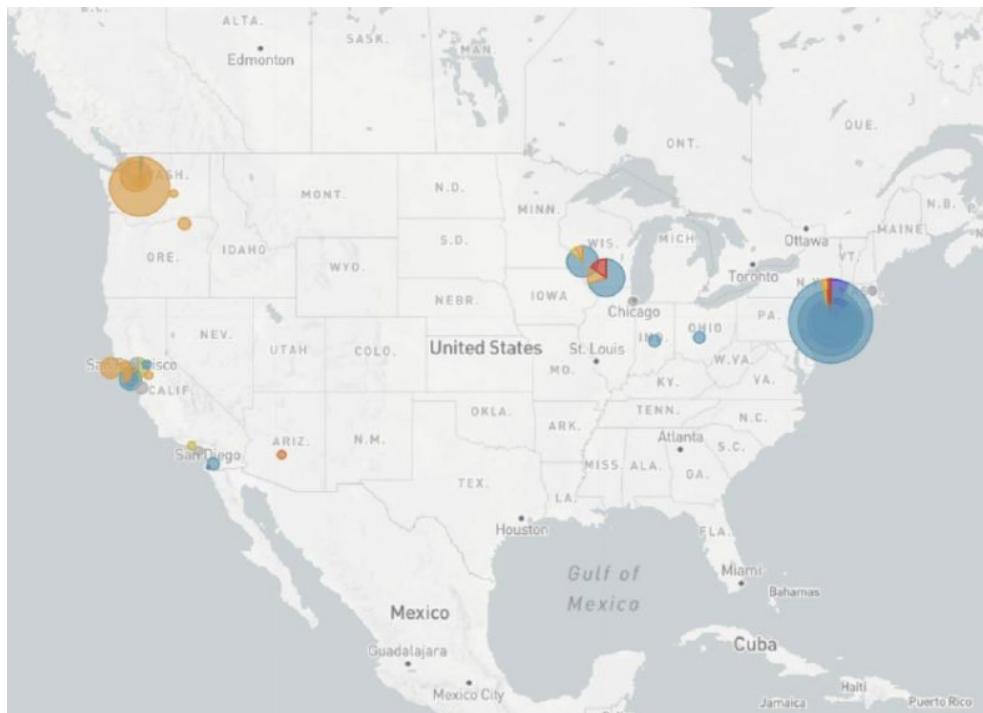


Figure 1: Dominant viral clades in the United States. Clade B1 (Orange) and Clade A2a (Blue)

Supporting pandemic response using genomics and bioinformatics: a case study on the emergent SARS-CoV-2 outbreak.

Bauer, Denis C; Tay, Aidan P; Wilson, Laurence O W; Reti, Daniel; Hosking, Cameron; McAuley, Alexander J; Pharo, Elizabeth; Todd, Shawn; Stevens, Vicky; Neave, Matthew J; Tachedjian, Mary; Drew, Trevor W; Vasan, S S

Transbound Emerg Dis

2020 Apr 19; PMID: 32306500

Level of Evidence: 5 – Mechanism-based reasoning

Article Type: Letter to the Editor

Summary: The authors compared two Australian isolates of covid-19 with known viral sequences from GISAID and validated their comparisons against known SARS and MERS sequences. They note that of the 6 strains of coronavirus being tracked, C3 (USA) is closest to a consensus model, but also that **there is not truly enough data to understand how many different strains have developed or are likely to develop.** This could present challenges when attempting to develop a vaccine. They recommend combining bioinformatics (i.e. sequencing and attempting to create

synthetic consensus sequences) with epidemiological and experimental data to choose which viral isolates to use for testing in the development of treatments and vaccines.

Abstract:

Pre-clinical responses to fast moving infectious disease outbreaks heavily depend on choosing the best isolates for animal models that inform diagnostics, vaccines and treatments. Current approaches are driven by practical considerations (e.g. first available virus isolate) rather than a detailed analysis of the characteristics of the virus strain chosen, which can lead to animal models that are not representative of the circulating or emerging clusters. Here, we suggest a combination of epidemiological, experimental and bioinformatics considerations when choosing virus strains for animal model generation. We discuss the currently chosen SARS-CoV-2 strains for international coronavirus disease (COVID-19) models in the context of their phylogeny as well as in a novel alignment-free bioinformatics approach. Unlike phylogenetic trees, which focus on individual shared mutations, this new approach assesses genome-wide co-developing functionalities and hence offers a more fluid view of the “cloud of variances” that RNA viruses are prone to accumulate. This joint approach concludes that while the current animal models cover the existing viral strains adequately, there is substantial evolutionary activity that is likely not considered by the current models. Based on insights from the non-discrete alignment-free approach and experimental observations, we suggest isolates for future animal models.

Symptoms and Severity

The Impact of 2019 Novel Coronavirus on Heart Injury: A Systemic Review and Meta-analysis.

Li JW, Han TW, Woodward M, Anderson CS, Zhou H, Chen YD, Neal B.

Prog Cardiovasc Dis

2020 Apr 16; PMID: 32305557

Level of Evidence: 2 – Systematic Review of Surveys that Allow Matching to Local Circumstances

Type of Article: Review

Summary: This meta-analysis of 28 observational studies with data on cardiac biomarkers (amounting to 4189 COVID-19 cases) assesses COVID-19’s association with acute cardiac injury. The analysis found that elevated cardiac injury biomarkers and acute cardiac injury were more common in more severe cases. Death was found to be more common in patients who experienced acute cardiac injury. The authors call for studies to determine whether cardiac supportive measures improve outcomes for COVID-19 patients.

Abstract:

Background: Evidence about COVID-19 on cardiac injury is inconsistent.

Objectives: We aimed to summarize available data on severity differences in acute cardiac injury and acute cardiac injury with mortality during the COVID-19 outbreak.

Methods: We performed a systematic literature search across Pubmed, Embase and pre-print from December 1, 2019 to March 27, 2020, to identify all observational studies that reported cardiac specific biomarkers (troponin, creatine kinase-MB fraction, myoglobin, or NT-proBNP) during COVID-19 infection. We extracted data on patient demographics, infection severity, comorbidity history, and biomarkers during COVID-19 infection. Where possible, data were pooled for meta-analysis with standard (SMD) or weighted (WMD) mean difference and corresponding 95% confidence intervals (CI).

Results: We included 4189 confirmed COVID-19 infected patients from 28 studies. More severe COVID-19 infection is associated with higher mean troponin (SMD 0.53, 95% CI 0.30 to 0.75,

$p < 0.001$), with a similar trend for creatine kinase-MB, myoglobin, and NT-proBNP. Acute cardiac injury was more frequent in those with severe, compared to milder, disease (risk ratio 5.99, 3.04 to 11.80; $p < 0.001$). Meta regression suggested that cardiac injury biomarker differences of severity are related to history of hypertension ($p = 0.030$). Also COVID19-related cardiac injury is associated with higher mortality (summary risk ratio 3.85, 2.13 to 6.96; $p < 0.001$). hsTnI and NT-proBNP levels increased during the course of hospitalization only in non-survivors.

Conclusion The severity of COVID-19 is associated with acute cardiac injury, and acute cardiac injury is associated with death. Cardiac injury biomarkers mainly increase in non-survivors. This highlights the need to effectively monitor heart health to prevent myocarditis in patients infected with COVID-19.

Smell and taste dysfunction in patients with COVID-19.

Xydakis, Michael S; Dehgani-Mobaraki, Puya; Holbrook, Eric H; Geisthoff, Urban W; Bauer, Christian; Hautefort, Charlotte; Herman, Philippe; Manley, Geoffrey T; Lyon, Dina M; Hopkins, Claire

Lancet Infect Dis

2020 Apr 19; PMID: 32304629

Level of Evidence: 5 - Expert Opinion

Type of Article: Letter

BLUF: [P]hysicians evaluating patients with acute-onset loss of smell or taste, particularly in the context of a patent nasal airway (ie, non-conductive loss), should have a high index of suspicion for concomitant SARS-CoV-2 infection.

SUMMARY: The American Academy of Otolaryngology--Head and Neck Surgery and the British Association of Otorhinolaryngology recommend that anosmia with or without dysgeusia be added to the list of primary screening symptoms for COVID-19. These symptoms may be seen early in the course of infection or in patients with mild or no constitutional symptoms. The traditional nasal cavity manifestations, such as nasal congestion or rhinorrhea, seen in other upper respiratory infections are commonly absent in patients with COVID-19, suggesting that SARS-CoV-2 is a neurotropic virus with a tropism for the olfactory system.

Symptom Screening at Illness Onset of Health Care Personnel With SARS-CoV-2 Infection in King County, Washington

Chow, Eric J.; Schwartz, Noah G; Tobolowsky, Farrell A; Zacks, Rachael L T; Huntington-Frazier, Melinda; Reddy, Sujan C; Rao, Agam K

JAMA

2020 Apr 17; PMID: 32301962

Level of evidence: 3 - Cohort Study

Type of Article: Research

BLUF: In a cohort of 50 healthcare personnel (HCP), screening with current COVID-19 guidelines and subsequent testing revealed that **not including myalgias and chills in screening guidelines** **inappropriately dismissed 7% of cases**, suggesting a need for an expanded screening criteria.

Abstract:

As the coronavirus disease 2019 (COVID-19) pandemic continues, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) exposures among US health care personnel (HCP) during health care delivery and from community contacts will increase. Results from real-time reverse transcriptase–polymerase chain reaction suggest that high viral loads may be detected soon after

illness onset, including in minimally symptomatic persons.¹ Current COVID-19 HCP screening guidance² includes assessing fever and respiratory symptoms (cough, shortness of breath, or sore throat) with clinical discretion for evaluation for other symptoms (eg, myalgias). We assessed the spectrum of symptoms at onset of COVID-19 among HCP and evaluated current screening criteria for identifying COVID-19 cases early in illness course.

Multicenter analysis of clinical characteristics and outcome of COVID-19 patients with liver injury.

Qi X, Liu C, Jiang Z, Gu Y, Zhang G, Shao C, Yue H, Chen Z, Ma B, Liu D, Zhang L, Wang J, Xu D, Lei J, Li X, Huang H, Wang Y, Liu H, Yang J, Pan H, Liu W, Wang W, Li F, Zou S, Zhang H, Dong J. *J Hepatol*

2020 Apr 16; PMID: 32305291

Level of Evidence: 4 - Case series

Article Type: Research

BLUF: COVID-19 increases the risk of liver injury, it is recommended to monitor liver function upon admission.

Summarizing Excerpt: "In our study, a longer time from illness onset to admission resulted in the risk of liver injury in patients with COVID-19, which highlighted the urgent need of early detection of SARS-CoV-2 infection. Since patients in the study did not receive therapy including antiviral drugs, traditional Chinese medicine and nonsteroidal antiinflammatory drugs before admission, and 67 (95.71%) of 70 patients had a nonsevere disease, 32 (45.71%) patients with liver injury on admission were more likely to be caused by SARS-CoV-2 infection...Therefore, we recommend dynamic monitoring the liver function of patients with liver injury, especially those in intensive care unit care."

Clinical characteristics of 80 hospitalized frontline medical workers infected with COVID-19 in Wuhan, China.

Wang X, Liu W, Zhao J, Lu Y, Wang X, Yu C, Hu S, Shen N, Liu W, Sun Z, Li W, Wang X, et al. *J Hosp Infect*.

2020 Apr 14; PMID: 32302722

Level of Evidence: 4 - Case control

Type of Article: Research

BLUF: A case series of 80 frontline medical workers hospitalized with COVID-19 found higher rates of diarrhea (18.75% vs 10%) and lower mortality rates (1.25% vs 4.3%) than the general population.

Summary: "More than 1,000 medical workers have been infected with COVID-19 in China. The 80 hospitalized patients included 57 SARS-CoV-2 confirmed and 23 clinically diagnosed. The median age was 39 years, 49 (61.25%) were women, and one patient died. **The most common symptoms at onset were fever (65, 81.25%), cough (47, 58.75%), fatigue (28, 35%), myalgia (19, 23.75%), expectoration (19, 23.75%), and diarrhea (15, 18.75%).** Patients of frontline medical workers at a single-center hospital showed some unique clinical and laboratory findings compared with other patients in Wuhan and outside of Wuhan. This study provides our experience for other frontline medical workers."

Diarrhea is associated with prolonged symptoms and viral carriage in COVID-19.

Wei XS, Wang X, Niu YR, Ye LL, Peng WB, Wang ZH, Yang WB, Yang BH, Zhang JC, Ma WL, Wang XR, Zhou Q

Clin Gastroenterol Hepatol

2020 Apr 17; PMID: 32311512

Level of Evidence: 4 -Retrospective case control

Type of Article: Research

BLUF: A retrospective, single site study of 84 patients in Wuhan comparing Covid-19 pneumonia patients with and without diarrhea finds that presence of diarrhea is associated with presence of several other symptoms (cough, headache, myalgia among others), longer duration of fever and dyspnea, higher likelihood of positive viral RNA in stool, and prolonged positive nasal and pharyngeal tests and hospital stay.

Abstract:

Background & aims: We compared clinical, laboratory, radiological, and outcome features of patients with SARS-CoV-2 infection (COVID-19) with pneumonia, with vs without diarrhea.

Methods: We performed a retrospective, single-center analysis of 84 patients with SARS-CoV-2 pneumonia in Wuhan Union Hospital, China, from January 19 through February 7, 2020. Cases were confirmed by real-time reverse-transcriptase PCR of nasal and pharyngeal swab specimens for SARS-CoV-2 RNA. Blood samples were analyzed for white blood cell count, lymphocyte count, alanine aminotransferase, creatine kinase, lactate dehydrogenase, D-dimer, C-reactive protein, and in some cases, immunoglobulins, complement, lymphocyte subsets, and cytokines. Virus RNA was detected in stool samples by real-time PCR.

Results: Of the 84 patients with SARS-CoV-2 pneumonia, 26 (31%) had diarrhea. The duration of fever and dyspnea in patients with diarrhea was significantly longer than those without diarrhea (all $P<.05$). Stool samples from a higher proportion of patients with diarrhea tested positive for virus RNA (69%) than from patients without diarrhea (17%) ($P<.001$). As of February 19, a lower proportion of patients with diarrhea had a negative result from the latest throat swab for SARS-CoV-2 (77%) than patients without diarrhea (97%) ($P=.010$), during these patients' hospitalization. Of 76 patients with a negative result from their latest throat swab test during hospitalization, a significantly higher proportion of patients with diarrhea had a positive result from the retest for SARS-CoV-2 in stool (45%) than patients without diarrhea (20%) ($P=.039$).

Conclusions: At a single center in Wuhan, China, 31% of patients with SARS-CoV-2 pneumonia had diarrhea. A significantly higher proportion of patients with diarrhea have virus RNA in stool than patients without diarrhea. Elimination of SARS-CoV-2 from stool takes longer than elimination from the nose and throat.

Risk factors of fatal outcome in hospitalized subjects with coronavirus disease 2019 from a nationwide analysis in China.

Chen R, Liang W, Jiang M, Guan W, Zhan C, Wang T, Tang C, Sang L, Liu J, Ni Z, Hu Y, Liu L, Shan H, Lei C, Peng Y, Wei L, Liu Y, Hu Y, Peng P, Wang J, Liu J, Chen Z, Li G, Zheng Z, Qiu S, Luo J, Ye C, Zhu S, Liu X, Cheng L, Ye F, Zheng J, Zhang N, Li Y, He J, Li S, Zhong N; Medical Treatment Expert Group for COVID-19.Chen R, et al.

Chest

2020 Apr 15; PMID: 32304772

Level of Evidence: 3 - Statistical modeling based on cohort study

Type of Article: Research

BLUF: A monogram model to predict clinical outcomes of patients with COVID-19 based on individual characteristics and risk factors were developed using data from a national cohort study of confirmed COVID-19 patients in China. While advanced age is the most significant predictor of fatal outcome, coronary heart disease, cerebrovascular disease, dyspnea at disease onset, and elevated procalcitonin and AST levels are additional independent risk factors associated with fatal outcomes.

Abstract:

Background: The novel coronavirus disease 2019 (COVID-19) has become a global health emergency. Cumulative number of new confirmed case and death are still increasing out of China. However, the independent predicted factors associated with the fatal outcome remain uncertain.

Methods: A retrospective cohort of 1590 hospitalized subjects with COVID-19 throughout China was established. The prognostic effects of variables, including clinical features and laboratory findings, were analyzed using Kaplan-Meier method and Cox proportional hazard model. A prognostic nomogram was formulated to predict the survival of patient with COVID-19.

Results: In this nationwide cohort, **non-survivors showed higher incidence of elderly people, subjects with co-existing chronic illness, dyspnea and laboratory abnormalities on admission, compared with survivors.** Multivariate Cox regression analysis showed that age \geq 75 (HR: 7.86, 95% CI: 2.44-25.35), age between 65-74 years (HR:3.43, 95%CI: 1.24-9.5), coronary heart disease (HR:4.28, 95%CI:1.14-16.13), cerebrovascular disease(HR:3.1, 95%CI:1.07-8.94), dyspnea (HR: 3.96, 95%CI:1.42-11), procalcitonin $>0.5\text{ng/ml}$ (HR:8.72, 95%CI:3.42-22.28), aspartate aminotransferase $>40\text{U/liter}$ (HR: 2.2, 95% CI: 1.1- 6.73) were independent risk factors associated with fatal outcome. A nomogram was established based on the results of multivariate analysis. The internal bootstrap resampling approach suggested the nomogram has sufficient discriminatory power with the C-index of 0.91 (95%CI 0.85-0.97). The calibration plots also demonstrated good consistency between the prediction and the observation.

Conclusions: The proposed nomogram accurately predict clinical outcomes of patients with COVID-19 based on individual characteristics. **Earlier identification, more intensive surveillance and appropriate therapy should be considered in patients with high risk.**

Risk factors for severe COVID-19: evidence from 167 hospitalized patients in Anhui, China.

Wei YY, Wang RR, Zhang DW, Tu YH, Chen CS, Ji S, Li CX, Li XY, Zhou MX, Cao WS, Han MF, Fei GH.

J Infect.

2020 Apr 16; PMID: 32305487

Level of Evidence: 4 – Case series

Type of Article: Letter to Editor

Summary: Severe cases of COVID-19 were associated with diabetes, decreased fingertip O₂ saturation, lymphopenia, elevated CRP, IL-6, fibrinogen, and decreased albumin when compared to non-severe cases of COVID-19. Rapid decline in T lymphocytes and significant increases in levels of inflammatory markers may be clinical warnings of severe infection.

Risk Factors Associated With Disease Severity and Length of Hospital Stay in COVID-19 Patients

Liu, Xiaofan; Zhou, Hong; Zhou, Yilu; Wu, Xiaojun; Zhao, Yang; Lu, Yang; Tan, Weijun; Yuan, Mingli; Ding, Xuhong; Zou, Jinjing Zou; Li, Ruiyun; Liu, Hailing; Ewing, Rob M; Hu, Yi; Nie, Hanxiang; Wang, Yihua

J Infect

2020 Apr 16; PMID: 32305490

Level of Evidence: 3 - Cohort Study

Type of Article: Letter to the Editor, Research

Summary: In an analysis of 99 patients who were categorized as having severe or moderate COVID-19 and discharged in the same time period, the authors found that hypertension, elevated CRP, and low lymphocyte count were independent risk factors for disease severity.

Cardiac Involvement in COVID-19 Patients: Risk Factors, Predictors, and Complications: A Review

Ghazal A, Benjamin GM, Luke BS, Frank WS

Journal of Cardiac Surgery

2020 Apr 19; PMID: 32306491

Level of Evidence: 5 - Literature Review

Type of Article: Research

BLUF: This literature review found that pre-existing cardiac issues, suchs a arrythmia and hypertension, were risk factors that have been tied to increase infection susceptibility, disease progression and likelihood of mortality.

Abstract:

Background: Respiratory complications have been well remarked in the novel coronavirus disease (SARS-CoV-2/COVID-19), yet an emerging body of research indicates that cardiac involvement may be implicated in poor outcomes for these patients.

Aims: This review seeks to gather and distill the existing body of literature that describes the cardiac implications of COVID-19.

Materials and methods: The English literature was reviewed for papers dealing with the cardiac effects of COVID-19.

Results: Notably, COVID-19 patients with pre-existing cardiovascular disease are counted in greater frequency in intensive care unit settings, and ultimately suffer greater rates of mortality. Other studies have noted cardiac presentations for COVID-19, rather than respiratory, such as acute pericarditis and left ventricular dysfunction. In some patients there has been evidence of acute myocardial injury, with correspondingly increased serum troponin I levels. With regard to surgical interventions, there is a dearth of data describing myocardial protection during cardiac surgery for COVID-19 patients.

Although some insights have been garnered in the study of cardiovascular diseases for these patients, these insights remain fragmented and have yet to cement clear guidelines for actionable clinical practice.

Conclusion: While some information is available, further studies are imperative for a more cohesive understanding of the cardiac pathophysiology in COVID-19 patients to promote more informed treatment and, ultimately, better clinical outcomes.

Diabetic patients with COVID-10 infection are at higher risk of ICU admission and poor short-term outcome.

Roncon L, Zuin M, Rigatelli G, Zuliani G, Roncon L, et al.

J Clin Virol.

2020 Apr 9; PMID: 32305882

Level of Evidence: 3 - Review of case-control studies

Type of Article: Research

BLUF: Review of case-control studies demonstrate higher risk of ICU admission and mortality in diabetic patients.

Abstract:

Background: The prognostic significance of diabetes mellitus (DM) in patients with coronavirus 2019 disease (COVID-19) remains unknown.

Objectives: To assess the risk of ICU admission and mortality risk in diabetic COVID-19 patients.

Study design: A **database search was conducted to identify studies comparing diabetic COVID-19 patients hospitalized in intensive care unit (ICU) and those reporting the overall mortality of these patients published up to March 25, 2020** within MEDLINE, Scopus and Web of Science. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in abstracting data and assessing validity. Quality assessment was performed using the Newcastle-Ottawa quality assessment scale. **The main outcome was the risk of ICU admission in diabetic patients with COVID-19 infection while the second was the mortality risk in overall diabetic COVID-19 patients.** Data were pooled using the Mantel-Haenszel random effects models with odds ratio (OR) as the effect measure with the related 95 % confidence interval (CI). Statistical heterogeneity between groups was measured using the Higgins I₂ statistic.

Results: Among 1382 patients (mean age 51.5 years, 798 males), DM resulted to be the second more frequent comorbidities. Diabetic patients resulted to have a significant increased risk of ICU admission (OR: 2.79, 95 % CI 1.85–4.22, p < 0.0001, I₂ = 46 %). In 471 patients (mean age 56.6 years, 294 males) analysed for the secondary outcome diabetic subjects resulted to be at higher mortality risk (OR 3.21, 95 % CI 1.82–5.64, p < 0.0001, I₂ = 16 %).

Conclusions: Diabetic patients with COVID-19 patients are at higher risk of ICU admission and show a higher mortality risk.

Disparities

The impact of nutrition on COVID-19 susceptibility and long-term consequences.

Butler MJ, Barrientos RM. Butler MJ, et al.

Brain Behav Immun.

2020 Apr 17; PMID: 32311498

Level of Evidence: 5 - Expert Opinion/Mechanism

Type of Article: Editorial

BLUF: The authors, relying heavily on animal studies, argue that a Western diet causes both innate and adaptive immune dysfunction that may be partially driving the poor outcomes observed in the elderly, underrepresented minorities, and those with comorbidities.

Abstract:

While all groups are affected by the COVID-19 pandemic, the elderly, underrepresented minorities, and those with underlying medical conditions are at the greatest risk. The high rate of consumption of diets high in saturated fats, sugars, and refined carbohydrates (collectively called Western diet, WD) worldwide, contribute to the prevalence of obesity and type 2 diabetes, and could place these populations at an increased risk for severe COVID-19 pathology and mortality. WD consumption

activates the innate immune system and impairs adaptive immunity, leading to chronic inflammation and impaired host defense against viruses. Furthermore, peripheral inflammation caused by COVID-19 may have long-term consequences in those that recover, leading to chronic medical conditions such as dementia and neurodegenerative disease, likely through neuroinflammatory mechanisms that can be compounded by an unhealthy diet. Thus, now more than ever, wider access to healthy foods should be a top priority and individuals should be mindful of healthy eating habits to reduce susceptibility to and long-term complications from COVID-19.

Women's Health

Pregnant Versus Non-Pregnant SARS-CoV-2 and COVID-19 Hospital Admissions: The First 4 Weeks in New York.

Tekbali A, Grünebaum A, Saraya A, McCullough L, Bornstein E, Chervenak FA.

Am J Obstet Gynecol

2020 Apr 15; PMID: 32304691

Level of Evidence: 3 – Local Non-Random Sample

Type of Article: Comment

BLUF: While admissions for COVID-19 rose over the month of March in New York for all patients, pregnant patients had much lower rates of COVID-19 related admissions than other patients.

Summary: The authors present data from admissions to a hospital group in New York in the month of March. The data shows an increase in COVID-19 admissions during this time. While admissions due to COVID-19 were higher in non-pregnant than pregnant patients, COVID-19 infection rates increased over the course of the month in both groups. The authors speculate the lower percentage of COVID-19 admission rate for pregnant patients could be attributed to the younger age and good health status of most pregnant patients, as well as the higher number of admissions for labor and delivery. The authors advocate for “ring-fencing” of hospital maternity services to ensure that this care can continue to be safely provided.

Pediatrics

Coronavirus Infections in Children Including COVID-19: An Overview of the Epidemiology, Clinical Features, Diagnosis, Treatment and Prevention Options in Children.

Zimmermann P, Curtis N. Zimmermann P, et al.

Pediatr Infect Dis J.

2020 May, PMID: 32310621

Level of Evidence: 2 - Systematic review

Article Type: Review

BLUF: The clinical, laboratory and radiologic features of human coronaviruses in children are similar for all novel CoVs: children experience less severe symptoms, lower mortality rates, and more GI symptoms. However, fever is observed at a higher rate in SARS-CoV than with SARS-CoV-2 or MERS-CoV. The author reports that currently proposed therapies (oral lopinavir/ritonavir, monoclonal antibodies, protease inhibitors, chloroquine, and RNA synthesis inhibitors) and most vaccines in development target the structural spike glycoprotein S or its receptor-binding domain (RBD).

Abstract: Coronaviruses (CoVs) are a large family of enveloped, single-stranded, zoonotic RNA viruses. Four CoVs commonly circulate among humans: HCoV2-229E, -HKU1, -NL63 and -OC43.

However, CoVs can rapidly mutate and recombine leading to novel CoVs that can spread from animals to humans. The novel CoVs severe acute respiratory syndrome coronavirus (SARS-CoV) emerged in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012. The 2019 novel coronavirus (SARS-CoV-2) is currently causing a severe outbreak of disease (termed COVID-19) in China and multiple other countries, threatening to cause a global pandemic. In humans, CoVs mostly cause respiratory and gastrointestinal symptoms. Clinical manifestations range from a common cold to more severe disease such as bronchitis, pneumonia, severe acute respiratory distress syndrome, multi-organ failure and even death. **SARS-CoV, MERS-CoV and SARS-CoV-2 seem to less commonly affect children and to cause fewer symptoms and less severe disease in this age group compared with adults, and are associated with much lower case-fatality rates.** Preliminary evidence suggests children are just as likely as adults to become infected with SARS-CoV-2 but are less likely to be symptomatic or develop severe symptoms. However, the importance of children in transmitting the virus remains uncertain. **Children more often have gastrointestinal symptoms compared with adults.** Most children with SARS-CoV present with fever, but this is not the case for the other novel CoVs. Many children affected by MERS-CoV are asymptomatic. The majority of children infected by novel CoVs have a documented household contact, often showing symptoms before them. In contrast, adults more often have a nosocomial exposure. **In this review, we summarize epidemiologic, clinical and diagnostic findings, as well as treatment and prevention options for common circulating and novel CoVs infections in humans with a focus on infections in children.**

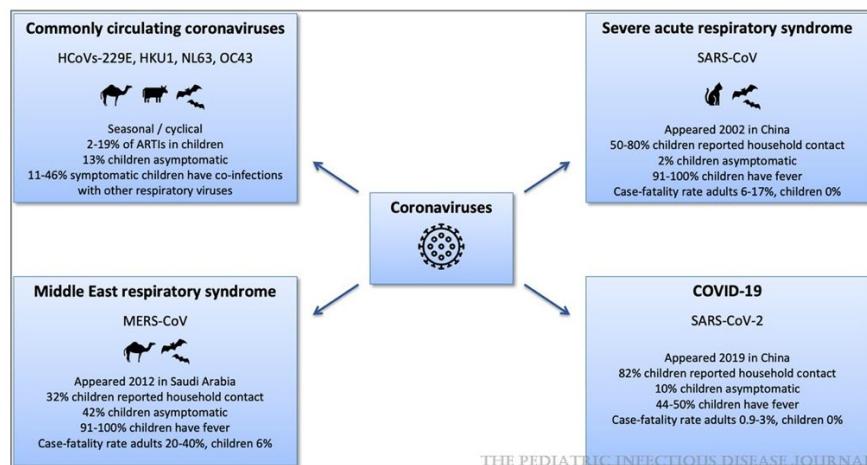


FIGURE 1: Summary of coronavirus diseases. COVID-19 indicates coronavirus disease 2019.

Adults: Original case definition from the Chinese CDC³⁸
A suspected or probable case is defined as a case that meets: (1) three clinical criteria or (2) two clinical criteria and one epidemiologic criterion
Clinical criteria:
1. Fever 2. Radiographic evidence of pneumonia or acute respiratory distress syndrome 3. Low or normal white blood cell count or low lymphocyte count
Epidemiologic criteria:
1. Living in Wuhan or travel history to Wuhan within 14 d before symptom onset 2. Contact with patients with fever and symptoms of respiratory infection within 14 d before symptom onset 3. Link to any confirmed cases or clusters of suspected cases
Adults: Case definition from the US CDC (February 13, 2020)¹⁴⁵
A. Fever or signs/symptoms of lower respiratory illness (eg, cough or shortness of breath) AND close contact with a laboratory-confirmed SARS-CoV-2 patient within 14 d of symptom onset B. Fever and signs/symptoms of lower respiratory illness (eg, cough or shortness of breath) AND a history of travel from Hubei Province, China within 14 d of symptom onset C. Fever or signs/symptoms of lower respiratory illness (eg, cough or shortness of breath) requiring hospitalization AND a history from mainland China within 14 d of symptom onset
Adults: Case definition from the World Health Organisation (WHO) (27th February 2020), which also form the basis for the European Centre for Disease Prevention and Control (ECDC) case definition¹⁴⁶
Suspected case
A. Patient with acute respiratory infection [fever and at least one sign/symptom of respiratory disease (eg, cough, shortness of breath)] AND with no other etiology that fully explains the clinical presentation AND a history of travel to or residence in a country/area or territory reporting local transmission of COVID-19 during the 14 days prior to symptom onset; OR B. A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to onset of symptoms; OR C. A patient with severe acute respiratory infection (as above) AND requiring hospitalization AND with no other etiology that fully explains the clinical presentation.
Children: Case definition by the National Clinical Research Center for Child Health, Zhejiang University School of Medicine (adapted from Chen et al⁷²)
A suspected or probable case is defined as a case that meets: two clinical criteria and one epidemiologic criterion
Clinical criteria:
1. Fever, fatigue, dry cough; some pediatric patients may have no fever 2. Patients with the following chest imaging findings: multiple small patchy shadows and interstitial changes, mostly in the lung periphery, bilateral multiple ground-glass opacity, infiltrating shadows, pulmonary consolidation on chest radiography or ground-glass opacities, bilateral segmental lung consolidation, especially in the periphery on chest CT 3. White blood cell counts are normal or decreased, or with decreased lymphocyte count
Epidemiologic criteria:
1. Children with a travel or residence history in Wuhan City and neighboring areas, or other areas with persistent local transmission within 14 d prior to disease onset 2. Children with a history of contacting patients with fever or respiratory symptoms who have a travel or residence history in Wuhan City and neighboring areas, or in other areas with persistent local transmission within 14 d prior to disease onset 3. Children with a history of contacting confirmed or suspected cases infected with SARS-CoV-2 within 14 d prior to disease onset 4. Children who are related with a cluster outbreak: in addition to this patient, there are other patients with fever or respiratory symptoms, including suspected or confirmed cases infected with SARS-CoV-2 5. Newborns delivered by suspected or confirmed SARS-CoV-2-infected mothers
A confirmed case is defined as a case that meets any of the following criteria:
1. Throat swab, sputum, stool or blood samples tested positive for SARS-CoV-2 nucleic acid using RT-PCR 2. Genetic sequencing of throat swab, sputum, stool or blood samples being highly homologous with the known SARS-CoV-2 3. SARS-CoV-2 granules being isolated by culture from throat swab, sputum, stool or blood samples

THE PEDIATRIC INFECTIOUS DISEASE JOURNAL

TABLE 2: Case Definitions for SARS-CoV-2 Infections in Adults and Children (as of February 2020)

Flash survey on severe acute respiratory syndrome coronavirus-2 infections in paediatric patients on anticancer treatment.

Hrusak O, et al.

Eur J Cancer

2020 Apr 7; PMID: 32305831

Level of Evidence: 4 - Case series

Type of Article: Research

BLUF: Pediatric patients receiving anticancer chemotherapy may have mild or asymptomatic disease based on the limited number of reported cases of COVID-19 in this population. Additional research on the epidemiology of SARS-CoV-2 and COVID-19 in pediatric patients with cancer or otherwise immunocompromised and the risk of severe disease is necessary to establish management parameters.

Abstract:

Introduction: Since the beginning of COVID-19 pandemic, it is known that the severe course of the disease occurs mostly among the elderly, whereas it is rare among children and young adults. Comorbidities, in particular, diabetes and hypertension, clearly associated with age, besides obesity and smoke, are strongly associated with the need for intensive treatment and a dismal outcome. A weaker immunity of the elderly has been proposed as a possible explanation of this uneven age distribution. Thus, there is concern that children treated for cancer may also be at risk for an

unfavourable course of infection. Along the same line, anecdotal information from Wuhan, China, mentioned a severe course of COVID-19 in a child treated for leukaemia.

Aim and methods: We made a **flash survey on COVID-19 incidence and severity among children on anticancer treatment**. Respondents were asked by email to fill in a short Web-based survey.

Results: We received reports from 25 countries, where approximately 10,000 patients at risk are followed up. At the time of the survey, more than 200 of these children were tested, nine of whom were positive for COVID-19. **Eight of the nine cases had asymptomatic to mild disease**, and one was just diagnosed with COVID-19. We also discuss preventive measures that are in place or should be taken and treatment options in immunocompromised children with COVID-19.

Conclusion: Thus, even **children receiving anticancer chemotherapy may have a mild or asymptomatic course of COVID-19**. While we should not underestimate the risk of developing a more severe course of COVID-19 than that observed here, the **intensity of preventive measures should not cause delays or obstructions in oncological treatment**.

Understanding the Pathology

Pathology

[COVID-19 Associated Hepatitis Complicating Recent Living Donor Liver Transplantation.](#)

Lagana SM, De Michele S, Lee MJ, Emond JC, Griesemer AD, Tulin-Silver SA, Verna EC, Martinez M, Lefkowitch JH.

Arch Pathol Lab Med.

2020 Apr 17; PMID: 32302212

Level of Evidence: 4 - Case report

Type of Article: Research

BLUF: Case report detailing the **first description of the histopathology of likely COVID-19 hepatitis identified in a liver biopsy**, leading to development of **moderate acute hepatitis**.

Abstract:

We present a case of **COVID-19 hepatitis** in a living donor liver allograft recipient whose donor subsequently tested positive for COVID-19. The patient is a female infant with biliary atresia (failed Kasai procedure). She recovered well, with improving liver function tests for 4 days. On post-operative day (POD) 4 the patient developed respiratory distress and fever. COVID-19 testing (polymerase chain reaction) was positive. Liver function tests increased approximately 5-fold. **Liver biopsy showed moderate acute hepatitis with prominent clusters of apoptotic hepatocytes and associated cellular debris. Lobular lymphohistiocytic inflammation was noted.** Typical portal features of mild to moderate acute cellular rejection were also noted.

[The Potential Role of Th17 Immune Responses in Coronavirus Immunopathology and Vaccine-induced Immune Enhancement](#)

Hotez, Peter J; Bottazzi, Maria Elena; Corry, David B

Microbes Infect

2020 Apr 16; PMID: 32305501

Level of Evidence: 5 - Expert opinion

Type of Article: Editorial

BLUF: Host Th17 inflammatory responses contribute to the inflammatory and cytokine responses seen in COVID-19 and experimental COVID-19 vaccines leading to severe lung pathology and mortality in lower respiratory infections.

Abstract:

Increasing evidence points to host Th17 inflammatory responses as contributing to the severe lung pathology and mortality of lower respiratory tract infections from coronaviruses. This includes host inflammatory and cytokine responses to COVID-19 caused by the SARS-2 coronavirus (SARS CoV2). From studies conducted in laboratory animals, there are additional concerns about immune enhancement and the role of potential host immunopathology resulting from experimental human COVID-19 vaccines. **Here we summarize evidence suggesting there may be partial overlap between the underlying immunopathologic processes linked to both coronavirus infection and vaccination, and a role for Th17 in immune enhancement.** Such findings help explain the link between viral-vectored coronavirus

vaccines and immune enhancement and its reduction through alum adjuvants. Additional research may also clarify links between COVID-19 pulmonary immunopathology and heart disease.

Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1, MERS-CoV and lessons from the past.

Giannis, Dimitrios; Ziogas, Ioannis A; Gianni, Panagiota

Journal of Clinical Virology

2020 Apr 20; PMID: 32305883

Level of Evidence: 5 - Expert Opinion

Type of Article: Research

BLUF: Thrombotic complications, including thrombocytopenia, elevated D-dimer/fibrin degradation products, prolonged prothrombin time, and development of DIC have been associated with COVID-19. The role and mechanism by which coagulation disorders presented in SARS-CoV-1 and MERS-CoV is also investigated.

Abstract: Coronavirus disease 2019 (COVID-19) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus strain disease, has recently emerged in China and rapidly spread worldwide. This novel strain is highly transmittable and severe disease has been reported in up to 16% of hospitalized cases. More than 600,000 cases have been confirmed and the number of deaths is constantly increasing. COVID-19 hospitalized patients, especially those suffering from severe respiratory or systemic manifestations, **fall under the spectrum of the acutely ill medical population, which is at increased venous thromboembolism risk.** Thrombotic complications seem to emerge as an important issue in patients infected with COVID-19. Preliminary reports on COVID-19 patients' clinical and laboratory findings include **thrombocytopenia, elevated D-dimer, prolonged prothrombin time, and disseminated intravascular coagulation.** As the pandemic is spreading and the whole picture is yet unknown, we highlight the importance of coagulation disorders in COVID-19 infected patients and review relevant data of previous coronavirus epidemics caused by the severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) and the Middle East Respiratory Syndrome coronavirus (MERS-CoV).

Severe COVID-19 Infection Associated With Endothelial Activation

Escher, Robert; Breakey, Neal; Lämmle, Bernhard

Thromb Res

2020 Apr 15; PMID: 32305740

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Letter

Summary: Based upon the levels of clotting factors of a COVID-19 patient these authors observed in the ICU, authors suggest treating severe COVID-19 patients with higher therapeutic doses of anticoagulation. Most notably, they based this observation on the high levels of von Willebrand factor and factor VIII of this patient. Based upon those levels, the authors increased the unfractionated heparin to therapeutic doses form prophylactic.

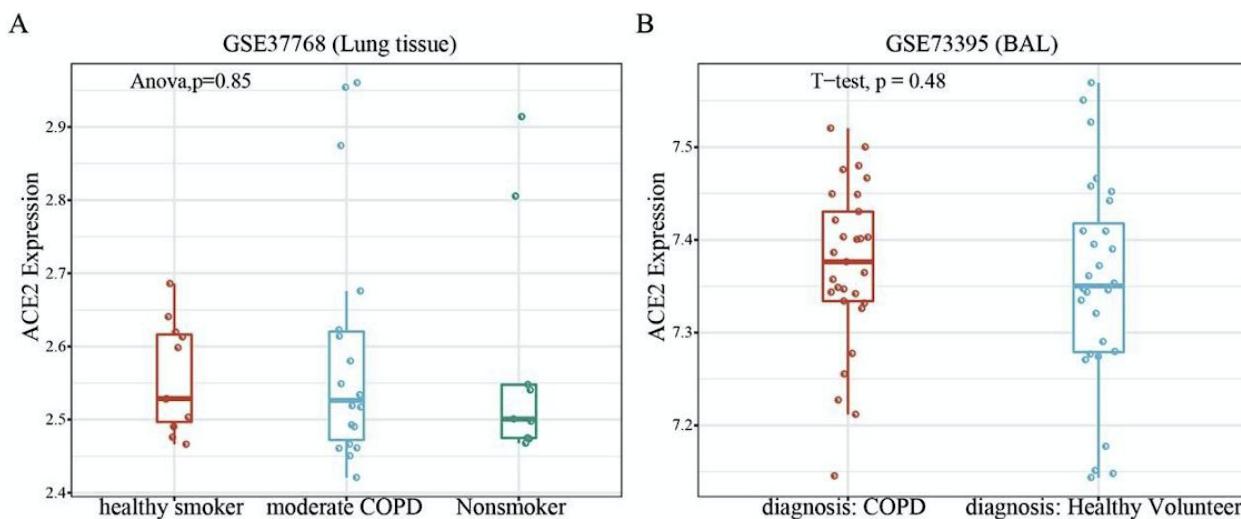
Biomechanics

Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19.

Li G, He X, Zhang L, Ran Q, Wang J, Xiong A, Wu D, Chen F, Sun J, Chang C.

BLUF: New analysis of existing data reveals **upregulation of ACE2 and other inflammatory proteins in SARS-CoV infected and in smokers' lung cells at baseline.** The title is somewhat misleading as the authors' conclusions assume SARS-CoV affects these pathways similarly to the current SARS-CoV-2 (Covid-19).

Abstract: It has been reported that **SARS-CoV-2 may use ACE2 as a receptor to gain entry into human cells, in a way similar to that of SARS-CoV.** Analyzing the distribution and expression level of ACE2 may therefore help reveal underlying mechanisms of viral susceptibility and post-infection modulation. In this study, we utilized previously uploaded information on **ACE2 expression in various conditions including SARS-CoV to evaluate the role of ACE2 in SARS-CoV and extrapolate that to COVID-19.** We found that the **expression of ACE2 in healthy populations and patients with underlying [COPD and asthma] diseases was not significantly different.** However, based on the elevated expression of ACE2 in cigarette smokers, we speculate that long-term smoking may be a risk factor for COVID-19. Analysis of ACE2 in SARS-CoV infected cells suggests that ACE2 is not only a receptor but is also involved in post-infection regulation, including immune response, cytokine secretion, and viral genome replication. Moreover, we constructed Protein-protein interaction (PPI) networks and identified hub genes in viral activity and cytokine secretion. Our findings may help clinicians and researchers gain more insight into the pathogenesis of SARS-CoV-2 and design therapeutic strategies for COVID-19.



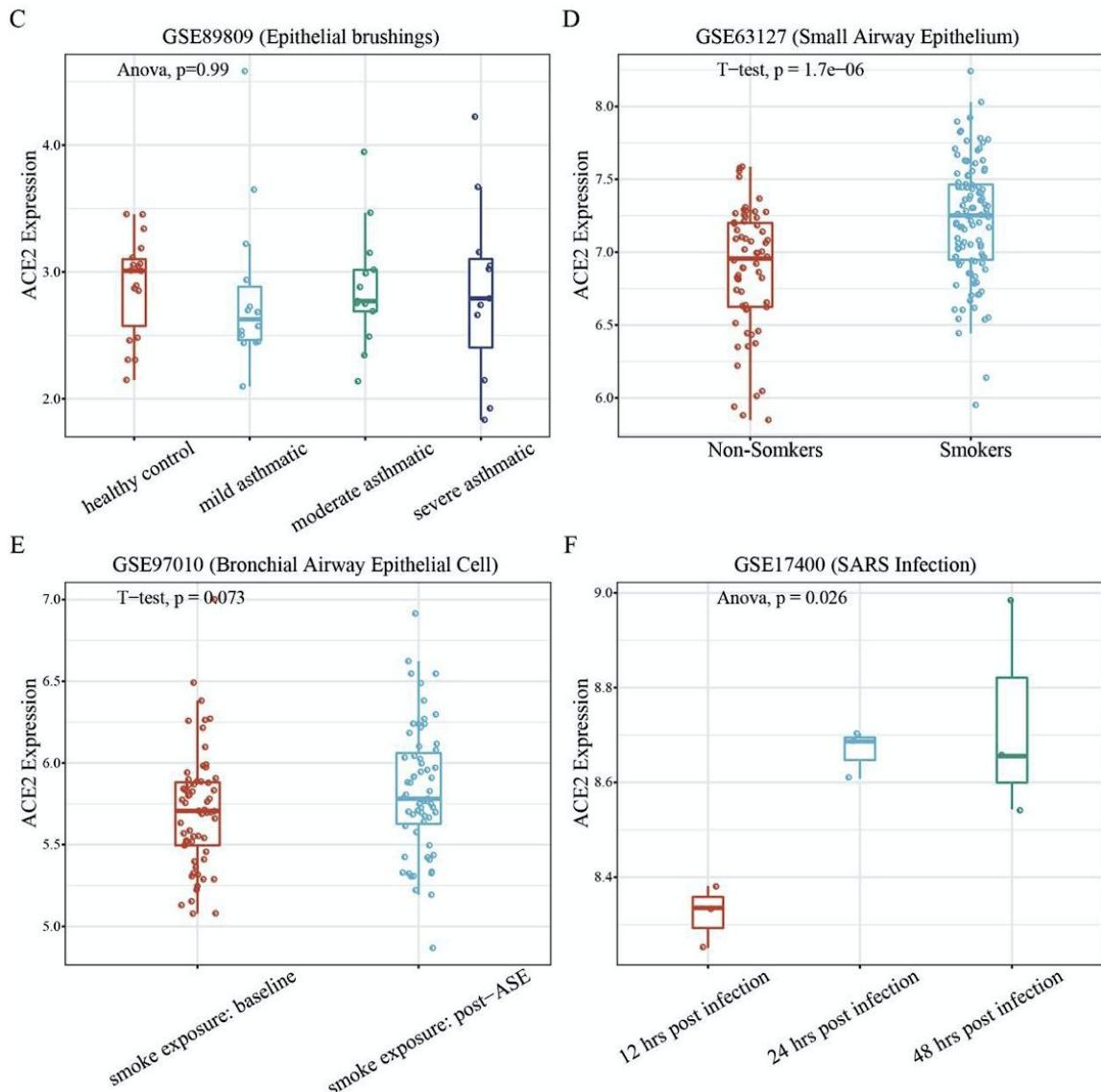


Figure 1. Shows a significant difference in ACE2 expression in BAL samples from smokers compared to non-smokers and in ACE2 expression at 12, 24, and 48 hours post infection

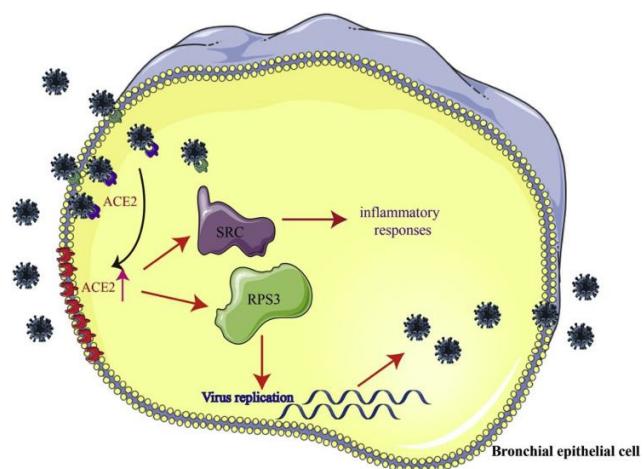


Figure 2. This figure shows a proposed pathway the effect of ACE2 on two proteins identified as major contributors to the inflammatory response in SARS-CoV infection

Clinical Implications of SARS-CoV2 Interaction with Renin Angiotensin System

Brojakowska A, Narula J, Shimony R, Bander J.

Journal of the American College of Cardiology

2020, April 14; PMID 32305401

Level of Evidence: 5 - Expert opinion

Type of Article: Literature Review

BLUF: Using a comprehensive literature review, the authors hypothesize that SARS-CoV2 downregulates the ACE2/Ang1-7/Mas pathway which could influence the systemic inflammation and dysregulation seen in COVID-19 patients. They postulate that ACE inhibitors, ARBs, and MRAs may benefit patients with an underlying cardiovascular disease via a compensatory upregulation of ACE2 expression, leading to decreased inflammation, decreased progression of disease, and providing anti-fibrotic and anti-thrombotic support.

Abstract:

SARS-CoV2 host cell infection is mediated by the binding to angiotensin-converting enzyme 2 (ACE2). Systemic dysregulation observed in SARS-CoV was previously postulated to be due to ACE2/Ang1-7/Mas axis downregulation, increased ACE2 activity was shown to mediate disease protection. Since angiotensin II receptor blockers (ARBs), ACE inhibitors, and mineralocorticoid receptor antagonists (MRAs) increase ACE2 receptor expression, it has been tacitly believed that the use of these agents may facilitate viral disease, thus they should not be used in high-risk patients with cardiovascular disease. Based on the anti-inflammatory benefits of the upregulation of the ACE2/Ang1-7/Mas axis and previously demonstrated benefits of lung function improvement in SARS-CoV infections, we hypothesize that the benefits of treatment with renin-angiotensin system inhibitors in SARS-CoV2 may outweigh the risks and at the very least should not be withheld.

Causes of hypogeusia/hyposmia in SARS-CoV2 infected patients.

Finsterer J, Stollberger C

J Med Virol.

2020 Apr 20; PMID: 32311107

Level of Evidence: 5 - Expert Opinion

Type of Article: Letter

BLUF: “[T]he most likely cause for transient hypogeusia and hyposmia in SARS-CoV2-infected patients is a direct contact and interaction of the virus with gustatory receptors or olfactory receptor cells.”

ABSTRACT: “It is well appreciated that SARS-CoV2 does not exclusively affect the lungs.^{1,2} Virus-RNA can be detected in most of the body compartments, including the cerebrospinal fluid (CSF).³ Neurological manifestations have been recently investigated in a retrospective study of 214 SARS-CoV2-infected patients.¹”

Immune response

Human Leukocyte Antigen Susceptibility Map for SARS-CoV-2.

Nguyen A, David JK, Maden SK, Wood MA, Weeder BR, Nellore A, Thompson RF.

J Virol

2020 Apr 17; PMID:32303592

Level of Evidence: 5 - Statistical modeling

Type of Article: Research

BLUF: This study presents an *in silico* analysis of individual genetic variability of HLA alleles in the context of SARS-CoV-2 infection. They speculate that HLA-B*46:01 may be particularly vulnerable to COVID-19, while HLA-B*15:03 may be protective. certain alleles may be associated with more severe disease. “Pairing HLA typing with COVID-19 testing where feasible could improve assessment of viral severity in the population. Following the development of a vaccine against SARS-CoV-2, the virus that causes COVID-19, individuals with high-risk HLA types could be prioritized for vaccination”

Abstract:

Genetic variability across the three major histocompatibility complex (MHC) class I genes (human leukocyte antigen [lsqb]HLA[rsqb] A, B, and C) may affect susceptibility to and severity of severe acute respiratory syndrome 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19). **We execute a comprehensive *in silico* analysis of viral peptide-MHC class I binding affinity across 145 HLA -A, -B, and -C genotypes for all SARS-CoV-2 peptides.** We further explore the potential for cross-protective immunity conferred by prior exposure to four common human coronaviruses. The SARS-CoV-2 proteome is successfully sampled and presented by a diversity of HLA alleles. However, **we found that HLA-B*46:01 had the fewest predicted binding peptides for SARS-CoV-2, suggesting individuals with this allele may be particularly vulnerable to COVID-19**, as they were previously shown to be for SARS. Conversely, we found that HLA-B*15:03 showed the greatest capacity to present highly conserved SARS-CoV-2 peptides that are shared among common human coronaviruses, suggesting it could enable cross-protective T-cell based immunity. Finally, we report global distributions of HLA types with potential epidemiological ramifications in the setting of the current pandemic.

IMPORTANCE Individual genetic variation may help to explain different immune responses to a virus across a population. In particular, understanding how variation in HLA may affect the course of COVID-19 could help identify individuals at higher risk from the disease. HLA typing can be fast and inexpensive. Pairing HLA typing with COVID-19 testing where feasible could improve assessment of viral severity in the population. Following the development of a vaccine against SARS-CoV-2, the virus that causes COVID-19, individuals with high-risk HLA types could be prioritized for vaccination

Comparative Computational Analysis of SARS-CoV-2 Nucleocapsid Protein Epitopes in Taxonomically Related Coronaviruses

Tilocca B, Soggiu A, Sanguinetti M, Musella V, Britti D, Bonizzi L, Urbani A, Roncada P
Microbes Infect

2020 Apr 14; PMID:32302675

Level of Evidence: Statistical model

Type of Article: Basic Research

Summary: This study provides an *in silico* analysis of the potential immunogenic epitopes found in the SARS-CoV-2 nucleoprotein and compares these epitopes to those from related coronaviruses. They hope to provide insight onto the host tropism of these viruses and better understand the potential immune responses that may be elicited.

Abstract:

Several research lines are currently ongoing to address the multitude of facets of the pandemic COVID-19. In line with the One-Health concept, extending the target of the studies to the animals which humans are continuously interacting with may favor a better understanding of the SARS-CoV-2 biology and pathogenetic mechanisms; thus, helping to adopt the most suitable containment measures. The last two decades have already faced severe manifestations of the coronavirus infection in both humans and animals, thus, circulating epitopes from previous outbreaks might confer partial

protection from SARS-CoV-2 infections. In the present study, we provide an **in-silico survey of the major nucleocapsid protein epitopes and compare them with the homologues of taxonomically-related coronaviruses with tropism for animal species that are closely interrelated with the human beings population all over the world**. Protein sequence alignment provides evidence of high sequence homology for some of the investigated proteins. Moreover, structural epitope mapping by homology modelling revealed a potential immunogenic value also for specific sequences scoring a lower identity with SARS-CoV-2 nucleocapsid proteins. These evidence provide a molecular structural rationale for a potential role in conferring protection from SARS-CoV-2 infection and identifying potential candidates for the development of diagnostic tools and prophylactic-oriented strategies.

Androgen hazards with COVID-19.

Sharifi N, Ryan C

Endocr Relat Cancer

2020 Apr 1; PMID: 32302975

Level of Evidence: 5 - Mechanism Based Reasoning

Type of Article: Editorial

BLUF: Androgen modulation of the immune system or androgen regulation of specific proteins may explain increased disease severity of COVID-19 in men, though the role of androgen antagonism/inhibition in treating the disease is unknown.

Summary with excerpts: Recent evidence has demonstrated poorer clinical outcomes and higher mortality for men infected with COVID-19 compared to women. “Although the etiology is probably multifactorial, the **physiological effects of androgens are one possible reason that may explain these sex-specific differences in outcomes.**” The authors posit two possible mechanisms for the role of androgen regulation in COVID-19:

1. The expression and function of TMPRSS2, a cellular protease required for SARS-CoV-2 infection (similar to ACE2 in this context), known for its androgen-regulated role in prostate cancer. If TMPRSS2 also responds to androgens in lung tissue, then inhibition of androgens could potentially impede SARS-CoV-2 cellular entry or activation via downregulation of this protein.
2. Androgens appear to have an immunosuppressive effect, but the degree of peripheral conversion of adrenal androgens to more potent androgens differs depending on a person’s genotype. Those with alleles that promote greater peripheral androgen conversion may be at risk for worsened clinical outcomes in COVID-19, suggested by the high frequency of this genotype in countries that have been severely affected by the disease like Italy and Spain.

SARS-CoV-2: A new aetiology for atypical lymphocytes.

Gerard D, Henry S, Thomas B.

Br J Haematol.

2020 Apr 20; PMID: 32311762

Level of Evidence: 5 - Case report

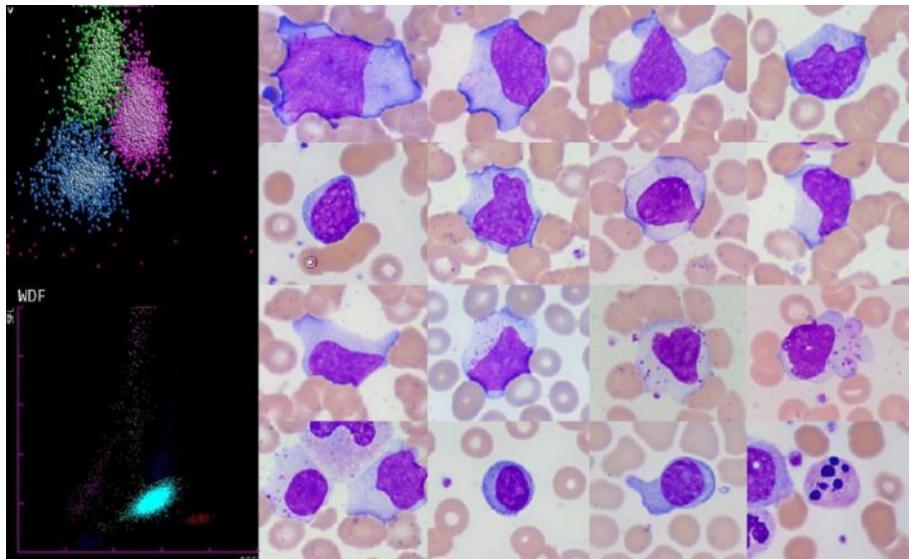
Type of Article: Images

BLUF: This report illustrates **atypical lymphocytes that may be present in cytological analysis of COVID-19-positive patients.**

Abstract:

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a newly emerging coronavirus, SARS-CoV-2. COVID-19 has a very variable clinical picture, ranging from asymptomatic

to severe acute respiratory syndrome that can lead to death. Our case, a 74-year-old female patient, presented with fever, moderate dyspnoea and leucocytosis (white blood cell count $21.6 \times 10^9 /l$, neutrophils $16.8 \times 10^9 /l$, lymphocytes $3.67 \times 10^9 /l$). RT-PCR for SARS-CoV-2 was performed, which confirmed COVID-19.



Scattergramm DxH800 (top left) and XN10 (bottom left). Atypical lymphocytes : basophilic or granular cytoplasm (right) and apoptotic cells (bottom right) (May-Grünwald Giemsa x 100)

SARS-CoV-2 and viral sepsis: observations and hypotheses.

Li H, Liu L, Zhang D, Xu J, Dai H, Tang N, Su X, Cao B

Lancet

2020 Apr 17; PMID: 32311318

Level of Evidence: 5- Mechanism based reasoning

Type of Article: Hypothesis

BLUF: A discussion of the current state of basic science on SARS-CoV-2 in addition to hypotheses on the mechanisms accounting for variable Covid-19 disease severity, including the cytokine storm and microvascular dysfunction, which together cause a “viral sepsis”, a concept that should be further evaluated.

Abstract: Since the outbreak of coronavirus disease 2019 (COVID-19), clinicians have tried every effort to understand the disease, and a brief portrait of its clinical features have been identified. In clinical practice, we noticed that many severe or critically ill COVID-19 patients developed typical clinical manifestations of shock, including cold extremities and weak peripheral pulses, even in the absence of overt hypotension. Understanding the mechanism of viral sepsis in COVID-19 is warranted for exploring better clinical care for these patients. With evidence collected from autopsy studies on COVID-19 and basic science research on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and SARS-CoV, we have put forward several hypotheses about SARS-CoV-2 pathogenesis after multiple rounds of discussion among basic science researchers, pathologists, and clinicians working on COVID-19. We hypothesise that a process called viral sepsis is crucial to the disease mechanism of COVID-19. Although these ideas might be proven imperfect or even wrong later, we believe they can provide inputs and guide directions for basic research at this moment.

Miller Fisher Syndrome and Polyneuritis Cranialis in COVID-19

Gutiérrez-Ortiz, Consuelo; Méndez, Antonio; Rodrigo-Rey, Sara; San Pedro-Murillo, Eduardo; Bermejo-Guerrero, Laura; Gordo-Mañas, Ricardo; de Aragón-Gómez, Fernando; Benito-León, Julián

Neurology

2020 Apr 17; PMID: 32303650

Level of Evidence: 5 - Case Study (2)

Type of Article: Research

BLUF: Two patients who tested positive for SARS-CoV-2 by RT-PCR also acutely presented with rare disorders Miller Fisher syndrome and polyneuritis cranialis, respectively, and made complete neurological recoveries. Neurological manifestations may be due to an aberrant immune response.

ABSTRACT:

Objective: To report two patients infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) who acutely presented with **Miller Fisher syndrome** and **polyneuritis cranialis**, respectively.

Methods: Patient data were obtained from medical records from the University Hospital "Príncipe de Asturias", Alcalá de Henares, Madrid, Spain and from the University Hospital "12 de Octubre", Madrid, Spain.

Results: The first patient was a **50-year-old man** who presented with **anosmia, ageusia, right internuclear ophthalmoparesis, right fascicular oculomotor palsy, ataxia, areflexia, albuminocytologic dissociation and positive testing for GD1b-IgG antibodies**. Five days before, he had developed a **cough, malaise, headache, low back pain, and a fever**. The second patient was a **39-year-old man** who presented with **ageusia, bilateral abducens palsy, areflexia and albuminocytologic dissociation**. Three days before, he had developed **diarrhea, a low-grade fever, and a poor general condition**. The oropharyngeal swab test for coronavirus disease 2019 (COVID-19) by qualitative real-time reverse-transcriptase-polymerase-chain-reaction assay was positive in both patients and negative in the cerebrospinal fluid. The first patient was treated with intravenous immunoglobulin and the second, with acetaminophen. Two weeks later, both patients made a **complete neurological recovery**, except for residual anosmia and ageusia in the first case.

Conclusions: Our two cases highlight the **rare occurrence of Miller Fisher syndrome and polyneuritis cranialis** during the COVID-2 pandemic. **Neurological manifestations may occur because of an aberrant immune response to COVID-19**. The full clinical spectrum of neurological symptoms in patients with COVID-19 remains to be characterized.

Transmission & Prevention

Developments in Transmission & Prevention

Impact of meteorological factors on the COVID-19 transmission: A multi-city study in China.

Liu J, Zhou J, Yao J, Zhang X, Li L, Xu X, He X, Wang B, Fu S, Niu T, Yan J, Shi Y, Ren X, Niu J, Zhu W, Li S, Luo B, Zhang K, Liu J, et al.

Sci Total Environ.

2020 Apr 9; PMID: 32304942

Level of Evidence: 3 - Cohort study

Type of Article: Research

BLUF:

In a retrospective cohort study examining the relationship between meteorological conditions and new cases of COVID-19, **increases in ambient temperature and diurnal temperature range were significantly correlated with a decline in daily case counts.**

Abstract:

The purpose of the present study is to explore the associations between novel coronavirus disease 2019 (COVID-19) case counts and meteorological factors in 30 provincial capital cities of China. We compiled a daily dataset including confirmed case counts, ambient temperature (AT), diurnal temperature range (DTR), absolute humidity (AH) and migration scale index (MSI) for each city during the period of January 20th to March 2nd, 2020. First, we explored the associations between COVID-19 confirmed case counts, meteorological factors, and MSI using non-linear regression. Then, we conducted a two-stage analysis for 17 cities with more than 50 confirmed cases. In the first stage, generalized linear models with negative binomial distribution were fitted to estimate city-specific effects of meteorological factors on confirmed case counts. In the second stage, the meta-analysis was conducted to estimate the pooled effects. Our results showed that among 13 cities that have less than 50 confirmed cases, 9 cities locate in the Northern China with average AT below 0 °C, 12 cities had average AH below 4 g/m³, and one city (Haikou) had the highest AH (14.05 g/m³). Those 17 cities with 50 and more cases accounted for 90.6% of all cases in our study. **Each 1 °C increase in AT and DTR was related to the decline of daily confirmed case counts, and the corresponding pooled RRs were 0.80 (95% CI: 0.75, 0.85) and 0.90 (95% CI: 0.86, 0.95), respectively.** For AH, the association with COVID-19 case counts were statistically significant in lag 07 and lag 014. In addition, we found the all these associations increased with accumulated time duration up to 14 days. In conclusions, meteorological factors play an independent role in the COVID-19 transmission after controlling population migration. **Local weather condition[s] with low temperature, mild diurnal temperature range and low humidity likely favor the transmission.**

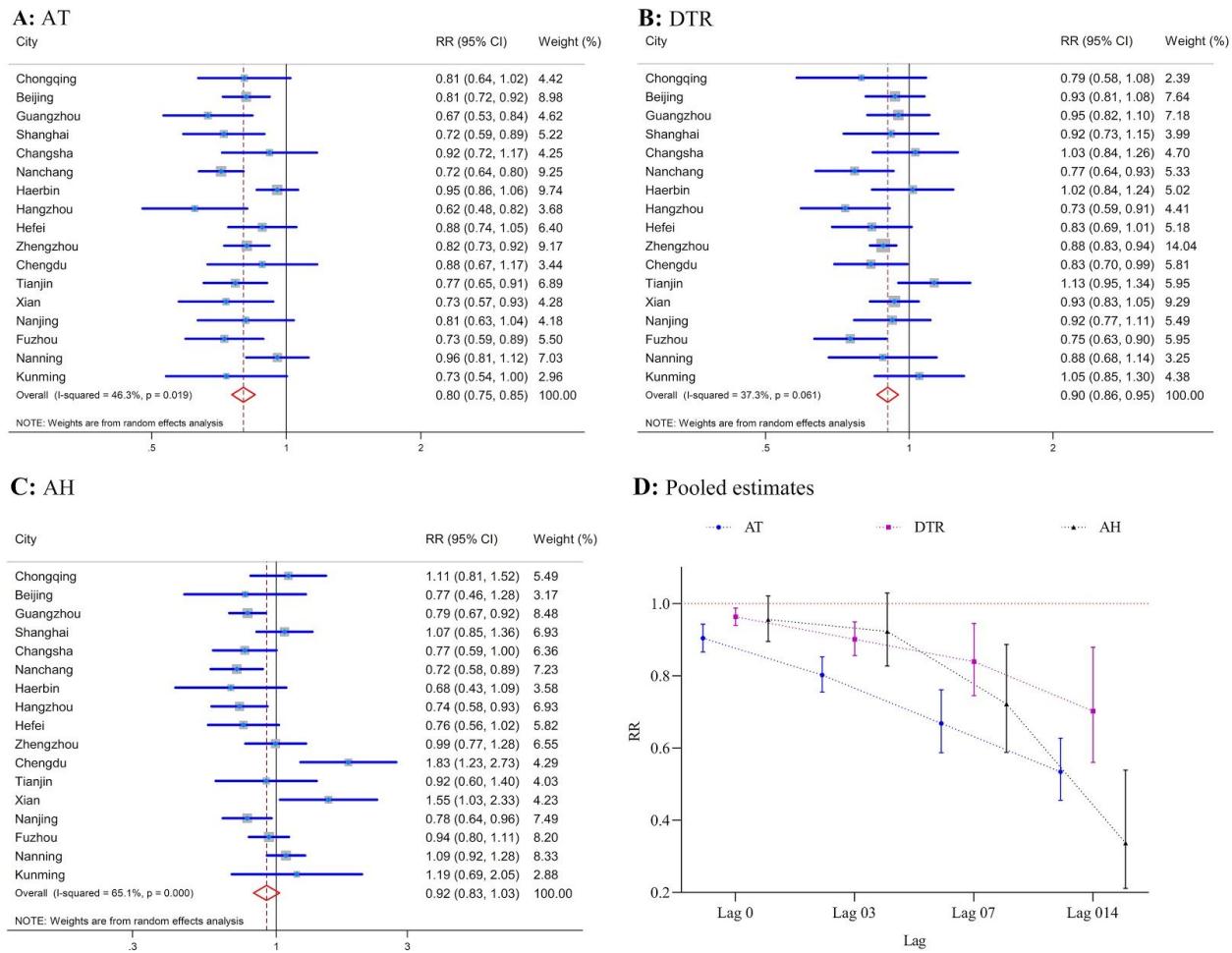


Figure 4. Meta-analysis for effects of meteorological factors on COVID-19 case counts in 17cities during the period of January 20th to March 2nd 2020. (A) [Ambient Temperature]; (B) [Diurnal Temperature Range]; (C) [Ambient Humidity]; (D) Pooled estimates in lag 0, lag 03, lag 07 and lag 014. The association of COVID-19 case counts with AT, AH and DTR in each city was evaluated by fitting generalized linear models respectively (Lag 03). The meta-analysis was conducted to combine the city-specific results. AT: Ambient Temperature; DTR: Diurnal Temperature Range; AH, Absolute Humidity. Fig. 4D showed associations between confirmed case counts and AT, DTR and AH in lag 0, lag 03, lag 07 and lag 014. The pooled effects of AT, DTR and AH became stronger with the increase of cumulative lag days.

Re-emergence of SARS-CoV2 in a discharged COVID-19 case.

Zhou M, Li Q, Cao L, Liu Y, Zha Y, Xie H, Zeng M, Shi X, Gao Y, Xie L, Luo M, Zeng Y

J Microbiol Immunol Infect

2020 Apr 2; PMID: 32303482

Level of Evidence: 4- Case report

Type of Article: Letter

Summary: The authors describe the disease course of a woman admitted to the hospital with Covid-19 diagnosed by nasopharyngeal swab. She tested negative 3 times before hospital release and then was readmitted days later with symptom recurrence and a positive swab.

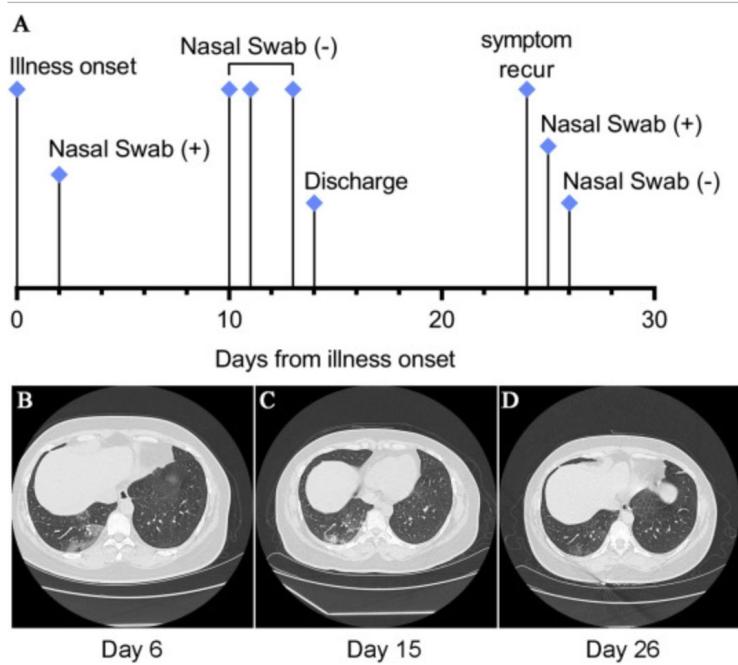


Figure 1. Clinical course of the patients. (A) Timeline for the clinical course in this patient and detection for SARS-CoV2; “+” and “-” indicates a positive or negative results for SARS-CoV2 by real-time RT-PCR assay, respectively; (B)–(D): Images of chest CT finds on day 6 (B), day 15 (C) and day 26 (D).

[Airborne Transmission of Severe Acute Respiratory Syndrome coronavirus-2 to Healthcare Workers: A Narrative Review](#)

Wilson, N M; Norton, A; Young, F P; Collins, D W

Anaesthesia

2020 Apr 20; PMID: 32311771

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Review

BLUF: The authors propose three mechanisms in which COVID-19 viral particles can transmit in the air, and suggest that it is rather time in the vicinity of aerosol-generating procedures instead of the procedure itself that correlates with infection risk.

Abstract:

Healthcare workers are at risk of infection during the severe acute respiratory syndrome (SARS) coronavirus-2 (SARS-CoV-2) pandemic. International guidance suggests direct droplet transmission is likely and airborne transmission occurs only with aerosol generating procedures.

Recommendations determining infection control measures to ensure healthcare worker safety follow these presumptions. Three mechanisms have been described for the production of smaller sized respiratory particles ('aerosols') that, if inhaled, can deposit in the distal airways. All require the surface tension of the respiratory tract lining fluid to be overcome by shear forces. These include: laryngeal activity such as talking and coughing; high velocity gas flow; and cyclical opening and closure of terminal airways. Sneezing and coughing are effective aerosol generators, but all forms of expiration produce particles across a range of sizes. The 5 µm diameter threshold used to differentiate droplet from airborne is an over-simplification of multiple complex, poorly understood biological and physical variables. The evidence defining aerosol-generating procedures comes largely from low-quality case and cohort studies where the exact mode of transmission is unknown as aerosol production was never quantified. **We propose that transmission is associated with time in**

proximity to SARS-CoV-1 patients with respiratory symptoms, rather than the procedures per-se. There is no proven relation between any aerosol-generating procedure with airborne viral content with the exception of bronchoscopy and suctioning. The mechanism for SARS-CoV-2 transmission is unknown but the evidence suggestive of airborne spread is growing. We speculate that infected patients who cough, have high work of breathing, increased closing capacity and altered respiratory tract lining fluid will be significant producers of pathogenic aerosols. We suggest several 'aerosol-generating procedures' may in fact result in less pathogen aerosolization than a dyspnoeic and coughing patient. Healthcare workers should appraise the current evidence regarding transmission and apply this to the local infection prevalence. Measures to mitigate airborne transmission should be employed at times of risk. However, the mechanisms and risk factors for transmission are largely unconfirmed. Whilst awaiting robust evidence, a precautionary approach should be considered to assure healthcare worker safety.

Preterm Delivery in Pregnant Woman With Critical COVID-19 Pneumonia and Vertical Transmission.

Zamaniyan M, Ebadi A, Mir SA, Rahmani Z, Haghshenas M, Azizi S.

Prenat Diagn

2020 Apr 17; PMID: 32304114

Level of Evidence: 5 – Case Report

Type of Article: Letter

BLUF: A possible case of vertically transmitted COVID-19 is presented.

Summary: The authors present a case report of a 22 year old patient with COVID-19 who delivered at 32 weeks by C-section in March at Imam Khomeini Hospital in Iran. A COVID-19 RT-PCR of amniotic fluid aspirated during the procedure tested positive. The neonate initially had negative nasal and throat swabs, but tested positive 24 hours later. The neonate developed fever and had a series of positive PCR tests but recovered. After delivery, the mother's condition worsened and she ultimately died a few weeks later as a result of COVID-19. The authors speculate that her severe disease course may have contributed to this possible case of vertical transmission.

Prevention in the community

Sustaining containment of COVID-19 in China.

Chen S, Zhang Z, Yang J, Wang J, Zhai X, Bärnighausen T, Wang C.

The Lancet

2020 Apr 18, PMID: 32305082

Level of Evidence: 5 - Expert Opinion

Article Type: Editorial

Summary: China is lifting their lockdown and resuming schools, businesses, and flights. Their rapid testing, tracing and changes in behaviors has resulted in containment of COVID-19.

Serological tests facilitate identification of asymptomatic SARS-CoV-2 infection in Wuhan, China.

Wu X, Fu B, Chen L, Feng Y, Wu X, et al.

J Med Virol.

2020 Apr 20; PMID: 32311142

Level of Evidence: 3 - Cohort Study

Article type: Commentary

BLUF: From April 3 - 15 at a hospital in Wuhan researchers collected NAT, chest CT scan, and serological SARS-CoV-2 IgG screening data from 1,021 individuals applying for a permission to resume work and 381 currently hospitalized non-COVID patients. Results showed no SARS-CoV-2 NAT positivity in the resuming group, and 1 in the hospital group with an overall SARS-CoV-2 IgG positive rate of 10%.

Abstract: The Wuhan City has ended the lockdown and people have been allowed to resume working since April 8 if meeting a set of COVID-19-associated tests including SARS-CoV-2 nucleic acid test (NAT) of nasopharyngeal swabs, chest CT scan or a SARS-CoV-2-specific serological test. Here, we reported the positive rate of COVID-19 tests based on NAT, chest CT scan and a serological SARS-CoV-2 test, from April 3 to 15 in one hospital in Qingshan District, Wuhan. **We observed a ~10% SARS-CoV-2-specific IgG positive rate from 1,402 tests. Combination of SARS-CoV-2 NAT and a specific serological test might facilitate the detection of COVID-19 infection, or the asymptomatic SARS-CoV-2-infected subjects.** Large-scale investigation is required to evaluate the herd immunity of the city, for the resuming people and for the re-opened city.

Preparedness for COVID-19 infection prevention in Korea: Single-center experience.

Kim, Youn Jeong; Jeong, Yeon Jeong; Kim, Si Hyun; Kim, Yeo Ju; Lee, Shin Young; Kim, Tae Yeong; Choi, Mi Sun; Ahn, Joong Hyun

J Hosp Infect

2020 Apr 18; PMID: 32302723

Level of Evidence: 6 - No data cited

Type of Article: Letter

BLUF: A hospital in Incheon, South Korea has implemented preparedness protocols for management of COVID-19 infection including a flow chart for actions in case of suspected COVID-19 infection, designation of three zones according to risk, and in-hospital RT-PCR.

SUMMARY: A flow chart (Figure 1) was developed to guide active in the case of a suspected COVID-19 infection, and checklists for patients at high risk were handed out to all medical staff and employees to assess all patients visiting the hospital. All entrances to the hospital excluding the main entrance were closed, and visitors were restricted. Proper PPE was distributed to staff. The hospital was divided into three zones (Figure 1B) according to flow chart risk: the main clinical hospital was the clean zone, a separate temporary building was the moderate-risk zone used for suspected COVID-19 cases, and a separate area at the emergency department was the high-risk zone. Staff in each zone were appropriately trained. Samples were labeled with warning labels and hand-delivered to the laboratory for RT-PCR testing. Laboratory personnel wore appropriate PPE.

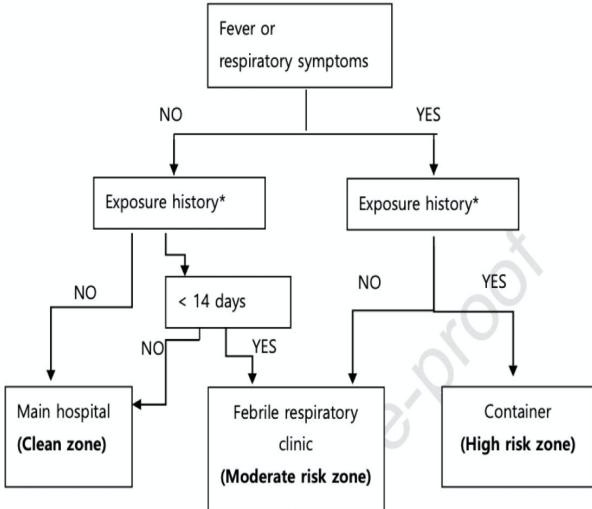


Fig 1A Response flow chart to a suspected COVID-19 case

Exposure history included contact with confirmed cases or travel history of risk area.



Recommendations for protecting against and mitigating the COVID-19 pandemic in long-term care facilities.

Yen MY, Schwartz J, King CC, Lee CM, Hsueh PR

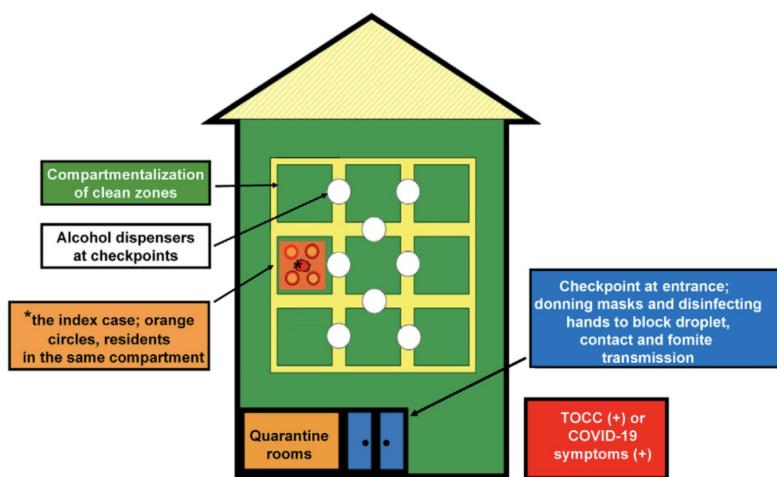
J Microbiol Immunol Infect.

2020 Apr 10; PMID: 32303480

Level of Evidence: 5 – Expert Opinion

Type of Article: Letter

Summary: The authors recommend adapting enhanced traffic control bundling (eTCB) to long-term care facilities, with further compartmentalization of clean zones plus active integrated syndromic and virological surveillance.



The immunological case for staying active during the COVID-19 pandemic.

Simpson RJ, Katsanis E.

Brain Behav Immun.

2020 Apr 17; PMID: 32311497

Level of Evidence: 5 - Expert opinion

Type of Article: Letter to the Editor

Summary: Exercise has been demonstrated to improve outcomes in patients with many viral illnesses through multifaceted mechanisms. These include the frequent mobilization and redistribution of effector lymphocytes and the release of various cytokines from the skeletal muscle (i.e. myokines) that can help maintain immune competency. Despite the closure of gyms and parks, **it is essential that physical activity be encouraged during this viral outbreak.**

[Primary and Secondary Prevention of Cardiovascular Disease in the Era of the Coronavirus Pandemic.](#)

Duffy EY, Cainzos-Achirica M, Michos ED.

Circulation

2020 Apr 20; PMID: 32310675

Level of Evidence: 6 - No evidence cited

Type of Article: Opinion

Summary: The authors discuss how it is important for people to maintain healthy lifestyles including physical activity, healthy diet, and reduced caloric intake during the COVID-19 pandemic. They argue that this pandemic provides an opportunity to “enhance patient empowerment and ownership in cardiovascular prevention.” They end on a hopeful point stating that the COVID-19 pandemic will likely lead to innovation in medicine and resilience that can be used to treat other pandemics such as obesity and heart disease.

[COVID-19 Mobile Positioning Surveillance and Contact Tracing, and Patient Privacy](#)

Ekong I, Chukwu E, Chukwu M

JMIR MHealth Uhealth

2020 Apr 19; PMID: 32310817

Level of Evidence: 5 - No evidence

Type of Article: Research

BLUF: The authors performed an exploratory internet search of technology approaches and responses to the COVID-19 pandemic and analyzed those results to see how different infection control agencies use technology, with consideration to data privacy regulations. Specifically in Nigeria, data from mobile phones can be used to track location while still staying within the confines of Nigerian privacy laws.

Abstract:

Background: The coronavirus disease pandemic is the biggest global economic and health challenge of the century. Its effect and impact are still evolving with deaths estimated to reach 40 million if not checked. One effective and complementary strategy to slow the spread and reduce the impact is to trace primary and secondary contacts using technology.

Objective: The objective of this paper is to survey strategies for digital contact tracing for COVID-19 pandemic and to present how using mobile positioning data conforms with Nigeria's data privacy regulations.

Methods: We conducted an exploratory review of current measures for COVID-19 contact tracing globally. We then analyzed how countries are using mobile positioning data technology in handling the COVID 19 pandemic spread. We made recommendations for how Nigeria can adopt this approach in context of Nigeria's Data protection Regulation (NDPR).

Results: Despite the potentials, digital contact tracing always comes in conflict with patient data privacy regulations. We found that Nigeria's response complies with the NDPR, and that it is possible to leverage telecommunications call detail registry (CDR) to complement current strategies within the NDPR regulation.

Conclusions: Our study show that mobile position data contact tracing is important for epidemic control as long as it conforms to relevant data privacy regulation. Implementation guideline will limit data misuse.

COVID-19: Health prevention and control in non-healthcare settings.

Belingheri M, Paladino ME, Riva MA. Belingheri M, et al.

Occup Med (Lond)

2020 Apr 20; PMID: 32311040

Level of Evidence: 6 - Expert opinion

Type of Article: Commentary

Summarizing statement: “Physicians, especially those in charge of occupational health services, should provide workers with accurate information and training about COVID-19, to ensure adequate risk perception and to improve compliance with prevention and control measures.” Suggested measures can be found in the table below:

Table 1.

Prevention and control measures in non-healthcare settings

➤ Provide information and education about COVID-19	➤ Stay home in case of symptoms or in case of a suspected transmission of COVID-19 virus (quarantine)	➤ Wash and clean hands with water and soap or with alcoholic solutions	➤ Maintain social distance (1 m) between people	➤ Clean surfaces, objects, clothes, and reduce the sharing of objects	➤ Ensure workplaces ventilation	➤ Do not recommend unnecessary PPE
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Prevention in the hospital

PPE and possible routes of airborne spread during the COVID-19 pandemic.

Brown J, Pope C.

Anaesthesia.

2020 Apr 20; PMID: 32311756

Level of Evidence: 5 - Expert Opinion

Type of Article: Letter

Summarizing excerpt: “There remains considerable debate about the extent to which airborne spread of SARS-CoV-2 occurs. Small droplets (< 5µm) are thought to remain suspended in the air and could theoretically be inhaled into the lungs causing infection. **Loose fitting "surgical" masks will not prevent such inhalation and only a tight-fitting filtering mask is adequate.** Conversely larger (> 5µm) particles do not remain suspended in the air and can only cause infection if they are immediately inhaled, or after contact with a surface they land on.”

Inactivation of severe acute respiratory syndrome coronavirus 2 in plasma and platelet products using a riboflavin and ultraviolet light-based photochemical treatment.

Keil SD, Ragan I, Yonemura S, Hartson L, Dart NK, Bowen R, Keil SD, et al.

Vox Sang.

2020 Apr 20; PMID: 32311760

Level of Evidence: 5 - Mechanism-based reasoning

Article type: Research

BLUF: The authors report on the efficacy of riboflavin and UV light against SARS-CoV-2 virus when tested in both plasma (n=5) and platelets (n=3) products. They observed that in plasma and platelet units the mean log reduction was ≥ 3.40 (Table 1) and ≥ 4.53 log (Table 2) respectively. Reducing both below to the limits of detection. These results suggest that this method could be effective in reducing the theoretical risk of transfusion-transmitted SARS-CoV-2.

Abstract:

Background and objective: Severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), is a member of the coronavirus family. Coronavirus infections in humans are typically associated with respiratory illnesses, however viral RNA has been isolated in serum from infected patients. Coronaviruses have been identified as a potential low-risk threat to blood safety. The Mirasol Pathogen Reduction Technology (PRT) System utilizes riboflavin and ultraviolet (UV) light to render blood-borne pathogens noninfectious, while maintaining blood product quality. Here we report on the efficacy of riboflavin and UV light against the pandemic virus SARS-CoV-2 when tested in both plasma and platelets units.

Materials and methods: Stock SARS-CoV-2 was grown in Vero cells and inoculated into either plasma or platelet units. Those units were then treated with riboflavin and UV light. The infectious titers of SARS-CoV-2 were determined by plaque assay using Vero cells. A total of five (n=5) plasma and three (n=3) platelet products were evaluated in this study.

Results: In both experiments the measured titer of SARS-CoV-2 was below the limit of detection following treatment with riboflavin and UV light. The mean log reductions in the viral titers were ≥ 3.40 and ≥ 4.53 for the plasma units and platelet units, respectively.

Conclusion: Riboflavin and UV light effectively reduced the titer of SARS-CoV-2 in both plasma and platelet products to below the limit of detection in tissue culture. The data suggest that the process would be effective in reducing the theoretical risk of transfusion-transmitted SARS-CoV-2.

Table 1: Log Reduction of SARS-CoV-2 after PRT Treatment – PF24 Plasma Units

Unit Number	Pre-Treatment Viral Load (Log PFU/mL)	Post-Treatment Viral Load (Log PFU/mL)	Log Reduction
1	4.58	≤ 1.22	≥ 3.36
2	4.79	≤ 1.22	≥ 3.57
3	4.48	≤ 1.22	≥ 3.26
4	4.85	≤ 1.22	≥ 3.63
5	4.38	≤ 1.22	≥ 3.16
Average	4.62	≤ 1.22	≥ 3.40
Std. Dev.	0.20	N/A	N/A
Stock Virus Titer	6.04 log PFU/mL		
Theoretical Pre-Treatment Titer*	4.73 log PFU/mL		

NOTE: Titers shown in italic font are at the limit of detection for the assay.

PFU= plaque forming unit

* Theoretical pre-treatment titer is based on a ~5% (12 mL) viral inoculum with a final product volume of 247 mL (200 mL plasma + 35 mL RB + 12 mL stock virus)

Unit Number	Pre-Treatment Viral Load (Log PFU/mL)	Post-Treatment Viral Load (Log PFU/mL)	Log Reduction
1	4.93	≤ 0.22	≥ 4.71
2	4.65	$\leq 0.30^*$	≥ 4.35
3	4.74	≤ 0.22	≥ 4.52
Average	4.77	≤ 0.25	≥ 4.53
Std. Dev.	0.14	N/A	N/A
Stock Virus Titer	6.11 log PFU/mL		
Theoretical Pre-Treatment Titer**	4.80 log PFU/mL		

NOTE: Titers shown in italic font are at the limit of detection for the assay.
PFU= plaque forming unit
* One of six wells in the 10^0 post-treatment sample was contaminated and removed from the final titer calculation.
** Theoretical pre-treatment titer is based on a ~5% (12 mL) viral inoculum with a final product volume of 247 mL (200 mL platelet + 35 mL RB + 12 mL stock virus)

COVID-19 putting patients at risk of unplanned extubation and airway providers at increased risk of contamination

Berkow, Lauren; Kanowitz, Arthur

Anesth Analg

2020 Apr 16; PMID: 32304463

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Letter

Summary: In this letter to the editor, authors discuss the numerous concerns and safety pitfalls surrounding managing critically ill COVID-19 patients, particularly those that could require emergent intubation or extubation. Donning PPE beforehand, whether for an emergent procedure or not, is recommended to all providers.

PPE & Decontamination Methods

Challenges and solutions for addressing critical shortage of supply chain for personal and protective equipment (PPE) arising from Coronavirus disease (COVID19) pandemic - Case study from the Republic of Ireland.

Rowan NJ, Laffey JG, Rowan NJ, et al.

Sci Total Environ.

2020 Apr 6; PMID: 32304970

Level of Evidence: 4 - Case Study

Type of Article: Research

Summary: In response to shortages of PPE, the authors discuss solutions being utilized in the Republic of Ireland including improved tracking and communication of existing stockpiles, production of made-to-order PPE, and reprocessing of single-use PPE with hydrogen peroxide or UV radiation.

Abstract:

Coronavirus (COVID-19) is highly infectious agent that causes fatal respiratory illnesses, which is of great global public health concern. Currently, there is no effective vaccine for tackling this COVID-19 pandemic where disease countermeasures rely upon preventing or slowing person-to-person transmission. Specifically, there is increasing efforts to prevent or reduce transmission to front-line healthcare workers (HCW). However, **there is growing international concern regarding the shortage in supply chain of critical one-time-use personal and protective equipment (PPE)**. PPE are heat sensitive and are not, by their manufacturer's design, intended for reprocessing. Most conventional sterilization technologies used in hospitals, or in terminal medical device sterilization providers, cannot effectively reprocess PPE due to the nature and severity of sterilization modalities. Contingency planning for PPE stock shortage is important. **Solutions in the Republic of Ireland include use of smart communication channels to improve supply chain, bespoke production of PPE to meets gaps, along with least preferred option, use of sterilization or high-level disinfection for PPE reprocessing.** Reprocessing PPE must consider material composition, functionality post treatment, along with appropriate disinfection. Following original manufacturer of PPE and regulatory guidance is important. Technologies deployed in the US, and for deployment in the Republic of Ireland, are eco-friendly, namely vaporised hydrogen peroxide (VH₂O₂), such as for filtering facepiece respirators and UV irradiation and High-level liquid disinfection (Actichlor+) is also been pursued in Ireland. Safeguarding supply chain of PPE will sustain vital healthcare provision and will help reduce mortality.

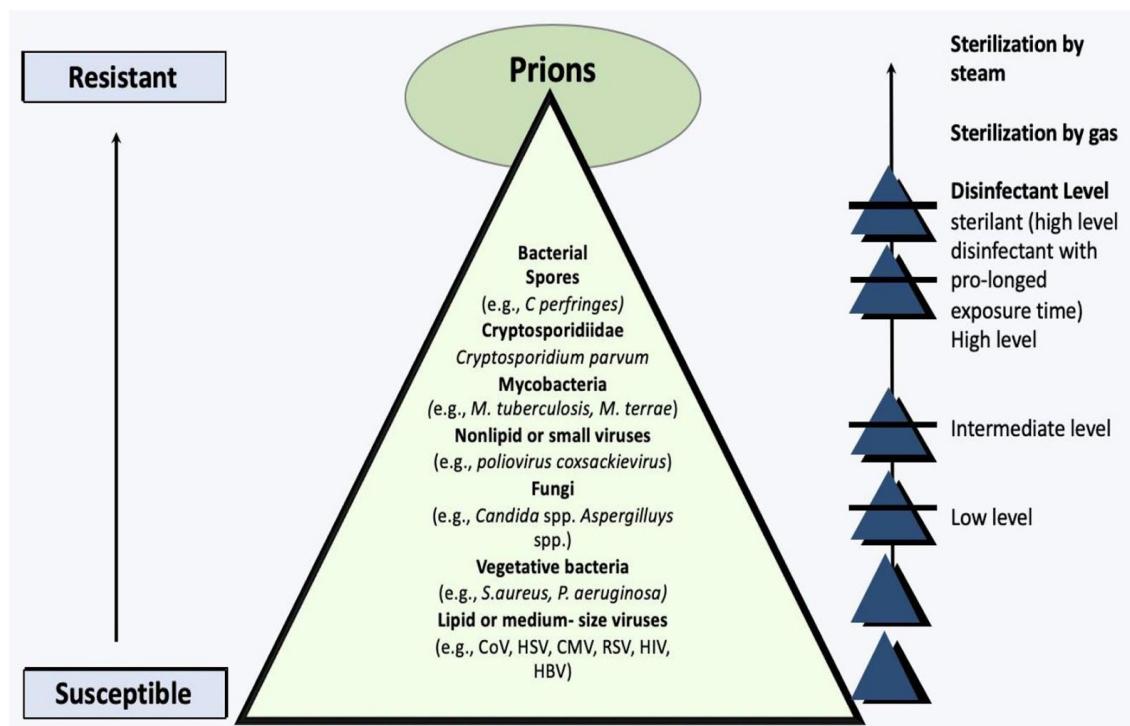


Fig. 4. Pyramid of resistance of increasing resistance to disinfection and sterilization.

SARS-CoV-2 RNA detection of hospital isolation wards hygiene monitoring during the Coronavirus Disease 2019 outbreak in a Chinese hospital.

Wang J, Feng H, Zhang S, Ni Z, Ni L, Chen Y, Zhuo L, Zhong Z, Qu T.

Int J Infect Dis.

2020 Apr 17; PMID: 32311449

Level of Evidence: 3 - Cross sectional study

Type of Article: Research article

BLUF: This cross sectional study of the 33 COVID-19 patients at First Affiliated Hospital of Zhejiang University, China, found that “routine disinfection measure of the air, object surface, and sewage” as well as staff hand hygiene was sufficient to decrease the prevalence of SARS-CoV-2 RNA.

Abstract:

Objectives: The aim of this paper was to monitor the presence of SARS-CoV-2 among hospital environment surfaces, sewage, and personal protective equipment (PPE) of staff in isolation wards in the First Affiliated Hospital of Zhejiang University, China.

Methods: **Surfaces of objects were routinely wiped with 1,000mg/L chlorine containing disinfectant.** Air and sewage disinfection was proceeded routinely and strictly. Hospital

environmental surfaces and PPE of staff in isolation wards were sampled using swabs. The sewage from various inlet and outlets were sampled. The respiratory and stool specimens of patients were collected. The respiratory specimens of staffs in the isolation wards were also sampled once a week. Quantitative real-time reverse transcription PCR (qRT-PCR) methods were used to confirm the existence of SARS-CoV-2 RNA. Viral culture was done for the samples positive for SARS-CoV-2 RNA.

Results: During the study period, 33 laboratory-confirmed patients were hospitalized in isolation wards in the hospital. None of SARS-CoV-2 RNA was detected among the 36 object surface samples and 9 staff PPE samples in isolation wards. Though the 3 sewage samples from the inlet of preprocessing disinfection pool were positive for SARS-CoV-2 RNA and the sample from the outlet of preprocessing disinfection pool was weakly positive, the sewage sample from the outlet of the last disinfection pool was negative. All of the 5 sewage samples from various points were negative by viral culture of SARS-CoV-2. None of the respiratory specimens of staff in the isolation wards were positive.

Conclusions: Though SARS-CoV-2 RNA of the sewage samples were positive from inlets of the sewage disinfection pool and negative from the outlet of the last sewage disinfection pool, no viable virus was detected by culture. **The monitoring data in this study suggested that the strict disinfection and hand hygiene could decrease the hospital-associated COVID-19 infection risk of the staff in isolation wards.**

Adaption of the Emergency Department Decontamination Room for Airway Management During COVID-19

Sampson CS

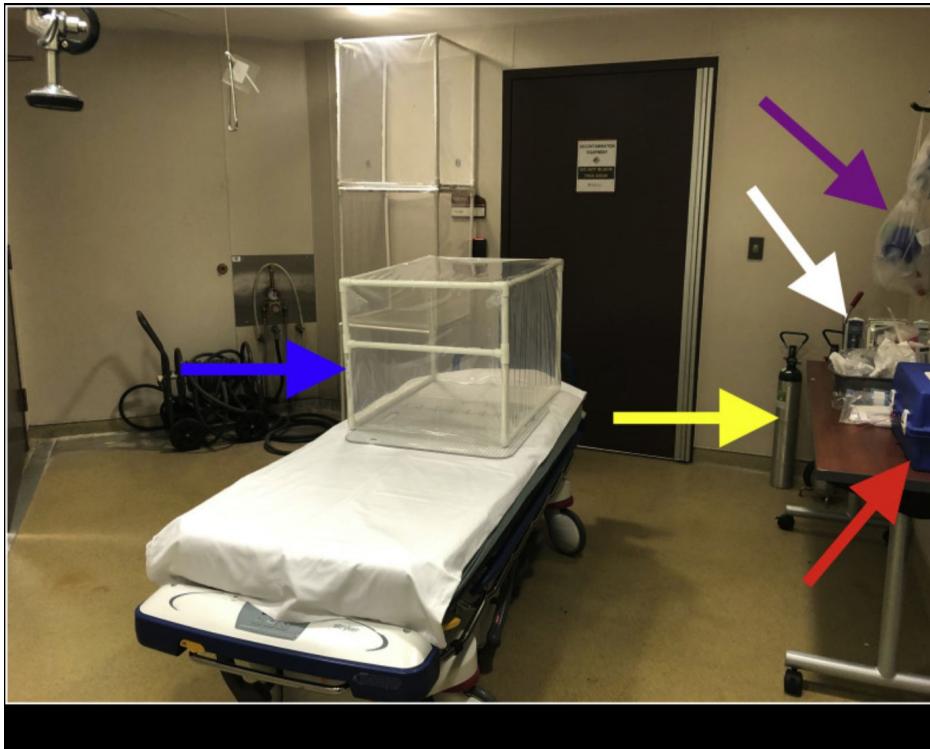
American Journal of Emergency Medicine

2020 Apr 15, PMID: 32305159

Level of Evidence: 6 - no data cited

Type of Article: Letter

Summary: This letter conveyed how one emergency department (ED) adapted their decontamination room and entry to the ED for COVID-19 patients in order to control infection and sustain an environment that could be readily sterilized. This letter aimed to provide practical information to encourage others to potentially learn from shared ideas.



[See this image and copyright information in PMC](#)

Image 1 Decontamination room setup. Blue arrow: Patient respiratory protection unit. Additional units stacked behind. Yellow arrow: Portable oxygen tank. Purple arrow: Adult bag valve mask with viral filter attached. White arrow: Infusion pump. Red arrow: Tackle box containing code medications.

Management

Healthcare workforce injuries from COVID-19 related changes

Covid-19: Countermeasure for N95 mask-induced pressure sore.

Yin Z.

J Eur Acad Dermatol Venereol.

2020 Apr 17; PMID: 32302449

Level of Evidence: 6 - Expert Opinion

Type of Article: Letter to the Editor

Summary: The author suggests a benzalkonium “band-aid” be placed over an existing pressure sore before an adhesive hydrocolloid dressing is placed as an improvement on using a hydrocolloid dressing alone for pressure sores from N95 mask use.



Figure 1. **A:** N95 health care respirator and surgical mask. **B:** Pressure sore on nose bridge. **C:** Application of benzalkonium chloride patch on nose bridge.

Skin Reactions to Non-glove Personal Protective Equipment: An Emerging Issue in the COVID-19 Pandemic.

Gheisari M, Araghi F, Moravvej H, Tabary M, Dadkhahfar S. Gheisari M, et al.

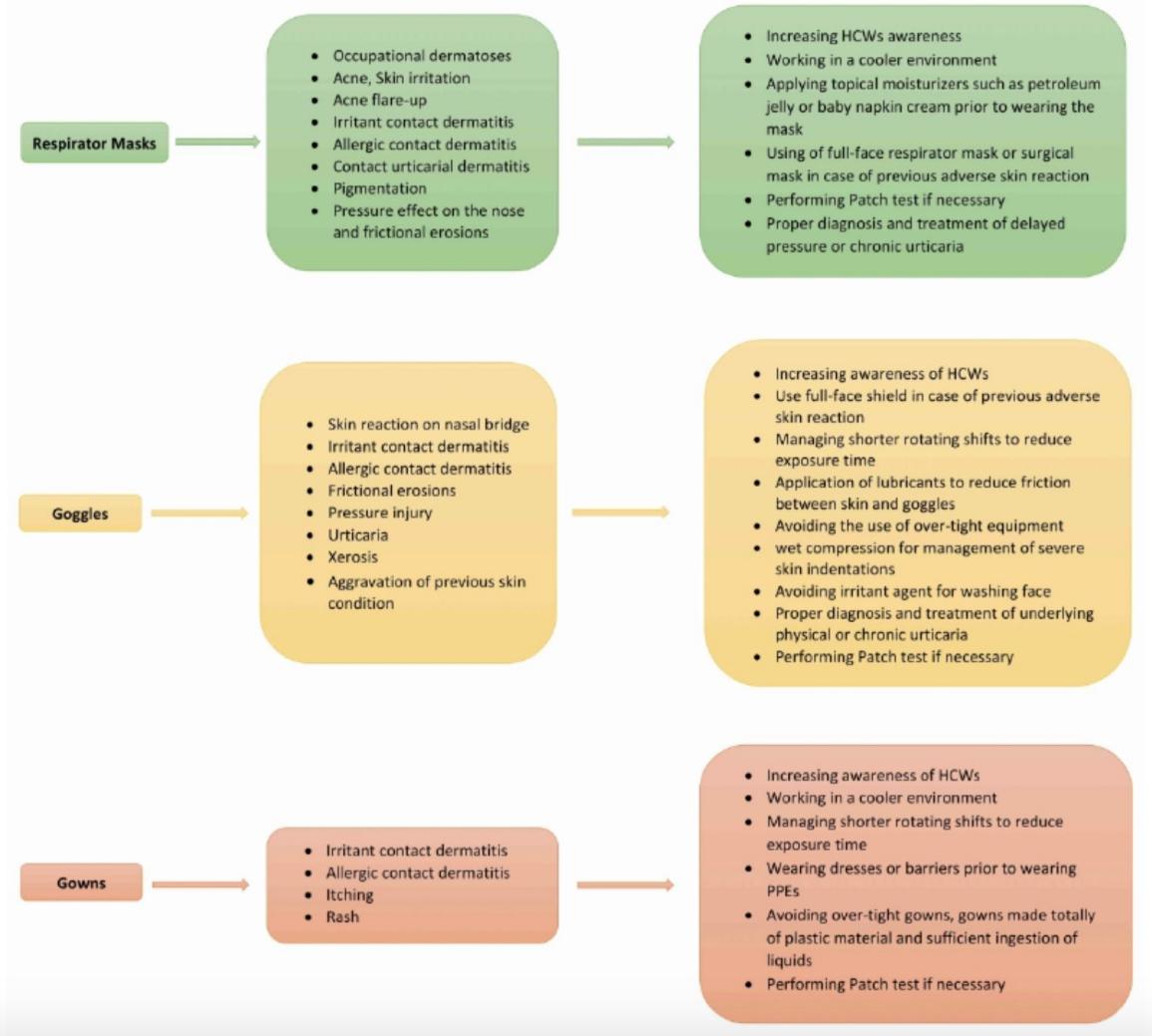
J Eur Acad Dermatol Venereol

2020 Apr 17; PMID: 32302444

Level of Evidence: 5 - Expert Opinion

Type of Article: Letter to the Editor

Summary: The authors review skin reactions in PPE other than gloves including respirators, gowns and goggles. **Figure 1 below lists these adverse reactions and provides management strategies.**



Acute care

Thromboembolic events and apparent heparin resistance in patients infected with SARS-CoV-2.

Beun R, Kusadasi N, Sikma M, Westerink J, Huisman A.

Int J Lab Hematol.

2020 Apr 20; PMID: 32311843

Level of Evidence: 4 - Case series

Type of Article: Letter to the Editor

BLUF: The rates of DIC and thromboembolic events in patients who have died of COVID-19 may be much higher than previously thought. COVID-19 patients had very high levels of Factor VIII which can cause heparin resistance, requiring high doses of unfractionated heparin to achieve a target aPTT and increasing the risk for life-threatening bleeding. The authors instead suggest aiming for a **target anti-Xa level of 0.3-0.7 U/L**.

Summarizing excerpts: “One of the most important clinical features of the infection is a profound coagulopathy. In a recent cohort study **71% of patients who eventually died matched the ISTH criteria for disseminated intravascular coagulation (DIC)**, while this percentage was only 0.6% in patients who survived. Although no data has been presented or published, clinical experience suggests that this coagulopathy is associated with an increased risk for both venous and arterial

thrombosis. **Treatment of thrombosis in the setting of profound coagulopathy may be hampered by the inability to use the aPTT ratio when treating with unfractionated heparin (UHF).** We provide data from our center and provide guidance for treatment of perceived heparin resistance associated with the coagulopathy in patients with SARS-CoV-2 infection.

Table 1. Thrombo-embolic events in patients with SARS-CoV-2 pneumonia.

	Number of patients (% of total)
Total number of patients admitted to ICU	75
Clinical suspicion of thrombo-embolic event	35 (46.6%)
Performed diagnostic approach	CT: 32 and ultrasound: 3
Pulmonary embolism in (sub)segmental arteries	16 (21.3%)
Pulmonary embolism in central artery	4 (5.3%)
Ischemic cerebrovascular accident	2 (2.7%)
Deep vein thrombosis	3 (4.0%)

Patients admitted to the ICU from March 16th until April 9th.

Table 2. Results of factor VIII, fibrinogen, d-dimer, antithrombin and the platelet count.

	Mean (min. – max.)	Reference range
Age (years)	60.5 (53 – 68)	n.a.
Gender (m/f)	2/2	n.a.
UFH (max. IU/24h)	48708 (36748 – 64576)	n.a.
Factor VIII (IU/mL)	4.45 (2.50 – 5.89)	0.60 – 1.50
Fibrinogen (g/L)	7.3 (6.9 – 7.6)	2.0 – 4.0
D-dimer (mg/L)	48.6 (13.8 – 100)	< 0.5
Antithrombin (IU/mL)	0.91 (0.67 – 1.19)	0.80 – 1.20
Platelet count ($\times 10^9/L$)	270 (223 – 302)	150 – 450

Blood samples were drawn on the day of admission to the ICU, or on the first day of signs of thromboembolic events. Conversion factor for factor VIII and antithrombin: 1.00 IU/mL = 100 IU/dL = 100%. n.a.: not applicable.

Emergency Medicine

Summary of 20 tracheal intubation by anesthesiologists for patients with severe COVID-19 pneumonia: retrospective case series.

Zhang L, Li J, Zhou M, Chen Z.

J Anesth.

2020 Apr 17, PMID: 32303885

Level of Evidence: 4 - Case series

Article Type: Research

BLUF: Patients critically ill from Covid-19 pneumonia are more likely to have a better outcome with early tracheal intubation before blood gas data deterioration.

Abstract: SARS-CoV-2 pandemic is announced and it is very important to share our experience to the critical care community in the early stage. Urgent intubation team was organized by anesthesiologists and was dispatched upon request. We have retrospectively reviewed medical charts of 20 **critically ill patients with Covid-19 pneumonia who required tracheal intubation** from February 17 to March 19 in Wuhan No.1 hospital, China. We collected their demographics, vital signs, blood gas analysis before and after tracheal intubation, and 7-day outcome after tracheal intubation. Out of 20 patients, 90% were over 60 years old and 15 were with at least one comorbidity. All meet the indication for tracheal intubation announced by treatment expert group. We had successfully intubated all patients using personal protective equipment without circulatory collapse during tracheal intubation. During the observational period, none of 17 anesthesiologists were infected. Although intubation improved SPO₂, reduced PaCO₂ and blood lactate, seven of 20 patients died within 7-days after tracheal intubation. Non-survivors showed significantly lower SPO₂ and higher PaCO₂ and blood lactate compared to survivors. For those who are **anticipated to deteriorate severe pneumonia with poor prognosis**, earlier respiratory support with **tracheal intubation** may be advised to **improve outcome**.

[Coronavirus Outbreak: Is Radiology Ready? Mass Casualty Incident Planning.](#)

Myers L, Balakrishnan S, Reddy S, Gholamrezanezhad A.

J Am Coll Radiol.

2020 Apr 3; PMID: 32304643

Level of Evidence: 5 - Expert opinion

Type of Article: Editorial

BLUF: The ACR does not recommend CT for screening for COVID-19. Use portable imaging equipment for patients suspected of COVID-19. Daily intradepartmental and interdepartmental communication is necessary for ongoing policy changes and needs for mobilization of resources.

Abstract: On March 11, 2020, the World Health Organization declared a coronavirus disease 2019 (COVID-19) pandemic. Health care systems worldwide should be prepared for an unusually high volume of patients in the next few weeks to months. Even the most efficient radiology department will undergo tremendous stress when victims of a mass casualty flood the emergency department and in turn the radiology department. A significant increase is expected in the number of imaging studies ordered for the initial diagnosis and treatment follow-up of cases of COVID-19. Here, we highlight recommendations for developing and implementing a mass casualty incident (MCI) plan for a viral outbreak, such as the current COVID-19 infection. The MCI plan consists of several steps, including **preparation, mobilization of resources, imaging chain, adjusting imaging protocols, and education, such as MCI plan simulation and in-service training.** Having an MCI plan in place for a viral outbreak will protect patients and staff and ultimately decrease virus transmission. The use of simulations will help identify throughput and logistical issues.

Table 1. Imaging chain: from order to communication with questions to provoke discussion

Imaging Chain (CT)	Considerations
Order	Who will order examinations for suspected COVID-19? Is there an algorithm used to determine which patients get a CT scan? Recommend indication or reason for examination to include the term "coronavirus precautions."
Protocol	Will you use a standard chest CT or low-dose chest CT coronavirus protocol?
Scheduling	Who determines the next patient and when imaging is available?
Transport to and from radiology	Is there a dedicated transport team?
Imaging	Image acquisition is based on protocol; see "Adjusting Imaging Protocols" section.
CT scanner cleaning	Determine if facilities management, ancillary staff, or CT technologist will clean the scanner.
Interpretation and communication	Determine communication of findings of COVID-19 cases: written or verbal communication. Consider templates specific for coronavirus.

COVID-19 = coronavirus disease 2019.

Table 2. Suggested questions to answer during MCI simulation

Questions for MCI Simulation (CT)	Considerations
What is the turnaround time from order to communication?	Provides information on efficiency and throughput
Where does the patient wait to be imaged?	Determines if the radiology department needs a waiting area that meets the CDC recommendations
What is the waiting area capacity?	Determines how many patients can wait in the radiology department
Who determines if a patient can come to radiology and who decides priority?	Radiology nurse, radiology nursing assistant, EM representative
Who transports the patient to and from radiology?	Dedicated versus general transporter, EM staff
Does the radiologist give a "wet read"?	Can decrease time to diagnosis, potentially more errors
Do coronavirus patients have priority over other patients?	Important to have an algorithm in place for patient priority

CDC = Centers for Disease Control and Prevention; EM = emergency medicine; MCI = mass casualty incident.

Which intravascular access should we use in patients with suspected/confirmed COVID-19?

Smereka J, Szarpak L, Filipiak KJ, Jaguszewski M, Ladny JR. Resuscitation.

Publication Date: April 15, 2020; PMID: 32304800,
Level of Evidence: 3 - Literature review

Type of Article: Letter to the Editor

Summary: “Medical personnel dressed in full protective gear as the preferred method of gaining intravascular access in patients with suspected/confirmed COVID-19 should choose intraosseous access.”

Comparing Rapid Scoring Systems in Mortality Prediction of Critical Ill (sic) Patients With Novel Coronavirus Disease

Hai H, Ni Y, Yanru Q

Academic Emergency Medicine (Society for Academic Emergency Medicine)

2020 Apr 20; PMID: 32311790

Evidence Level: 4 - Chart Review Case Series

Type of Article: Research

BLUF: This study used records from 138 COVID-19 critical patients to explore rapid scoring systems using calculated Modified Early Warning Score (MEWS) and Rapid Emergency Medicine Score (REMS). They found that the REMS could be a valuable tool, especially for patients under the age of 65.

Abstract:

Objectives: Rapid and early severity-of-illness assessment appears to be important for critical ill patients with novel coronavirus disease (COVID-19). This study aimed to evaluate the performance of the rapid scoring system on admission of these patients.

Methods: 138 medical records of critical ill patients with COVID-19 were included in the study. Demographic and clinical characteristics on admission used for calculating Modified Early Warning Score (MEWS) and Rapid Emergency Medicine Score (REMS) and outcomes (survival or death) were collected for each case and extracted for analysis. All patients were divided into two age subgroups (<65 and ≥65years). The receiver operating characteristic curve analyses were performed for overall patients and both subgroups.

Results: The median [25%quartile, 75%quartile] of MEWS of survivors versus non-survivors were 1[1, 2] and 2[1, 3] and that of REMS were 5[2, 6] and 7[6, 10], respectively. In overall analysis, the area under the receiver operating characteristic curve for the REMS in predicting mortality was 0.833 (95% CI: 0.737-0.928), higher than that of MEWS (0.677, 95% CI 0.541-0.813). An optimal cut-off of REMS (≥6) had a sensitivity of 89.5%, a specificity of 69.8%, a positive predictive value of 39.5%, and a negative predictive value of 96.8%. In the analysis of subgroup of patients aged<65years, the area under the receiver operating characteristic curve for the REMS in predicting mortality was 0.863 (95% CI: 0.743-0.941), higher than that of MEWS (0.603, 95% CI 0.462-0.732).

Conclusion: To our knowledge, this study was the first exploration on rapid scoring systems for critical ill patients with COVID-19. The REMS could provide emergency clinicians with an effective adjunct risk stratification tool for critical ill patients with COVID-19, especially for the patients aged<65 years. The effectiveness of REMS for screening these patients is attributed to its high negative predictive value.

Critical Care

Blood transfusion strategies and ECMO during the COVID-19 pandemic.

Koeckerling, David; Pan, Daniel; Mudalige, N Lakmal; Oyefeso, Oluwatobiloba; Barker, Joseph
Lancet Respir Med

2020 Apr 16; PMID: 32305078

Level of Evidence: 5 – Expert opinion

Article Type: Letter to the Editor

Summary: Authors note ECMO is frequently accompanied by hemorrhage and coagulopathy, citing daily transfusion requirements of up to 2-5 units PRBCs and 3-9 units of platelets. They note that the American Red Cross is likely to experience blood shortages, and cite the TRICC trial and a 2015 *Ann Thorac Surg* article reporting on a blood conservation protocol in ECMO for ARDS patients as

evidence that being more judicious with blood supply is likely to be safe for patients and wise for the long-term support of patient care.

Hypercoagulability of COVID-19 patients in Intensive Care Unit. A Report of Thromboelastography Findings and other Parameters of Hemostasis.

Panigada, Mauro; Bottino, Nicola; Tagliabue, Paola; Grasselli, Giacomo; Novembrino, Cristina; Chantarangkul, Veena; Pesenti, Antonio; Peyvandi, Fora; Tripodi, Armando

J Thromb Haemost

2020 Apr 17; PMID: 32302438

Level of Evidence: 3 - Cohort Study

Type of Article: Research

BLUF: After analysis of coagulation factors and platelet counts in a cohort of 24 patients admitted to the ICU due to COVID-19, authors conclude that the severe inflammatory state in COVID-19 is not consistent with DIC.

Abstract:

Background: The severe inflammatory state secondary to Covid-19 leads to a severe derangement of hemostasis that has been recently described as a state of disseminated intravascular coagulation (DIC) and consumption coagulopathy, defined as decreased platelet count, increased fibrin(ogen) degradation products such as D-dimer as well as low fibrinogen.

Aims: Whole blood from 24 patients admitted at the intensive care unit because of Covid-19 was collected and evaluated with thromboelastography by the TEG point-of-care device on a single occasion and six underwent repeated measurements on two consecutive days for a total of 30 observations. Plasma was evaluated for the other parameters of hemostasis.

Results: TEG parameters are consistent with a state of hypercoagulability as shown by decreased R and K values, and increased values of K angle and MA. Platelet count was normal or increased, prothrombin time and activated partial thromboplastin time were near(normal). Fibrinogen was increased and D-dimer was dramatically increased. C-reactive protein was increased. Factor VIII and von Willebrand factor (n=11) were increased. Antithrombin (n=11) was marginally decreased and protein C (n=11) was increased.

Conclusion: The results of this cohort of patients with Covid-19 are not consistent with acute DIC, rather they support hypercoagulability together with a severe inflammatory state. These findings may explain the events of venous thromboembolism observed in some of these patients and support antithrombotic prophylaxis/treatment. Clinical trials are urgently needed to establish the type of drug, dosage and optimal duration of prophylaxis.

Chinese Expert Consensus on Diagnosis and Treatment of Coagulation Dysfunction in COVID-19

Song, JC; Wang, G; Zhang, W; Zhang, Y; Li, WQ; Zhou, Z; People's Liberation Army Professional Committee of Critical Care Medicine, Chinese Society on Thrombosis and Haemostasis

Military Medical Research

2020, April 20; PMID: 32307014

Level of Evidence: 5- Expert Opinion

Type of Article: Position

BLUF: The authors cite recent studies showing that 71% of patients with COVID-19 related deaths have met the criteria for the diagnosis of disseminated intravascular coagulation (DIC). The article reviews the coagulation dysfunction caused by COVID-19 and details numerous recommendations provided by experts from Wuhan, summarized below:

Evaluation of blood coagulation function:

- Verify history of underlying disease (ex. hypertension, diabetes) and coagulation function.
- Assess prothrombin time/INR, platelet count, fibrinogen, D-Dimer, and APTT routinely to assess for changing coagulation function.
- Use ISTH/CDCC DIC scores to diagnose coagulation dysfunction.
- Use viscoelastic tests to evaluate coagulation function in patients with an underlying coagulopathy.

Anticoagulation therapy (for severe COVID-19 patients with coagulation dysfunction):

- **Unfractionated Heparin/low-molecular-weight Heparin are recommended** to prevent the depletion of coagulation substrates. Carefully monitor when administering to a patient on ECMO.
- Avoid local anticoagulation in patients requiring continuous renal replacement therapy (no anticoagulation or systemic is recommended).
- Topical citrate anticoagulation should be used for patients who require CRRT due to active bleeding.
- Use argatroban/bivalirudin in the setting of heparin-induced thrombocytopenia.

Replacement treatment

- Use goal directed replacement therapy with routine coagulation indicators, TEG parameters and Sonoclot/Centruclyt indices.
- Factor VII is recommended if hemorrhage is not corrected by active replacement therapy and a hypocoagulation state is present.

Supportive treatment (for patients with severe symptoms and coagulopathy)

- Artificial liver support system (ALSS) to facilitate plasma exchange is recommended for patients with liver failure.

Prevention

- Avoid heparin flush during vascular access placement.
- Maintain strict control of infusion dose of synthetic colloids, while ensuring adequate tissue perfusion.
- Actively control coagulation dysfunction for patients on ECLS.

Abstract: Since December 2019, a novel type of coronavirus disease (COVID-19) in Wuhan led to an outbreak throughout China and the rest of the world. To date, there have been more than 1,260,000 COVID-19 patients, with a mortality rate of approximately 5.44%. Studies have shown that coagulation dysfunction is a major cause of death in patients with severe COVID-19. Therefore, the People's Liberation Army Professional Committee of Critical Care Medicine and Chinese Society on Thrombosis and Hemostasis grouped experts from the frontline of the Wuhan epidemic to come together and develop an expert consensus on diagnosis and treatment of coagulation dysfunction associated with a severe COVID-19 infection. This consensus includes an overview of COVID-19-related coagulation dysfunction, tests for coagulation, anticoagulation therapy, replacement therapy, supportive therapy and prevention. The consensus produced 18 recommendations which are being used to guide clinical work.

First Successful Treatment of COVID-19 Induced Refractory Cardiogenic Plus Vasoplegic Shock by Combination of pVAD and ECMO - A Case Report

Bemtgen X, Krüger K, Supady A, Dürschmied D, Schibilsky D, Bamberg F, Bode C, Wengenmayer T, Staudacher DL

ASAIO J

2020 Apr 16; PMID: 32304394

Level of Evidence: 5 – Case Report

Type of Article: Research

BLUF: This article discusses the first case report of **treatment of refractory mixed cardiogenic and vasoplegic shock** in a patient who **later developed COVID-19-associated ARDS**. The authors suggest that **ECMO and pVAD** might be useful to manage cardiogenic and vasoplegic **shock**, respectively, **secondary to COVID-19 disease**.

Abstract:

The novel coronavirus SARS-CoV-2 is infecting hundreds of thousands of humans around the globe. The coronavirus disease COVID-19 is known to generate mild as well as critical courses. Complications on the intensive care units include acute respiratory distress syndrome, acute cardiac and kidney injury as well as shock. Here, we present the **first case report of a successful treatment of a COVID-19 patient presenting with ARDS plus refractory combined cardiogenic and vasoplegic shock**, which could be successfully stabilized after implantation of a percutaneous ventricular assist device (**pVAD**) plus an extracorporeal membrane oxygenation (**ECMO**). While such intense treatment **might not be feasible** in case of a health care disaster as described for the **hot spots of the COVID-19 pandemic**, it might encourage treatment of younger patients on intensive care units not overcrowded by critically ill patients.

A process for daily checks when using anaesthetic machines to ventilate the lungs of COVID-19 patients: the 'domino switch' technique.

Greig PR, Dixson T, McCorkell S.

Anaesthesia.

2020 Apr 19; PMID: 32311759

Level of Evidence: 6 - Expert opinion without evidence

Type of Article: Letter

BLUF: Dräger Primus anaesthetic machines provide an alternative for ventilators during the COVID-19 pandemic but require regular (within 72 hours) maintenance checks. The authors describe how they use a "domino" system where they exchange a used machine with a clean and freshly maintained machine. The used machine is then cleaned and checked before being used to replace other used machines that require cleaning and maintenance.

Abstract: The COVID-19 pandemic has increased demand for ventilators. Anaesthetic machines offer an alternative, but these are not designed to run continuously. Our department uses Dräger Primus anaesthetic machines which require daily checks. Dräger company representatives have indicated that checks can be deferred for up to 72 h [1], but this might increase the risk of malfunctions. Checks take several minutes, so an alternative means of ventilation is required to cover this period, necessitating two circuit disconnections per patient. Each disconnection potentially generates an infectious aerosol, and risks tracheal tube displacement and lung derecruitment, even with precautions such as tracheal tube clamping. We concluded that multiple circuit disconnections were unsatisfactory and devised a process for daily checks with a single disconnection per patient. We call this process 'domino switching'.

Radiology

Contributory Role of Positron Emission Tomography in a Left Ventricular Assist Device Recipient at the time of COVID-19 pandemic.

PMID: 32304393

Publication Date: Apr 16, 2020

Loforte A, Gliozzi G, Martin Suarez S, Pacini D. Loforte A, et al.

ASAIO Journal

Level of Evidence: 4 - Case Report

Type of Article: Research

BLUF: A case report is presented where a patient with a left ventricular assist device (LVAD) was sensitive to PET scan examination that was indicative of COVID-19 even though there were no symptoms and a negative wound site swab test. Along with PET- scans, CT-scans have also been found to be sensitive in “case[s] of clinically and laboratoristically asymptomatic or less symptomatic patients.” Thus, these methods, especially the 18F-FDG PET scan, have high diagnostic value in “detecting the localization and extension of infection to internal LVAD components” and are recommended for the LVAD recipient population “during routine ambulatory outpatients.”

Abstract:

We report on the role of fluorine 18-fluorodeoxyglucose (F-FDG) positron emission tomography (PET) scan examinations to contribute in the diagnosis of COVID-19 respiratory syndrome even in the case of asymptomatic left ventricular assist device (LVAD) recipients. Thus, warm caution and thoughtful approaches for timely detection should be taken for our delicate LVAD population especially if patients are currently living in a high density COVID-19 infected area and the potential intention for LVAD treatment is bridge to transplantation.

Review of Artificial Intelligence Techniques in Imaging Data Acquisition, Segmentation and Diagnosis for COVID-19.

Shi F, Wang J, Shi J, Wu Z, Wang Q, Tang Z, He K, Shi Y, Shen D.

IEEE Rev Biomed Eng.

2020 Apr 16; PMID: 32305937

Level of Evidence: 5 – Qualitative data

Type of Article: Literature Review

Summary: The application of artificial intelligence techniques can eliminate the need for close contact between patients and imaging technicians. The use of segmentation techniques such as U-Net can be utilized to assist radiologists in distinguishing COVID-19 from other lung pathology based on X-ray and CT images. Machine-learning can further assist radiologists by providing insight into severity assessment.

Anesthesiology

Consensus guidelines for managing the airway in patients with COVID-19.

Kearsley R

Anaesthesia

2020 Apr 20; PMID: 32311772

Level of Evidence: 5- Expert opinion

Type of Article: Letter

Summary: The author expresses concern about a new method of possibly decreasing aerosol exposure during intubation called an “**aerosol box**,” which has gained traction on social media despite **no conclusive evidence that it provides increased safety to medical personnel** and no evidence about its effects on timely intubation of a patient at risk of desaturation.

Extubation of patients with COVID-19.

D'Silva DF, McCulloch TJ, Lim JS, Smith SS, Carayannidis D

Br J Anaesth

2020 Apr 9; PMID: 32303376

Level of Evidence: 5 - Expert opinion

Type of Article: Letter

Summary Excerpt: "...A summary of our extubation guidelines for COVID-19 patients, including description of an extubation technique aimed at minimising staff exposure to SARS-CoV-2." See image below.



Fig 1. Mask-Over Tube Extubation Technique. (a) Tracheal tube positioned at one corner of the mouth with ties cut. (b) Facemask with airway filter positioned to create a seal over the face and tracheal tube. (c) The assistant withdraws the tracheal tube from under the side of the facemask using a two-handed technique to control the tracheal tube. (d) Tracheal tube has been detached and circuit has been connected to the second airway filter on the facemask.

Internal Medicine

Acute pulmonary embolism in a patient with COVID-19 pneumonia.

Cellina M, Oliva G. Cellina M, et al.

Diagn Interv Imaging.

2020 Apr 10; PMID: 32303472

Level of Evidence: 4 – Case Study

Type of Article: Case Study

Summary: An overweight 60-year-old man admitted for COVID-19 developed dyspnea and oxygen desaturation on day 3 of admission and was found to have CT findings of acute bilateral pulmonary embolism. Elevated D-dimer values are common in COVID-19 patients, even in the absence of thrombophlebitis and acute pulmonary embolism. The authors recommend chest CT angiography in patients with COVID-19 pneumonia presenting with worsening clinical respiratory symptoms.

Pulmonary embolism in patients with COVID-19: Time to change the paradigm of computed tomography.

Rotzinger DC, Beigelman-Aubry C, von Garnier C, Qanadli SD.

Thromb Res.

2020 Apr 11; PMID: 32302782

Level of Evidence: 5 - Expert opinion

Type of Article: Letter

Summarizing excerpt: “**Patients requiring hospital admission for COVID-19 pneumonia should receive prophylactic LMWH to prevent thromboembolism**, in the absence of contraindication. Furthermore, CT has quickly become a cornerstone in both the diagnostic workup and follow-up of SARS-CoV-2 infection and is usually performed without intravenous contrast agent injection. Though, patients with known COVID-19 disease may have acute pulmonary embolism. **In the case of elevated D-dimer levels on admission or sudden clinical worsening, CT pulmonary angiography should be considered since pulmonary embolism is a life-threatening but potentially treatable condition.**”

D-dimer Levels on Admission to Predict In-Hospital Mortality in Patients With Covid-19

Zhang, Litao; Yan, Xinsheng; Fan, Quingkuk; Liu, Haiyan; Liu, Xintian; Liu, Zejin; Zhang, Zhenlu
Journal of Thrombosis and Haemostasis

2020, April 19; PMID: 32306492

Level of Evidence: 3- Retrospective Cohort Study

Type of Article: Brief Report

BLUF: Researchers at Wuhan Asia General Hospital found that 12 of the 13 patients that died of COVID-19 in their study had D-dimer levels over 2.0 ug/ml on admission, making it a significant predictor of death ($P<.001$). They concluded that **elevated D-dimer levels can be a useful marker to aid in the management of patients with COVID-19.**

Abstract:

Background: The outbreak of the coronavirus disease 2019 (Covid-19) shows a global spreading trend. Early and effective predictors of clinical outcomes [are urgently] needed to improve management of Covid-19 patients.

Objective: The aim of the present study was to evaluate whether elevated D-dimer levels could predict mortality in patients with Covid-19.

Methods: Patients with laboratory confirmed Covid-19 were retrospective[ly] enrolled in Wuhan Asia General Hospital from January 12, 2020 to March 15, 2020. D-dimer levels on admission, and death events were collected to calculate the optimum cutoff using receiver operating characteristic curve. According to the cutoff, the subjects were divided into two groups. Then the in-hospital mortality between two groups were compared to assess the predictive value of D-dimer level.

Results: A total of 343 eligible patients were enrolled in the study. The optimum cutoff value of D-dimer to predict in-hospital mortality was 2.0 $\mu\text{g}/\text{ml}$ with a sensitivity of 92.3% and a specificity of 83.3%. There were 67 patients with D-dimer $\geq 2.0 \mu\text{g}/\text{ml}$, and 267 patients with D-dimer $< 2.0 \mu\text{g}/\text{ml}$ on admission. 13 deaths occurred during hospitalization. Patients with D-dimer levels $\geq 2.0 \mu\text{g}/\text{ml}$ had a higher incidence of mortality when comparing to those who with D-dimer levels $< 2.0 \mu\text{g}/\text{ml}$ (12/67 vs 1/267, $P<0.001$, HR:51.5, 95%CI:12.9-206.7).

Conclusions: D-dimer on admission greater than 2.0 $\mu\text{g}/\text{mL}$ (fourfold increase) could effectively predict in-hospital mortality in patients with Covid-19, which indicated D-dimer could be an early and helpful marker to improve management of Covid-19 patients.

ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection.

Barazzoni, Rocco; Bischoff, Stephan C; Breda, Joao; Wickramasinghe, Kremlin; Krznaric, Zeljko; Nitzan, Dorit; Pirlich, Matthias; Singer, Pierre
Clin Nutr

Pre-publication; PMID: 32305181

Level of Evidence: 5 – Expert opinion

Article Type: Letter to the Editor

Summarizing excerpt: “The European Society for Clinical Nutrition and Metabolism (ESPEN) aims at providing concise guidance for nutritional management of COVID-19 patients by proposing 10 practical recommendations.” See figure below.

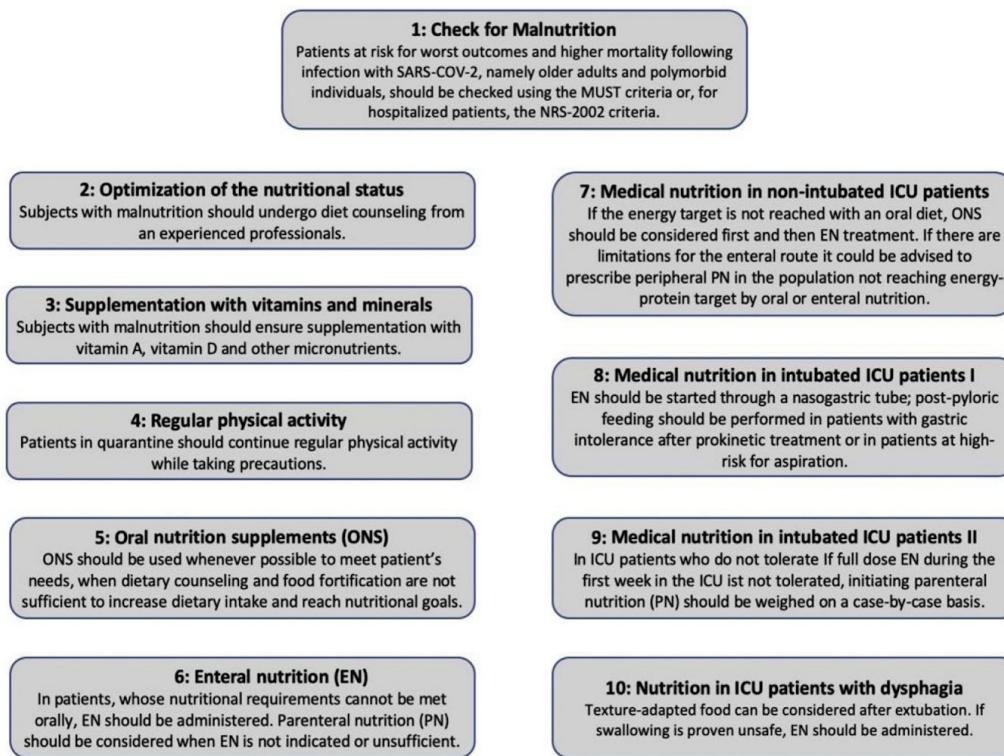


Fig. 1. Nutritional management in individuals at risk for severe COVID-19, in subjects suffering from COVID-19, and in COVID-19 ICU patients requiring ventilation. For details, see text.

Dermatology

Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients.

Marzano AV, Genovese G, Fabbrocini G, Pigatto P, Monfrecola G, Piraccini BM, Veraldi S, Rubegni P, Cusini M, Caputo V, Rongioletti F, Berti E, Calzavara-Pinton P.

Journal of the American Academy of Dermatology

2020, April 16; PMID: 32305439

Level of Evidence: 4- Case Series

Type of Article: Letter to the Editor

Summary: Eight Italian Dermatology Units collected data on 22 COVID-19 patients that developed a papulovesicular exanthem characteristic of varicella, a rare but specific finding (see figure 1). If these findings are validated in further studies, this manifestation of COVID-19 could serve as an early predictor of disease in asymptomatic patients.

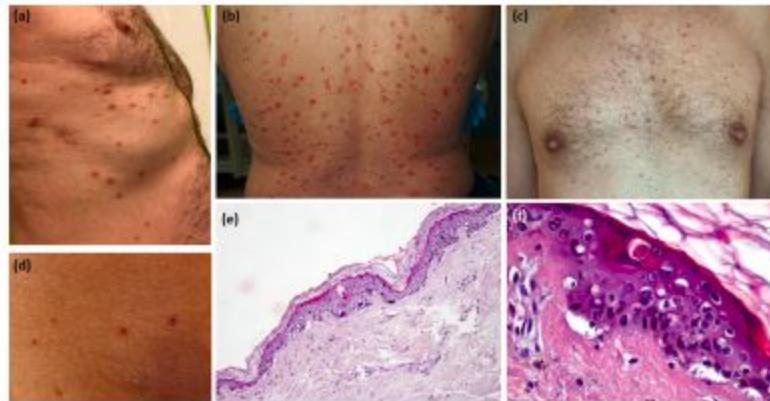


FIGURE 1. A, B, C, D. Papulovesicular exanthem on the trunk in four patients with COVID-19.

In three patients (A, B and C), predominance of papules is seen. In another patient (D) mainly presenting with vesicles, exanthem resolution with crusts is evident; E, Basket-wave hyperkeratosis, slightly atrophic epidermis, vacuolar degeneration of the basal layer with multinucleate, hyperchromatic keratinocytes and dyskeratotic cells. Note the absence of inflammatory infiltrate. Hematoxylin and eosin stain original magnification. F, Close-up with atrophic epidermis, vacuolar alteration with disorganized keratinocytes lacking orderly maturation, enlarged and multinucleate keratinocytes with dyskeratotic (apoptotic) cells. Hematoxylin and eosin stain, original magnification:

Cardiology

Considerations for Drug Interactions on QTc in Exploratory COVID-19 (Coronavirus Disease 2019) Treatment.

Roden DM, Harrington RA, Poppas A, Russo AM

Heart Rhythm

2020 Apr 14; PMID: 32302703

Level of Evidence: 5 - Expert opinion

Type of Article: Practice guideline

BLUF: Guidelines are presented to reduce the risk of arrhythmia in Covid-19 patients, given that several drugs being used to combat the virus increase the risks of arrhythmias.

Summary Excerpt: “Hydroxychloroquine and azithromycin have been touted for potential prophylaxis or treatment for COVID-19 (coronavirus disease 2019) infection. Both drugs are listed as definite causes of torsade de pointes at crediblemeds.org. ...

Mechanisms to minimize arrhythmia risk include:

- Electrocardiographic/QT interval monitoring
 - Withhold the drugs in patients with baseline QT prolongation (eg, QTc \geq 500 msec) or with known congenital long QT syndrome.
 - Monitor cardiac rhythm and QT interval; withdrawal of the drugs if QTc exceeds a preset threshold of 500 msec.
 - In patients critically ill with COVID-19 infection, frequent caregiver contact may need to be minimized, so optimal electrocardiographic interval and rhythm monitoring may not be possible.
- Correction of hypokalemia to levels of >4 mEq/L and hypomagnesemia to levels of >2 mg/dL. •Avoid other QTc prolonging agents whenever feasible.”

Management of Acute Myocardial Infarction During the COVID-19 Pandemic.

Mahmud E, Dauerman HL, Welt FG, Messenger JC, Rao SV, Grines C, Mattu A, Kirtane AJ, Jauhar R, Meraj P, Rokos IC, Rumsfeld JS, Henry TD.

Catheter Cardiovasc Interv.

2020 Apr 20; PMID: 32311816

Level of Evidence: 5 - Expert Opinion

Type of Article: Comment

BLUF: This document endorsed by The American College of Cardiology, the American College of Emergency Physicians, and the Society for Cardiovascular Angiography and Interventions suggest that primary percutaneous coronary intervention (PCI) remains the SOC for STEMI when administered quickly, in an PCI-capable hospital's dedicated cath lab, and with proper PPE.

Fibrinolysis applies only in certain circumstances or in facilities that do not have PCI capabilities.

Abstract: The worldwide pandemic caused by the novel acute respiratory syndrome coronavirus 2 (SARS-CoV2) has resulted in a new and lethal disease termed coronavirus disease 2019 (COVID-19). Although there is an association between cardiovascular disease and COVID-19, the majority of patients who need cardiovascular care for the management of ischemic heart disease may not be infected with COVID-19. The objective of this document is to provide recommendations for a systematic approach for the care of patients with an acute myocardial infarction (AMI) during the COVID-19 pandemic. There is a recognition of two major challenges in providing recommendations for AMI care in the COVID-19 era. Cardiovascular manifestations of COVID-19 are complex with patients presenting with AMI, myocarditis simulating a ST-elevation MI presentation, stress cardiomyopathy, non-ischemic cardiomyopathy, coronary spasm, or nonspecific myocardial injury and the prevalence of COVID-19 disease in the US population remains unknown with risk of asymptomatic spread. **This document addresses the care of these patients focusing on 1) the varied clinical presentations; 2) appropriate personal protection equipment (PPE) for health care workers; 3) role of the Emergency Department, Emergency Medical System and the Cardiac Catheterization Laboratory; and 4) Regional STEMI systems of care.** During the COVID-19 pandemic, **primary PCI remains the standard of care for STEMI patients at PCI capable hospitals when it can be provided in a timely fashion, with an expert team outfitted with PPE in a dedicated CCL room. A fibrinolysis-based strategy may be entertained at non-PCI capable referral hospitals or in specific situations where primary PCI cannot be executed or is not deemed the best option.**

Neurology

Meningoencephalitis without Respiratory Failure in a Young Female Patient with COVID-19 Infection in Downtown Los Angeles, Early April 2020.

Duong L, Xu P, Liu A.

Brain Behav Immun.

2020 Apr 16; PMID: 32305574

Level of Evidence: 4 - Case report

Type of Article: Research

Summary: The authors report a case of Covid-19 presenting as isolated meningoencephalitis in a 41-year old female without respiratory involvement.

Letter: COVID-19 Infection Affects Surgical Outcome of Chronic Subdural Hematoma.

Panciani PP, Saraceno G, Zanin L, Renisi G, Signorini L, Fontanella MM. Panciani PP, et al. Neurosurgery.

2020, Apr 18; PMID: 32304213

Level of Evidence: 4 - Case Series

Article Type: Letter to Editor

BLUF: 5 patients with COVID-19 and chronic subdural hematomas were studied. 4 patients developed interstitial pneumonia after undergoing surgical or endovascular interventions, 1 patient survived with conservative management only.

his case series of 5 COVID-19 positive patients with chronic subdural hematomas observed severe interstitial pneumonia in patients who received endovascular or surgical treatment. Only one patient who received conservative treatment survived without observed respiratory failure post-surgery.

Summary: The authors relate their surgical experience of chronic subdural hematomas (CSDH) in 5 COVID-19 positive patients (Table, February 21, 2020 to March 23, 2020) at the Neurosurgical Department of Brescia University Hospital. Surgery or endovascular treatment was performed in 4 COVID-19 patients once the CSDH was symptomatic and the maximum thickness was greater than 1 cm (Figures 1-4). One patient did not present severe neurological impairment and was treated conservatively (Figure 5). Post-procedure complications and findings include mild thrombocytopenia with rebleeding in 2 patients, dyspnoea and fatigue in all patients, and severe interstitial pneumonia (IP) in four cases (Figure 1-4). Th conservative-treated patient did not have respiratory failure, observed a normal chest x-ray (Figure 5), and was the only patient to survive. The authors compare this case series' mortality rate of 80% to their previous 3.7% mortality rate in their prior case series of 142 pre-COVID-19 CSDH (May 2018 and September 2019). Since overloaded intensive care units in Lombardy have influenced resuscitation possibilities of elderly patients, the authors cannot exclude that these results could be affected by the health emergency status. The authors propose that conservative treatment should be performed whenever surgery can be postponed.

TABLE. Clinical Features of our Cohort

Sex	Age	CIRS	AT	Side	COVID-19	IP	TP*	Surgery	Time to death(d)
M	82	13	Yes	Left	+	+	No	Burr-hole	14
M	86	18	No	Bilateral	+	+	No	MMA embolization	10
M	77	20	No	Right	+	+	Yes	Craniotomy	5
M	85	22	Yes	Left	+	+	Yes	Burr-hole	5
M	78	19	Yes	Left	+	-	No	NO	Alive

*TP (Thrombocytopenia): $100.000 < \text{PLTs} < 150.000$

All patients developed IP after surgery. Thrombocytopenia was observed in 2 cases (40%). The patients suffered rebleeding and showed a shorter time to death. CIRS (Cumulative Illness Rating Scale), AT (antithrombotic drugs), IP (Interstitial Pneumonia), COVID-19 (Coronavirus Disease 2019).

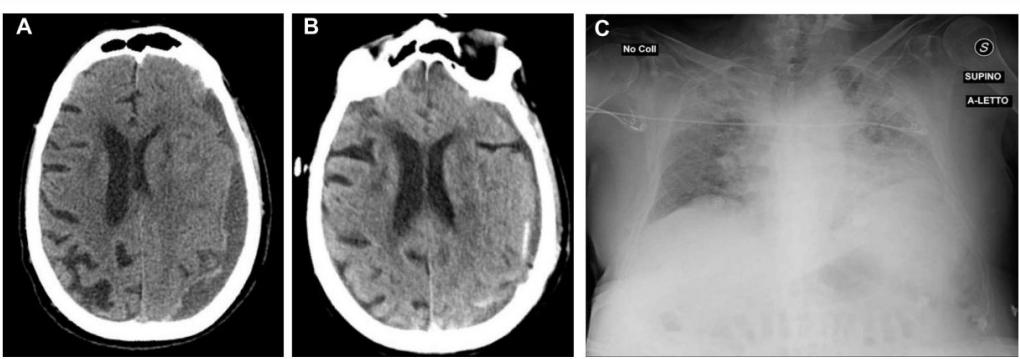


FIGURE 1. A and B, Head CT scan, axial view: pre- and postoperative CDSH. C, CXR showing bilateral and diffuse IP.

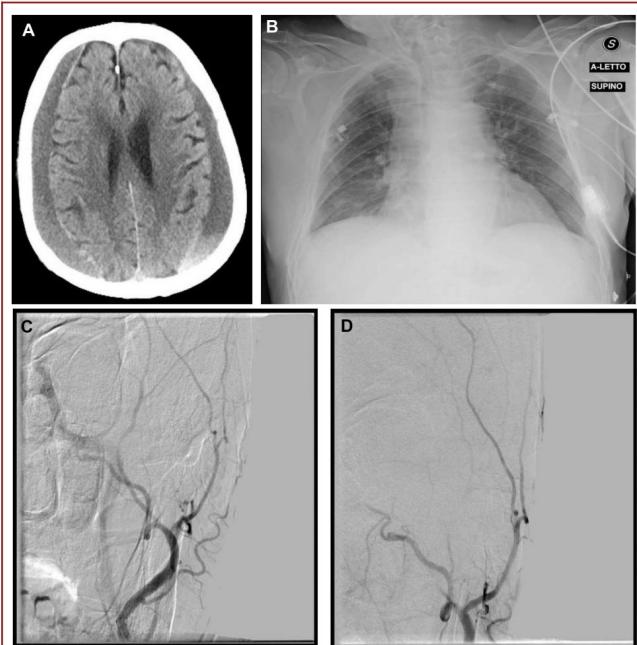


FIGURE 2. **A.** Head CT scan, axial view: bilateral CSDH. **B.** CXR showing bilateral and diffuse IP. **C** and **D**, MMA embolization procedure.

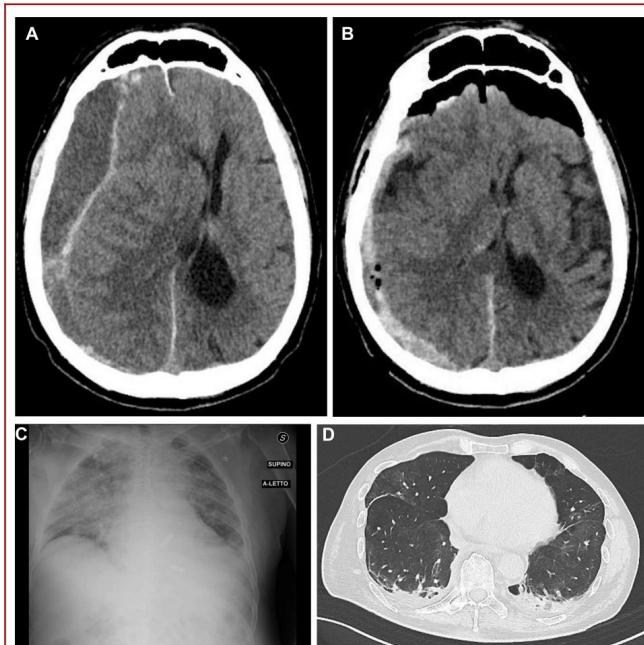


FIGURE 3. **A.** Head CT scan, axial view: preoperative CSDH. **B.** Head CT scan, axial view: postoperative CSDH with signs of recent rebleeding. **C.** CXR showing bilateral IP. **D.** Chest CT scan, axial view, showing ground glass opacity.

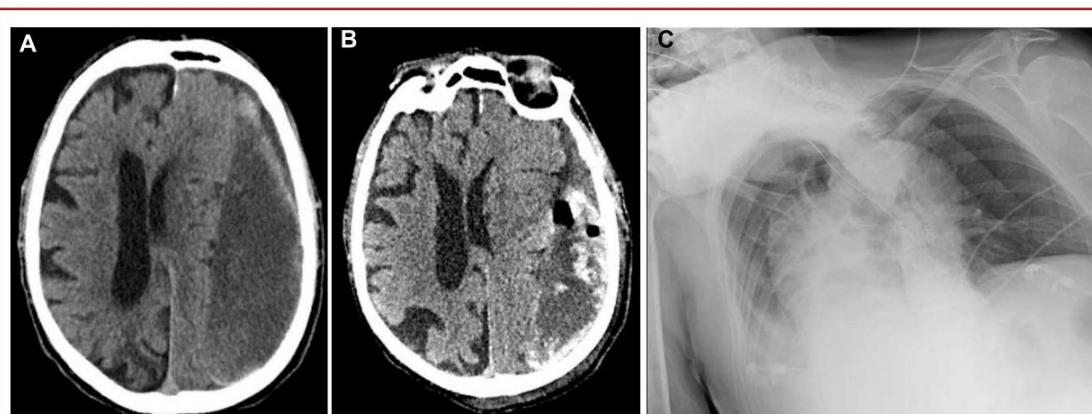


FIGURE 4. **A.** Head CT scan, axial view: preoperative left CSDH. **B.** Head CT scan, axial view: postoperative CSDH with signs of recent rebleeding. **C.** CXR showing bilateral IP.

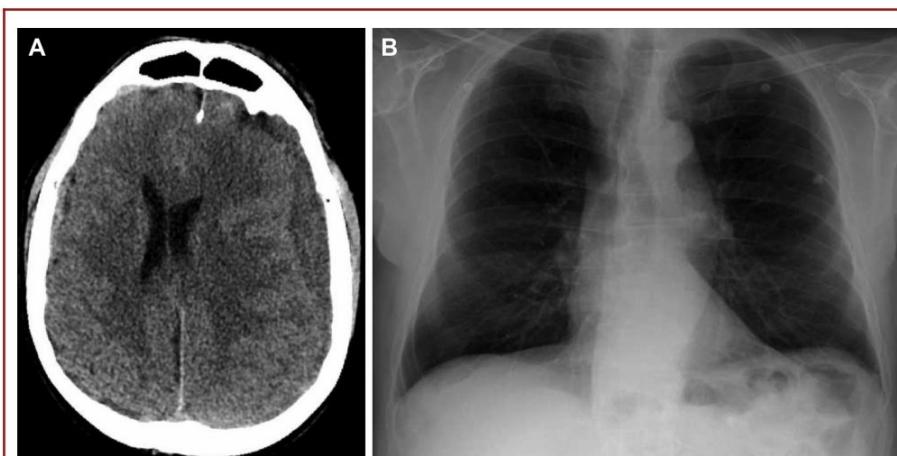


FIGURE 5. **A.** Head CT scan, axial view: left CSDH. **B.** normal CXR.

Immunology

COVID-19 in patients with HIV: clinical case series.

Blanco JL, Ambrosioni J, Garcia F, Martínez E, Soriano A, Mallolas J, Miro JM; COVID-19 in HIV Investigators.

Lancet HIV

2020 Apr 15; PMID: 32304642

Level of Evidence: 4 - Case Series

Type of Article: Research

Summary: 5 patients from the Hospital Clinic in Barcelona who were SARS-CoV-2 and HIV-positive (4 of whom were on ART) were started on a coronavirus regimen that included various combinations of coronavirus-boosted-protease inhibitors (lopinavir-boosted-ritonavir and dopenavir-boosted-cobicistat), azithromycin, IFN beta 1-b, and hydroxychloroquine. Preliminary results highlight the efficacy of boosted protease inhibitor treatment, but require further trials to confirm.

Thromboinflammation and the hypercoagulability of COVID-19.

Connors, Jean M; Levy, Jerrold H

J Thromb Haemost

2020 Apr 17; PMID: 32302453

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Comment

BLUF: Through analysis of previous research into hypercoagulability and the cytokine storm that can be associated with COVID-19, the authors suggest a **risk adapted approach to anticoagulation** in COVID-19 patients as well as monitoring fibrinogen, PT, PTT, and renal function when considering severe COVID and acute lung injury. **There does not seem to be a benefit in increasing anticoagulant dosing but authors admit more research is needed to be certain.**

Abstract:

The pathogenic coronavirus has been wreaking havoc worldwide since January. Infection with SARS-CoV-2 is problematic as no one has prior immunity, and no specific antiviral treatments are available. While many people with COVID-19 develop mild to moderate symptoms, some develop profound seemingly unchecked inflammatory responses leading to acute lung injury and hypoxic respiratory failure, the most common cause for death.

Oncology

Rapid Detection of Asymptomatic COVID-19 by CT Image-Guidance for Stereotactic Ablative Radiotherapy.

McGinnis GJ, Ning MS, Nitsch PL, O'Reilly M, McAleer MF, Koong AC, Chang JY. et al.

J Thorac Oncol.

2020 Apr 17; PMID: 32311499

Level of Evidence: 4 - Case Report

Type of Article: Comment

Summary: The authors at MD Anderson Cancer Center in Houston, Texas share a patient with recurrent nonsquamous cell lung cancer who was detected to have COVID-19 incidentally part of routine set-up for stereotactic ablative radiotherapy. The patient's CT compared to initial records revealed development of new multifocal ground glass opacities of the lung. The patient was screened

per COVID-19 pandemic policies and found to be positive. She was subsequently quarantined and her treatment was withheld until she was tested negative per department policy. This case report highlights the importance of early recognition in asymptomatic communities via streamlined COVID19 protocols, particularly among the vulnerable oncological population.

Surgery

Vascular

[Venous thrombosis and arteriosclerosis obliterans of lower extremities in a very severe patient with 2019 novel coronavirus disease: a case report.](#)

Zhou B, She J, Wang Y, Ma X, Zhou B, et al.

J Thromb Thrombolysis

2020 Apr 18; PMID: 32306290

Level of Evidence: 4 - Case series

Type of Article: Research

BLUF: Case report of a 69 year old man hospitalized with COVID-19 and found to have bilateral venous thrombosis and arteriosclerosis obliterans. The authors posit a connection between this case, the development of thromboses, and the systemic inflammation caused by COVID-19.

Abstract:

The outbreak of 2019 novel coronavirus disease (COVID-19) began since early December 2019, and has been declared as a public health emergency by the World Health Organization. Due to the hypercoagulable state, blood stasis and endothelial injury, severe patients with COVID-19 are at high risk for thrombosis. We report a case of very severe COVID-19 complicated with venous thrombosis and arteriosclerosis obliterans of lower extremities. Risk stratification for deep vein thrombosis and peripheral arterial disease are of vital importance for the prognosis of COVID-19.

Neurosurgery

[A COVID-19 Patient Who Underwent Endonasal Endoscopic Pituitary Adenoma Resection: A Case Report.](#)

Zhu, Wende; Huang, Xing; Zhao, Hongyang; Jiang, Xiaobing

Neurosurgery

2020 Apr 18; PMID: 32302399

Level of Evidence: 5 - Case Study

Type of Article: Research

BLUF: A 70-year-old man underwent endonasal endoscopic pituitary adenoma resection was confirmed positive for COVID-19 via nasal swab 12 days later and died of respiratory failure 4 weeks after surgery. 14 medical staff members were diagnosed with COVID-19, not including any of the operating staff, and the epidemic was limited by patient quarantine, proper PPE, and social distancing.

ABSTRACT:

Background and importance: A pituitary adenoma patient who underwent surgery in our department was diagnosed with COVID-19 and 14 medical staff were confirmed infected later. This case has been cited several times but without accuracy or entirety, we feel obligated to report it and share our thoughts on the epidemic among medical staff and performing endonasal endoscopic surgery during COVID-19 pandemic.

Clinical presentation: The patient developed a fever 3 d post endonasal endoscopic surgery during which cerebrospinal leak occurred, and was confirmed with SARS-CoV-2 infection later. Several **medical staff outside the operating room were diagnosed with COVID-19**, while the **ones who participated in the surgery were not**.

Conclusion: The deceptive nature of COVID-19 results from its most frequent onset symptom, fever, a cliché in neurosurgery, which makes it hard for surgeons to differentiate. The COVID-19 epidemic among medical staff in our department was deemed as postoperative rather than intraoperative transmission, and **attributed to not applying sufficient personal airway protection**. Proper personal protective equipment and social distancing between medical staff contributed to limiting epidemic since the initial outbreak. **Emergency endonasal endoscopic surgeries are feasible** since COVID-19 is still supposed to be containable when the surgeries are performed in negative pressure operating rooms with personal protective equipment and the patients are kept under quarantine postoperatively. However, **we do not encourage elective surgeries** during this pandemic, which might put patients in conditions vulnerable to COVID-19.

Pediatric surgery

[**Pediatric Endoscopy in the Era of Coronavirus Disease 2019: A North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Position Paper.**](#)

Walsh CM, Fishman DS, Lerner DG; NASPGHAN Endoscopy and Procedures Committee
J Pediatr Gastroenterol Nutr.

2020 Apr 14; PMID: 32304561

Level of Evidence: 5 - Expert Opinion

Article Type: Commentary

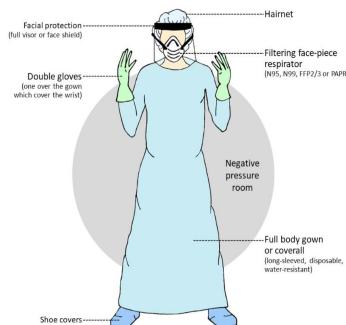
BLUF: NASPGHAN Endoscopy and Procedures Committee offers guidelines, specifically PPE recommendations, risk stratification to procedures, and practical considerations for pre-, intra-, and post-procedures, in order to minimize COVID-19 transmission.

Abstract: The delivery of endoscopic care is changing rapidly in the era of Coronavirus Disease 2019 (COVID-19). The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) Endoscopy and Procedures Committee has formulated this statement to offer practical guidance to help standardize endoscopy services for pediatric patients with the aim of minimizing COVID-19 transmission to staff, patients, and caregivers and to conserve personal protective equipment (PPE) during this critical time. Appropriate use of PPE is essential to minimize transmission and preserve supply. Pediatric endoscopic procedures are considered at high risk for COVID-19 transmission. We recommend that all pediatric endoscopic procedures are done in a negative pressure room with all staff using proper airborne, contact, and droplet precautions regardless of patient risk stratification. This includes appropriate use of a filtering face-piece respirator (N95, N99, FFP2/3, or PAPR), double gloves, facial protection (full visor and/or face shield), full body water-resistant disposable gown, shoe covers and a hairnet. In deciding which endoscopic procedures should proceed, it is important to weigh the risks and benefits to optimize healthcare delivery and minimize risk. To inform these decisions, we propose a framework for stratifying procedures as emergent (procedures that need to PROCEED), urgent (PAUSE, weigh the benefits and risks in deciding whether to proceed) and elective (POSTPONE procedures). This statement was based on emerging evidence and is meant as a guide. It is important that all endoscopy facilities where pediatric procedures are performed follow current recommendations from public health agencies within their jurisdiction regarding infection prevention and control of COVID-19.

Table 2: Risk stratification of pediatric endoscopic procedures. Voted on by 31 members of the NASPGHAN Endoscopy and Procedures Committee

Emergent → Proceed <ul style="list-style-type: none"> ➤ Endoscopic procedure for intervention and/or diagnosis of potentially life-threatening conditions and/or for conditions where if left untreated has significant morbidity/mortality. ➤ <i>Need to continue.</i> <ul style="list-style-type: none"> • Potentially life-threatening gastrointestinal bleeding • Small bowel endoscopy for ongoing transfusion dependent bleeding • Foreign bodies classified by NASPGHAN clinical report as emergent (e.g., esophageal button battery, multiple magnet ingestions)³⁹ • Bowel obstruction amenable to endoscopic therapy • Evaluation of caustic injury, if unable to tolerate oral intake and/or placement of NG required under direct visualization • Tissue sampling required to diagnose a life-threatening disease, including graft-versus-host disease, post-transplant lymphoproliferative disorders and suspected intestinal graft rejection • Volvulus decompression • Endoscopic vacuum therapy for perforations/leaks • Acute biliary obstruction/decompression secondary to stone, lesion or cholangitis • Endoscopic ultrasound for infected pancreatic necrosis or walled off necrosis • Liver biopsy ± PTC for neonatal cholestasis, suspicious for biliary atresia • Liver biopsy ± PTC for acute liver failure, or impending acute liver failure (e.g., hepatitis with rising INR) 	<ul style="list-style-type: none"> • Removal or exchange of temporary stent • EUS for symptomatic pancreatic fluid collection • Urgent initial nutrition support (e.g., PEG/NJ) • Urgent replacement PEG/NJ • Suspected gastrointestinal malignancy • Planned polypectomy, EMR/ESD for complex/high-risk lesions • Inflammatory bowel disease (IBD): (a) high suspicion of new IBD diagnosis; (b) guide treatment decisions (including flare) in patient with moderate to severe activity; (c) guide treatment decisions for complications of established/new diagnosis IBD (e.g., partial bowel obstruction) • Severe and progressive failure to thrive, unresponsive to medical management • Severe chronic diarrhea, unresponsive to medical management • Severe <i>Clostridioides difficile</i> colitis refractory to medical therapy for fecal transplant* • Anorectal manometry or suction rectal biopsy for suspected Hirschsprung's disease • Liver biopsy for hepatitis of uncertain cause with one of elevated aminotransferases (persisting or rising), jaundice, rising INR, and/or serological evidence for autoimmune hepatitis; liver transplant rejection; or suspected malignant tumor
Elective → Postpone <ul style="list-style-type: none"> ➤ Endoscopic procedure that can be postponed and/or managed alternatively; encompasses conditions not considered emergent or urgent. ➤ <i>Postpone.</i> <ul style="list-style-type: none"> • Staged ligation of esophageal varices • Foreign bodies classified by NASPGHAN clinical report as elective³⁹ • Mild dysphagia • Upper GI endoscopy for eosinophilic esophagitis diagnosis or re-evaluation • Staged dilation of gastointestinal stricture • Staged ERCP with stent exchange (e.g., q3mo planned exchange) • ERCP cases - stones where there has been no recent cholangitis and a stent is in place; therapy for chronic pancreatitis; ampullectomy follow up • EUS for suspected autoimmune pancreatitis or EUS for 'benign' indications - biliary dilatation, possible stones, submucosal lesions, pancreatic cysts without high-risk features • Non-urgent initial nutritional support or replacement (e.g., PEG, NJ) • Polyposis surveillance • Polypectomy; considered to be at low risk for malignancy • Inflammatory bowel disease; to guide therapy in patients with mild disease activity • Endoscopy and/or biopsy for clinical trials or other research diseases • Upper GI endoscopy to diagnose suspected celiac disease or to re-stage • Upper GI endoscopy for <i>Helicobacter pylori</i> culture/sensitivity (non-bleeding) • Upper GI endoscopy for abdominal pain with reasonable medical alternatives available and/or low suspicion of organic disease, routine symptomatic referrals; low risk follow-up and repeat endoscopy (e.g., re-assessment of eosinophilic esophagitis) • Esophageal manometry with concern for primary motility disorder (e.g., achalasia), or prior to fundoplication • Anorectal manometry for patients with fecal incontinence • Colonic manometry • POEM • Bariatric endoscopy 	

Figure 1: Enhanced personal protective equipment (PPE) recommended for pediatric endoscopic procedures to ensure airborne, contact and droplet precautions



- pH impedance, breath tests
- Liver biopsy for NAFLD/ NASH or to assess histologic remission in AIH

*donor stool should be tested

EMR: endoscopic mucosal resection; ERCP: endoscopic retrograde cholangiopancreatography; ESD: endoscopic surgical dissection; EUS: Endoscopic ultrasound; IBD: Inflammatory bowel disease; INR: International normalized ratio; NAFLD: non-alcoholic fatty liver disease; NASH: non-alcoholic steatohepatitis; NASPGHAN: North American Society of Pediatric Gastroenterology, Hepatology and Nutrition; NJ: nasojejunal; PEG: Percutaneous endoscopic gastrostomy; POEM: per-oral endoscopic myotomy; PTC: percutaneous transhepatic cholangiography.

Pediatrics

Neonatal COVID-19: Little Evidence and the Need for More Information

Prochanoy, Renato S; Silveira, Rita C; Manzoni, Paolo; Sant'Anna, Guilherme J Pediatr (Rio J)

2020 Apr 11; PMID: 32298645

Level of Evidence: 5 - Mechanism-based Reasoning

Type of Article: Editorial

Summary: In this article regarding neonatal care and COVID-19, authors point out that knowledge on neonatal health in this pandemic is limited due to the number of case reports but at this point neonates do not seem to be severely impacted by this pandemic.

They recommend:

1. not intubating neonatal patients solely based on COVID-19 positive labs

2. to follow practice recommendations for suspected or positive COVID-19 patients during delivery and care with PPE use
3. as well as careful monitoring and isolation of suspected COVID-19 infected neonates. In addition, they do recommend careful use of viral filters and bubble CPAP due to the potential harm with prolonged use.

Managing COVID-19-Positive Maternal-Infant Dyads: An Italian Experience.

Salvatori G, De Rose DU, Concato C, Alario D, Olivini N, Dotta A, Campana A.

Breastfeed Med

2020 Apr 20, PMID: 32311273

Level of Evidence: 4 - Case series

Article Type: Research

Summarizing Excerpt: "We confirm that SARS-CoV-2 seems to spare breast milk and horizontal transmission from mother to neonate could occur through respiratory droplets rather than through milk. Therefore, when SARS-CoV-2 is identified both in the mother and in the child, there is no reason to stop breastfeeding and separate them. Whenever direct breastfeeding is not possible, the use of expressed mother's milk should be considered and promoted to take advantage of its unquestionable benefits."

Adjusting Practice during COVID-19

Acute care

Emergency Medicine

Practical diagnosis and treatment of suspected venous thromboembolism during COVID-19 Pandemic.

Obi, Andrea T; Barnes, Geoff D; Wakefield, Thomas W; Brown Rvt, Sandra; Eliason, Jonathon L; Arndt, Erika; Henke, Peter K

J Vasc Surg Venous

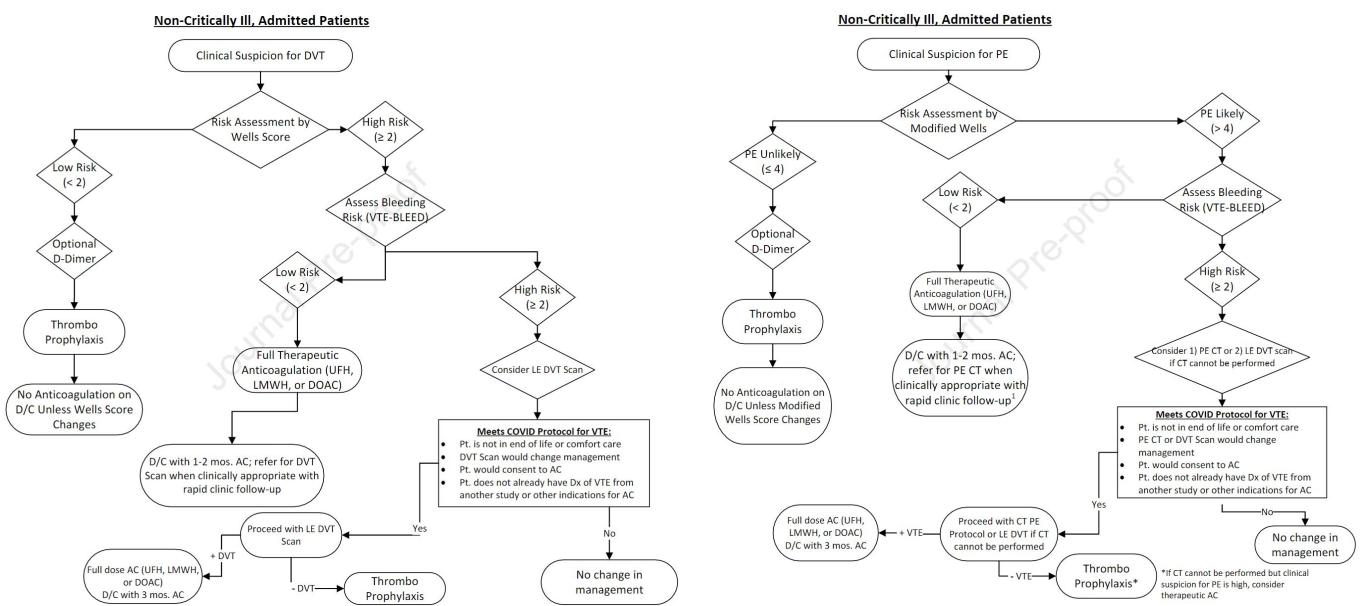
2020 Apr 20; PMID: 32305585

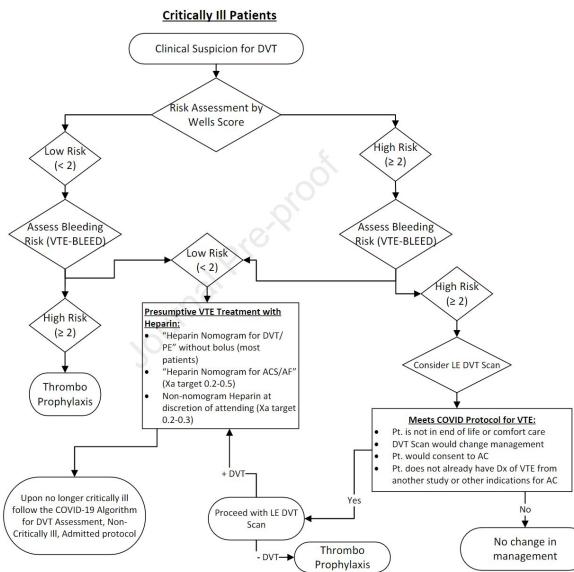
Level of Evidence: 5 - Expert Opinion

Type of Article: Research

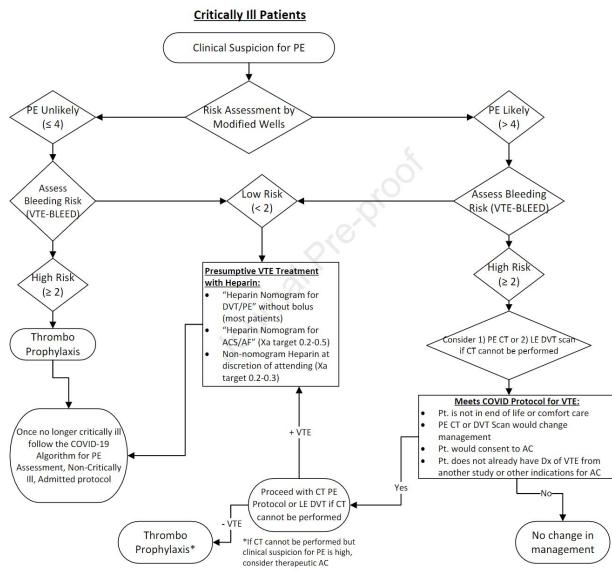
BLUF: This article provides expert-evaluated and evidence-based algorithms for the evaluation and recommended therapies of VTE events in the context of COVID-19 positive patients (figures below).

Abstract: A markedly increased demand for vascular ultrasound laboratory and other imaging studies in COVID-19 positive patients has occurred, due to most with markedly elevated D-dimer, and a presumed prothrombotic state in many of the very ill patients. This article **summarizes a broad institutional consensus focusing on evaluation and recommended empirical therapy for COVID-19 positive patients.** We recommend following the algorithms with the idea that as more data becomes available that this may well change.





Figures 1-2: Algorithms for patients with clinical suspicion for DVT.



Figures 3-4: Algorithms for patients with clinical suspicion for PE.

Internal Medicine

Dermatology

Overzealous hand hygiene during COVID 19 pandemic causing increased incidence of hand eczema among general population

Singh, Mehak; Pawar, Manoj; Bothra, Atul; Choudhary, Nishant

J Am Acad Dermatol

2020 Apr 16; PMID: 32305441

Level of Evidence: 5 - Expert opinion

Type of Article: Letter

Summary:

In the fight against COVID-19, handwashing and the overuse of hand sanitizers may lead to hand eczema. Through telemedicine consultations of patients in India and a recent study of health care workers in China, it was found that **frequent hand washing leads to depletion of protective surface lipids in the skin which not only leads to dermatitis but could also create a route of entry for SARS-CoV-2**. Education on proper techniques in handwashing is essential to prevent this.

Recommendations for Treatment of Cutaneous Lymphomas During the COVID-19 Pandemic.

Zic JA, Ai W, Akilov OE, Carter JB, Duvic M, Foss F, Girardi M, Gru AA, Kim E, Musiek A, Olsen EA, Schieke SM, Shinohara M, Zain JM, Geskin LJ

J Am Acad Dermatol.

2020 Apr 16; PMID: 32305443

Level of Evidence: 5 - Expert Opinion

Type of Article: Editorial

Summary: The following editorial by the United States Cutaneous Lymphoma Consortium is a set of recommended strategies for treating primary cutaneous lymphomas in low, intermediate, and high-risk patient categories. Generally speaking, **low-risk patient regimens consist of topical retinoids and creams, intermediate-risk consist of oral retinoids, and high-risk consist**

of immunotherapy, chemotherapy, and radiotherapy. The images depicted below are the specific categories and treatments.

Cutaneous Lymphomas:

- A. Low risk: pagetoid reticulosis, acral CD8(+) T-cell lymphoma (TCL), CD4(+) pleomorphic small/medium T-cell lymphoproliferative disorder, lymphomatoid papulosis, and mycosis fungoïdes (MF) stage IA, MF stage IB (patch only or limited body surface area), primary cutaneous (PC) marginal zone or PC follicle center B-cell lymphoma
- B. Intermediate-low risk: primary cutaneous anaplastic large cell lymphoma, folliculotropic MF, granulomatous MF, granulomatous slack skin, MF stage IB (extensive patches/plaques) and IIA (reactive lymphadenopathy), subcutaneous panniculitis-like TCL.
- C. Intermediate-high risk: MF stage IIB (tumors) and III (erythrodermic), PC diffuse large B-cell lymphoma (DLBCL) (not leg type).
- D. High risk: Sézary syndrome, MF Stage IV or transformed, primary cutaneous gamma-delta T-cell lymphoma, CD8(+) aggressive epidermotropic cytotoxic T-cell lymphoma, extranodal NK/T-cell lymphoma, PC-DLBCL, leg-type.

Therapies:

- A. Low risk: topical retinoids, mechlorethamine gel or ointment, topical steroids with or without occlusion, imiquimod, home narrowband UVB phototherapy (NBUVB), heliotherapy, oral antibiotics, oral antipruritics, dilute vinegar or bleach soaks/baths, and aggressive moisturization.
- B. Intermediate risk: oral retinoids (bexarotene, acitretin, isotretinoin), methotrexate, oral steroids, vorinostat, and interferons (alpha or gamma).
- C. High risk: pralatrexate, romidepsin, mogamulizumab, brentuximab, gemcitabine and other chemotherapies. Skin radiotherapy, photopheresis and office-based UV therapy are high risk due to travel.

Phototherapeutic approach to dermatological patients during the 2019 Coronavirus pandemic: Real-life Data from the Italian Red Zone.

Pacifico A, Ardigò M, Frascione P, Damiani G, Morrone A. Pacifico A, et al.

Br J Dermatol

2020 Apr 17; PMID: 32302419

Level of Evidence: 6 - No Data Cited

Type of Article: Research Letter

Summary: A hospital in Italy, during the red-zone declaration, implemented a new internal protocol for approaching immunosuppressed at-risk dermatological patients. The protocol involved using telemedicine to pre-triage for COVID-19, then triage cleared patients in-person at the hospital, and finally treat patients with phototherapy using sanitary methods to minimize COVID-19 exposure. Providers assigned phototherapy treatment priority based on disease morbidity, severity, and risk of erythroderma.

Cardiology

'COVID-19 Pandemic' Anxiety induced Tako-tsubo Cardiomyopathy.

Chadha S.

QJM

2020 Apr 20; PMID: 32311043

Level of Evidence: 5 - Case report

Type of Article: Letter

Summary: Case report of an 85-year old female with no past medical history or cardiac risk factors who was diagnosed with Takotsubo Cardiomyopathy as a result of stress related to the COVID-19 pandemic. Physicians should keep Takotsubo Cardiomyopathy in mind as a potential cause of sudden onset chest pain, especially for patients experiencing stress or anxiety.

Adapting to a Novel Disruptive Threat: Nuclear Cardiology Service in the Time of the Coronavirus (COVID-19) Outbreak 2020 (SARS REBOOT).

Loke KSH, Tham WY, Bharadwaj P, Keng FYJ, Huang Z, Idu MB, Wong YM, Tan PKS, Zaheer S, Khor YM, Ng DCE, Wong WY, Tong AK.

Nucl Cardiol

2020 Apr 19; PMID: 32306210

Level of Evidence: 5 – Expert Opinion

Type of Article: Comment

BLUF: The authors present measures that a nuclear cardiology service in a Singaporean hospital group used to minimize COVID-19 transmission.

Summary: This article reviews the multipronged COVID-19 response employed by the nuclear cardiology service of a hospital group in Singapore. Experience with the 2003 SARS epidemic informed their response.

Measures included:

1. Use of appropriate PPE and hand hygiene by medical staff
2. Screening patients upon arrival for sick contacts, recent travel, fever, and flu-like symptoms
3. Application of social distancing policies in waiting rooms,
4. Use of isolation rooms for patients with suspected COVID-19
5. Separating waiting room areas or appointment times for high risk and low risk patients
6. Using pharmacological cardiac stress testing over treadmill exercise stress testing to minimize risk of droplet transmission
7. Minimizing time patients spent in the department
8. Requiring review of CT scans to identify findings suspicious for COVID-19 before allowing patients to leave the department
9. Dividing the healthcare staff into two teams to work alternate shifts so that a team exposed to an unexpected COVID-19 case can stand down while the other team takes over.

Neurology

Cerebrovascular disease is associated with an increased disease severity in patients with Coronavirus Disease 2019 (COVID-19): A pooled analysis of published literature.

Aggarwal G, Lippi G, Michael Henry B

Int J Stroke.

2020 Apr 20; PMID: 32310015

Level of Evidence: 1 - Pooled Analysis

Type of Article: Research

BLUF: In a pooled analysis of six studies, cerebrovascular disease was associated with a statistically significant 2.5 fold increased risk of a severe form of COVID-19, and there was a non-significant trend when evaluating cerebrovascular disease and enhanced risk of mortality. Age may have been a confounding variable.

ABSTRACT:

Introduction: There is an urgent need to identify patients at high risk during the ongoing coronavirus disease (COVID-19) pandemic. Whether a history of stroke is associated with increased severity of disease or mortality is unknown.

Method: We pooled studies from published literature to assess the association of a history of stroke with outcomes in patients with COVID-19.

Results: A **pooled analysis** of 4 studies showed a **~2.5-fold increase in odds of severe COVID-19**. While a trend was observed, there was **no statistically significant association of stroke with mortality** in patients with COVID-19 infection.

Discussion: Our findings are limited by a small number of studies and sample size.

Conclusion: There is a ~2.5-fold increase in odds of severe COVID-19 illness with a history of cerebrovascular disease.

EXPRESS: COVID-19 and Stroke - A Global World Stroke Organization perspective.

Markus HS

Int J Stroke.

2020 Apr 20; PMID: 32310017

Level of Evidence: 5 - Expert Opinion

Type of Article: Editorial

BLUF: Stroke patients may be at higher risks of complications and death from COVID-19 infection, but reorganization of healthcare systems and reallocation of personnel and supplies could have negative impacts on stroke treatment and follow-up care.

SUMMARY: “The COVID-19 pandemic affecting all parts of the world is having major implications for stroke care, both direct and indirect. **Stroke patients themselves appear particularly susceptible to developing complications and death when suffering COVID-19 infection**, as highlighted in a pooled analysis of the available data published by Aggarwal et al in International Journal of Stroke.(1) They therefore need to be protected from contact with infected individuals. However the pandemic is having a much wider impact on stroke care, with **significant pressures on delivery of stroke services**, meaning the [sic] the outcome of patients presenting with stroke but without COVID-19 may be worse than at normal times.”

Multiple sclerosis and the risk of infection: considerations in the threat of the novel coronavirus, COVID-19/SARS-CoV-2.

Willis MD, Robertson NP. Willis MD, et al.

J Neurol.

2020 Apr 17; PMID: 32303837

Level of Evidence: 4 - Case-control or historically controlled studies

Type of Article: Review

BLUF: Three case-control studies reviewed by the authors found higher rates of infections (data collected prior to COVID-19) among individuals with MS, and some evidence of increased risk of infection among those treated with second generation disease modifying therapies. The authors advocate consideration of risks and benefits in treatment approach during current pandemic.

Summary:

The article reviews three observational studies that examine the relationship between individuals with multiple sclerosis (MS), disease-modifying therapies (DMTs), and risk of infection.

1. The first study found that “[t]he incidence of infection was higher in MS patients compared with non-MS patients: [United States Dept. of Defense database) (IRR 1.76; 95% CI 1.72–1.80) and [United Kingdom Clinical Practice Research database] (IRR 1.25; 95% CI 1.21–1.29). Compared to patients without MS, the rate of infections causing hospitalisation in MS patients was higher in both databases (US-DOD IRR 2.43; 95% CI 2.23–2.63 and UK-CPRD IRR 2.00; 95% CI 1.84–2.17).”
2. The study examined the risk of serious infection requiring hospitalization associated with use of several commonly used MS DMTs. “In the most adjusted model taking into account potential confounders and when comparing against [interferon beta] and [glatiramer], only rituximab had a statistically significant increased risk (HR, 1.70 [95% CI 1.11–2.61]) although point estimates for fingolimod and natalizumab were still greater than 1.00 (HRs, 1.30 [95% CI 0.84–2.03] and 1.12 [95% CI 0.71–1.77], respectively).”
3. The third case “investigated the association between MS DMTs [(either first generation interferon beta or glatiramer or second generation natalizumab, fingolimod, or dimethyl fumarate)] and risk of infections in a population-based retrospective cohort study...In comparison to first generation DMTs, the second generation drugs showed a 53% greater hazard for infection (aHR 1.53; CI 1.21–1.95).”

Parkinson's disease and COVID-19: Perceptions and implications in patients and caregivers.

Prasad S, Holla VV, Neeraja K, Surisetti BK, Kamble N, Yadav R, Pal PK. Prasad S, et al. Mov Disord.

2020 Apr 17; PMID: 32304118

Level of Evidence: 3 - Local non-random sample

Type of Article: Letter

Summary: Though there is no evidence that patients with Parkinson's disease have a higher risk of contracting COVID-19 or have worse outcomes, a survey in India found that a small percentage of patients (8%) and caregivers (4%) perceived Parkinson's as conferring higher risk. In addition, 11% of patients reported new or worsening symptoms that they attributed to the pandemic.

Gastroenterology

Plexiglass barrier box to improve ERCP safety during the COVID-19 pandemic.

Ljubicic N, Stojavljevic-Shapeski S, Virovic-Jukic L, Nikolic M, et al.

Gastrointest Endosc

2020 Apr 16; PMID: 32305346

Level of Evidence: 5 - Expert Opinion

Type of Article: Opinion

Summarizing excerpt: “With the idea of minimizing the spread of aerosols during endoscopy, [the authors] are using a specially designed transparent plexiglass box (length 90 cm, width 70 cm, height 60 cm) with a smaller opening on the side for the endoscope (diameter 60 mm) and 2 openings for the anesthesiologist maneuvers and passage of various equipment cables (each diameter 150 mm).” The authors did not test the plexiglass box model’s ability to limit aerosol spread but found that it “did not limit necessary access to the patient, the endoscopic procedure, or the quality of the diascopy view.”



Figures1-2: The plexiglass barrier box developed to improve ERCP safety.

ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic.

Gralnek IM, Hassan C, Beilenhoff U, Antonelli G, Ebigbo A, Pellisè M, Arvanitakis M, Bhandari P, Bisschops R, Van Hooft JE, Kaminski MF, Triantafyllou K, Webster G, Pohl H, Dunkley I, Fehrke B, Gazic M, Gjergek T, Maasen S, Waagenes W, de Pater M, Ponchon T, Siersema PD, Messmann H, Dinis-Ribeiro M. Gralnek IM, et al

Endoscopy.

2020 Apr 17; PMID: 32303090

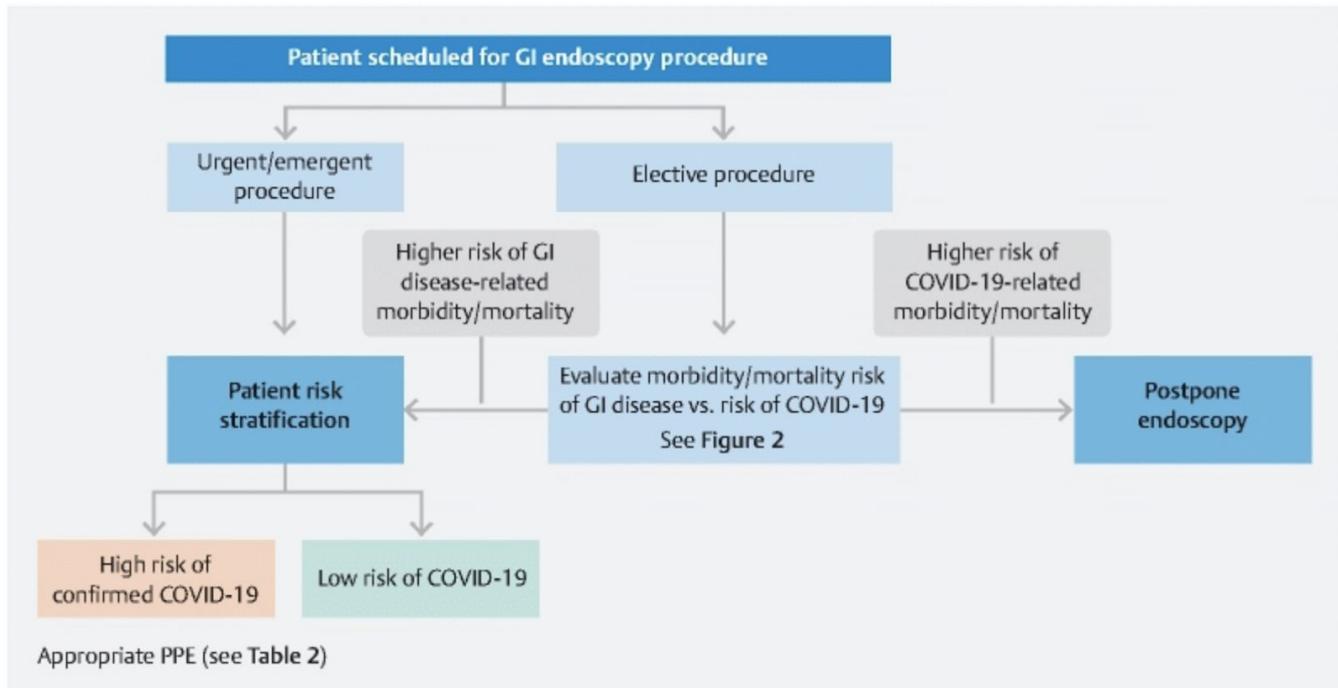
Level of Evidence: 5 - Expert Consensus

Type of Article: Review of Guidelines

Summary: This article provides a comprehensive review of recommendations for endoscopy compiled from the WHO, CDC and major GI societies, with risk management strategies in the pre-procedure, intra-procedure and post-procedure settings. The figures below address how to stratify patients during the COVID-19 pandemic and identify which patients need endoscopy urgently and which can be postponed to a later date.

Abstract: We are currently living in the throes of the COVID-19 pandemic that imposes a significant stress on health care providers and facilities. Europe is severely affected with an exponential increase in incident infections and deaths. The clinical manifestations of COVID-19 can be subtle, encompassing a broad spectrum from asymptomatic mild disease to severe respiratory illness. Health care professionals in endoscopy units are at increased risk of infection from COVID-19. Infection prevention and control has been shown to be dramatically effective in assuring the safety of both health care professionals and patients. The European Society of Gastrointestinal Endoscopy (www.esge.com) and the European Society of Gastroenterology and Endoscopy Nurses and Associates (www.esgena.org) are joining forces to provide guidance during this pandemic to help assure the highest level of endoscopy care and protection against COVID-19 for both patients and endoscopy

unit personnel. This guidance is based upon the best available evidence regarding assessment of risk during the current status of the pandemic and a consensus on which procedures to perform and the priorities on resumption. We appreciate the gaps in knowledge and evidence, especially on the proper strategy(ies) for the resumption of normal endoscopy practice during the upcoming phases and end of the pandemic and therefore a list of potential research questions is presented. New evidence may result in an updated statement.



| **Fig.1** Decision pathway for GI endoscopic procedures during the COVID-19 pandemic. GI, gastrointestinal; PPE, personal protective equipment.|

Table1
Risk stratification for potential COVID-19 infection in patients requiring gastrointestinal endoscopy.

Low-risk patient	No symptoms (eg, cough, fever, shortness of breath or diarrhea) AND No history of contact with COVID positive individual AND No travel or residence in a location reporting community transmission of COVID-19 during previous 14 days Negative testing for COVID 19 (with adequate accuracy and proper epidemiological setting)
High-risk patient	Presence of symptoms with adequate sensitivity (eg, cough, fever, shortness of breath or diarrhea) OR Travel or residence in a location reporting community transmission of COVID-19 during previous 14 days (eg, most European regions in April 2020) OR Contact with COVID-19 positive (or very likely to be positive) individual

Table2
Health-professional personal protective equipment stratified by patient risk

Low-Risk Patient	High-risk or Positive patient
Surgical mask[1]	Respiratory PPE (FFP2/FFP3 mask)[2]
Gloves[3]	Two pairs of gloves[3]
Booties/shoe covers	Booties/shoe covers
Disposable hairnet	Disposable hairnet
Protective eyewear (goggles or disposable face shield)	Protective eyewear (goggles or disposable face shield)
Water-proof disposable gowns[4]	Water-proof disposable gowns[4]

Perform always <ul style="list-style-type: none"> ▪ Acute upper/lower GI bleeding with hemodynamic instability ▪ Capsule/enteroscopy for urgent/emergent bleeding ▪ Anemia with hemodynamic instability ▪ Foreign body in esophagus and/or high-risk foreign body in the stomach ▪ Obstructive jaundice ▪ Acute ascending cholangitis 	Case by case management – high priority <ul style="list-style-type: none"> ▪ Endoscopic treatment of high-grade dysplasia (HGD) or early intra-mucosal cancer in the esophagus, stomach, or large colonic polyps at high-risk of submucosal invasion ▪ Malignant stricture stenting ▪ PEG/PEJ/NJ tube ▪ Upper GI fistula/leakage ▪ Dysphagia or dyspepsia with alarm symptoms present ▪ Upper GI bleeding without hemodynamic instability ▪ Rectal bleeding ▪ Colonoscopy for melena after negative upper-GI endoscopy ▪ Severe anemia with no hemodynamic instability ▪ Tissue acquisition needed for the initiation of systemic therapy/surgery ▪ Colonoscopy within organized FOBT+ CRC screening programme ▪ Foreign body in the stomach, low-risk ▪ Benign stricture requiring dilation/stenting ▪ Radiologic evidence of mass ▪ Lymph node EUS sampling ▪ Gallstone-related pancreatitis ▪ Pancreatic mass/stricture ▪ Biliary stricture dilation ▪ Pancreatico-biliary stent replacement for non-urgent indication ▪ Necrosectomy 	Case by case management – low priority <ul style="list-style-type: none"> ▪ Endoscopic treatment of esophageal or gastric low-grade dysplasia (LGD) ▪ Duodenal polyp ▪ Ampullectomy ▪ Band ligation/non-emergency ▪ Iron deficiency anemia ▪ Pancreatic cyst (depending on risk features) ▪ Biliary stricture/no urgency (no cholangitis, no jaundice, etc.) ▪ Submucosal lesion EUS sampling ▪ Achalasia (POEM, balloon dilatation) ▪ gFOBT/FIT+ (outside of an organized regional/national screening program)
Postpone always		
<ul style="list-style-type: none"> ▪ Surveillance for <ul style="list-style-type: none"> – Barrett's Esophagus without dysplasia or Low-Grade Dysplasia or after endoscopic treatment – Gastric atrophy/Intestinal Metaplasia – Inflammatory Bowel Disease – Primary Sclerosing Cholangitis ▪ Post-endoscopic resection (including immediate endoscopy after resection), surgical resection of cancer or post-polypectomy surveillance ▪ Diagnosis/surveillance of Lynch syndrome and other hereditary syndromes ▪ Diagnosis of Irritable Bowel Syndrome-like symptoms ▪ Diagnosis of reflux disease, dyspepsia (no alarm symptoms) ▪ Screening in high risk patients for esophageal cancer, gastric cancer, colon cancer (primary screening endoscopy) or pancreatic cancer ▪ Bariatric GI endoscopy procedures (e.g., intra-gastric balloons, endoscopic sleeve gastroplasty) 		

Fig. 2 List of indications for endoscopic procedures according to rescheduling recommendations and priority.

Covid-19 and immunomodulation in IBD.

Neurath MF.Neurath MF.

Gut.

2020 Apr 17; PMID: 32303609

Level of Evidence: 2 - Literature Review

Article Type: Commentary

BLUF: The author reviews the recent advances in basic science regarding COVID-19 pathophysiology and the potential implications this may have for immunomodulation and biological therapy in IBD. The author highlights the key messages of his review as follows:

- “Severe patients with covid-19 may suffer from progressive pneumonia, acute respiratory distress syndrome and multiorgan failure due to hyperinflammation and a cytokine storm syndrome; the interleukin-6R antibody” (Figure 1, 2)
- **“The receptor ACE2 is highly expressed in ileal and colonic tissue and ACE2 IBD.”**

- “**There is currently no evidence for an increased frequency of COVID-19 cases in IBD**; a recent study suggesting decreased disease activity in IBD requires further investigations.”
- “**Based on the currently available limited data, immunomodulatory and biological therapies can be continued in patients with IBD in remission**; however, close attention to new results should be paid in the dynamic pandemic situation.” (Boxes 1 and 2 demonstrate recommendations for IBD management during the COVID-19 pandemic)

Abstract: The current coronavirus pandemic is an ongoing global health crisis due to covid-19, caused by severe acute respiratory syndrome coronavirus 2. Although covid-19 leads to little or mild flu-like symptoms in the majority of affected patients, the disease may cause severe, frequently lethal complications such as progressive pneumonia, acute respiratory distress syndrome and organ failure driven by hyperinflammation and a cytokine storm syndrome. This situation causes various major challenges for gastroenterology. In the context of IBD, several key questions arise. For instance, it is an important question to understand whether patients with IBD (eg, due to intestinal ACE2 expression) might be particularly susceptible to covid-19 and the cytokine release syndrome associated with lung injury and fatal outcomes. Another highly relevant question is how to deal with immunosuppression and immunomodulation during the current pandemic in patients with IBD and whether immunosuppression affects the progress of covid-19. Here, the current understanding of the pathophysiology of covid-19 is reviewed with special reference to immune cell activation. Moreover, the potential implications of these new insights for immunomodulation and biological therapy in IBD are discussed.

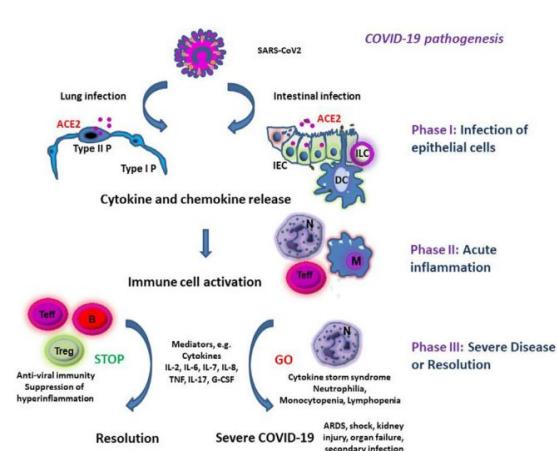


Figure 1 Hypothetical pathogenesis of covid-19. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infects ACE2 expressing epithelial cells in the lung and/or the intestine. This is followed by production of mediators causing immune cell activation. Overwhelming immune cell activation may lead to severe complications including acute respiratory distress syndrome (ARDS), shock and kidney or multiorgan failure. B, B lymphocytes; IEC, intestinal epithelial cell; ILC, innate lymphoid cell; M, monocyte/macrophage; N, neutrophils; Teff, effector T cells; Treg, regulatory T cell; Type I P, type I pneumocytes; Type II P, type II pneumocytes.

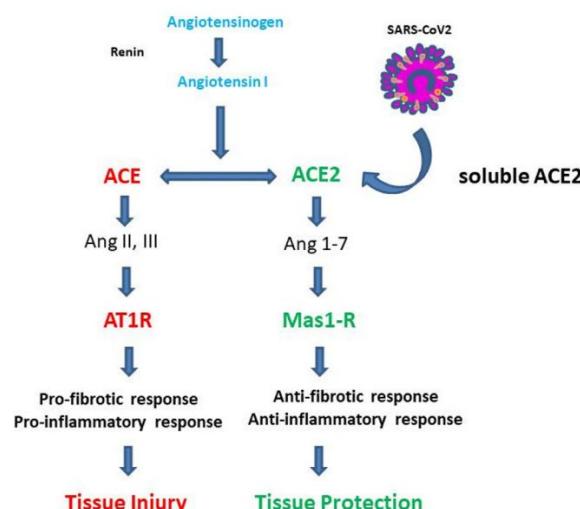


Figure 2 The ACE/ACE2 receptor system (modified according to Zhang et al⁵²). The classical renin-angiotensin-aldosterone system ACE/angiotensin II/angiotensin type 1/2 receptor (AT1-R) and ACE2/Ang 1–7/MAS-1 receptor (MAS1-R) systems are shown.^{49–52} The ACE/AT1-R system has been mainly implicated in pro-inflammatory immune responses and tissue injury. In contrast, the ACE2/MasR system appears to play a key role in many anti-inflammatory pathways controlling tissue protection.

Box 1 Recommendations for managing patients with IBD during the covid-19 pandemic

Consider potential risk situations for severe acute respiratory syndrome coronavirus 2 infection

- Patients with inflammatory bowel disease (IBD) on immunosuppressive agents.
- Patients with active-stage IBD with malnutrition
- Elderly patients with IBD
- Patients with IBD frequently visiting medical clinic
- Patients with IBD with underlying health conditions, such as hypertension and diabetes mellitus
- Patients with IBD who are pregnant
- Patients receiving experimental COVID-19 therapy plus IBD specific medications (potential drug drug interactions).

Medication for patients with IBD

- Continue current treatment if disease is stable and discuss suitable medicine if disease has flared.
- Use of mesalamine should be continued and should not increase the risk of infection.
- Corticosteroid use can be continued, but be cautious of possible side effects.
- A new prescription of immunosuppressant or increase in dose of an ongoing immunosuppressant is not recommended in epidemic areas.
- Use of biologics such as the antitumour necrosis factors infliximab or adalimumab should be continued.
- If infliximab infusion is not accessible, switching to adalimumab injection at home should be considered.
- Vedolizumab use can be continued due to the specificity of the drug for the intestine.
- Ustekinumab use can be continued, but starting ustekinumab requires infusion centre visits and therefore should be discussed before initiation of therapy.
- Enteral nutrition might be used if biologics are not accessible.
- Tofacitinib should not be newly prescribed in epidemic areas unless there are no other alternatives.

Surgery and endoscopy

- Postpone elective surgery and endoscopy.
- Consider screening for covid-19 (complete blood count, nucleic acid detection and chest CT) before surgery.

Patients with IBD and fever

- Fever is the most common reported symptom in covid-19.
- Contact your IBD doctor about potential option to visit outpatient clinic with personal protection provisions if temperature continues over 38°C.
- Suspend the use of immunosuppressant and biological agents after consultation with your IBD doctor, and follow appropriate local guidance for suspected covid-19 if covid-19 cannot be ruled out.

Modified according to Mao et al.⁹⁶

Box 2 Recommendations for IBD centres in covid-19 risk situations

Advise patients to strictly follow the WHO recommendations for covid-19 prevention

- Wash your hands regularly.
- Keep potentially contaminated surfaces clean.
- Respect social distancing.
- Avoid to touch eyes, nose and mouth.
- Stay home if you feel unwell.
- Wear a mask to avoid infecting other people.
- Reduce the risk of hand contamination (eg, by wearing gloves).
- Avoid to use public toilets.

Consider to restructure your IBD patient care under consideration of the local situation

- Strictly separate areas for care of patients with suspected/proven covid-19 and patients with IBD in the hospital.
- Assign-specific physicians to inpatient care, endoscopy and remote monitoring.
- Convert multidisciplinary team meetings into virtual meetings.
- Consider to avoid elective surgery.
- Avoid crowding in the waiting area of the outpatient unit.
- Consider to wear personal protective equipment and follow the WHO recommendations to prevent any contamination.
- Consider to limit the number of patients in the outpatient clinic by focusing on infusion treatment.
- Secure home delivery and adequate drug supply to all patients given subcutaneous and oral drugs.
- Provide help in individual cases by using emails and telephone calls.
- Send newsletters or information material by email.
- Secure communication between local gastroenterologists and primary care doctors with your centre.
- Consider alternative and safer ways of administration and remote monitoring of patients with IBD.

Modified according to Danese et al and Fiorino et al.^{97 98}

British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic.

Kennedy NA, Jones GR, Lamb CA, Appleby R, Arnott I, et al.

Gut. Jnl

2020 Apr 17; PMID: 32303607

Level of Evidence: 5 - Expert Opinion

Type of Article: Commentary

Summarizing excerpt: “The British Society of Gastroenterology has set the following recommendations for patients with Irritable Bowel Disease:

1. Patients with IBD are advised not to stop or reduce their medication without discussing with their IBD team.
2. IBD centers are encouraged to identify an experienced person to oversee blood tests, initiation of biologics and prescribing of biologics, and support patients accordingly. 3) Administrative support should be identified to ensure prescriptions for subcutaneous biologics are forwarded to home care in a timely manner.
3. Patients should be given helpline details to arrange contact for advice regarding delayed deliveries.
4. Maintaining a functional infusion service throughout the pandemic should be a priority.”

Prevention of COVID-19 in patients with inflammatory bowel disease in Wuhan, China.

An P, Ji M, Ren H, Su J, Ding NS, Kang J, Yin A, Zhou Q, Shen L, Zhao L, Jiang X, Xiao Y, Tan W, Lv X, Li J, Liu S, Zhou J, Chen H, Xu Y, Liu J, Chen M, Cao J, Zhou Z, Shen L, Tan S, Yu H, Dong W, Ding Y.

Lancet Gastroenterol Hepatol.

2020 Apr 17; PMID: 32311321

Level of Evidence: 3 - Cohort Study

Type of Article: Correspondence

BLUF: “Establishing a method of communication between patients and their IBD teams was effective in mitigating risk of disease in this vulnerable population.” They accomplished this by alerts/messages promoting appropriate hygiene and safety measures over 3 months.

Summary: Patients with inflammatory bowel disease (IBD) are at an increased risk of opportunistic infections, and thus, particular attention is required for these patients amidst the ongoing COVID-19 pandemic. 318 patients with IBD were registered in a prospective database at the Regional Medical IBD Center of China, Renmin Hospital of Wuhan University, Wuhan, China between January 1, 2020 and December 8, 2019. Educational and instructional alerts and messages were communicated to each of these patients on January 3, 2020. Within three days, most patients reported that they maintained good hand hygiene, sought medical assistance online rather than in-person, and kept track of fever and respiratory symptoms. Subsequent messages pertaining to appropriate hygiene and safety measures were communicated over the next three months. As of March 30, none of the registered patients with IBD had reported concern over respiratory symptoms, and none had confirmed or suspected COVID-19.

Potential implications of COVID-19 in non-alcoholic fatty liver disease.

Prins, Grietje H; Olinga, Peter

Liver Int

2020 Apr 19; PMID: 32306495

Level of Evidence: 5 – Expert opinion/mechanism-based reasoning

Article Type: Letter to the Editor

Summary: ACE inhibitors (often used to treat patients with diabetes and hypertension) may up-regulate ACE2, and ACE2 is a means of entry for covid-19. So patients with metabolic syndrome are likely to be at increased risk from covid-19. Patients with metabolic syndrome also frequently have some degree of NAFLD, and liver dysfunction has already been seen in covid-19 patients regardless of their history. Therefore, the authors recommend investigation into whether patients with NAFLD are more vulnerable to covid-19, and whether covid-19 “may increase NAFLD progression to non-alcoholic steatohepatitis in the long term.”

Endocrinology

Managing New-Onset Type 1 Diabetes During the COVID-19 Pandemic: Challenges and Opportunities.

Garg SK, Rodbard D, Hirsch IB, Forlenza GP.

Diabetes Technol Ther.

2020 Apr 17; PMID: 32302499

Level of Evidence: 4 - Case study

Type of Article:

BLUF: In this article, the authors make an argument based on two case studies that concludes that telemedicine would provide adequate and cost effective care for patients with Type I Diabetes.

Abstract: The current COVID-19 pandemic provides an incentive to expand considerably the use of telemedicine for high-risk patients with diabetes, and especially for the management of type 1 diabetes (T1D). Telemedicine and digital medicine also offer critically important approaches to improve access, efficacy, efficiency, and cost-effectiveness of medical care for people with diabetes. Two case reports are presented where telemedicine was used effectively and safely after day 1 in person patient education. These aspects of the management of new-onset T1D patients (adult and pediatric) included ongoing diabetes education of the patient and family digitally. The patients used continuous glucose monitoring with commercially available analysis software (Dexcom Clarity and Glooko) to generate ambulatory glucose profiles and interpretive summary reports. The adult subject used multiple daily insulin injections; the pediatric patient used an insulin pump. The subjects were managed using a combination of e-mail, Internet via Zoom, and telephone calls. These two cases show the feasibility and effectiveness of use of telemedicine in applications in which we had not used it previously: new-onset diabetes education and insulin dosage management. **The present case reports illustrate how telemedicine can be used safely and effectively for new-onset T1D training and education for both pediatric and adult patients and their families.** The COVID-19 pandemic has acutely stimulated the expansion of the use of telemedicine and digital medicine. We conclude that telemedicine is an effective approach for the management of patients with new-onset T1D.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic.

Erkan Cure, Medine Cumhur Cure

Diabetes Metab Syndr

2020 Apr 15; PMID: 32311651

Level of Evidence: 5 - Mechanism based reasoning

Type of Article: Letter

BLUF: The COVID-19 virus has been shown to attach to the ACE2 enzyme at low cytosolic pH. Due to Medications such as ACEIs and ARBs leading to an increased ACE2 level and low cytosolic pH, the combined use of ACEis and ARBs during the COVID-19 outbreak could lead to a markedly raised ACE2 level and viral load. As a result, the authors speculate that the use of ACEIs and ARBs in patients with diabetes may lead to increased morbidity and mortality of COVID-19.

Abstract: The novel coronavirus disease 2019 (COVID-19) outbreak once again demonstrated the importance of the renin-angiotensin system (RAS) in patients with diabetes. Activation of the RAS increases in patients with diabetes. **The virus attaches to the ACE2 enzyme at low cytosolic pH values and enters into the cell and causes infection.** Especially in the presence of diabetes mellitus and accompanying comorbid conditions such as hypertension, obesity, old age, and smoking, cytosolic pH is low, thus the virus easily may enter the cell by attaching to ACE2. **ACEIs and ARBs lead to a reduction in angiotensin II level by increasing the ACE2 level, thus they cause a low cytosolic pH.** Increased cardiac ACE2 levels due to ACEIs and ARBs can trigger cardiac arrhythmias and myocarditis by causing the virus to easily enter the heart tissue. There is ACE2 activity in the rostral ventrolateral medulla in the brain stem. The release of angiotensin 1-7 in the brain stem leads to the activation of the sympathetic nervous system. This activation causes systemic vasoconstriction and the patient's blood pressure increases. The most important event is the increased sympathetic activity via the central stimulation, this activity increases pulmonary capillary

leaking, causing the ARDS. As the cytosolic pH, which is already low in patients with diabetes will decrease further with the mechanisms mentioned above, the viral load will increase and the infection will be exacerbated. As a result, the use of ACEIs and ARBs in patients with diabetes can lead to increased morbidity and mortality of COVID-19.

Diabetes self-management amid COVID-19 pandemic.

Banerjee M, Chakraborty S, Pal R.

Diabetes Metab Syndr.

2020 Apr 13; PMID: 32311652

Level of Evidence: 5 - Expert opinion

Type of Article: Editorial

BLUF: Diabetic patients in quarantine face a unique set of challenges regarding diet, medication compliance, symptom management, exercise, and psychosocial issues. Cooperation and communication between patients and a multidisciplinary team of healthcare professionals is critical to the health of these patients, and telemedicine should be utilized when possible to safely and effectively communicate with patients in quarantine.

Abstract:

Background and aims: COVID-19 pandemic has challenged the physician-centered approach of diabetes care in India that is primarily based on routine clinic visits. We aim to review the various aspects of patient-centered care via diabetes self-management education based on available literature.

Methods: This is a narrative review using Pubmed, EMBASE and Google Scholar search till March 29, 2020. Search terms were "COVID-19", "diabetes self-care", "diabetes self-management education", "DSME", "diabetes self-management in India", "diabetes self-care in India" and "DSME in India".

Results: We have discussed an educational plan on diabetes self-management that can be adopted for people with diabetes mellitus in our country amid the ongoing pandemic. We have also identified the barriers to diabetes self-management in the current scenario and suggested possible solutions to overcome those.

Conclusions: We have reemphasized the need for a simultaneous **patient-centered approach in routine diabetes care that has to be coordinated by a multidisciplinary team amid the ongoing COVID-19 pandemic.**

Rheumatology

Should SARS-CoV-2 influence immunosuppressive therapy for autoimmune blistering diseases?

Di Altobrando A, Patrizi A, Bardazzi F.

J Eur Acad Dermatol Venereol.

2020 Apr 17; PMID: 32302437

Level of Evidence: 5 - Expert opinion

Type of Article: Letter

BLUF: This article discusses the lack of evidence for the use of immunosuppressive therapies in patients infected with SARS-CoV-2 and autoimmune bullous disease. The authors stress the importance of sharing information about these patients.

Abstract: "In this dramatic period where the whole world is affected by the outbreak of coronavirus disease 19 (COVID-19), scientific data relating to the causative virus SARS-CoV-2 as well as the

subsequent therapeutic repercussions on the management of other diseases should be divulged in order to share as much information as possible among experts in a timely manner.”

Hematology

American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group Position Statement on Pharmacy Practice Management and Clinical Management for COVID-19 in Hematopoietic Cell Transplant and Cellular Therapy Patients in the United

Mahmoudjafari Z, Alexander M, Roddy J, Shaw R, Shigle TL, Timlin C, Culos K.
Biol Blood Marrow Transplant.

2020 Apr 16; PMID: 32305359

Level of Evidence: 5 - Expert opinion

Type of Article: Recommendations

BLUF: The American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group Steering Committee offers recommendations on the following: initial preparations, inpatient pharmacist practice, optimizing technology resources, students/interns/resident learners, clinical management considerations, chloroquine/hydroxychloroquine, remdesivir, ribavirin, convalescent plasma, tocilizumab, and ruxolitinib.

Abstract:

The coronavirus-19 (COVID-19) pandemic poses a significant risk to patients undergoing hematopoietic stem cell transplantation (HCT) or cellular therapy. The American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group Steering Committee aims to provide pharmacy practice management recommendations for how to transition clinical HCT or cellular therapy pharmacy services using telemedicine capabilities in the inpatient and outpatient settings to maintain an equivalent level of clinical practice while minimizing viral spread in a high-risk, immunocompromised population. In addition, the Steering Committee offers clinical management recommendations for COVID-19 in HCT and cellular therapy recipients based on the rapidly developing literature. As the therapeutic and supportive care interventions for COVID-19 expand, collaboration with clinical pharmacy providers is critical to ensure safe administration in HCT recipients. Attention to drug-drug interactions (DDIs) and toxicity, particularly QTc prolongation, warrants close cardiac monitoring and potential cessation of concomitant QTc-prolonging agents. Expanded indications for hydroxychloroquine and tocilizumab have already caused stress on the usual supply chain. Detailed prescribing algorithms, decision pathways, and specific patient population stock may be necessary. The COVID-19 pandemic has challenged all members of the healthcare team, and we must continue to remain vigilant in providing pharmacy clinical services to one of the most high-risk patient populations while also remaining committed to providing compassionate and safe care for patients undergoing HCT and cellular therapies.

Table 1
Inpatient and Outpatient Considerations for Pharmacy Practice Management

Inpatient Considerations	Outpatient Considerations
Limiting exposure to staff and patients	
<ul style="list-style-type: none"> Limiting physical presence Attending clinical rounds or huddles virtually Rotating pharmacy staff on- and off-site Pharmacists to avoid accessing patient rooms (not seeing patients directly) If rounding in person, maintaining 6 feet from other team members 	<ul style="list-style-type: none"> Limiting physical presence Concentrating visits on particular days to allow for non-patient visit days Rotating pharmacy staff on- and off-site Pharmacists to avoid accessing patient rooms (not seeing patients directly)
Distribution of services	
<ul style="list-style-type: none"> Onsite Urgent/emergent needs (rapid responses/codes) Collaboration with other team members Discharge education <ul style="list-style-type: none"> Offsite Medication education and reconciliation Patient own medication identification Therapeutic drug monitoring Order verification, including chemotherapy Medication adjustments based on renal and liver function Drug-drug interaction management 	<ul style="list-style-type: none"> Onsite Urgent/emergent needs (rapid responses/codes) Help maintain clinic workflow efficiency/throughput Collaboration with other team members <ul style="list-style-type: none"> Offsite Medication education and reconciliation Oral chemotherapy education and follow-up Conditioning and transplant education Laboratory follow up Therapeutic drug monitoring Order verification Chemotherapy order preparation
Technology	
<ul style="list-style-type: none"> Messaging Chat mechanisms (EMR real-time, Cureatr, Voatle, Skype for Business) EMR messaging functions Email Handouts or medication calendars sent to patient via EMR or through programs such as MedActionPlanPro <ul style="list-style-type: none"> Audiovisual Audio call resources (Doximity, Jabber phone, blocked calls from personal line) Virtual visit capabilities (eg, webcam) Zoom/Webex/Skype for Business (for communicating with team members) (if approved for use by IT department) 	

Table 2
Drug Interactions with Experimental COVID-19 Therapies and Common Immunosuppressants [32]

Drug	CQ/HCQ	RDV	RBV	LPV/r	TCZ	RUX
Tacrolimus	↑	↔	↔	↑	↓ (weak)	↔
Cyclosporine	↑	↔	↔	↑	↓ (weak)	↔
Sirolimus	↑	↔	↔	↑ (strong)	↓ (weak)	↔
Mycophenolate	↔	↔	↔	↔	↔	↔
ATG	↔	↔	↔	↔	↔	↔

RDV indicates remdesivir; RBV, ribavirin; LPV/r, lopinavir/ritonavir; TCZ, tocilizumab; RUX, ruxolitinib; ATG, antithymocyte globulin.

Arrow depicts the effect on immunosuppressant concentration.

Oncology

Strategies for patient with cancer during COVID-19 pandemic.

Zhao Z, Yang C, Li C.

Asia Pac J Clin Oncol.

2020 Apr 20; PMID: 32311820

Level of Evidence: 5 - Expert Opinion

Type of Article: Letter

Summary: A surgical oncology team at Chongqing university medical center weigh in on the approach to cancer treatment during the COVID-19 pandemic. Their recommendations: **surgically, only rapidly growing, majorly-involving organs, or life threatening tumors need emergent surgical treatment. High dose chemotherapy and radiotherapy with myelotoxicity needs to be limited or halted.** A three-step prevention for admitted cancer patients may also be followed.

Surgery

ENT/otolaryngology

COVID-19 in otolaryngologist practice: a review of current knowledge.

Krajewska J, Krajewski W, Zub K, Zatoński T.

Eur Arch Otorhinolaryngol

2020 Apr 18; PMID: 32306118

Level of Evidence: 5 - Expert Opinion

Article Type: Literature Review

BLUF: Otolaryngologists should wear protective equipment when seeing patients and postpone non-urgent appointments as patients may present with COVID-19 ENT related symptoms before testing positive for COVID-19.

Abstract:

PURPOSE: Otorhinolaryngological manifestations are common symptoms of COVID-19. This study provides a brief and precise review of the current knowledge regarding COVID-19, including disease transmission, clinical characteristics, diagnosis, and potential treatment. The article focused on COVID-19-related information useful in otolaryngologist practice.

METHODS: The Medline and Web of Science databases were searched without a time limit using terms "COVID-19", "SARS-CoV-2" in conjunction with "otorhinolaryngological manifestation", "ENT", and "olfaction".

RESULTS: The most common otolaryngological dysfunctions of COVID-19 were cough, sore throat, and dyspnea. Rhinorrhea, nasal congestion and dizziness were also present. COVID-19 could manifest as an isolated sudden hyposmia/anosmia. Upper respiratory tract (URT) symptoms were commonly observed in younger patients and usually appeared initially. They could be present even before the molecular confirmation of SARS-CoV-2. Otolaryngologists are of great risk of becoming infected with SARS-CoV-2 as they cope with URT. ENT surgeons could be easily infected by SARS-CoV-2 during performing surgery in COVID-19 patients.

CONCLUSION: Ear, nose and throat (ENT) symptoms may precede the development of severe COVID-19. During COVID-19 pandemic, patients with cough, sore throat, dyspnea, hyposmia/anosmia and a history of travel to the region with confirmed COVID-19 patients, should be considered as potential COVID-19 cases. **An otolaryngologist should wear FFP3/N95 mask, glasses, disposable and fluid resistant gloves and gown** while examining such individuals.

Not urgent ENT surgeries should be postponed. Additional studies analyzing why some patients develop ENT symptoms during COVID-19 and others do not are needed. Further research is needed to determine the mechanism leading to anosmia.

Cardiothoracic

Cardiovascular Surgery in the COVID-19 Pandemic

Mavioglu M, Unal E

J Card Surgery

2020 Apr 19; PMID: 32306474

Level of Evidence: 5 - Expert opinion

Type of Article: Letter

Summary: Elective case triage is difficult for cardiovascular procedures; deciding to defer a procedure should be based on the capacity of the healthcare system, availability of surgical/anesthesia staff, and the need for other supplies and equipment. The patient's status must be accounted for when

deciding to defer or perform the procedure. If surgery is to be performed, extra precautions should be taken by the operative staff to utilize proper PPE and maintain sterility.

Vascular

Early Experience in the COVID-19 pandemic from a Vascular Surgery Unit in a Singapore Tertiary Hospital.

Tan, Glenn Wei Leong; Chandrasekar, Sadhana; Lo, Zhiwen Joseph; Hong, Qiantai; Yong, Enming; Lingam, Pravin; Zhang, Li; Quek, Lawrence Han Hwee; Pua, Uei
J Vasc Surg

2020 Apr 20; PMID: 32305387

Level of Evidence: 5 – Expert opinion

Article Type: Letter to the Editor

Summary: Authors describe their hospital changes which included deploying a large segment of consultants to emergency department care to screen COVID-19 patients, cancelling all leave/vacation, conference attendance, other educational events, developing a back-up on-call system for vascular surgery in case a physician develops COVID-19 symptoms, and a triage system for outpatient clinic. They note that measures taken have been strict, but they have had no COVID-19 transmission amongst surgeons in their hospital.

Urology

Endourological Stone Management in the Era of the COVID-19.

Proietti S, Gabardi F, Giusti G. Proietti S, et al.

Eur Urol

2020 Apr 14; PMID: 32303384

Level of Evidence: 5 - Expert Opinion

Type of Article: Editorial

Summary with excerpts: The authors make several recommendations for endourologic management of stones:

1. Renal colic patients should be managed conservatively if possible and patients with stones should be evaluated based on surgical priority.
2. Stenting or percutaneous nephrostomy can be used in obstructed/infected kidneys. “In the current pandemic scenario, it is advisable to take extra effort to avoid the latter because of the high risk of inadvertent removal and likely long delay to subsequent surgical lithotripsy. Whenever possible, the ureteral stent or nephrostomy tube should be placed under local anesthesia, sparing a ventilator”
3. Previously stented patients for complicated nephrolithiasis should be considered with priority in order to avoid prolonged delays in stent removal.

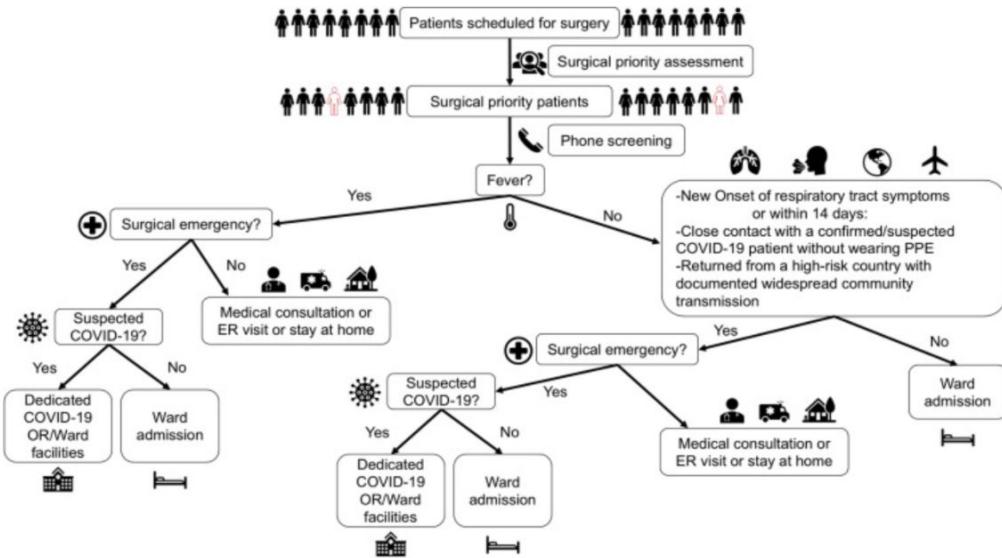
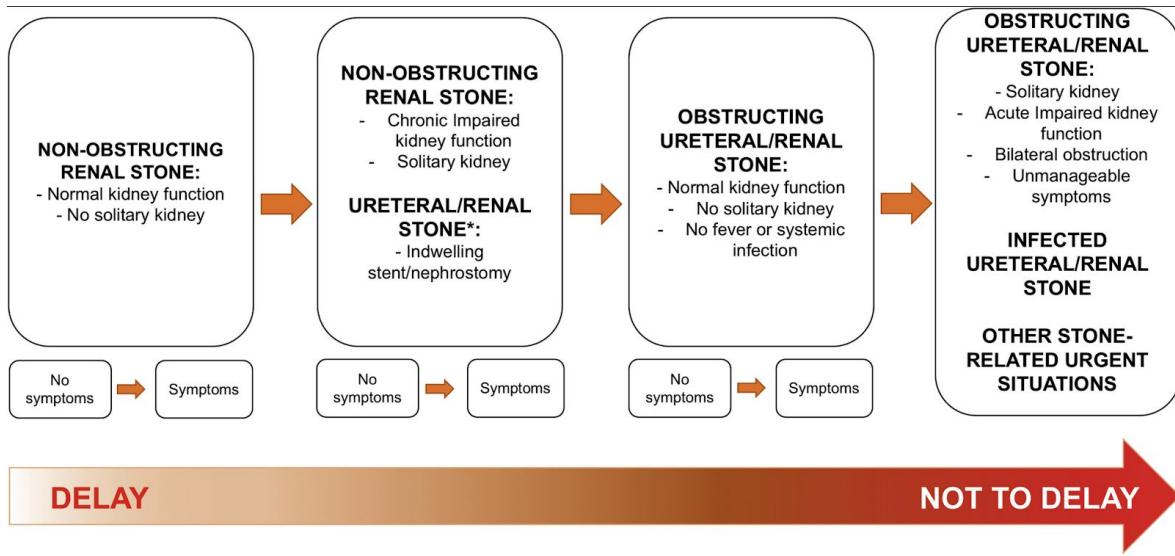


Fig. 1. Flowchart for triage of urological patients during the COVID-19 pandemic.



*depending on stent indwelling time, urinary infections, symptoms

Fig. 2. Prioritization scheme for stone patients scheduled for surgery during the COVID-19 pandemic.

OBGYN

COVID19 during pregnancy: a systematic review of reported cases.

Della Gatta AN, Rizzo R, Pilu G, Simonazzi G. Della Gatta AN, et al.

Am J Obstet Gynecol

2020 Apr 17; PMID: 32311350

Level of Evidence: 4 - Systematic review (poor quality data available)

Type of Article: Research

BLUF: 46 of 48 late-term pregnant women with known COVID-19 underwent an elective cesarean. The indications for these procedures is unclear at this time and further study is needed.

Abstract:

Objective: to conduct a systematic review of the outcomes reported for pregnant patients with COVID 19.

Data sources: we searched electronically Pubmed, Cinahl, Scopus using combination of keywords “Coronavirus and/ or pregnancy”; “COVID and/or pregnancy”; “COVID disease and/or pregnancy”; “COVID pneumonia and/or pregnancy. There were no restriction of languages in order to collect as much cases as possible.

Study eligibility criteria: all pregnant women, with a COVID19 diagnosed with acid nucleic test, with reported data about pregnancy and, in case of delivery, reported outcomes.

Study appraisal and synthesis methods: all the studies included have been evaluated according the tool for evaluating the methodological quality of case reports and case series described by Murad et al.

Results: 6 studies including 51 women were eligible for the systematic review. Three pregnancies were ongoing at the time of the report; of the remaining 48, 46 were delivered with a cesarean section and 2 vaginally; there was 1 stillbirth and 1 neonatal death.

Conclusions: although vertical transmission of SARS-Cov2 has been excluded thus far and the outcome for mothers and fetuses has been generally good, the high rate of preterm cesarean delivery is a reason for concern. These interventions were typically elective, and it is reasonable to question whether they were warranted or not. COVID-19 associated with respiratory insufficiency in late pregnancies certainly creates a complex clinical scenario.

No-Test Medication Abortion: A Sample Protocol for Increasing Access During a Pandemic and Beyond.

Raymond EG, Grossman D, Mark A, Upadhyay UD, Dean G, Creinin MD, Coplon L, Perritt J, Atrio JM, Taylor D, Gold M.

Contraception

2020 Apr 16; PMID: 32305289

Level of Evidence: 5 – Expert Opinion

Type of Article: Commentary

Summary: The article presents a protocol for medical abortion provision that minimizes in-person contact with healthcare providers, with the goal of ensuring access to abortion services during the pandemic. The protocol entails a strategy for provision of mifepristone and misoprostol therapy to patients with a first trimester pregnancy, excluding patients likely to have an ectopic pregnancy and using telehealth modalities for follow up visits unless symptoms of a failed medical abortion are present that would necessitate in-person follow up. The authors indicate this protocol can help to enable abortion access both during the COVID-19 pandemic and after its resolution.

Pediatrics

Rapid Development of Telehealth Capabilities within Pediatric Patient Portal Infrastructure for COVID-19 Care: Barriers, Solutions, Results.

Patel PD, Cobb J, Wright D, Turer R, Jordan T, Humphrey A, Kepner AL, Smith G, Rosenbloom ST. J Am Med Inform Assoc.

2020 Apr 17; PMID: 32302395

Level of Evidence: 4 - Cases series

Type of Article: Research

BLUF: The authors discuss how they used the status of Vanderbilt University Medical Center as a "...large, private, nonprofit, academic medical center with telehealth capabilities integrated into its patient portal" to their advantage to increase their telehealth capabilities by developing processes for

remote enrollment, utilizing allowable video conferencing tools, and using both of these methods to confirm identities.

Abstract:

The COVID-19 national emergency has led to surging care demand and the need for unprecedented telehealth expansion. Rapid telehealth expansion can be especially complex for pediatric patients. From the experience of a large academic medical center, **this report describes a pathway for efficiently increasing capacity of remote pediatric enrollment for telehealth** while fulfilling privacy, security, and convenience concerns. **The design and implementation of the process took two days. Weekly enrollment subsequently increased 10-fold for children (age 0-12 years) and 1.2-fold for adolescents (age 13-17 years). Weekly telehealth visits increased 200-fold for children and 90-fold for adolescents.** The obstacles and solutions presented in this report can provide guidance to health systems for similar challenges during the COVID-19 response and future disasters.

Paediatric Anaesthetic implications of COVID-19 - A Review of Current Literature.

Lee-Archer P, von Ungern-Sternberg BS

Paediatr Anaesth

2020 Apr 19; PMID: 32306440

Level of Evidence: 5- Expert opinion

Type of Article: Review

BLUF: A thorough but not exhaustive review of literature on pediatric COVID-19 followed by recommendations for anesthetists in the context of COVID-19. The authors highlight the need for careful training and supervision to correctly use PPE, **recommend practice simulations as a way to increase safety**, and stress the need for careful communication strategies and **attention to physical space such as the use of negative pressure rooms.**

Abstract: Paediatric anaesthetists have an important role to play in the management of patients suspected or confirmed to have COVID-19. In many institutions, the COVID-19 intubation teams are staffed with anaesthetists as the proceduralists working throughout the hospitals also in the ICU and Emergency Departments. As practitioners who perform aerosol generating procedures involving the airway, we are at high risk of exposure to the virus SARS-CoV-2 and need to ensure we are well-prepared and trained to manage such cases. This article reviews the relevant paediatric literature surrounding COVID-19 and summarises the key recommendations for anaesthetists involved in the care of children during this pandemic.

Transplant medicine

Pharmacologic treatment of transplant recipients infected with SARS-CoV-2: considerations regarding therapeutic drug monitoring and drug-drug interactions.

Elens, Laure; Langman, Loralie J; Hesselink, Dennis A; Bergan, Stein; Moes, Dirk Jan A R; Molinaro, Mariadelfina; Venkataraman, Raman; Lemaitre, Florian

Therapeutic Drug Monitoring

2020 Apr 19; PMID: 32304488

Level of Evidence: 5 - Mechanism-based Reasoning

Type of Article: Research

BLUF: In the context of hospitalized transplant patients with COVID-19, management of drug-drug interactions between immunosuppressant drug therapies (ISD) and investigational anti-SARS-CoV-2 drugs is complicated. Recommendations regarding therapeutic drug monitoring and dose adjustments were given with attention to the following classes of drugs: hydroxychloroquine, protease inhibitors, calcineurin inhibitors/mTORi, mycophenolate mofetil, glucocorticoids, remdesivir, and tocilizumab.

Abstract:

Background:

COVID-19 is a novel infectious disease caused by the severe acute respiratory distress (SARS)-corona virus-2 (SARS-CoV-2). Several therapeutic options are currently emerging but none with universal consensus or proven efficacy. Solid organ transplant recipients are perceived to be at increased risk of severe COVID-19 because of their immunosuppressed conditions due to chronic use of immunosuppressive drugs. It is therefore likely that solid organ transplant recipients will be treated with these experimental antivirals.

Methods:

This article is not intended to provide a systematic literature review on investigational treatments tested against COVID-19; rather, the authors aim to **provide recommendations for therapeutic drug monitoring of immunosuppressive drugs in transplant recipients infected with SARS-CoV-2 based on a review of existing data in the literature.**

Results:

Management of drug-drug interactions between investigational anti-SARS-CoV-2 drugs and immunosuppressants is a complex task for the clinician. Adequate immunosuppression is necessary to prevent graft rejection while, if critically ill, the patient may benefit from pharmacotherapeutic interventions directed at limiting SARS-CoV-2 viral replication. Maintaining immunosuppressive drug concentrations within the desired therapeutic range requires a highly individualized approach that is complicated by the pandemic context and lack of hindsight.

Conclusions:

With the present manuscript, the authors **inform the clinician about the potential interactions of experimental COVID-19 treatments with immunosuppressive drugs used in transplantation.** Recommendations regarding **therapeutic drug monitoring and dose adjustments** in the context of COVID-19 are provided.

Palliative Care

Emergency Palliative Care Planning and Support in a COVID-19 Pandemic.

Chidiac C, Feuer D, Naismith J, Flatley M, Preston N

J Palliat Med

2020 Apr 20; PMID: 32311287

Level of Evidence: 5 - Expert opinion

Type of Article: Letter

Summary: The authors outline their approach to optimize and improve access to palliative care during COVID-19. Major recommendations include the following:

- “**Developing service capacity**” - creating resources, processes and support systems.
- “**Educating the generalist workforce**” - providing communication strategies, remote and face to face teaching opportunities, and encouraging advanced care planning outside the hospital.
- “**Care of family caregivers**” - using technology to allow video visits to hospitalized family, training home caregivers to administer certain medications.

R&D: Diagnosis & Treatments

Current Diagnostics

Detection and analysis of nucleic acid in various biological samples of COVID-19 patients.

Wu J, Liu J, Li S, Peng Z, Xiao Z, Wang X, Yan R, Luo J.
Travel Med Infect Dis.

2020 Apr 17; PMID: 32311437

Level of Evidence: 3 - Cross sectional study

Type of Article: Letter

BLUF: “The detection of multiple biological samples of COVID-19 cases can improve the detection rate of 2019-nCoV nucleic acid, guide clinical diagnosis and treatment, reduce the false negative rate of discharged cases, and play a very important role in determining and cutting off the route of transmission and preventing the further development of the epidemic.”

Abstract:

COVID-19 (coronavirus disease 2019) is a kind of acute severe pneumonia caused by 2019-nCoV (2019-nCoV) infection. Since December 2019, it has been found in Wuhan, Hubei Province, and then spread to the whole country. Some parts of the world also showed an outbreak trend [1-3]. Real-time fluorescence quantitative reverse transcriptase polymerase chain reaction (reverse transcriptase-polymerase chain reaction, RT-PCR) and viral gene sequencing are the gold standard for the diagnosis of COVID-19. At present, upper respiratory tract nasopharyngeal swabs are mostly used as nucleic acid detection samples in China, but the positive rate is low. However, there are few reports on clinical application of 2019-nCoV nucleic acid detection in other biological samples.

METHODS: The East Section of Renmin Hospital of Wuhan University is a designated COVID-19 hospital in Wuhan City, Hubei Province, China. This observation study included 132 patients diagnosed with COVID-19 in the infectious disease areas of the East Section of Renmin Hospital of Wuhan University from 2020.1.31 to 2020.2.29. COVID-19 diagnostic criteria: according to China's 《pneumonia diagnosis and treatment Program of novel coronavirus infection (trial version 7)》, in accordance with the relevant epidemiological and clinical manifestations, nasopharyngeal swabs real-time fluorescence RT-PCR detection of 2019-nCoV nucleic acid positive, COVID-19 cases were divided into mild, ordinary, severe and severe. The nasopharyngeal swabs of 132 cases of COVID-19 were positive for 2019-nCoV nucleic acid on admission, including 72 males and 60 females, with an average age of 66.7 ± 9.1 years, including 80 cases of common type, 44 cases of severe type and 8 cases of critical type. During the period of admission, under the condition of tertiary protection, nasopharyngeal swabs, sputum, blood, feces and anal swabs of COVID-19 cases were collected many times in the isolation ward for 2019-nCoV nucleic acid detection. All biological samples are sealed and transferred to the laboratory in strict accordance with the standard process. The RT-PCR test kits (BioGerm) were recommended by the Chinese Center for Disease Control and Prevention. The same technician and brand of test kit was used for all RT-PCR testing reported; both internal controls and negative controls were routinely performed with each batch of tests.

RESULTS: 132 the results of 2019-nCoV nucleic acid test of various biological samples during the treatment of confirmed COVID-19 cases are as follows: the positive rate of 2019-nCoV nucleic acid test of nasopharyngeal swab is 38.13% (180/472 times), the positive rate of 2019-nCoV nucleic acid test of sputum is 48.68% (148/304 times), the positive rate of blood 2019-nCoV nucleic acid test is 3.03% (4/132 times), and the positive rate of 2019-nCoV nucleic acid test of feces is 9.83% (24/244 times). The positive rate of 2019-nCoV nucleic acid detection in anal swabs is 10.00% (12/120 times).

DISCUSSION: In this study, it was found that the positive rate of 2019-nCoV nucleic acid in sputum of 132 patients with COVID-19 was higher than that of nasopharyngeal swabs, and viral nucleic acids were also detected in blood and digestive tract (fecal/anal swabs). Simple detection of nasopharyngeal swab 2019-nCoV nucleic acid detection positive rate is not high, multi-sample 2019-nCoV nucleic acid detection can improve the accuracy, reduce the false negative rate, better guide clinical treatment and evaluate the therapeutic effect.

A report of three COVID-19 cases with prolonged viral RNA detection in anal swabs.

Hu Y, Shen L, Yao Y, Xu Z, Zhou J, Zhou H

Clin Microbiol Infect

2020 Apr 15; PMID: 32304746

Level of Evidence: 4- Case series

Type of Article: Letter

Summary: The authors describe three patients in China with mild Covid-19 illness with no gastrointestinal symptoms who tested positive for viral RNA by anal swab even after 2 of the 3 had begun testing negative by nasopharyngeal swab. They caution that “RNA detection by PCR does not correlate with the risk of transmission.” As yet, “there is no conclusive evidence that SARS-CoV-2 virus can be transmitted through oral-fecal route.”

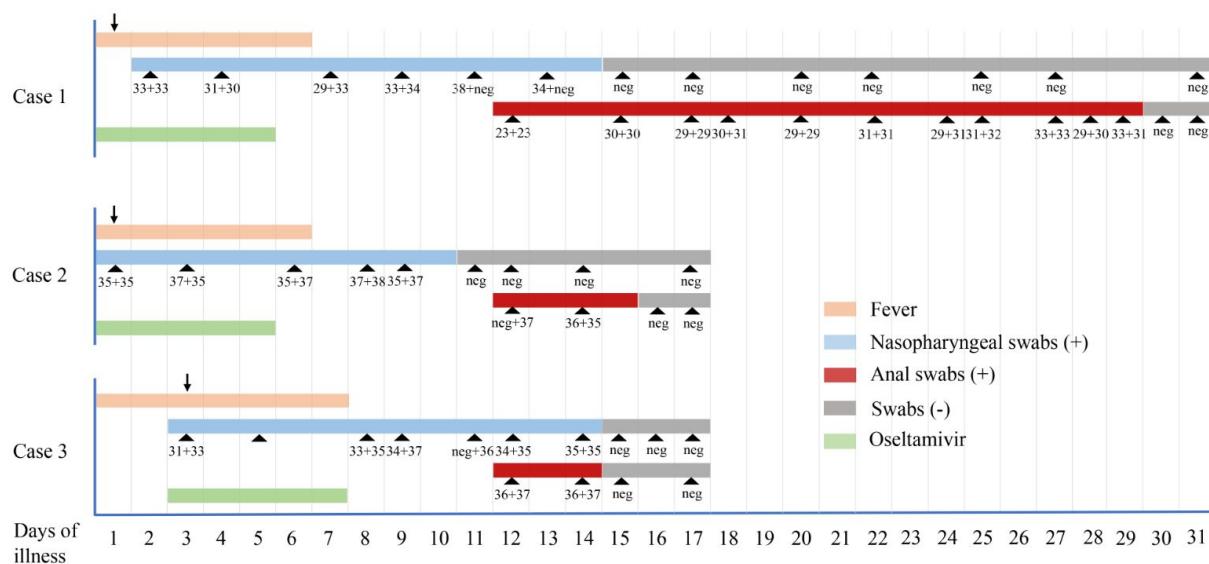


Figure 1. Diagram of viral detection, fever, and oseltamivir administration of the three cases. The time when SARS-CoV-2 nucleic acids turned negative was 15 and 5 days later in the anal swabs than in the nasopharyngeal swabs in cases 1 and 2, respectively. Illness day represents the patients with clear clinical symptoms such as fever which is labelled. The black arrows point to the admission day of each case. Virus nucleic acids were tested by real-time RT-PCR. Ct values are shown as Orfiab+N genes. Oseltamivir was administered in an oral dose of 75 mg twice daily.

Testing for SARS-CoV-2: Can We Stop at Two?

Lee TH, Lin RJ, Lin RTP, Barkham T, Rao P, Leo YS, Lye DC, Young B; National Centre for Infectious Diseases COVID-19 Outbreak Research Team.

Clinical Infectious Diseases

2020 Apr 19; PMID: 32306042

Level of Evidence: 4- Case Series

Type of Article: Brief Report

BLUF: A study conducted at the National Center for Infectious Diseases, Singapore found that while 88.6% (62/70) of symptomatic COVID-19 patients tested positive upon presentation, the remaining portion tested negative initially, with follow up testing conducted days later indicating a positive result. **The authors recommend taking caution when interpreting a negative result in a symptomatic patient**, and using a diagnostic matrix or chest CT to indicate whether or not follow up testing is necessary.

Abstract: The COVID-19 epidemic requires accurate identification and isolation of confirmed cases for effective control. This report describes the effectiveness of our testing strategy and highlights the importance of repeat testing in suspect cases in our cohort.

SARS-CoV-2: What Can Saliva Tell Us?

Braz-Silva PH, Pallos D, Giannecchini S, To KK

Oral Dis

2020 Apr 20; PMID: 32311181

Level of Evidence: 5 – Expert Opinion

Type of Article: Letter

BLUF: In this letter to the editor, a case is made for **SARS-CoV-2 detection using saliva instead of nasopharyngeal swabs**, highlighting the possibility for **rapid testing and self-collection** amidst a **growing asymptomatic case load**.

Abstract:

An epidemic pneumonia was first reported in the city of Wuhan, China, in the end of December 2019, had its aetiological agent identified as a new coronavirus (Zhu et al., 2020). The World Health Organisation (WHO) declared on 11 March 2020 that the epidemic of the new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a pandemic now called COVID-19.

Detection of SARS-CoV-2 RNA and Antibodies in Diverse Samples: Protocol to Validate the Sufficiency of Provider-Observed Home-Collected Blood, Saliva and Oropharyngeal Samples

Sullivan PS, Sailey C, Guest JL, Guarner J, Siegler AJ, Valentine-Graves M, Gravens L, Del Rio C, Sanchez TH

JMIR Public Health Surveill

2020 Apr 19; PMID: 32310815

Level of Evidence: 5 – Protocol

Type of Article: Research

BLUF: This article proposes a provisional protocol for patient self-collection of salivary swabs to detect SARS-CoV-2. The protocol seeks to employ multi-step sample quality checks to ensure uniformity of sample processing.

Abstract:

Background: The US response to the SARS-CoV-2 epidemic has been hampered by a lack of aggressive testing for infection. Testing for SARS-CoV-2 infection is the cornerstone of an effective public health response. However, efforts to test have been hampered by limited reagents, limitations in the availability of swabs used for collection of nasopharyngeal swab (NPS) specimens, limitations in personal protective equipment (PPE) for healthcare providers collecting the NPS specimens, and limitations in viral transport media for transporting the specimens. Therefore, more flexible options

for screening for SARS-CoV-2 RNA and serologic responses are critical to inform clinical and public health responses.

Objective: We aim to **document the ability of patients to self-collect specimens** for SARS-CoV-2 viral detection and serology.

Methods: In this protocol, patient collection of samples will be done with **observation by a provider during a telemedicine session**. Participants will be **mailed a specimen collection kit**, engage in a telehealth session with a healthcare provider through a HIPAA-compliant video meeting, and collect specimens while observed by the provider. **Providers will record whether they are confident in the sufficiency of the specimen** for laboratory testing that would inform clinical decision making. We will objectively **assess the laboratory evidence of sufficient biological material** in the mailed-in specimens.

Conclusions: Defining a **conceptual framework** for assessing the sufficiency of patient-collected samples for the detection of SARS-CoV-2 RNA and serologic responses to infection is critical for facilitating public health responses and providing PPE-sparing options to increase testing. Validation of alternative specimen collection should include objective measures of the sufficiency of specimens for testing. A strong evidence base for diversifying testing modalities will improve the tools to guide public health responses to the COVID-19 epidemic.

The Appropriate Use of Testing for COVID-19.

Zitek T.Zitek T.

West J Emerg Med.

2020 Apr 13;. PMID: 32302278

Level of Evidence: 4 - Review of studies

Type of Article: Expert Commentary

BLUF: "While the exact sensitivity and specificity of RT-PCR tests for COVID-19 are not known, it appears that a positive test is highly suggestive of true COVID-19, but a negative test does not rule out the disease."

Summary: The sensitivity and specificity of nasopharyngeal swabs using RT-PCR for the diagnosis of COVID-19 cannot be precisely determined with the published data to this point. However, the available in vitro data along with minimal clinical data suggest that **the test has very high specificity. On the other hand, the sensitivity is moderate (perhaps between 63-78%).** Among the various ways of performing RT-PCR, pharyngeal swabs seem to have lowest sensitivity; nasal swabs may be a bit more sensitive than pharyngeal swabs. RT-PCR analysis of BAL fluid seems to be the most accurate means of virologic confirmation, but BAL fluid can only reasonably be collected on the sickest cohort of patients.

Developments in Diagnostics

CRISPR-Cas12-based Detection of SARS-CoV-2

Broughton JP, Deng X, Yu G, Fasching CL, Servellita V, Singh J, Miao X, Streithorst JA, Granados A , Sotomayor-Gonzalez A, Zorn K, Gopez A, Hsu E, GuW, Miller S, Pan CY, Guevara H, Wadford DA, Chen JS, Chiu CY

Nat Biotechnology

2020 Apr 16; PMID: 32300245

Level of Evidence: 5- Basic Research

Type of Article: Letter

Summary: Here the authors report a novel CRISPR-Cas12 based diagnostic assay to detect SARS-CoV-2 from extracted RNA called SARS-CoV-2 DNA Endonuclease-Targeted CRISPR Trans Reporter (DETECTR). The assay is based on RT-LAMP and CAS12 mediated reporter cleavage.

Abstract:

An outbreak of betacoronavirus severe acute respiratory syndrome (SARS)-CoV-2 began in Wuhan, China in December 2019. COVID-19, the disease associated with SARS-CoV-2 infection, rapidly spread to produce a global pandemic. **We report development of a rapid (<40 min), easy-to-implement and accurate CRISPR-Cas12-based lateral flow assay for detection of SARS-CoV-2 from respiratory swab RNA extracts.** We validated our method using contrived reference samples and clinical samples from patients in the United States, including 36 patients with COVID-19 infection and 42 patients with other viral respiratory infections. Our CRISPR-based DETECTR assay provides a visual and faster alternative to the US Centers for Disease Control and Prevention SARS-CoV-2 real-time RT-PCR assay, with 95% positive predictive agreement and 100% negative predictive agreement.

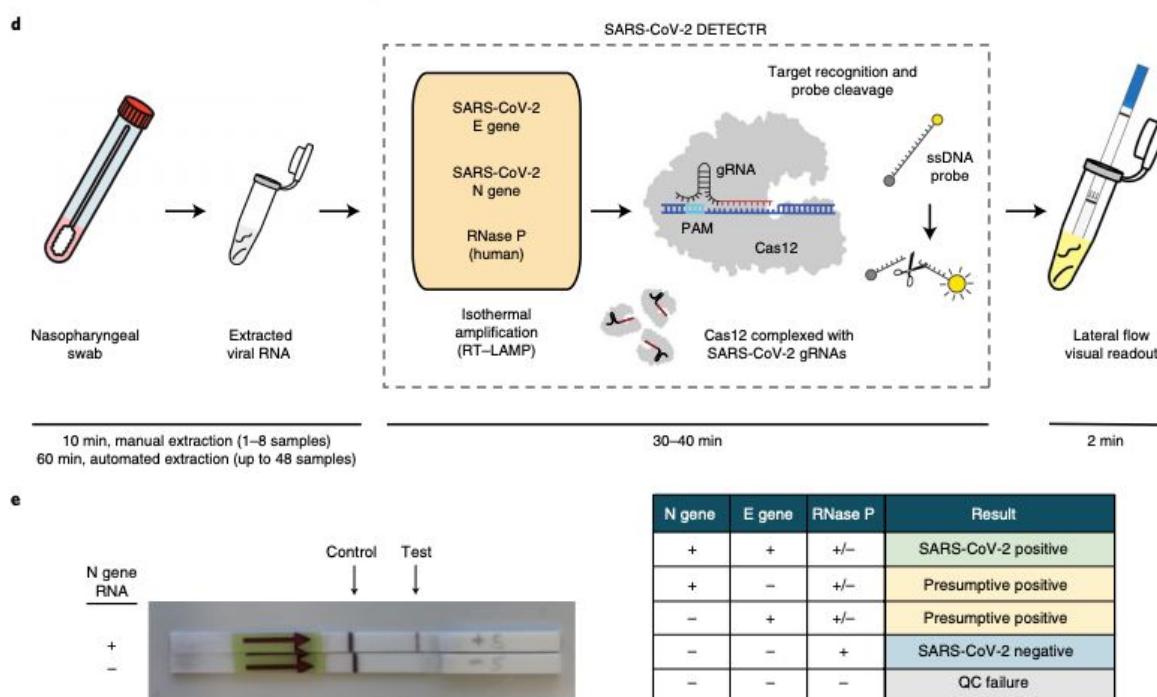


Fig. 1 | A CRISPR–Cas12-based assay for detection of SARS-CoV-2. a, Genome map showing primers, probes and gRNAs...
d, Schematic of SARS-CoV-2 DETECTR workflow. Conventional RNA extraction can be used as an input to DETECTR (LAMP preamplification and Cas12-based detection for E gene, N gene and RNase P), which is visualized by a fluorescent reader or lateral flow strip. e, Lateral flow strip assay readout. A positive result requires detection of at least one of the two SARS-CoV-2 viral gene targets (N gene or E gene, as indicated in the interpretation matrix). QC, quality control.

Development of a reverse transcription-loop-mediated isothermal amplification as a rapid early-detection method for novel SARS-CoV-2

Baek YH, Um J, Antigua KJC, Park JH, Kim Y, Oh S, Kim YI, Choi WS, Kim SG, Jeong JH, Chin BS, Nicolas HDG, Ahn JY, Shin KS, Choi YK, Park JS, Song MS

Emerg Microbes Infect

Apr 20 ,2020; PMID: 32306853

Level of Evidence: 5 - Basic research

Type of Article: Research

BLUF: The authors outline the development of their version of the reverse transcription loop-mediated isothermal amplification (RT-LAMP) assay, a type of test that shows promise due to its ease of use and quick turnaround time.

Abstract:

The previous outbreaks of SARS-CoV and MERS-CoV have led researchers to study the role of diagnostics in impeding further spread and transmission. With the recent emergence of the novel SARS-CoV-2, the availability of rapid, sensitive, and reliable diagnostic methods is essential for disease control. Hence, **we have developed a reverse transcription loop-mediated isothermal amplification (RT-LAMP) assay for the specific detection of SARS-CoV-2.**

The primer sets for RT-LAMP assay were designed to target the nucleocapsid gene of the viral RNA, and displayed a detection limit of 10² RNA copies close to that of qRT-PCR. Notably, the assay has exhibited a rapid detection span of 30 min combined with the colorimetric visualization. **This test can detect specifically viral RNAs of the SARS-CoV-2 with no cross-reactivity to related coronaviruses, such as HCoV-229E, HCoV-NL63, HCoV-OC43, and MERS-CoV as well as human infectious influenza viruses (type B, H1N1pdm, H3N2, H5N1, H5N6, H5N8, and H7N9), and other respiratory disease-causing viruses (RSVA, RSVB, ADV, PIV, MPV, and HRV).** Furthermore, the developed RT-LAMP assay has been evaluated using specimens collected from COVID-19 patients that exhibited high agreement to the qRT-PCR. Our RT-LAMP assay is simple to perform, less expensive, time-efficient, and can be used in clinical laboratories for preliminary detection of SARS-CoV-2 in suspected patients. In addition to the high sensitivity and specificity, this isothermal amplification conjugated with a single-tube colorimetric detection method may contribute to the public health responses and disease control, especially in the areas with limited laboratory capacities.

Routine Blood Tests as a Potential Diagnostic Tool for COVID-19

Ferrari, Davide; Motta, Andrea; Strollo, Marta; Banfi, Giuseppe; Locatelli, Massimo

Clin Chem Lab Med

2020 Apr 16; PMID: 32301746

Level of Evidence: 3 - Cohort Study

Type of Article: Research

BLUF: Researchers in this study compared WBC, CRP, AST, ALT, and LDH values between 207 patients admitted for COVID-19 who were then subsequently tested with PCR. **By setting empiric cutoffs for AST and LDH, the authors were able to confirm COVID-19 positive or negative patients, suggesting a use for routine labs in settings where PCR is not readily available.**

Abstract:

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to date, the epidemic has gradually spread to 209 countries worldwide with more than 1.5 million infected people and 100,000 deaths. Amplification of viral RNA by rRT-PCR serves as the gold standard for confirmation of infection, yet it needs a long turnaround time (3-4 h to generate results) and shows false-negative rates as large as 15%-20%. In addition, the need of certified laboratories, expensive equipment and trained personnel led many countries to limit the rRT-PCR tests only to individuals with pronounced respiratory syndrome symptoms. Thus, there is a need for alternative, less expensive and more accessible tests. Methods We analyzed the plasma levels of white blood cells (WBCs), platelets, C-reactive protein (CRP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ -glutamyl transpeptidase (GGT), alkaline phosphatase and lactate dehydrogenase (LDH) of 207 patients who, after being admitted to the emergency room of the San Raffaele Hospital (Milan, Italy)

with COVID-19 symptoms, were rRT-PCR tested. Of them, 105 tested positive, whereas 102 tested negative. Results Statistically significant differences were observed for WBC, CRP, AST, ALT and LDH. **Empirical thresholds for AST and LDH allowed the identification of 70% of either COVID-19-positive or -negative patients on the basis of routine blood test results.**

Conclusions Combining appropriate cutoffs for certain hematological parameters could help in identifying false-positive/negative rRT-PCR tests. Blood test analysis might be used as an alternative to rRT-PCR for identifying COVID-19-positive patients in those countries which suffer from a large shortage of rRT-PCR reagents and/or specialized laboratory.

The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients

Yang, Ai-Ping; Liu, Jian-Ping; Tao, Wen-Qiang; Li, Hui-Ming

Int Immunopharmacol

2020 Apr 13; PMID: 32304994

Level of Evidence: 3 - Retrospective Study

Type of Article: Research

BLUF: In their analysis of 69 random non-severe and 24 severe cases of COVID-19, both age and neutrophil to lymphocyte ratio were independent risk factors for poor clinical outcomes.

Abstract:

Aim: To accumulate evidence that indicated the key role played by virus-triggered inflammation in the 2019-novel coronavirus disease (COVID-19) which emerged in Wuhan City and rapidly spread throughout China.

Methods: Age, neutrophil(NEU)-to-lymphocyte (LYM) ratio (NLR), lymphocyte-to-monocyte (MON) ratio, platelet-to-lymphocyte ratio (PLR), and C-reactive protein (CRP) of 93 patients with laboratory confirmed COVID-19 were investigated and compared. The receiver operating characteristic curve was applied to determine the thresholds for five bio-markers, and their prognostic values were assessed via the Kaplan-Meier curve and multivariate COX regression models.

Results: The median age was 46.4 years old, and 37cases were females. A total of 27.8% of patients had been to Wuhan, and 73.1% had contacted with people from Wuhan. Fever (83.8%) and cough (70.9%) were the two most common symptoms. Elevated NLR and age were significantly associated with illness severity. The binary logistic analysis identified elevated NLR (hazard risk [HR] 2.46, 95% confidence interval [CI] 1.98-4.57) and age (HR 2.52, 95% CI 1.65-4.83) as independent factors for poor clinical outcome of COVID-19. NLR exhibited the largest area under the curve at 0.841, with the highest specificity (63.6%) and sensitivity (88%).

Conclusions: Elevated age and NLR can be considered independent biomarkers for indicating poor clinical outcomes.

Antibody Detection and Dynamic Characteristics in Patients with COVID-19.

Xiang F, Wang X, He X, Peng Z, Yang B, Zhang J, Zhou Q, Ye H, Ma Y, Li H, Wei X, Cai P, Ma WL. Clin Infect Dis.

2020 Apr 19; PMID: 32306047

Level of Evidence: 3 – Cross Sectional Study

Type of Article: Research

BLUF: ELISA-based IgM and IgG demonstrate outstanding specificity and PPV, suggesting that seropositive IgM and/or IgG can help to establish diagnosis of COVID-19 pneumonia, especially in patients with a protracted course of disease.

Summary: This cross-sectional study investigated the sensitivity, specificity, PPV, NPV and consistency rate of ELISA-based IgM and IgG testing, using nucleic acid testing by RT-PCR as a gold standard. The specificity and PPV of IgM were both 100%; however, the sensitivity and NPV were 73.2% and 80.0%, respectively, indicating that acute infection may still be missed based on seronegative IgM. The specificity and NPV of IgG were 95.0% and 94.8%, respectively, suggesting that patients can be diagnosed with COVID-19 pneumonia based on seropositive IgG. To avoid misdiagnosis, patients with early seronegative antibodies should be retested after 10 days of onset.

Figure 1

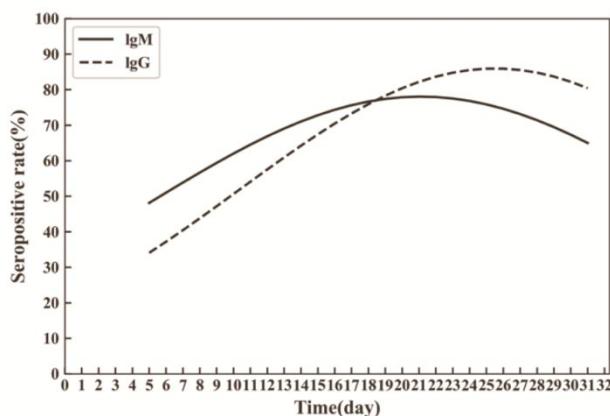


Figure 1. Detection of IgM and IgG antibodies in different periods. A log-distribution was used to describe the distribution time period of seropositive rate of the two types of antibodies. Serological IgM and IgG antibodies tested by ELISA in patients with confirmed diagnosis. The IgM and IgG antibodies were detected as positive as early as on the 4th day after onset, the seropositive rate of IgM increased gradually; however, IgG was increased sharply on the 12th day after onset.

Figure 2

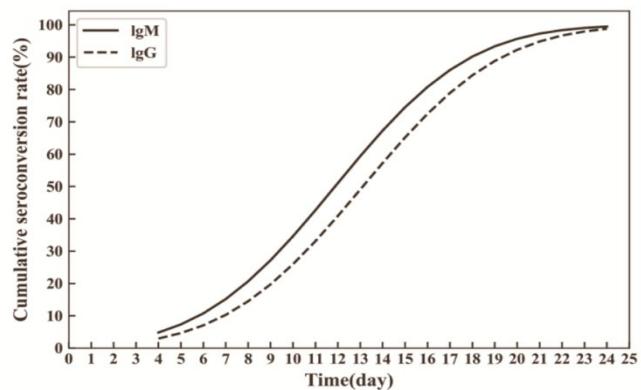


Figure 2. The timelines of initial seroconversion of IgM and IgG antibodies. A log-distribution was used to describe the distribution time period of cumulative seroconversion rate of the two antibodies. IgM cumulative seroconversion increased quickly from nearly the 8th day as well as IgG increased from nearly the 10th day after symptom onset.

Table 3. Diagnostic Roles of IgM and IgG Antibodies for COVID-19 Pneumonia *

	IgM against SARS-CoV-2		IgG against SARS-CoV-2	
	Confirmed case group	Control group	Confirmed case group	Control group
Positive	51	0	55	3
Negative	15	60	11	57
total	66**	60	66**	60

* Diagnostic value of serological IgM and IgG antibodies for COVID-19 pneumonia was evaluated in 66 patients with positive nucleic acid tests. Serum samples were obtained from patients with disease courses greater than or equal to 13 days and less than 29 days.

** 66 patients were included in the 85 confirmed cases, and their disease courses were greater than or equal to 13 days and less than 29 days.

Table 4. Detection of IgM and IgG Seropositivity for Suspected COVID-19 Pneumonia Patients *

	IgM against SARS-CoV-2		IgG against SARS-CoV-2	
	Suspected case group	Control group	Suspected case group	Control group
Positive	21	0	17	3
Negative	3	60	7	57
total	24	60	24	60

* Diagnostic value of serological IgM and IgG antibodies for suspected COVID-19 pneumonia patients was evaluated in 24 patients with negative nucleic acid tests.

Developments in Treatments

Comparative Pathogenesis of COVID-19, MERS, and SARS in a Nonhuman Primate Model

Rockx B, Thijs Kuiken T, Sander Herfst S, Theo Bestebroer T, Lamers MM, Oude Munnink BB, de Meulder D, van Amerongen G, van den Brand J, Okba NMA, Schipper D, van Run P, Leijten L, Sikkema R, Verschoor E, Verstrepen B, Bogers W, Langermans J, Drosten C, van Vlissingen NF, Fouchier R, de Swart R, Koopmans M, Haagmans BL
Science

2020 Apr 17; PMID: 32303590

Level of Evidence: 5- Basic Research

Type of Article: Report

Summary: The development of COVID-19 drugs and vaccines relies on the establishment and use of a suitable animal model for the disease. Here the authors describe a non-human primate model for SARS-CoV-2 infection and use SARS-CoV and MERS-CoV as comparison infections.

Abstract:

The current pandemic coronavirus, SARS-CoV-2, was recently identified in patients with an acute respiratory syndrome, COVID-19. To compare its pathogenesis with that of previously emerging coronaviruses, we inoculated cynomolgus macaques with SARS-CoV-2 or MERS-CoV and compared the pathology and virology with historical reports of SARS-CoV infections. In SARS-CoV-2-infected macaques, virus was excreted from nose and throat in the absence of clinical signs, and detected in type I and II pneumocytes in foci of diffuse alveolar damage and in ciliated epithelial cells of nasal, bronchial, and bronchiolar mucosae. In SARS-CoV-infection, lung lesions were typically more severe, while they were milder in MERS-CoV infection, where the virus was detected mainly in type II pneumocytes. These data show that SARS-CoV-2 causes COVID-19-like disease in macaques, and provides a new model to test preventive and therapeutic strategies.

A Detectable Serum SARS-CoV-2 Viral Load (RNAaemia) Is Closely Correlated With Drastically Elevated Interleukin 6 (IL-6) Level in Critically Ill COVID-19 Patients

Chen X, Zhao B, Qu Y, Chen Y, Xiong J, Feng Y, Men D, Huang Q, Liu Y, Yang B, Ding J, Li F
Clin Infect Dis

2020 Apr 17; PMID: 32301997

Level of Evidence: 3- Cohort study

Type of Article: Basic Research

Summary: Study of 48 patients in Wuhan, China examining serum RNA levels of SARS-CoV-2. They find a trend of higher levels of viremia and IL-6 associated with more severe disease.

Abstract:

Background: Although the detection of SARS-CoV-2 viral load in respiratory specimens has been widely used to diagnose coronavirus disease-19 (COVID-19), it is undeniable that serum SARS-CoV-2 nucleic acid (RNAaemia) could be detected in a fraction of COVID-19 patients. However, it is not clear whether testing for RNAaemia is correlated with the occurrence of cytokine storms or with the specific class of patients.

Methods: This study enrolled 48 patients with COVID-19 admitted to the General Hospital of Central Theater Command, PLA, a designated hospital in Wuhan, China. The patients were divided into three groups according to the "Diagnosis and Treatment of New

Coronavirus Pneumonia (6th edition)" issued by the National Health Commission of China. The clinical and laboratory data were collected. The serum viral load and IL-6 levels were determined. .

Results: Clinical characteristics analysis of 48 cases of COVID-19 showed that RNAaemia was diagnosed only in the critically ill group and seemed to reflect the severity of the disease. Furthermore, the level of inflammatory cytokine IL-6 in critically ill patients increased significantly, almost 10 times that in other patients. More importantly, the extremely high IL-6 level was closely correlated with the detection of RNAaemia ($R = 0.902$).

Conclusions: Detectable serum SARS-CoV-2 RNA(RNAaemia) in COVID-19 patients was associated with elevated IL-6 concentration and poor prognosis. Because the elevated IL-6 may be part of a larger cytokine storm which could worsen outcome, IL-6 could be a potential therapeutic target for critically ill patients with an excessive inflammatory response.

Keywords: Coronavirus disease-19 (COVID-19); IL-6; RNAaemia; critically ill patients; cytokine storm; pneumonia.

[**Weak Induction of Interferon Expression by SARS-CoV-2 Supports Clinical Trials of Interferon Lambda to Treat Early COVID-19**](#)

O'Brien TR, Thomas DL, Jackson SS, Prokunina-Olsson L, Donnelly R, Hartmann R

Clin Infect Dis

2020 Apr 17; PMID: 32301957

Level of Evidence: 5- Basic Research

Type of Article: Research Article

Summary: Using lung tissue from six human donors authors compare interferon production in response to SARS-CoV and SARS-CoV-2 infection. Because SARS-CoV-2 seemed to very weakly induce interferon in their in-vitro studies they make a case for the use of interferon lambda as a treatment option.

[**Clinical Pharmacology Perspectives on the Antiviral Activity of Azithromycin and Use in COVID-19.**](#)

Damle, Bharat; Vourvahis, Manoli; Wang, Erjian; Leany, Joanne; Corrigan, Brian

Clin Pharmacol Ther

2020 Apr 17; PMID: 32302411

Level of Evidence: 5 - Mechanism-Based Reasoning

Type of Article: Review

BLUF: A brief overview of the safety trials done with azithromycin (AZ) with comment upon recent studies not showing increased QT-prolongation with AZ and hydroxychloroquine. The authors also suggest AZ may play a role in reducing overall inflammation and covering COVID-19 patients with bacterial co-infection.

Abstract:

Azithromycin (AZ) is a broad-spectrum macrolide antibiotic with a long half-life and a large volume of distribution. It is primarily used for the treatment of respiratory, enteric, and genitourinary bacterial infections. AZ is not approved for the treatment of viral infections, and there is no well-controlled, prospective, randomized clinical evidence to support AZ therapy in COVID-19 (Coronavirus Infectious Disease-2019). Nevertheless, there are anecdotal reports that some hospitals have begun to include AZ in combination with hydroxychloroquine (HCQ) or chloroquine (CQ) for treatment of COVID-19. It is essential that the clinical pharmacology (CP) characteristics of AZ be considered in planning and conducting clinical trials of AZ alone or in combination with other agents, to ensure safe study conduct and to increase the probability of achieving definitive answers regarding efficacy of AZ in the

treatment of COVID-19. The safety profile of AZ used as an antibacterial agent is well-established.(1) This work assesses published in vitro and clinical evidence for AZ as an agent with antiviral properties. It also provides basic CP information relevant for planning and initiating COVID-19 clinical studies with AZ, summarizes safety data from healthy volunteer studies, and safety and efficacy from Phase 2 and Phase 2/3 studies in patients with uncomplicated malaria, including a Phase 2/3 study in pediatric patients following administration of AZ and CQ in combination. This paper may also serve to facilitate the consideration and use of a priori-defined control groups for future research.

Novel 2019 Coronavirus Structure, Mechanism of Action, Antiviral drug promises and rule out against its treatment.

Boopathi, Subramanian; Poma, Adolfo B; Kolandaivel, Ponmalai

J Biomol Struct Dyn

2020 Apr 20; PMID: 32306836

Level of Evidence: 5 – Mechanism-based reasoning

Article Type: Letter to the Editor

Summary: This article reviews various components of the covid-19 virion and recommends that institutions use computational simulations to help determine probable effectiveness of various medications including chloroquines, protease inhibitors, and nucleoside inhibitors.

The BTK-inhibitor ibrutinib may protect against pulmonary injury in COVID-19 infected patients.

Treon SP, Castillo J, Skarbnik AP, Soumerai JD, Ghobrial IM, Guerrera ML, Meid KE, Yang G

Blood

2020 Apr 17; PMID: 32302379

Level of Evidence: 5 - Expert opinion

Type of Article: Letter

Summary: Early evidence from several patients diagnosed with COVID-19 while taking ibrutinib as well as mechanism based reasoning based on prior uses and mouse models suggest that ibrutinib may be a useful therapy in decreasing lung injury and hypoxia among COVID-19 patients. Clinical trials more closely examining this potential have been initiated.

Coronavirus drugs: Using plasma from recovered patients as a treatment for COVID-19

Alzoughool F, Alanagreh L

International Journal of Risk & Safety in Medicine,

2020 Apr 13; PMID: 32310190

Level of Evidence: 5 - Expert opinion

Type of Article: Article Commentary / Literature review

Summary: Authors review history of passive immunization (PI) using convalescent plasma (CP) from recovered patients which allows for collection of large volumes per session with frequent donations without any impact on donor's hemoglobin. CP could be screened for antibodies using ELISA IgG. Authors reference positive results from use of CP in previous SARS-CoV outbreak.

Abstract

The ongoing COVID-19 pandemic has infected nearly 400,000 individuals with 17000 deaths since it was first identified in human populations in December 2019, in Wuhan, China. No antiviral therapies or vaccines are available for their treatment or prevention. Passive immunization PI through broadly neutralizing antibodies that bind to the specific antigens of SARS-CoV 2 might be a potential solution to address the immediate health threat of COVID-19 pandemic while vaccines are being developed. The PI approach in treating COVID-19 is discussed herein, including a summary of its historical applications to confront epidemics.

Peptide-like and Small-Molecule Inhibitors Against COVID-19

Pant S, Singh M, Ravichandiran V, Murty USN, Srivastava HK

J Biomol Struct Dyn

2020 Apr 20; PMID: 32306822

Level of Evidence: 5 – Mechanism-based Reasoning

Type of Article: Research

BLUF: Using recently published crystal structure of the SARS-CoV-2 main protease, the authors virtually screened compounds, including 66 FDA-approved drugs, using drug-protein docking simulations. They computationally validated the binding of current drugs of interest ritonavir and darunavir, and also uncovered 4 potential compounds with comparable or improved binding energies to SARS-CoV-2.

Abstract:

Coronavirus disease strain (SARS-CoV-2) was discovered in 2019, and it is spreading very fast around the world causing the disease Covid-19. Currently, more than 1.6 million individuals are infected, and several thousand are dead across the globe because of Covid-19. Here, we utilized the in-silico approaches to identify possible protease inhibitors against SARS-CoV-2. Potential compounds were **screened from the CHEMBL database, ZINC database, FDA approved drugs and molecules under clinical trials.** Our study is based on **6Y2F and 6W63 co-crystallized structures available in the protein data bank (PDB).** Seven hundred compounds from ZINC/CHEMBL databases and fourteen hundred compounds from drug-bank were selected based on positive interactions with the reported binding site. All the selected compounds were subjected to standard-precision (SP) and extra-precision (XP) mode of docking. Generated docked **poses were carefully visualized for known interactions within the binding site.** Molecular mechanics-generalized born surface area (MM-GBSA) calculations were performed to screen the best compounds based on docking scores and binding energy values. Molecular dynamics (MD) simulations were carried out on four selected compounds from the CHEMBL database to validate the stability and interactions. MD simulations were also performed on the PDB structure 6YF2F to understand the differences between screened molecules and co-crystallized ligand. We screened 300 potential compounds from various databases, and 66 potential compounds from FDA approved drugs. **Cobicistat, ritonavir, lopinavir, and darunavir are in the top screened molecules from FDA approved drugs.** The screened drugs and molecules may be helpful in fighting with SARS-CoV-2 after further studies.

Mental Health & Resilience Needs

[ADHD management during the COVID-19 pandemic: guidance from the European ADHD Guidelines Group.](#)

Cortese S, Asherson P, Sonuga-Barke E, Banaschewski T, Brandeis D, Buitelaar J, Coghill D, Daley D, Danckaerts M, Dittmann RW, Doepfner M, Ferrin M, Hollis C, Holtmann M, Konofal E, Lecendreux M, Santosh P, Rothenberger A, Soutullo C, Steinhagen HC, Taylor E, Van der Oord S, Wong I, Zuddas A, Simonoff E; European ADHD Guidelines Group.

Lancet Child Adolesc Health.

2020 Apr 17; PMID: 32311314

Level of Evidence: 5 - Expert Opinion

Type of Article: Comment

BLUF: Guidance of assessment and monitoring of ADHD during the COVID-19 pandemic. For families: use behavioral parenting strategies and avoid increasing medication doses as well as drug "holidays". For health care providers: continue virtual care, postpone face-to-face care, initiate pharmacological care if indicated. For regulatory authorities: allow flexibility around restrictions on ADHD medication.

Summarizing Excerpt:

"COVID-19 and the related physical distancing measures are presenting many challenges for children, young people, and their families, and these challenges are likely to be considerably greater for those with ADHD. It will therefore be important to draw upon the strategies routinely recommended in parent focused ADHD interventions, as well as mental-wellbeing interventions for children and young people. The inability to do routine, face-to-face clinical visits to initiate and monitor medication should not be viewed as an absolute contraindication to pharmacotherapy. Instead, the risks and benefits of initiating or maintaining medication under the COVID-19 restrictions implemented in some countries should be carefully considered. If the use of medication is deemed desirable, strategies for remote monitoring should be implemented."

[Public Health Approach of Ayurveda and Yoga for COVID-19 Prophylaxis.](#)

Girish Tillu 1, Sarika Chaturvedi 2, Arvind Chopra 3, Bhushan Patwardhan 1

J Altern Complement Med.

2020 Apr 20; PMID: 32310670

Level of Evidence: 5 - Expert opinion

Type of Article: Editorial

Summary: From local prophylaxis to immunomodulation, Tillu et al. described the various practices and health benefits of Ayurveda and Yoga. They propose that when used appropriately, Ayurveda, Yoga, and meditation may be effective in improving host immunity through the modulation of key targets relevant to COVID-19.

Silver Linings

World Leaders' Usage of Twitter in Response to the COVID-19 Pandemic: A Content Analysis

Rufai, Sohaib R; Bunce, Catey

J Public Health (Oxf)

2020 Apr 20; PMID: 32309854

Level of Evidence: 4 - Qualitative analysis

Type of Article: Research

BLUF: Twitter is an effective way for world leaders to rapidly communicate essential information including public health information to citizens at a time of crisis.

Summary:

Eight of nine G7 world leaders had verified and active twitter accounts with a total following of 85.7 million, that were used during the COVID-19 pandemic to communicate directly with the public.

About 82.5% of these tweets were classified to be informative and relayed public health information, 9.4% were morale boosting and 6.9% were political. **Twitter can be used as a powerful tool by world leaders to rapidly communicate public health information to citizens.**

Resources

Epidemiology and clinical features of COVID-19: A review of current literature.

Siordia JA Jr.

J Clin Virol.

2020 Apr 10; PMID: 32305884

Level of Evidence: 5 - Review

Type of Article: Review

Abstract:

Coronavirus disease 2019 is a pandemic influencing the first half of the year 2020. The virus has rapidly spread to many countries. Studies are rapidly published to share information regarding epidemiology, clinical and diagnostic patterns, and prognosis.

Acknowledgements

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