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Daily COVID-19 Literature Surveillance Summary

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NOW LIVE!

COVID-19 Daily Literature Surveillance

COVID19LST

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

Coming soon:

The Swab

Jasmine Rah

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

April 20th, 2020
Executive Summary

Climate

- Inuit communities are at higher risk for COVID-19 due to the tuberculosis epidemic in their communities.
    - This coupled with secluded locations, basic health care facilities, and insufficient COVID-19 testing led to the Ilisaqsivik Society and SeeChange Initiative, which has been developed to mitigate some of these issues by training personnel and using radio services to share information, among other efforts.
- Individuals who smoke and chew tobacco are recommended to discontinue use to decrease potential COVID-19 spread by decreasing coughing and spitting of tobacco in public areas.
- A cross-sectional survey found ~25% of Chineses ex-pats faced various forms of discrimination and violent overreaction during the outbreak of COVID-19.

Epidemiology

- A French study of 14 COVID-19 patients who developed skin lesions found that half were characterized as inflammatory lesions and half were vascular lesions.
    - In addition these dermatologists reported a large number of chilblain lesions in persons who had close contact with COVID-19 patients but exhibited no other symptoms, leading to speculation that in some people, rash is the only symptom of COVID-19.
- Retrospective hematologic analysis of 69 COVID-19 patients in Singapore found that lymphopenia, elevated LDH, and older age are associated with ICU admission.
- There are growing concerns that discontinuation of antiviral therapy may be the reason for recovered COVID-19 patients testing positive again.
- A patient in France who was admitted to the hospital for chest pain and fatigue without fever or respiratory symptoms was found to be positive for COVID-19, suggesting that myocarditis can reveal COVID-19 infection in the absence of other symptoms.

Understanding the Pathology

- Some researchers are considering the use of 3D organoids derived from induced pluripotent stem cell, specifically 3D lung bud organoids, as a possible model for ex vivo study of COVID-19 that can offer clinical translatability that other methods of using cell lines and animal models don't provide.
- Preliminary gene and protein mapping found increased expression of ACE2, which correlated with better prognosis in COVID-10 positive patients with Kidney Renal Papillary Cell Carcinoma and Uterine Corpus Endometrial Carcinoma.

Transmission & Prevention

- Evaluation of 30 nursing homes in the US found that 70% of essential long-term care workers felt that when they are sick they are still obligated to come to work. This contributes to increased risk of transmission to nursing home residents
- Experts emphasize the importance of a healthy diet rich in omega-3 fatty acids and micronutrients as a protective factor against viral infections.

Management

- A retrospective study found a high level of CRP, an acute phase reactant, is associated with poor outcomes for COVID-19 patients and thus could be used to risk stratify infected patients.
- Another retrospective cohort study found artificial intelligence significantly improved the performance of distinguishing chest CT scans of COVID-19 pneumonia from non-COVID-19 pneumonia when compared to radiologists.
- A new method for percutaneous tracheostomy where the bronchoscope is put next to instead of inside the ET tube was demonstrated safely for the 98 COVID-19 patients.
    - This method could mitigate viral aerosolization during these procedures.
- Based on a qualitative survey of patients with connective tissue disease, continued therapy is speculated to be safe if given within proper safety precautions.
- More data is needed for managing renal transplant recipients infected with SARS-CoV-2 but current recommendations are to avoid corticosteroids in severe disease.
- The International Society of Infectious Disease in Obstetrics and Gynecology (ISIDOG) has published guidelines on how to diagnose, treat, manage, and protect SARS-CoV-2 infected pregnant patients.
    - Furthermore a case series found lung ultrasound to be more sensitive than chest x-ray for detecting COVID-19 positive pregnant patients.

Adjusting Practice during COVID-19

- There are warnings to not make rash medical decisions about medication and COVID risk before there's evidence:
    - Dermatologists urge that there is insufficient evidence that psoriasis medications increase the risk of COVID-19 and argue that there is a possibility that they would be protective against COVID-19-induced cytokine storms.
- Guidelines have recently been developed in the following areas:
    - Treatment strategy for acute myocardial infarction, focusing on personal protective equipment.
    - Perioperative considerations during emergency general surgery
    - Management of swallowing disorders and recent dysphonia
    - Thyroid surgery
- Experts remind that fibrinolytic therapy can be an effective alternative to percutaneous coronary intervention during the pandemic, providing a less time and personnel intensive treatment option.
    - Though, two directors of cardiac catheterization labs stress that percutaneous coronary intervention is still the best option for reperfusion in suspected STEMI.
- A database review for topical agents used against coronaviruses found that Povidone-iodine has the potential of reducing viral load aerosolization during upper airway surgery.

- A report of everolimus toxicity in a transplant patient treated with chloroquine and lopinavir/ritonavir highlights the importance of drug interaction awareness during the COVID-19 pandemic.

R&D: Diagnosis & Treatments

- An intention-to-treat randomized control trial studied the effect of two doses of chloroquine diphosphate as adjuvant therapy in 81 inpatients with suspected or confirmed COVID-19
    - The recommendation was against the high-dose regimen of 600mg. The low statistical power of the study prevented conclusions on overall chloroquine diphosphate safety or efficacy.

Mental Health & Resilience

- Experts are calling for better psychological preparedness for traumatic events as well as reducing stigma and repercussions for seeking help.
- Over 10% of people returning to work in China during the pandemic met the criteria for post traumatic stress disorder, a recent survey found.

Silver linings:

- Experts argue that the widespread contact tracing that has been implemented for COVID-19 may provide a unique opportunity to also conduct widespread HIV testing to address two epidemics at once.

Table of Contents

Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections.

Prevention in the Hospital

Medical mask or N95 respirator: When and how to use?

COVID-19 and Risks Posed to Personnel During Endotracheal Intubation.

Working schedule, sleep quality and susceptibility to COVID-19 in healthcare workers.

Using effective hand hygiene practice to prevent and control infection.

Management

Acute care

Emergency Medicine

Predictive factors of poor outcomes in the COVID-19 epidemic: consider the inflammatory response.

Diagnostic Radiology

AI Augmentation of Radiologist Performance in Distinguishing COVID-19 from Pneumonia of Other Etiology on Chest CT

Critical Care

Novel Percutaneous Tracheostomy for Critically Ill Patients with COVID-19

Regional Planning for Extracorporeal Membrane Oxygenation Allocation During COVID-19.

Neurology

COVID-19 may induce Guillain-Barré syndrome.
Medical subspecialties

Inpatient Medicine

ISTH interim guidance on recognition and management of coagulopathy in COVID-19.

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19.

Dermatology

Potential role of Janus kinase inhibitors in COVID-19.

Cardiology

Clinical impact of renin-angiotensin system inhibitors on in-hospital mortality of patients with hypertension hospitalized for COVID-19.

Hematology and Oncology

Determining risk factors for mortality in liver transplant patients with COVID-19.

COVID-19 and its implications for thrombosis and anticoagulation.

Rheumatology

Incidence and clinical course of COVID-19 in patients with connective tissue diseases: a descriptive observational analysis.

Sleep medicine

Correspondence COVID-19: Melatonin as a potential adjuvant treatment.

Surgical Subspecialties

General Surgery

Performing abdominal surgery during the COVID-19 epidemic in Wuhan, China: a single-centred, retrospective, observational study.

Transplant Surgery

Two distinct cases with COVID-19 in kidney transplant recipients.

Managing COVID-19 in Renal Transplant Recipients: A Review of Recent Literature and Case Supporting Corticosteroid-sparing Immunosuppression.

OBGYN

ISIDOG Recommendations Concerning COVID-19 and Pregnancy.

Ophthalmology

COVID-19 Associated Pulmonary Aspergillosis.

Adjusting Practice During COVID-19

COVID-19 and the role of 3D printing in medicine.

Acute care

Neurology

The Value of Headache-Specific Recommendations During COVID-19.

Medical subspecialties

Inpatient Medicine

Inpatient Care of Patients with COVID-19: A Guide for Hospitalists.

Dermatology

No evidence of increased risk for COVID-19 infection in patients treated with Dupilumab for atopic dermatitis in a high-epidemic area - Bergamo, Lombardy, Italy.

Changes in emergency service access after spread of COVID19 across Italy.

Biologics for psoriasis in COVID-19 era: what do we know?

Cardiology

STEMI Care and COVID-19: The Value Proposition of Pharmacoinvasive Therapy.

COVID-19 and cardiovascular disease: What we know, what we think we know, and what we need to know.

A treatment strategy for acute myocardial infarction and personal protection for medical staff during the COVID-19 epidemic: the Chinese experience.

Why Fibrinolytic Therapy for STEMI in The COVID-19 Pandemic is Not Your New Best Friend.

Endocrinology

COVID-19 and diabetes: is metformin a friend or foe?

Hematology and Oncology

The After Diagnosis Head and Neck cancer-specific Patient Concerns Inventory (HaNC-AD) as a pre-treatment preparation aid during the COVID-19 pandemic.

Addressing the impact of the Coronavirus Disease (COVID-19) pandemic on hematopoietic cell transplantation: Learning networks as means for sharing best practices.

Primary Care

Do you know how COVID-19 is changing general practice/family medicine education?

Surgical Subspecialties

General Surgery

Perioperative Considerations During Emergency General Surgery in the Era of COVID-19: A U.S. Experience.

COVID-19 a Short-Term Challenge, Telewound a Lifetime Change.

Otolaryngology

Guidelines of clinical practice for the management of swallowing disorders and recent dysphonia in the context of the COVID-19 pandemic.

Topical preparations to reduce SARS-CoV-2 aerosolization in head and neck mucosal surgery.

Thyroid surgery during COVID-19 pandemic: Principles and philosophies.

Transplant Surgery

Severe COVID-19 in a renal transplant recipient: A focus on pharmacokinetics.

High-Immunological Risk Living Donor Renal Transplant during the COVID-19 Outbreak: Uncertainties and Ethical Dilemmas.

Urology

Experience from Malaysia During the COVID-19 Movement Control Order.

Urologic surgery and COVID-19: How the pandemic is changing the way we operate.

OBGYN

Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis.

Psychiatry

Access to evidence-based care for eating disorders during the COVID-19 crisis.

R&D: Diagnosis & Treatments

Current Diagnostics

Profile of IgG and IgM antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Classification of COVID-19 patients from chest CT images using multi-objective differential evolution-based convolutional neural networks.

COVID-19 and chest CT: do not put the sensitivity value in the isolation room and look beyond the numbers.

Developments in diagnostics

Clinical role of lung ultrasound for the diagnosis and monitoring of COVID-19 pneumonia in pregnant women.

The Use of Digital Health in the Detection and Management of COVID-19.

Developments in Treatments

Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Clinical Trial

The Role of Adipocytes and Adipocyte-Like Cells in the Severity of COVID-19 Infections

Probiotics and COVID-19: one size does not fit all.

Kallikrein-kinin blockade in patients with COVID-19 to prevent acute respiratory distress syndrome.

Mental Health & Resilience Needs

COVID-19's Impact on Healthcare Workforce

Experiences and Insights from the Early US COVID-19 Epicenter: A Rapid Assessment Procedure Informed Clinical Ethnography Case Series.

Response to and Recovery from the COVID-19 Pandemic: What Will It Take?

Medical personnel, COVID-19 and emotional impact.

Preserving mental health and resilience in frontline healthcare workers during COVID-19.

Impact on Public Mental Health

Is Returning to Work during the COVID-19 Pandemic Stressful? A Study on Immediate Mental Health Status and Psychoneuroimmunity Prevention Measures of Chinese Workforce.

Focus on Mental Health During the Coronavirus (COVID-19) Pandemic: Applying Learnings from the Past Outbreaks.

COVID 19 and its mental health consequences.

Resources

Interactive web-based graphs of novel coronavirus COVID-19 cases and deaths per population by country.

Covid-19 treatment update: follow the scientific evidence.

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

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

Climate

Global

Coronavirus, ageism, and Twitter: An evaluation of tweets about older adults and COVID-19.
Jimenez-Sotomayor MR, Gomez-Moreno C, Soto-Perez-de-Celis E.Jimenez-Sotomayor MR, et al.
J Am Geriatr Soc.
2020 Apr 27; PMID: 32338787
Level of Evidence: 4 - Qualitative study
Type of Article: Research
BLUF: A qualitative review of twitter content related to older adults during the time period between 3/12 and 3/21/2020. A sample of 351 tweets were analyzed out of a total 18,128 tweets. In this sample ~⅔ were personal opinions or tweets intended to be informative and ~⅛ were "likely intended to ridicule or offend". The methodology is generally well defined, however, the criteria for determining saturation or explanation of the chosen sample size was not adequately explained.

Abstract:
Objectives: In March 2020, the World Health Organization declared coronavirus disease 2019 (COVID-19) a pandemic. High morbidity and mortality rates of COVID-19 have been observed among older adults, and this has been widely reported in both mainstream and social media. The objective of this study was to analyze tweets related to COVID-19 and older adults, and to identify ageist content.
Design and settings: We obtained a representative **sample of original tweets** posted between March 12 and March 21, 2020, **containing the keywords "elderly", "older", and/or "boomer" plus the hashtags "#COVID19" and/or "#coronavirus".**
Measurements: We identified the type of user and number of followers for each account. **Tweets were classified by three raters** as: 1) informative; 2) personal accounts; 3) personal opinions; 4) advice seeking; 5) jokes; and 6) miscellaneous. Potentially offensive content, as well as that downplaying the severity of COVID-19 because it mostly affects older adults, was identified.
Results: **18,128 tweets were obtained, of which a random sample of 351 was analyzed.** Most accounts **(91.7%) belonged to individuals. The most common types of tweets were personal opinions (31.9%), followed by informative tweets (29.6%), jokes/ridicule (14.3%), and personal accounts (13.4%). Seventy-seven tweets (21.9%) likely intended to ridicule or offend someone, while 21.1% had content which implied that the life of older adults was less valuable,** or downplayed the relevance of COVID-19.
Conclusions: Most COVID-19 and older adults-related tweets contained personal opinions, personal accounts, and jokes. Almost a quarter of analyzed tweets had ageist or potentially offensive content towards older adults.

Diagnosing malaria and other febrile illnesses during the COVID-19 pandemic
Dittrich, S; Lamy, M; Acharya, S; Thu, HK; Datta, R; Blacksell, SD; Hein, PS; Mercado, CEG; Ding, XC; Chebbi, A
Lancet Glob Health
2020 Apr 24; PMID: 32339472
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
Summarizing Excerpt: "To ensure that malaria efforts stay on track, health-care workers' toolkits could be expanded to include improved tools and training to safely identify patients with malaria. Adapted health-care packages that include pragmatic advice on PPE options, training on appropriate such as respiratory rate measurements, and digital tools to support data collection and contact tracing could all support health-care workers in their task in the short term, as well as building the foundation for more integrated fever management in the future."

Inuit communities can beat COVID-19 and tuberculosis.
Kiddell-Monroe R, Ranta M, Enook S, Saranchuk P
Lancet Public Health
2020 Apr 24, PMID: 32339479
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence
Summarizing excerpt: Inuit communities are at high risk for COVID-19 due to the ongoing epidemic of tuberculosis their community faces. Communities in Nunavut, Canada are "reachable only by air, have very basic medical care facilities, and have insufficient COVID-19 testing available." "Community organisations, such as Ilisaqsivik Society and SeeChange Initiative, have developed a unique collaborative mode" that develops emergency readiness plans, radio and outline platforms to share culturally relevant COVID-19 information, train community members, and promote surveys and mask wearing.

COVID-19: home poisoning throughout the containment period.
Le Roux G, Sinno-Tellier S, Descatha A.Le Roux G, et al.
Lancet Public Health.
2020 Apr 24; PMID: 32339480
Level of Evidence: 5 - Expert Opinion
Type of Research: Correspondence
Summary: This article discusses the increase in use of home cleaners and other dangerous substances that have led to more exposures and reports of poisoning. They discussed exposures due to having children at home more and heightened levels of precautionary cleaning among COVID-19. They emphasized prevention of these cases is key as the health system is strained currently and made a call to action for data on this to learn from after the pandemic has subsided.

COVID-19 pandemic: It is time to temporarily close places of worship and to suspend religious gatherings.
Yezli S, Khan A.
J Travel Med.
2020 Apr 27; PMID: 32339236
Level of Evidence: 6 - Opinion

Type of Article: Opinion
Summary: The authors state that practicing social distancing and quarantining has been a major part of the fight against COVID-19. The authors believe "temporary closure of places of worship for group prayers and religious services should be implements *[sic]* by countries around the world (especially those with local COVID-19 transmission) regardless of faiths involved, with alternatives offered if possible, to help fight the pandemic."

Tobacco use and vaping in the COVID-19 era.
Singh AG, Chaturvedi P.
Head Neck.
2020 Apr 27; PMID: 32338805
Level of Evidence: 5 - Expert Opinion
Type of Article: Correspondence
BLUF: In this correspondence, head and neck oncology specialists in Mumbai urge individuals to discontinue smoking and chewing tobacco. Their goals are to decrease coughing and spitting of tobacco in public places and they support banning tobacco products in order to prevent further spread of COVID-19.

Abstract:
Health crises have become a popular topic of discussion. In the wave of the ongoing pandemic, experts have suggested the role of vaping and other tobacco product use exemplifying the vulnerability of the population to contract the COVID-19 *[sic]*. We discuss some of the events that led up to these conclusions and also **offer a unique insight into another form of tobacco use that is potentially propagating its spread especially in the South Asian region-chewed tobacco**. Both of these have been a perennial issue that head and neck cancer surgeons have been dealing with. Governments and head and neck cancer care providers now have an opportunity to deal with a common enemy in the midst of this pandemic.

Disparities
COVID-19 Policies can Perpetuate Violence Against Transgender Communities: Insights from Peru.
Perez-Brumer A, Silva-Santisteban A
AIDS Behav
2020 Apr 27; PMID: 32338329
Level of Evidence: 5- Expert opinion
Type of Article: Notes from the field
Summary: Recounting the failed implementation of a gender-based movement restriction policy in Peru, the authors make the argument that blanket government policies often overlook the harmful impact on already marginalized groups. They state that "It is imperative to name and document violence and, importantly, respect and learn from rapidly evolving grassroots mobilization efforts to establish broader-scale interventions and policies that will equitably protect vulnerable communities as we jointly live through and emerge from the COVID-19 pandemic."

Epidemiology

Modeling

Mathematic Modeling of COVID-19 in the United States.
Tang Y, Wang S.
Emerg Microbes Infect.
2020 Apr 26. PMID: 32338150
Level of Evidence: 5 - Mechanism-based
Type of Article: Research
Summary: The authors applied mathematical modeling using an exponential decay formula for daily growth rate to estimate various parameters concerning the COVID-19 pandemic: peak, daily new cases, and total number of cases. For the USA as a whole, the model predicted the peak to be on April 8, 2020, less than 100 new cases a day in early June, and about 1.1 million total cases in total by the end of June. The authors also performed the same analysis in individual states: Michigan, New York, and California.

COVID-19 deaths in Lombardy, Italy: data in context.
Odone A, Delmonte D, Scognamiglio T, Signorelli C
Lancet Public Health
2020 Apr 24; PMID: 32339478; No abstract available
Level of Evidence: 5 - Expert Opinion
Type of Article: Correspondence
Summary: Regional-level COVID-19 surveillance data throughout Italy show varying case fatality rates. For example, COVID-19 related deaths in Lombardy was 6x higher than in the rest of Italy. However, this data can be explained in that Lombardy was hit by the COVID-19 outbreak much earlier than other regions were, with a possibly delayed public health response and uncontrolled transmission between asymptomatic individuals at the community level.

Symptoms and Clinical Presentation

Adults

Vascular Skin Symptoms in COVID-19: A French Observational Study
Bouaziz JD et. al
J Eur Acad Dermatol Venereol
2020 Apr 27; PMID: 32339344
Level of Evidence: 3 – Retrospective cohort study
Type of Article: Research/Letter to the Editor
BLUF: This correspondence reports two categories of skin lesions observed in both outpatients and in-patients who were consulted on by the dermatologic team during a month of the COVID-19 pandemic (March-April 2020) in France. The authors describe these inflammatory eruptions and vascular lesions as appearing a few days after the virus' general symptoms in COVID-19 positive patients, but also note that a specific vascular lesion (chilblain) developed in 40 other patients that were not tested or were negative for SARS-CoV-2.

Summary: A retrospective study of **skin lesions** consulted on from March 18 – April 6, 2020, performed in an ambulatory setting of **French dermatologists and 2 French hospitals**, found **14 COVID-19 patients that developed skin lesions days after the appearance of the virus' general symptoms** of fever, fatigue, dry cough, and dyspnea. **Seven COVID-19 patients** were reported to have **inflammatory lesions** while **seven other COVID-19 patients** developed **vascular lesions**. 40 other patients with vascular lesions (chilblain subtype) were consulted on but their RT-PCR for COVID-19 detection was either negative (n = 6) or not performed (n = 34). French dermatologists also reported **numerous chilblain lesions** in **persons that had close contact with COVID-19+ patients** without COVID-19 PCR confirmation and without general symptoms of COVID-19 infections. They provide **three suggestions as to why these lesions may be showing up in those without confirmed COVID-19**, stating that 1) the lesions may be due to a confounding factor other than COVID-19; 2) the lesions may be a post-viral immunological reaction in asymptomatic COVID-19 patients; 3) the lesions may be a skin presentation in a subgroup of patients with a "peculiar" anti-viral response.

Fig 1. Vascular lesions were reported in 7 patients: violaceous macules with "porcelain-like" appearance (n=1, Figure 1A), livedo (n= 1, Figure 1B), non-necrotic purpura (n=1, Figure 1 C), necrotic purpura (n=1, Figure 1D), chilblain appearance with Raynaud's phenomenon (n=1, Figure 1E), chilblain (n=1, Figure 1F), eruptive cherry angioma (n=1, Figure 1G)

Hematologic parameters in patients with COVID-19 infection.
Fan BE.
Am J Hematol.
2020 Apr 27; PMID: 32339335
Level of Evidence: 4 - Case Series
Type of Article: Letter
Summary: Retrospective hematologic analysis of 69 COVID-19 patient samples, taken from Singapore, was performed to determine correlations between cell and platelet levels with frequency of ICU stays. Although the research is limited based on some missing patient samples and patient data post-transfer to other institutions, **preliminary conclusions demonstrate lymphopenia, raised LDH, and older age to be associated with ICU admission for patients with COVID-19 infection.**

Olfactory and rhinological evaluations in SARS-CoV-2 patients complaining of olfactory loss.
Ottaviano G, Carecchio M, Scarpa B, Marchese-Ragona R
Rhinology
2020 Apr 27; PMID: 32338254
Level of Evidence: 4 - Case Series
Type of Article: Research
BLUF: Authors at a hospital in Italy describe a case series of six patients who reported sudden smell loss that tested positive for SARS-CoV-2 via RT-PCR, suggesting that individuals who complain of sudden smell loss should undergo COVID-19 diagnostic testing. There was an overall improvement in smell and taste, although all but one patient still complained of hyposmia and hypogeusia following resolution of infection.

Abstract: Since December 2019, a novel coronavirus SARS-CoV-2 (Covid-19) outbreak emerged in China and spread rapidly in several countries. As of April 5, 2020, 1.218.474 cases were confirmed with 65.884 deaths worldwide. The clinical manifestations of Covid-19 range from asymptomatic carrier status to severe pneumonia. In a study of 7,736 Covid-19 patients in China, of all the clinical symptoms, hyposmia was not reported in any patient. **Anyway, it is now clear that olfactory dysfunction may also be present in these patients as the only or prevalent manifestation.**

Abnormalities of peripheral blood system in patients with COVID-19 in Wenzhou, China.
Sun S, Cai X, Wang H, He G, Lin Y, Lu B, Chen C, Pan Y, Hu X.
Clin Chim Acta.
2020 Apr 24; PMID: 32339487
Level of Evidence: 3 – Retrospective Study
Type of Article: Research
BLUF: The purpose of this study was to analyze the clinical application value of routine blood parameters in diagnosis and treatment of COVID-19. Specifically, the changes of routine peripheral blood parameters of 116 patients with COVID-19 in Wenzhou were retrospectively tracked and analyzed. It was noted that dynamic surveillance of eosinophils is helpful in the prediction of severe COVID-19 cases.

Abstract:
Background: In December 2019, coronavirus disease 2019 (COVID-19) was first found in Wuhan, China and soon was reported all around the world.
Methods**:** All confirmed cases with COVID-19 in Wenzhou from January 19 to February 20, 2020, were collected and analyzed. Of the 116 patients with COVID-19, 27 were diagnosed as severe cases. Among severe cases, 9 were treated in ICU. The data of blood routine examination were analyzed and compared among common patients (as common group), severe patients admitted to intensive care unit (as severe ICU group) and severe patients not admitted to ICU (as severe non-ICU group). The blood routine examination results were dynamically observed in the above groups after admission.
Results**:** Patients with COVID-19 have lower counts of leucocytes, lymphocytes, eosinophils, platelets, and hemoglobin, but have higher neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR), which were compared with controls ($P<0.001$). In severe ICU group, patients have the lowest count of lymphocytes, but the highest neutrophil count and NLR among the above three groups (all P values <0.05); NLR and MLR indicators were combined for diagnostic efficacy analysis of severe COVID-19, and its area under the curve reached 0.925. The odds ratio of the delay in days to the start of the increase of eosinophil count for predicting the outcome of patients with severe COVID-19 was 2.291 after age adjusted.
Conclusions: Patients with COVID-19 have abnormal peripheral blood routine examination results. Dynamic surveillance of peripheral blood system especially eosinophils is helpful in the prediction of severe COVID-19 cases.

Computed Tomography Manifestations of COVID-19 Pneumonia.
An P, Liu B
J Hosp Med
2020 Mar 11; PMID: 32339019
Level of Evidence: 4 - Case report
Type of Article: Case report
Summary: This report of a 44 year-old female presenting with fevers to a clinic in Hubei, China demonstrates the radiographic findings in a patient with COVID-19. Upon a positive nucleic acid test for SARS-CoV-2, initial CT showed bilateral multifocal ground glass opacities with consolidation (Figure 1). After 10 days of treatment (supplemental O_2, IV cefuroxime, oral arbidol, and lopinavir/ritonavir) her symptoms and infection foci resolved (Figure 2) and returned two negative SARS-CoV-2 nucleic acid tests.

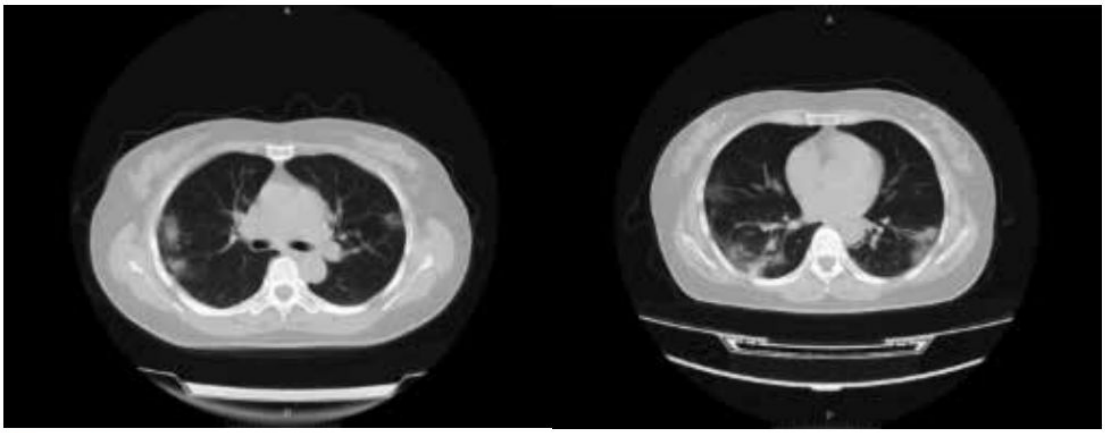


Figure 1. A 44-year-old woman presented with fever and positive polymerase chain reaction assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Representative axial thin-section chest computed tomography images show multifocal ground-glass opacities with consolidation.

Figure 2. Eight days later, her computed tomography results had returned to normal. The infection foci of both lungs were absorbed and disappeared.

Discontinuation of antiviral drugs may be the reason for recovered COVID-19 patients testing positive again.
Wu F, Zhang W, Zhang L, Wang D, Wan Y.
Br J Hosp Med (Lond)
2020 Apr 2; PMID: 32339007
Level of Evidence: 4 - Case Report
Type of Article: Case Report
BLUF: This study is a case report of a COVID-19 patient who tested positive again after testing negative and being discharged from the hospital. The authors believe that some patients who have been treated for COVID-19 and discharged have tested positive again because the discontinuation of antiviral drugs allowed lung lesions that were not completely absorbed to re-aggravate.

Summary: A 46 year old woman experienced a dry cough, throat discomfort, and fatigue after coming in close contact with a COVID-19 patient 10 days earlier. After 5 days of symptoms she was admitted to the hospital and her throat swab nucleic acid was positive for SARS-CoV-2. One day after admission she was given oxygen inhalation and antiviral therapy (lopinavir/ritonavir 400mg twice daily by mouth). 9 and 10 days after admission her symptoms improved and her nucleic acid test from her throat swab was negative both days. She was discharged and lopinavir/ritonavir was discontinued. 3 days after discharge her nucleic acid test from her throat swab was negative, however, 3 days after that (6 days after discharge) it became positive. She had only mild symptoms and was given aerosol inhalation of recombinant human interferon a1b. 3 and 4 days later her nucleic acid tests from her throat swab were both negative and she was discharged the next day. This patient was quarantined in an isolation room so subsequent exposure was unlikely and the authors concluded that the discontinuation of antiviral drugs allowed her pulmonary lesions to re-aggravate resulting in subsequent positive tests.

Myocarditis revealing COVID-19 infection in a young patient.
Paul JF, Charles P, Richaud C, Caussin C, Diakov C.

Eur Heart J Cardiovasc Imaging.
2020 Apr 27; PMID: 32338706.
Level of Evidence: 4 - Case study
Type of Article: Research
Summary: This article details the clinical presentation of a 35-year-old male who was admitted to the hospital for chest pain and fatigue without fever or respiratory signs. He tested positive for COVID-19 suggesting that the **SARS-CoV-2 infection may be atypically revealed by acute myocarditis without fever or pulmonary involvement**.

Pediatrics
First reported nosocomial outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a pediatric dialysis unit.
Schwierzeck V, König JC, Kühn J, Mellmann A, Correa-Martínez CL, Omran H, Konrad M, Kaiser T, Kampmeier S.Schwierzeck V, et al.
Clin Infect Dis.
2020 Apr 27; PMID: 32337584
Level of Evidence: 4 – Case Series
Article Type: Case Series
Summary: A COVID-19 outbreak among 48 people (28 healthcare workers, 13 patients, 7 accompanying persons) on a pediatric dialysis unit is described. Contact tracing revealed person-to person transmission was responsible. Two infected children with chronic kidney disease (CKD) were asymptomatic, but most had flu-like symptoms and/or loss of taste and smell. Authors report that their experience highlights that, **"contact tracing, assessment of exposure and optimal symptom-based testing strategies are essential to prevent outbreaks of SARS-CoV-2 within hospital settings**."

Abstract:
Background: Coronavirus disease 2019 (COVID-19) is a life-threatening respiratory condition caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was initially detected in China in December 2019. Currently, in Germany over 140,000 cases of COVID-19 are confirmed. Here we report a nosocomial outbreak of SARS-CoV-2 infections in the pediatric dialysis unit of the University Hospital of Münster (UHM).
Methods: Single-step real-time RT-PCR from nasopharyngeal swaps *[sic]* was used to diagnose the index patient and identify infected contacts. Epidemiological links were analyzed by patient interviews and chart reviews. In addition, each contact was assessed for exposure to the index case and monitored for clinical symptoms. Threshold cycle (Ct) values of all positive test results were compared between symptomatic and asymptomatic cases.
Results: Forty-eight cases were involved in this nosocomial outbreak. Nine contact cases developed laboratory confirmed COVID-19 infections. Two SARS-CoV-2 positive cases remained clinically asymptomatic. Eleven cases reported flu-like symptoms without positive results. Ct values were significantly lower in cases presenting typical COVID-19 symptoms, suggesting high viral shedding (p =0.007).
Conclusion: Person-to-person transmission was at the heart of a hospital outbreak of SARS-CoV-2 between healthcare workers (HCWs) and patients in the pediatric dialysis unit at the UHM. Semi quantitative real-time RT-PCR results suggest that individuals with high viral load pose a risk to spread SARS-CoV-2 in the hospital setting. Our epidemiological observation highlights the need to develop strategies to trace and monitor SARS-CoV-2 infected HCWs in order to prevent COVID-19 outbreaks in the hospital setting.

Additional hypotheses about why COVID-19 is milder in children than adults.
Ruggiero A, Attinà G, Chiaretti A.
Acta Paediatr
2020 Apr 27, PMID: 32339307
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
Summarizing excerpt: In response to an editorial discussing why COVID-19 has been mild in children, the authors suggest that perhaps **age and dysregulation of the immune response involving T lymphocytes are factors impacting disease severity**. The authors suggest that "the functional and phenotypic features of children's immune systems should be included when explaining their age-dependent susceptibility to COVID-19 and the severity of any disease."

Understanding the Pathology

Early risk factors for the duration of SARS-CoV-2 viral positivity in COVID-19 patients.
Lin A, He ZB, Zhang S, Zhang JG, Zhang X, Yan WH.
Clin Infect Dis.
2020 Apr 27; PMID: 32337591
Level of Evidence: 3 – Cohort Study
Type of Article: Research
Summary: The authors found that among a cohort of 137 patients with COVID-19, the median SARS-CoV-2 viral positive duration is 12 days (range: 4~45 days). They also found that the following characteristics were associated with a shorter viral positivity duration: younger age, higher count of lymphocytes, eosinophils, and CD8+ T cells, and lower level of IL-6 and IL-10.

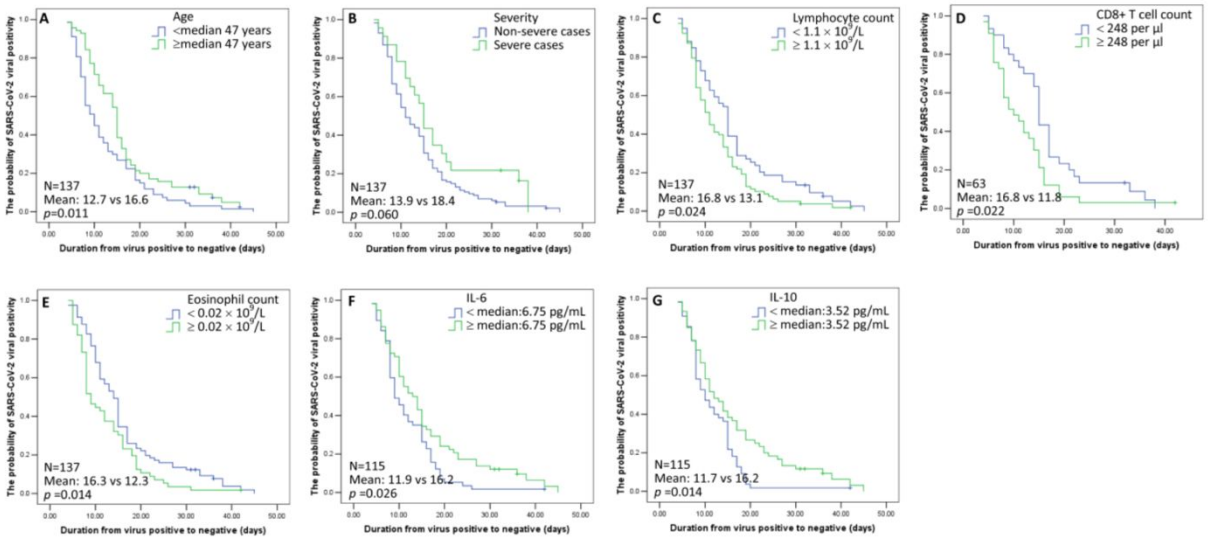


Figure 1. Kaplan-Meier method with Log-rank test was performed to evaluate the significance of clinical variables for the duration of SARS-CoV-2 viral positivity. Comparison between the groups of (A) patients age (p = 0.011); (B) severe and non-severe cases (p = 0.060); (C) lymphocytes (p = 0.024); (D) CD8+ T cells (p = 0.022); (E) eosinophils counts (p = 0.014); and (F) IL-6 (p = 0.026) and (G) IL-10 levels (p = 0.014).

ACE inhibitors and COVID-19: We don't know yet.
Khashkhusha TR, Chan JSK, Harky A.Khashkhusha TR
J Card Surg
2020 April 27; PMID: 32340070
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
BLUF: SARS-CoV-2 gains access to human cells through ACE2 receptors which poses a concern for individuals taking ACE inhibitors due to its upregulation of ACE2 receptor; however, ACE inhibitors also serve as a protective agent by blocking the renin-angiotensin-aldosterone system thus reducing inflammation in COVID-19 pneumonia.

Summary: Similar to SARS-CoV outbreak in 2003, SARS-CoV-2 the causative agent of COVID-19 gains access to the human cells via ACE2 receptor. This raises concerns for individuals with a history of hypertension or diabetes who are taking ACE inhibitors for management due to the upregulation of ACE2 receptors from ACE inhibitors. In return, this increases the risk for infection with COVID-19 for individuals taking ACE inhibitors. On the other hand, there are protective effects with the use of ACE inhibitors due to its ability to block the renin-angiotensin-aldosterone system that reduces inflammation in COVID-19 pneumonia. Overall, the concerns regarding ACE inhibitors use remains unclear due to insufficient clinical evidence.

Does apolipoprotein E genotype predict COVID-19 severity?
Goldstein MR, Poland GA, Graeber CW
QJM
2020 Apr 27; PMID: 32339247
Level of Evidence: 5 - Expert opinion
Type of Article: Correspondence
Summary excerpt: "It is possible that having one or two copies of apoE4 predisposes one to be at high risk to progress to severe illness from SARS-CoV-2, by virtue of a sequence of robust innate immune response, followed by cytokine storm, and resulting ARDS. Furthermore, apoE polymorphism may explain in part why African-Americans appear to be disproportionately affected with severe illness from COVID-19, in addition to other well known socioeconomic inequalities and risk factors."

Issues on Coronavirus Disease 2019 (COVID-19) Pathogenesis.
Silva Júnior JVJ, Lopes TRR, de Oliveira PSB, Weiblen R, Flores EF

Viral Immunol
2020 Apr 27; PMID: 32339089
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
Summary: The authors raise questions about whether antibody-dependent enhancement could be an important consideration in COVID-19 infections, possibly contributing to the increased disease severity among older patients. They also wonder whether positive tests after presumed recovery with a documented negative test indicate that SARS-CoV-2 persists in human cells allowing intermittent shedding, which has been shown to happen in a gamma-coronavirus infecting chickens.

A Potential Ex Vivo Infection Model of Human Induced Pluripotent Stem cell-3D Organoids Beyond Coronavirus Disease 2019
Zhou H, Liu LP, Fang M, Li YM, Zheng YW
Histol Histopathol
2020 Apr 27; PMID: 32339250
Level of Evidence: 5 – Mechanism-based Reasoning
Type of Article: Review
BLUF: This article reviews the use of **3D organoids derived from iPSCs** as **potential models for ex vivo study of disease** and drug screening in the advent of the COVID-19 pandemic. The authors compare commonly adopted strategies involving **cell lines and animal models**, focusing mainly on the **lack of direct clinical translatability** for either technology. Citing the ability to mimic human organs at a micro- and macroscopic level, they posit that **3D lung bud organoids might offer this clinical translatability**.

Abstract:
The novel coronavirus disease 2019 (COVID-19) outbreak began in the city of Wuhan, whereupon it rapidly spread throughout China and subsequently across the world. Rapid transmission of COVID-19 has caused wide-spread panic. Many established medications have been used to treat the disease symptoms; however, no specific drugs or vaccines have been developed. **Organoids derived from human induced pluripotent stem cells** (iPSCs) **may serve as suitable infection models** for ex vivo mimicking of the viral life cycle and drug screening. Human iPSC-3D organoids, self-organised tissues with multiple cell environments, have a **similar structure and function as real human organs**; hence, these organoids allow greater viral infection efficiency, **mimic the natural host-virus interactions**, and are suitable for long-term experimentation. Here, we suggest the use of a functional human iPSC-organoid that could act as a reliable and feasible ex vivo infection model for investigation of the virus. This approach will provide much needed insight into the underlying molecular dynamics of COVID-19 for the development of novel treatment and prevention strategies.

In silico
ACE2 correlated with immune infiltration serves as a prognostic biomarker in endometrial carcinoma and renal papillary cell carcinoma: implication for COVID-19.
Yang J, Li H, Hu S, Zhou Y.
Aging (Albany NY).
2020 Apr 27; PMID: 32339157
Level of Evidence: 5 - Mechanism-based reasoning
Type of Article: Research
BLUF: Gene and protein mapping analysis was performed to determine ACE2 expression and prognosis of KIRP and UCEC in the context of the COVID-19 pandemic. **Preliminary conclusions suggest that increased ACE2 expression correlates with better prognosis in these two cancers, but SARS-CoV-2 infection downregulates these receptors.**

Abstract: Angiotensin-converting enzyme 2 (ACE2) is a member of the renin-angiotension system, however, the correlation between ACE2 and prognosis in UCEC (Uterine Corpus Endometrial Carcinoma) and KIRP (Kidney Renal Papillary Cell Carcinoma) is not clear. We analyzed the expression levels of ACE2 in the Oncomine and TIMER databases, the correlation between ACE2 and overall survival in the PrognoScan, GEPIA and Kaplan-Meier plotter databases. The correlation between ACE2 and immune infiltration level and the type markers of immune cells was investigated in TIMER database. A prognosis analysis based on the expression levels of ACE2 was further performed in related immune cells subgroup. The ACE2 promoter methylation profile was tested in the UALCAN database. In addition, we used GSE30589 and GSE52920 databases to elucidate the changes of ACE2 expression in vivo and in vitro after SARS-CoV infection. ACE2 was elevated in UCEC and KIRP, and high ACE2 had a favorable prognosis. The expression of ACE2 was positively correlated with the level of immune infiltration of macrophage in KIRP, B cell, CD4+T cell, neutrophil and dendritic cell immune infiltration levels in UCEC. ACE2 was significantly positively correlated with the type markers of B cells and neutrophils, macrophages in UCEC, while ACE2 in KIRP was positively correlated with the type markers of macrophages. High ACE2 expression level had a favorable prognosis in different enriched immune cells subgroups in UCEC and KIRP. And the promoter methylation levels of ACE2 in UCEC and KIRP were significantly reduced. What's more, we found that the expression of ACE2 decreased in vivo and in vitro after SARS-CoV infection. In conclusion, ACE2 expression increased significantly in UCEC and KIRP, elevated ACE2 was positively correlated with immune infiltration and prognosis. Moreover, tumor tissues may be more susceptible to SARS-CoV-2 infection in COVID-19 patients with UCEC and KIRP, which may worsen the prognosis.
SARS-CoV-2 RNA dependent RNA polymerase (RdRp) targeting: An *in silico* perspective.
Elfiky, Abdo A
J Biomol Struct Dyn
2020 Apr 26; PMID: 32338164
Level of Evidence: 5 - Mechanism-based Reasoning
Type of Article: Research
BLUF: Molecular modeling, docking, and dynamics simulations are used to develop a model of the viral protein RNA-dependent RNA polymerase (RdRp) and test its binding affinity to different drug therapy candidates for COVID-19. Results yielded a list of FDA-approved antiviral treatments that exhibit binding to the SARS-CoV-2 RdRp and need to be further investigated as drug therapy options for COVID-19.

Abstract:
New treatment against SARS-CoV-2 now is a must. Nowadays, the world encounters a huge health crisis by the COVID-19 viral infection. Nucleotide inhibitors gave a lot of promising results in terms of its efficacy against different viral infections. In this work, **molecular modeling, docking, and dynamics simulations are used to build a model for the viral protein RNA-dependent RNA polymerase (RdRp) and test its binding affinity to some clinically approved drugs and drug candidates.** Molecular dynamics is used to equilibrate the system upon binding calculations to ensure the successful reproduction of previous results, to include the dynamics of the RdRp, and to understand how it affects the binding. The results

show the effectiveness of **Sofosbuvir, Ribavirin, Galidesivir, Remdesivir, Favipiravir, Cefuroxime, Tenofovir, and Hydroxychloroquine**, in binding to SARS-CoV-2 RdRp. Additionally, **Setrobuvir, YAK, and IDX-184**, show better results, while **four novel IDX-184 derivatives** show promising results in attaching to the SARS-CoV-2 RdRp. There is an urgent need to specify drugs that can selectively bind and subsequently inhibit SARS-CoV-2 proteins. The availability of a punch of FDA-approved anti-viral drugs can help us in this mission, aiming to reduce the danger of COVID-19. The compounds 2 and 3 may tightly bind to the SARS-CoV-2 RdRp and so may be successful in the treatment of COVID-19.

Transmission & Prevention

A Novel Use of Zip Lock Bags: Preserving A Sense of Humanity During COVID-19 Pandemic
McGarvey CGA, Maher-Donnelly M, Walsh PA,Moriarty JP, Keane RJ
QJM
2020 Apr 27; PMID: 32339240
Level of Evidence: 5 – Expert opinion
Type of Article: Letter to the Editor
Summary: The authors of this correspondence developed a **cost-effective way to combat the tragic isolation of patients** receiving end of life care in a COVID-19 ward in Ireland while minimizing risk of contraction: **polyethylene zip lock bags as protective covers on smart devices** that have video/call functionality.

Prevention in the Community
Essential Long-Term Care Workers Commonly Hold Second Jobs and Double- or Triple-Duty Caregiving Roles.
Van Houtven CH, DePasquale N, Coe NB.Van Houtven CH, et al.
J Am Geriatr Soc.
2020 Apr 27; PMID: 32338767
Level of Evidence: 4- Secondary Analysis
Type of Article: Research
Summary: The authors evaluate 30 nursing home facilities in the US and measure long-term health care workers characteristics. They find **over 70% of these workers agreed or strongly agreed** with the following statement: "**When you are sick, you still feel obligated to come into work.**" One-sixth had a second job, where they worked an average of 20 hours per week, and over 60% held double- or triple-duty caregiving roles. To slow the spread of COVID-19, both the paid and unpaid activities of these employees warrant consideration.

Contact tracing for COVID-19: An opportunity to reduce health disparities and End the HIV/AIDS Epidemic in the US.
Nosyk B, Armstrong WS, Del Rio C.
Clin Infect Dis.
2020 Apr 27; PMID: 32339245
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
Abstract: "SARS-CoV2 testing and contact tracing have been proposed as critical components of a safe and effective COVID-19 public health strategy. We argue that COVID-19 contact tracing may provide a unique opportunity to also conduct widespread HIV testing, among other health promotion activities."

Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections.
Calder PC, Carr AC, Gombart AF, Eggersdorfer M
Nutrients
2020 Apr 23; PMID: 32340216
Level of Evidence: 5 - Expert Opinion
Type of Article: Review
BLUF: In addition to handwashing and getting vaccinations to prevent the transmission of infections, nutritional status is also an important factor against the viral impact. This review article highly recommends supplementing with micronutrients and omega-3 fatty acids to support optimal immune function, and therefore reduce the risk and consequences of infections.

Abstract:
Public health practices including handwashing and vaccinations help reduce the spread and impact of infections. Nevertheless, the global burden of infection is high, and additional measures are necessary. Acute respiratory tract infections, for example, were responsible for approximately 2.38 million deaths worldwide in 2016. The role nutrition plays in supporting the immune system is well-established. A wealth of mechanistic and clinical data show that vitamins, including **vitamins A, B6, B12, C, D, E, and folate; trace elements, including zinc, iron, selenium, magnesium, and copper; and the omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid play important and complementary roles in supporting the immune system**. Inadequate intake and status of these nutrients are widespread, leading to a decrease in resistance to infections and as a consequence an increase in disease burden. Against this background the following **conclusions are made: (1) supplementation with the above micronutrients and omega-3 fatty acids is a safe, effective, and low-cost strategy to help support optimal immune function; (2) supplementation above the Recommended Dietary Allowance (RDA), but within recommended upper safety limits, for specific nutrients such as vitamins C and D is warranted; and (3) public health officials are encouraged to include nutritional strategies in their recommendations to improve public health.**

Prevention in the Hospital
Medical mask or N95 respirator: When and how to use?
Azap A, Erdinç FŞ.Azap A, et al.Turk J Med Sci.
2020 Apr 27; PMID: 32336079
Turk J Med Sci.
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
Summary: This article described face masks in reducing health care workers' COVID-19 risk, citing the dependence on setting, type of personnel, and activity. They agreed with most guidelines that patients should wear medical surgical masks, but added that the N95 masks studies claiming they were more effective against COVID-19 often were underpowered or lacked control groups. They noted a study recently which showed that N95 and medical surgical masks were equally effective. Finally, they made mask recommendations. (see figure below)

Abstract:
COVID-19 pandemic is now a global threat on human health reaching up to 2 million infected people all around the World. Since its first recognition in Wuhan, many topics were discussed intensively about COVID-19, both in the public and scientific community. Personal protective equipments *[sic]* and

especially masks *[sic]* were among the hottest topics during this pandemic. Regardless of which mask is used, performing hand hygiene frequently with an alcohol-based hand rub or with soap and water if hands are dirty; is the most effective preventive measure for COVID-19. The type of mask used when caring for COVID-19 patients will vary according to the setting, type of personnel/person, and activity. Although the main transmission route for COVID-19 is droplets, during aerosol generating procedures airborne transmission may occur. Keeping the distancing and medical masks and eye protection during close contact efficiently protects against respiratory diseases transmitted via droplets. Airborne precautions include goggles and respiratory protection with the use of an N95 or an equivalent mask respirator to prevent airborne transmission.

Table. The type of mask used when caring for COVID-19 patients [3,5].

Setting	Target personnel or patients	Activity	Type of mask
Inpatient facilities			
Screening	HCWs	Preliminary contact not involving direct contact	If physical distance (1 m) is feasible, no need for face mask; when not feasible, use a medical mask.
	Patients with symptoms suggestive of COVID-19	Any	Medical mask
	Patients without symptoms suggestive of COVID-19	Any	If the incidence of COVID-19 is low, no need for medical mask. When the incidence is high, cloth face masks/ coverings may be used.
Patient room	HCWs	Providing direct care (no aerosol-generating procedures)	Medical mask
	HCWs	Direct care (aerosol-generating procedures are frequently in place)	N95/FFP2 respirators
	Cleaners	Entering the room of COVID-19 patients	Medical mask
Areas of transit where patients are not allowed	All staff, including HCWs	Any activity that does not involve contact with COVID-19 patients	No masks are required. Maintain physical distance (if not feasible, cloth face coverings/masks may be used).
Laboratory	Lab technician	Manipulation of respiratory samples of suspected COVID-19 patients	N95/FFP2 respirators
Administrative areas	All staff, including HCWs	Administrative tasks that do not involve contact with COVID-19 patients.	No masks are required Maintain physical distance (if not feasible, cloth face coverings/masks may be used).
Outpatient facilities			
Screening/triage	HCWs	Preliminary contact not involving direct contact	If physical distance (1 m) is feasible, no need for face mask; when not feasible use a medical mask.
	Patients with symptoms suggestive of COVID-19	Any	Medical mask
	Patients without symptoms suggestive of COVID-19	Any	Mask is not required if physical distance is maintained.
Waiting room	Patients with symptoms suggestive of COVID-19	Any	Medical mask
	Patients without symptoms suggestive of COVID-19	Any	Mask is not required if physical distance is maintained.
Consultation room	HCWs	Physical examination	Medical mask
	Patients	Any	Medical mask
	Cleaners	After and between consultations with patients with respiratory symptoms.	Medical mask

Administrative areas	All staff, including HCWs	Administrative tasks	No masks are required. Maintain physical distance (if not feasible, cloth face coverings/masks may be used).
Home care			
Home	Patients with symptoms suggestive of COVID-19	Any	Medical mask (except sleeping)
	Caregiver	Entering the patients room but not providing direct care or assistance	Medical mask
	Caregiver	Providing direct care	Medical mask
	HCWs	Providing direct care	Medical mask
Community Settings			
	Anyone	Indoor environment	Maintain physical distance (if not feasible, cloth face coverings/masks may be used).
		Outdoor environment	Maintain physical distance. No mask required.

COVID-19 and Risks Posed to Personnel During Endotracheal Intubation.
Weissman DN, de Perio MA, Radonovich LJ Jr
JAMA
2020 Apr 27; PMID: 32338710
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
Summary: Authors discuss the high risk to health care personnel during endotracheal intubation (significantly increased odds ratio of 6.6 when compared to other aerosolizing procedures) and note that viral particles may land on uncovered facial skin, hair, and shoes, suggesting the need for adherence to hand hygiene and the possible benefit of using powered air-purifying respirators. Protection of SARS-CoV-2 susceptible tissues (eyes, nose, mouth) is crucial.

Working schedule, sleep quality and susceptibility to COVID-19 in healthcare workers.
Belingheri M, Paladino ME, Riva MA
2020 Apr 27; Clin Infect Dis.
PMID: 32339218
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
BLUF: The authors respond to a recent paper by Ran et al., which found that healthcare workers with longer duty hours may be at higher risk for infection. Based on their findings, Ran et al. suggested limiting shift work for healthcare workers to <10 hours/day. In response, Belingheri and colleagues suggest that shift work and sleep quality could be important predisposing factors to COVID-19 in healthcare workers, thus should be considered in future studies.

Summarizing statement: "**A recent prospective cohort study showed that shift workers in healthcare had 20% more acute respiratory infection and influenza-like illness than non-shift workers [7].** These infections also appeared to be more severe also. Perceived sleep quality seems to be an underlying mechanism in the relation between shift work and increase infection susceptibility [8]. **No studies have been still conducted on the association between shift work, sleep quality and COVID-19 infection,** but it is presumed that the mechanisms are similar. Stress could also played a determinant role in worsening sleep quality, as already evidenced in previous studies [4]. Undoubtedly, during the COVI-19 outbreak, HCWs are exposed to an unprecedented stressful situation of unknown duration,with an important emotional involvement. For these reasons, recommendations to healthcare staff on working schedule –including the considerations of Ran et al. on prolonged hours –should be widespread in the hospitals and well known by hospital managers.
Finally, **we believe that future studies on susceptibility of HCWs to COVID-19 should not limit to analyze the demographic characteristics of workers and the presence of protective equipment, but they should also consider working conditions in the hospital, including an analysis of shift work and its effects of sleep quality**. The study by Ran et al. could be a starting point."

Using effective hand hygiene practice to prevent and control infection.
Hillier Mark Dexter MD
Nurs Stand
2020 April 29; PMID: 32337862
Level of Evidence: 5 Expert Opinion
Type of Article: Educational
BLUF: "The COVID-19 pandemic has emphasised the importance of effective hand hygiene practice. However, it is important to stress that healthcare staff should maintain hand hygiene standards at all times, not simply during challenging circumstances."

Summary: Decontamination using hand hygiene remains one of the most important and effective methods for reducing healthcare-associated infections and cross-infection between patients. In 1860, Florence Nightingale wrote that nurses should wash their hands frequently throughout the day, demonstrating an early awareness of the effectiveness of this simple procedure. The COVID-19 pandemic has demonstrated that effectively applied hand hygiene is a vital intervention that can be used to prevent the spread of disease. This article details the correct procedure required for effective hand hygiene and emphasises the need for nurses to keep up to date with evidence-based guidelines. The article also outlines the differences between hand decontamination using alcohol-based hand gels and soap and water, and the complex factors that can interfere with effective hand hygiene compliance.

Management

Acute care

Emergency Medicine

Predictive factors of poor outcomes in the COVID-19 epidemic: consider the inflammatory response.

Razanamahery J, Malinowski L, Humbert S, Brunel AS, Lepiller Q, Chirouze C, Bouiller K

Med Mal Infect

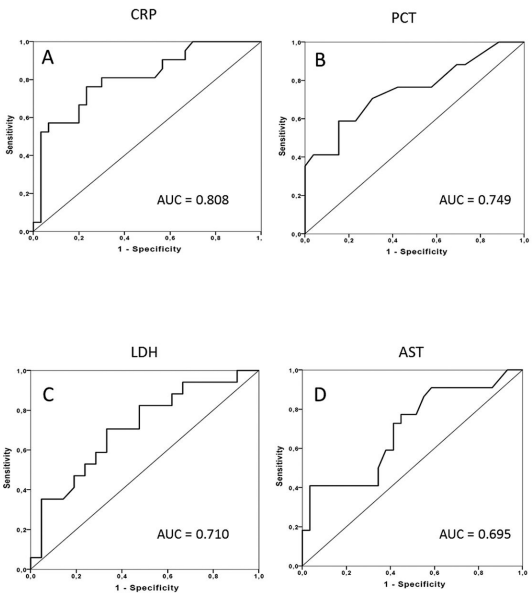
2020 Apr 24; PMID: 32339596

Level of Evidence: 3 - Retrospective Cohort Study

Type of Article: Letter to Editor/Research

BLUF: The authors conducted a retrospective cohort study on 52 hospitalized COVID-19 patients at the Besancon University Hospital in France and found that high CRP levels was associated with poor outcomes (ICU transfer or death) and thus could most accurately be used in risk stratification for patients infected with COVID-19.

Summary: This research was conducted at the Besancon University Hospital in France in response to C-reactive protein levels in the early stage of COVID-19 by Wang et al, which suggested that CRP levels were positively correlated with lung lesions and COVID-19 disease severity. This retrospective cohort study analyzed various labs including acute phase reactants (CRP, PCT, ferritin, fibrinogen), CBC and metabolic panels in 52 hospitalized patients at this tertiary care center in France to correlate them with severe disease leading to poor outcomes (defined as ICU transfer or death). They found that high levels of CRP, PCT, AST and LDH were associated with poor outcomes, though high CRP levels were the most accurate at predicting poor outcomes (AUC 0.808 [figure 1]). The authors then conclude that their data concurred with that of Wang et al suggesting that CRP levels had the best predictive value in regard to predicting disease severity.



CRP value (mg/L)	Sensitivity	1-specificity
0,00	1,00	1,00
2,00	1,00	0,97
3,50	1,00	0,90
5,00	1,00	0,87
8,00	1,00	0,80
10,50	1,00	0,77
11,50	1,00	0,73
13,00	1,00	0,70
15,00	0,95	0,67
18,50	0,91	0,67
24,50	0,91	0,63
29,50	0,91	0,60
31,50	0,91	0,57
36,50	0,86	0,57
41,50	0,81	0,53
44,50	0,81	0,50
47,50	0,81	0,43
49,00	0,81	0,40
52,50	0,81	0,37
56,50	0,81	0,33
63,00	0,81	0,30
69,00	0,76	0,30
73,00	0,76	0,23
85,50	0,71	0,23
96,00	0,67	0,23
98,50	0,67	0,20
102,50	0,62	0,20
107,50	0,57	0,20
115,50	0,57	0,17
123,50	0,57	0,13
130,50	0,57	0,10
137,50	0,57	0,07
147,50	0,52	0,07
158,00	0,52	0,03
166,50	0,43	0,03
179,00	0,38	0,03
187,50	0,33	0,03
198,00	0,29	0,03
232,00	0,24	0,03
261,50	0,19	0,03
278,50	0,14	0,03
293,50	0,10	0,03
297,50	0,05	0,03
389,00	0,05	0,00
480,00	0,00	0,00

Figure 1. Receiver operating characteristic (ROC) curves for CRP (A), PCT (B), LDH (C), and AST (D) in the prediction of poor outcome. AUC: area under the curve

Diagnostic Radiology

AI Augmentation of Radiologist Performance in Distinguishing COVID-19 from Pneumonia of Other Etiology on Chest CT

Bai, HX; Wang, R; Xiong, Z; Hsieh, B; Chang, K; Halsey, K; Tran, TML; Choi, JW; Wang, DC; Shi, LB; Mei, J; Jiang, XL; Pan, I; Zeng, QH; Hu, PF; Li, YH; Fu, FX; Huang, RY; Sebro, R; Yu, QZ; Atalay, MK; Liao, WH

Radiology

2020 Apr 27; PMID: 32339081

Level of Evidence: 3 - Retrospective Cohort Study

Type of Article: Research

BLUF: Authors performed a study comparing radiologist performance in distinguishing COVID-19 pneumonia versus non-COVID-19 with or without the use of artificial intelligence (AI). AI was found to improve performance significantly. The study was performed with retrospectively selected cases, 521 confirmed COVID-19 patients with abnormal chest computed tomography (CT) and 665 non-COVID-19 pneumonia CTs.

Abstract:

Background COVID-19 and pneumonia of other etiology share similar CT characteristics, contributing to the challenges in differentiating them with high accuracy. Purpose To establish and evaluate an artificial intelligence (AI) system in differentiating COVID-19 and other pneumonia on chest CT and assess radiologist performance without and with AI assistance.

Methods 521 patients with positive RT-PCR for COVID-19 and abnormal chest CT findings were retrospectively identified from ten hospitals from January 2020 to April 2020. 665 patients with non-COVID-19 pneumonia and definite evidence of pneumonia on chest CT were retrospectively selected from three hospitals between 2017 and 2019. To classify COVID-19 versus other pneumonia for each patient, abnormal CT slices were input into the EfficientNet B4 deep neural network architecture after lung segmentation, followed by two-layer fully-connected neural network *[sic]* to pool slices together. Our final cohort of 1,186 patients (132,583 CT slices) was divided into training, validation and test sets in a 7:2:1 and equal ratio. Independent testing was performed by evaluating model performance on separate hospitals. Studies were blindly reviewed by six radiologists without and then with AI assistance.

Results Our final model achieved a test accuracy of 96% (95% CI: 90-98%), sensitivity 95% (95% CI: 83-100%) and specificity of 96% (95% CI: 88-99%) with Receiver Operating Characteristic (ROC) AUC of 0.95 and Precision-Recall (PR) AUC of 0.90. On independent testing, our model achieved an accuracy of 87% (95% CI: 82-90%), sensitivity of 89% (95% CI: 81-94%) and specificity of 86% (95% CI: 80-90%) with ROC AUC of 0.90 and PR AUC of 0.87. Assisted by the models' probabilities, the radiologists achieved a higher average test accuracy (90% vs. 85%, Δ=5, p<0.001), sensitivity (88% vs. 79%, Δ=9, p<0.001) and specificity (91% vs. 88%, Δ=3, p=0.001).
Conclusion AI assistance improved radiologists' performance in distinguishing COVID-19 from non-COVID-19 pneumonia on chest CT.

Novel Percutaneous Tracheostomy for Critically Ill Patients with COVID-19
Angel, L; Kon, ZN; Chang, SH; Rafeq, S; Shekar, SP; Mitzman, B; Amoroso, N; Goldenberg, R; Sureau, K; Smith, D; Cerfolio, RJ
Ann Thorac Surg
2020 Apr; PMID: 32339508
Level of Evidence: 4 - Case Series
Type of Article: Research
BLUF: Authors present a new method for percutaneous tracheostomy - putting the bronchoscope next to but not inside the ET tube - alongside a case series in the patients who required it, demonstrating safety for the 98 COVID-19 patients involved in the study. The authors also propose this will mitigate viral aerosolization during percutaneous tracheostomy procedures.

Abstract:
Background: COVID-19 is a worldwide pandemic, with many patients requiring prolonged mechanical ventilation. Tracheostomy is not recommended by current guidelines as it is considered a super-spreading event due to aerosolization that unduly risks healthcare workers.
Methods: Patients with severe COVID-19 that were on mechanical ventilation ≥ 5 days were evaluated for percutaneous dilational tracheostomy. We developed a novel percutaneous tracheostomy technique that placed the bronchoscope alongside the endotracheal tube, not inside it. This improved visualization during the procedure and continued standard mechanical ventilation after positioning the inflated endotracheal tube cuff in the distal trachea. This technique offers a significant mitigation for the risk of virus aerosolization during the procedure.
Results: From March 10 to April 15, 2020, 270 patients with COVID-19 required invasive mechanical ventilation at New York University Langone Health Manhattan's campus of which 98 patients underwent percutaneous dilational tracheostomy. The mean time from intubation to the procedure was 10.6 days (SD ±5 days). Currently, thirty-two (33%) patients do not require mechanical ventilatory support, 19 (19%) have their tracheostomy tube downsized and 8 (8%) were decannulated. Forty (41%) patients remain on full ventilator support, while 19 (19%) are weaning from mechanical ventilation. Seven (7%) died as result of respiratory and multiorgan failure. Tracheostomy related bleeding was the most common complication (5 patients). None of health care providers have developed symptoms or tested positive for COVID-19.
Conclusions: Our percutaneous tracheostomy technique appears to be safe and effective for COVID-19 patients and safe for healthcare workers.

Regional Planning for Extracorporeal Membrane Oxygenation Allocation During COVID-19.
Prekker ME, Brunsvold ME, Bohman JK, Fischer G, Gram KL, Litell JM, Saavedra-Romero R, Hick JL.Prekker ME, et al.
Chest
2020 Apr 24; PMID: 32339510
Level of Evidence: 5 – Expert Opinion
Article Type: Editorial
Summary: Working from the expectation that hospitals will be overfull and critical care resources spread thin, the authors suggest critical care experts work with incident response networks to develop a system to maintain situational awareness about extracorporeal membrane oxygenation (ECMO) available in the local geographic area, to preserve availability of experts for consultation on ECMO, and to triage resources such that ECMO can be used for patients most likely to benefit. They present a framework for decision-making when ECMO resources are limited (table below).

Tier (Predicted survival)	Short Duration ECMO Anticipated (≤5 days)	Long Duration ECMO Anticipated (>5 days)
Tier 1 (>60%)	Acute hypercarbic respiratory failure due to status asthmaticus Cardiac arrest or cardiogenic shock due to severe accidental hypothermia (i.e. extracorporeal rewarming) Pediatric pre- and post-cardiotomy cardiogenic shock Neonatal meconium aspiration syndrome	Acute respiratory failure due to infection (especially influenza or coronavirus) with single-organ failure Acute respiratory failure due to trauma (drowning, pulmonary contusion, etc.) with single-organ failure Pediatric myocarditis Other neonatal indications (including sepsis, congenital diaphragmatic hernia, and persistent pulmonary hypertension of the newborn)
Tier 2 (30-60%)	Poisoning-induced cardiogenic shock Massive pulmonary embolism	Acute respiratory failure from any cause with multi-organ failure (including kidney injury requiring dialysis or hypotension requiring vasopressor support) Pediatric/neonatal cardiac arrest from a cardiac etiology
Tier 3 (<30%)	Adult post-cardiotomy cardiogenic shock Out-of-hospital, refractory cardiac arrest with favorable prognostic features (i.e. extracorporeal cardiopulmonary resuscitation [E-CPR]) Cardiac arrest with non-shockable rhythm or unfavorable prognostic features (including most adults with in-hospital cardiac arrest)	Bridge to lung transplantation for irreversible respiratory failure Acute respiratory failure and severe immunocompromise (e.g. stem cell transplant <240 days post-transplant) Cardiovascular collapse refractory to vasopressors in the setting of multi-organ failure of any cause (e.g. septic shock)

Journal Pre-proof

Table 1: Framework for prioritizing common ECMO indications during a disaster, by predicted survival and duration of support

Neurology

COVID-19 may induce Guillain-Barré syndrome.

Camdessanche JP, Morel J, Pozzetto B, Paul S, Tholance Y, Botelho-Nevers E.Camdessanche JP, et al.
Rev Neurol (Paris)
2020 Apr 15; PMID: 32334841
Level of Evidence: 4 - Case Report
Article Type: Editorial

Summary: A 64 year-old man with no significant PMH was admitted to the hospital after a fall and rotator cuff tear, and found incidentally positive for COVID-19. He subsequently developed weakness, difficulty swallowing, and respiratory insufficiency. Motor nerve conduction tests suggested demyelination most consistent with GBS. Authors note that such cases precipitated by COVID-19 could be mistaken for ICU-related deconditioning and weakness, and advocate caution and vigilance.

Medical subspecialties

Inpatient Medicine

ISTH interim guidance on recognition and management of coagulopathy in COVID-19.

Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, Clark C, Iba T.
J Thromb Haemost.
2020 Mar 25. PMID: 32338827
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary

Summary: High D-dimer levels are associated with higher mortality in COVID-19 patients. This paper recommends to order the following for all COVID-19 patients: D-dimer, prothrombin time, platelet count; fibrinogen is useful too, but assays may not be widely available. If admitted for suspected coagulopathy, the recommended drug is prophylactic low molecular weight heparin.

Dermatology

Potential role of Janus kinase inhibitors in COVID-19.

Napolitano M, Fabbrocini G, Patruno C
J Am Acad Dermatol
2020 Apr 24; PMID: 32339701
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter to the Editor

BLUF: Authors suggest that patients taking Janus Kinase inhibitors such as Baricitinib or Upatacinib for atopic dermatitis should continue to take these medications in the setting of COVID-19. Despite a recent article expressing concerns for these medications decreasing antiviral activity, these authors point out other literature that suggest that these medications could actually be protective of COVID-19 by blocking viral entry or dampening the cytokine storm.

Summary: This letter is in response to The use of Janus kinase inhibitors in the time of SARS-CoV-2 by Peterson et al, which suggests that these medications be discontinued during initial COVID-19 infection to promote antiviral activity via JAK-STAT dependent interferons. Authors of this letter point out that more recent literature would suggest that Janus Kinase inhibiting drugs such as Baricitinib could actually be beneficial in treating COVID-19 due to its capability to reduce viral entry into lung cells by inhibiting AP2-associated protein kinase 1. Additionally they suggest that Upatacinib (selective JAK1 inhibitor) could also be beneficial in treatment of COVID-19 rather than detrimental due to its ability to reduce levels of IL-6 which is a cytokine known to cause lung damage in COVID-19. Both Baricitinib and Upatacinib are medications that are currently either being used or trialed in treatment of atopic dermatitis and the authors suggest that evidence would point towards patients with atopic dermatitis continuing rather than discontinuing these medications in the setting of the COVID-19 pandemic.

Cardiology

Clinical impact of renin-angiotensin system inhibitors on in-hospital mortality of patients with hypertension hospitalized for COVID-19.

Tedeschi S, Giannella M, Bartoletti M, Trapani F, Tadolini M, Borghi C, Viale P.
Journal Clinical Infectious Disease
2020 Apr 27; PMID: 32339215
Level of Evidence: 3- Prospective Cohort
Type of Article: Letter to the Editor

Summary: A multicenter prospective cohort study of 311 hospitalized COVID-19 patients with hypertension found that independent predictors of in-hospital mortality were sequential organ failure assessment **(SOFA) score on admission** (aHR 1.32, 95% CI 1.20-1.45; p<0.001) and **age** (aHR 1.05, 95% CI 1.03-1.07). **Chronic use of renin-angiotensin inhibitors were not associated with outcome.** Limitations include lack of randomization and selection bias for sicker patients (all cause mortality 29%).

Hematology and Oncology

Determining risk factors for mortality in liver transplant patients with COVID-19.

Webb GJ, Moon AM, Barnes E, Barritt AS, Marjot T.
Lancet Gastroenterol Hepatol.
2020 Apr 24; PMID: 32339474
Level of Evidence: 4 – Case series
Type of Article: Research

BLUF: Nine (23%) of 39 liver transplant patients who contracted COVID-19 died from respiratory failure; comorbidities in patients who died did not significantly differ from those who survived.

Summary:
Two collaborating international registries (SECURE Cirrhosis, covering the Americas, China, Japan, and South Korea; and COVID-Hep covering the rest of the world) worked to collate details of patients with chronic liver disease and post-liver transplantation who develop COVID-19. Submissions to the registries were received from 21 countries. **Details from the 39 liver transplant recipients who developed COVID-19 are summarized herein.**

COVID-19 and its implications for thrombosis and anticoagulation.

Connors JM, Levy JH.
Blood
2020 Apr 27; PMID: 32339221
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

BLUF: COVID-19 is associated with a coagulopathy consistent with DIC, presenting with prominent elevation of D-dimer and fibrin/fibrinogen degradation products and treated with the standard supportive-care measures for DIC. Monitoring of D-dimer and fibrinogen levels is suggested, but full intensity anticoagulation doses are not recommended unless otherwise clinically indicated.

Abstract:
The SARS-CoV-2 coronavirus (COVID-19) induced infection can be associated with a coagulopathy, findings consistent with infection induced inflammatory changes as observed in patients with disseminated intravascular coagulopathy (DIC). The lack of prior immunity to COVID-19 has resulted in large numbers of infected patients across the globe and uncertainty regarding management of the complications that arise in the course of this viral illness. The lungs are the target organ for COVID-19; patients develop acute lung injury which can progress to respiratory failure, although multiorgan failure can also occur**. The initial coagulopathy of COVID-19 presents with prominent elevation of D-dimer and fibrin/fibrinogen degradation products,** while abnormalities in prothrombin time, partial thromboplastin time, and platelet counts are relatively uncommon in initial presentations. **Coagulation test screening, including the measurement of D-dimer and fibrinogen levels, is suggested.** COVID-19 associated coagulopathy should be managed as it would be for any critically ill patient, following the established practice of using thromboembolic prophylaxis for critically ill hospitalized patients, and standard supportive care measures for those with sepsis-induced coagulopathy or DIC. Although D-dimer, sepsis physiology, and consumptive coagulopathy are indicators of mortality, **current data do not suggest the use of full intensity anticoagulation doses unless otherwise clinically indicated**. Even though there is an associated coagulopathy with COVID-19, bleeding manifestations, even in those with DIC, have not been reported. If bleeding does occur, standard guidelines for the management of DIC and bleeding should be followed.

Rheumatology
Incidence and clinical course of COVID-19 in patients with connective tissue diseases: a descriptive observational analysis.
Favalli EG, Agape E, Caporali R.
J Rheumatol.
2020 Apr 25, PMID: 32335513
Level of Evidence: 5 - Qualitative survey
Article Type: Research
BLUF: The authors conducted a survey on patients with connective tissue disease to determine the impact COVID-19 has on their disease. Of the 123 patients included in the study 115 did not experience flare ups and have continued with rheumatological therapy. One 32-year old patient with systemic scleroderma developed interstitial pneumonia and died from respiratory complications while others with suspected infection developed mild symptoms. The authors concluded it is safe to continue therapy for patients with connective tissue disease with proper safety precautions.

Abstract:
The outbreak of COVID-19 in December 2019 in China has very quickly become a global health emergency with almost two million of infected patients worldwide. Along with the spread of the pandemic, there has been a growing concern about the management of fragile rheumatic patients, for whom there is still very little data available. In particular, subjects affected by connective tissue diseases (CTD) are known to have an increased infectious risk compared to the healthy population due to a general impairment of the immune system intrinsic to the autoimmune disease itself, the iatrogenic effect linked to the use of immunosuppressive drugs, and the high number of comorbidities that often complicate the clinical picture.

Sleep medicine
Correspondence COVID-19: Melatonin as a potential adjuvant treatment.
Salles C.
Life Sci.
2020 Apr 22; PMID: 32334009
Level of Evidence: 5 - Review
Type of Article: Letter
Summary: This correspondence provides a comment on the recent review article by Zhang et al., which summarizes the likely benefits of melatonin in the attenuation of COVID-19 based on its putative pathogenesis. Specifically, the article reviews data indicating that melatonin limits virus-related diseases and would also likely be beneficial in COVID-19 patients. This letter raises two follow-up questions to the original article including: Is sleep deprivation able to negatively interfere with the lung picture of COVID-19? Would the use of melatonin, especially in elderly patients in sleep deprivation with COVID-19, in an early and even preventive way, be able to reduce the injury in the lung tissue of these patients?

Surgical Subspecialties
Major Head and Neck Reconstruction During the COVID-19 Pandemic: The University of Pittsburgh Approach
Ranasinghe V et al.
Head Neck
2020 Apr 27; PMID: 32338790
Level of Evidence: 5 – Expert Opinion
Type of Article: Guidelines
BLUF: The authors propose major head and neck reconstruction guidelines tailored to the COVID-19 pandemic, with goals to mitigate infectious risk while continuing to provide timely care in surgical cases deemed emergent.

- **Outpatient care**
  - Preoperative assessments transitioned to telemedicine
  - Postoperative visits to include surgical mask or N95 (aerosolizing procedure), eye protection
- **Preoperative testing**
  - Testing for SARS-CoV-2: Those that are positive will be postponed and patients who test negative will proceed with surgery, although still with full PEE and N95 masks due to 25% false negative rate
- **Case and flap selection**
  - Development of tiered structure to classify oncology cases based on urgency (Table 1)
  - Weekly Zoom reconstructive surgery conferences to discuss scheduled cases and the reconstructive plan
  - Simplifying reconstruction and reduction of surgical duration when possible
    - Reconstruction done in stages when acceptable
    - Substituting locoregional flap reconstruction when feasible
    - Limiting cases of microvascular reconstruction except when absolutely necessary
  - Prioritization of reconstructive cases in a tiered system (Table 2)
  - Consideration to perform soft tissue reconstruction without the addition of bone reconstruction, if functionally feasible
  - Use of virtual surgical planning (VSP) for complex oromandibular reconstructions

- **Intraoperative care**
  - All head and neck free flap cases involving mucosal surfaces are performed with N95 masks for all operating room (OR) staff
  - Reduction in operative team to four surgeons (two attendings and two assistants)
  - Flap harvest done concurrently with flap ablation in a two-team approach, minimizing delay
  - Decreased amount of times scrubbing in and out during a case
  - Use of full muscle relaxant during tracheostomy to prevent coughing, holding ventilation prior to airway entry, and only resuming ventilation after tube has been placed with cuff inflated
  - Strategic team breaks during prolonged cases for recovery of N95-induced headaches
- **Postoperative care**
  - Division of head and neck service into two independent teams, with minimization of interaction between teams
    - Separate rounding times and now once daily
  - Decreased frequency of flap checks for intraoral flaps: checked every 6 hours or if there is a change in Doppler signal
    - Due to dependence on Doppler sonography, now performing implantation of both arterial and venous probe on all intraoral flap cases
- **Education**
  - Due to decreased volume of cases for residents and educational experiences such as cadaver labs being postponed, the residents are now more able to engage in research, studying, and alternative didactic opportunities

Abstract: The 2019 novel coronavirus (COVID-19) pandemic has created **significant challenges** to the delivery of care for patients with **advanced head and neck cancer requiring multimodality therapy**. Performing major head and neck ablative surgery and reconstruction is a particular concern given the extended duration and aerosolizing nature of these cases. In this manuscript, **we describe our surgical approach to provide timely reconstructive care and minimize infectious risk to the providers, patients, and families.**

Tier 1
All benign pathology (eg, benign parotid tumors)
All benign indication for minor procedures (eg, esophageal dilation, TEP)
Nonmelanoma skin cancer <2 cm
Tier 2
Low-grade malignancy (eg, well differentiated thyroid cancer, low-grade parotid cancer)
Nonmelanoma skin cancer >2 cm
Diagnostic biopsy of cervical lymph node
Tier 3
Mucosal squamous cell carcinoma
Advanced stage malignancies (well differentiated thyroid cancer with local invasion)
Poorly differentiated thyroid cancer
Melanoma
Direct laryngoscopy and biopsy (with clinical concern for malignancy)

Table 1: University of Pittsburgh, Division of Head and Neck Surgery tiered prioritization of cancer surgery

Tier 1: Stage reconstruction with wound care, skin grafting, or local flap
Small oral cavity defect without neck communication
Small oroantral fistula after maxillectomy
External skin defect without exposed critical structures
Facial nerve reanimation (functional muscle transfer)
Traumatic maxillofacial injuries requiring free tissue transfer
Tier 2: Consider free flap reconstruction, substitute locoregional flaps if feasible
Maxillectomy defects[a]
Lateral mandibular defects
Tongue, floor of mouth defects <50% without large neck communication
Patch or overlay reconstruction after laryngectomy
Radical neck dissection with exposed great vessels
Large external skin defects with exposed vital structures/ bone
Tier 3: Free flap reconstruction required
Anterior oromandibular defects
Tongue, floor of mouth defects >50% with neck communication
Total laryngopharyngectomy defects requiring tubed reconstruction
Skull base defects with exposed intracranial structures/CSF leak

[a]Consider prosthetic obturator when feasible.

Table 2: University of Pittsburgh, Division of Head and Neck Surgery tiered prioritization of reconstructive head and neck surgery

General Surgery

Performing abdominal surgery during the COVID-19 epidemic in Wuhan, China: a single-centred, retrospective, observational study.

Cai M, Wang G, Zhang L, Gao J, Xia Z, Zhang P, Wang Z, Cai K, Wang G, Tao K.
Br J Surg.
2020 Apr 27; PMID: 323392590
Level of Evidence: 4 – Case Series
Type of Article: Letter to the Editor

Summary: The authors present baseline characteristics, laboratory findings, and CT findings of eight patients with COVID-19 and 22 without COVID-19 who underwent surgery from 1/15/2020 to 3/15/2020. They conclude that for mildly infected or asymptomatic patients, postoperative recovery seemed not to be affected. They acknowledge their study is limited by a lack of clinical cases.

Transplant Surgery

Two distinct cases with COVID-19 in kidney transplant recipients.

Kim Y, Kwon O, Paek JH, Park WY, Jin K, Hyun M, Lee JY, Kim HA, Han S.
Am J Transplant.
2020 Apr 26; PMID: 32337859
Level of Evidence: 4 - Case series
Type of Article: Letter to the Editor

BLUF: This article details the treatment of two COVID-19 patients who had kidney transplants (KT). They suggest that the treatment of KT recipients with concurrent SARS-CoV-2 infections does not significantly differ from non-transplant individuals and early diagnostic screening is recommended. Lastly, authors state that lopinavir/ritonavir should be cautiously used in KT recipients with tacrolimus.

Abstract:
The fatality of novel coronavirus disease (COVID-19) is precipitously increased in patients with underlying comorbidities or elderly people. Kidney transplant (KT) recipients are one of the vulnerable populations for infection. COVID-19 infection in KT recipients might be a complicated and awkward situation, but there has been a lack of reports concerning this group. Herein, we demonstrated two distinct cases with different clinical progress. The first case was a 36-year-old man who underwent KT 3 years ago. He was diagnosed with COVID-19 expressing relevant symptoms. Following administration of lopinavir/ritonavir and hydroxychloroquine with reduced immunosuppressant, he recovered from COVID-19. However, the unexpected fluctuations in tacrolimus trough levels needed to be managed because of drug-to-drug interaction. The second case was developed in a 56-year-old man without any symptoms. He took the second KT from an ABO-incompatible donor 8 years ago. He was diagnosed with COVID-19 by screening due to exposure history. During the hospitalization period, the chest infiltrative lesion showed a wax and wane, but he successfully recovered by hydroxychloroquine with azithromycin. These apparently different cases suggest that assertive screening and management could improve the clinical course. In addition, antiviral agents should be used cautiously, especially in patients on calcineurin inhibitors.

Managing COVID-19 in Renal Transplant Recipients: A Review of Recent Literature and Case Supporting Corticosteroid-sparing Immunosuppression.

Johnson K, Belfer J, Peterson G, Boelkins M, Dumkow L. Johnson K, et al.
Journal Pharmacotherapy
2020 Apr 27; PMID: 32339304
Level of Evidence: 5- Literature Review
Type of Article: Review

Summary: A review of the literature on immunosuppression management strategies in renal transplant patients infected with SARS-CoV-2 found **no randomized clinical trials and a lack of guidelines on standard of care,** especially regarding steroid-sparing regimens and immunosuppressant modifications. More data is needed, but current recommendations are to **avoid corticosteroids in severe COVID-19 disease.**

Abstract:
Novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome virus (SARS-CoV-2) has become a global healthcare crisis. The Centers for Disease Control and Prevention (CDC) lists immunocompromised patients, including **those requiring immunosuppression** following renal transplantation, as **high-risk for severe disease from SARS-CoV-2**. Treatment for other viral infections in renal transplant recipients often includes a reduction in immunosuppression, however, there are **no current guidelines recommending the optimal approach to managing immunosuppression in the patients who are infected with SARS-CoV-2.** It is currently recommended to **avoid corticosteroids in the treatment of SARS-CoV-2 outside of critically ill patients**. Recently published cases describing the inpatient care of COVID-19 in renal transplant recipients differ widely in disease severity, time from transplantation, baseline immunosuppressive therapy, and the modifications made to immunosuppression during COVID-19 treatment. The purpose of this review is to summarize and compare inpatient immunosuppressant management strategies of recently published reports in the renal transplant population infected with SARS-CoV-2 and to discuss the limitations of corticosteroids in managing immunosuppression in this patient population.

OBGYN

ISIDOG Recommendations Concerning COVID-19 and Pregnancy.

Donders F, Lonnée-Hoffmann R, Tsiakalos A, Mendling W, Martinez de Oliveira J, Judlin P, Xue F, Donders GGG, Isidog Covid-Guideline Workgroup.
Diagnostics (Basel).
2020 Apr 22; PMID: 32338645
Level of Evidence: 5 - Expert opinion
Type of Article: Literature Review

BLUF: This article discusses guidelines that should be used to diagnose, treat, manage, and protect pregnant patients with concurrent SARS-CoV-2 infection. They are summarized below:

- Pregnant women are considered "high risk" due to the likelihood of altered immune responses and the difficulty of delivering intensive care, these patients should take more extensive preventative measures to avoid infection.
- Pregnant women working in high-risk settings (such as ICU, or respiratory wards) should be moved to lower risk jobs for the time being.
- Although there is limited information regarding COVID-19, historically pregnant women have been more susceptible and have experienced more severe symptoms with respiratory viruses.
- Potential risks of COVID-19 infection during pregnancy include preterm delivery and fetal distress.
- Multidisciplinary teams should be assembled to design individualized delivery plans.
- Fetal growth should be monitored carefully in COVID-19 positive pregnant women.
- No data has shown vertical transmission; however, postnatal transmission is possible and precautions including masks, hand washing and physical distancing should be taken.
- Due to the rates of false negative [RT-]PCR tests, an additional test should be administered at least 24 hours later if patients with suspicious symptoms have a negative result.
- Providers in contact with COVID-19 patients should always wear full PPE, and self-quarantine for a minimum of 14 days if symptomatic.
- Patients should call the healthcare facility prior to arrival, allowing the provider to determine the level of emergency and take appropriate precautions.
- Assessment of respiratory function in laboring patients is critical, although it is advised to account for normal oxygen saturation adaptations during pregnancy.
- Labor induction should not be postponed in suspected COVID-19 patients and high doses of oxytocin should be avoided as it can cause fluid overload and cardiovascular decompensation.
- A staff member trained in neonatal resuscitation should be present at delivery.
- Methylergometrine should be avoided for the management of uterine atony.
- Avoid the use of general/inhaled anesthesia.

Abstract:
Providing guidelines to health care workers during a period of rapidly evolving viral pandemic infections is not an easy task, but it is extremely necessary in order to coordinate appropriate action so that all patients will get the best possible care given the circumstances they are in. With these International Society of Infectious Disease in Obstetrics and Gynecology (ISIDOG) guidelines we aim to provide detailed information on how to diagnose and manage pregnant women living in a pandemic of COVID-19. Pregnant women need to be considered as a high-risk population for COVID-19 infection, and if suspected or proven to be infected with the virus, they require special care in order to improve their survival rate and the well-being of their babies. Both protection of healthcare workers in such specific care situations and maximal protection of mother and child are envisioned.

Ophthalmology

COVID-19 Associated Pulmonary Aspergillosis.

Koehler P, Cornely OA, Böttiger BW, Dusse F, Eichenauer DA, Fuchs F, Hallek M, et al.
Journal Mycoses.
2020 Apr 27; PMID: 32339350
Level of Evidence: 4- Retrospective Chart Review
Type of Article: Research

BLUF: An interdisciplinary group at the University Hospital of Cologne, Germany conducting a retrospective chart review of all COVID-19 patients admitted to the intensive care unit (ICU) with acute respiratory distress syndrome (ARDS) found **Aspergillosis positivity in five of 19**

consecutively tested patients, suggesting a possible mechanism of viral or ARDS-induced immunosuppression causing susceptibility to invasive aspergillosis. Criticisms from the study are:

- Difficult to **distinguish invasive disease vs normal respiratory colonization.**
- Respiratory tract sampling requires **increased PPE use and exposure risk**
- No evidence that treating these COVID-19 patients with antifungals affects mortality.

Abstract:
Objectives: Patients with acute respiratory distress syndrome (ARDS) due to viral infection are at risk for secondary complications like invasive aspergillosis. Our study evaluates Coronavirus disease 19 (COVID-19) associated invasive aspergillosis at a single center in Cologne, Germany.
Methods: A retrospective chart review of all patients with COVID-19 ARDS admitted to the medical or surgical intensive care unit at the University Hospital of Cologne, Germany.
Results: COVID-19 associated invasive pulmonary aspergillosis was found in five of 19 consecutive critically ill patients with **moderate to severe ARDS.**
Conclusion: Clinicians caring for patients with ARDS due to COVID-19 should consider invasive pulmonary aspergillosis and subject respiratory samples to comprehensive analysis to detect co-infection.

Adjusting Practice During COVID-19

COVID-19 and the role of 3D printing in medicine.
Tino R, Moore R, Antoline S, Ravi P, Wake N, Ionita CN, Morris JM, Decker SJ, Sheikh A, Rybicki FJ, Chepelev LL.Tino R, et al.
3D Print Med.
2020 Apr 27; PMID: 32337613
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
Summary: This editorial is initiating a discussion on evolving ready-to-print models when aiding urgent medical resources, highlighting recent (4/1/20) initiatives and collaborations by companies, hospitals, and researchers. The editorial does not claim clinical effectiveness of the devices, rather suggest 3D printing experts to keep an open communication with local hospital supply chains and potentially the national strategic stockpile holders. As "safe implementation of unregulated parts is essential, and risk/benefit ratios can change very rapidly as medical supplies become unavailable."

Acute care

Neurology

The Value of Headache-Specific Recommendations During COVID-19.
Wells RE, Strauss LD
2020 May; Headache
PMID: 32337725
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial
BLUF: Wells and Strauss applaud the the recently published expert guidelines for migraine care during the Covid-19 Pandemic by Szperka and colleagues in the Headache journal, while also highlighting its limitations. These include:

- lack of evidence-based non-pharmacological treatments for chronic migraine and
- failure to point out the unknown potential interactions between the new CGRP medications and COVID-19.

They suggest several additional questions be addressed in future papers:

- When or if in-person urgent headache care visits are needed
- How to address new-onset headache that could be a manifestation of COVID-19,
- If there are new headache conditions unique to COVID-19.

The authors conclude that the rapid turnaround of the guidelines largely outweigh any limitations which may have been addressed with a longer review process.

Summarizing statement: "In summary, this publication is an extraordinary effort by a group of dedicated headache specialists with unique expertise in Headache Management with "real-world" strategies during this pandemic. This will help headache providers continue to provide excellent care without the risks involved with in-person visits during COVID-19. **It is helpful at both the provider level, with specific and concrete recommendations for acute, preventive, and bridge treatment approaches, and at the administrative level, as it provides recommendations that can help inform decision making regarding the ability to provide care in the absence of in-person visits that could potentially avoid unnecessary and potentially dangerous ED visits.** This paper also serves as a model for other providers to consider – as recommendations for disease-specific treatment options during COVID will enable patients to continue to receive non-COVID care during this pandemic. This paper could also help inform the development of future evidenced-based guidelines. **The limitations described are minimal compared to the benefit of the rapid turnaround of this manuscript at this time of crisis**."

Medical subspecialties

Inpatient Medicine

Inpatient Care of Patients with COVID-19: A Guide for Hospitalists.
Yetmar ZA, Issa M, Munawar S, Burton MC, Pureza V, Sohail MR, Mehmood T.
Am J Med.
2020 Apr 24; PMID: 32339477
Level of Evidence: 4 – Review
Type of Article: Review
BLUF: This entry highlights methods of controlling the COVID-19 pandemic primarily through effective implementation of the following strategies:

- "Interventions to help a health system prepare for patients with COVID-19 include establishing a committee for logistic planning and information dissemination, creating a service dedicated to caring for patients with COVID-19, and building contingency plans for anticipated staffing needs.
- Common findings of COVID-19 include fever, cough, dyspnea, lymphopenia, and normal procalcitonin.
- Supportive care is the mainstay of therapy, though several medications including hydroxychloroquine and remdesivir are undergoing clinical trials."

Abstract:
Since its emergence in December 2019, the virus known as severe acute respiratory syndrome coronavirus 2 has quickly caused a pandemic. This virus causes a disease now known as coronavirus disease 2019, or COVID-19. As an increasing proportion of the at-risk population becomes infected, and patients with severe illness are hospitalized, it is essential for hospitalists to remain current on how to best care for people with suspected or confirmed disease. Establishing a system for logistical planning, and accurate information sharing is strongly recommended. Infection control remains the ultimate goal. As such, healthcare workers should be educated on universal and isolation precautions, and the appropriate use of personal protective equipment. Social distancing should be encouraged to prevent the spread of infection, and creative and innovative ways to reduce contact may need to be considered. Moreover, it is imperative to prepare for contingencies as medical staff will inevitably get sick or become unavailable. Hospitalists have the difficult task of caring for patients, while also adapting to the many logistical and social elements of a pandemic.

Dermatology

No evidence of increased risk for COVID-19 infection in patients treated with Dupilumab for atopic dermatitis in a high-epidemic area - Bergamo, Lombardy, Italy.

Carugno A, Raponi F, Locatelli AG, Vezzoli P, Gambini DM, Di Mercurio M, Robustelli Test E, Sena P.Carugno A, et al.
J Eur Acad Dermatol Venereol.
2020 Apr 27; PMID: 32339362
Level of Evidence: 4 - Case series
Type of Article: Letter

BLUF: The authors examined their patient population currently on treatment with dupilumab (n=30) to see if they were at an increased risk of contracting infection by COVID-19. They found that none of the patients studied had tested positive for COVID-19 or had symptoms suggestive of infection. The authors recommend standard precautions like hand-washing, social distancing, and use of protective gear to mitigate infection risk in this patient population.

Abstract: Atopic dermatitis (AD) is a chronic inflammatory skin disease. Patients with AD have increased infection risk, including skin infections and systemic infections. Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin-4 (IL-4) and IL-13. Dupilumab is approved for inadequately controlled moderate-to-severe AD.

Changes in emergency service access after spread of COVID19 across Italy.

Tartari F, Guglielmo A, Fuligni F, Pileri A.Tartari F, et al.
J Eur Acad Dermatol Venereol.
2020 Apr 27; PMID: 32339340
Level of Evidence: 5 - Expert Opinion
Article Type: Letter to the Editor

BLUF: This study observed a decrease of unjustified consultations, specifically dermatoses, to their emergency services unit when comparing two different weeks before and after COVID-19. The authors propose a solution to avoid misuse of emergency services: 1) implement the number of scheduled exams by recruiting more dermatologists, 2) have more outpatients during the daytime, 3) train general practitioners to diagnose the most commonly occurring dermatosis.

Abstract: The Italian National Health System is currently living through some catastrophic days, owing to the rapid spread of COVID-19 across the country. **At the time of writing, our Government has passed emergency laws (March 11, 2020), with a view to preventing widespread viral infection among the population**, which may well lead to an increase in the number of people requiring intensive care unit (ICU) hospital treatment. **Currently, most of the northern Italian regions are close to saturation point in terms of the number of available ICU inpatient beds.**

Table 1: principal characteristics of our patients

	Total number of access	Justified access	Non-justified access	Median age (years)	Male	Female
Pre-COVID	106	46	60	61	56	50
COVID	19	14	5	44	6	13

Biologics for psoriasis in COVID-19 era: what do we know?

Megna M, Napolitano M, Patruno C, Fabbrocini G.
Dermatol Ther
2020 Apr 27; PMID: 32338424
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

BLUF: There is insufficient evidence to say that the biologics used to treat psoriasis increase the risk of COVID-19, therefore these medications should not be discontinued. Additionally, there is a possibility that these biologics could be beneficial in preventing a cytokine storm in COVID-19 patients.

Summary: This is a response to an article by Conforti et al. stressing the importance of a therapeutic reassessment of psoriatic patients on immunosuppressive drugs during the COVID-19 pandemic. The authors argue that this topic needs more investigation as definitive evidence that anti-psoriatic biologics increase the risk of infectious complications and promote the spread of COVID-19 are lacking. The Italian Society of Dermatology and the International Psoriasis council recommend only stopping biologic treatment of psoriasis in documented cases of COVID-19 and in those with active symptoms. Additionally, the immune response against COVID-19 could cause a cytokine storm which further damages organs and causes complications. In these cases the biologics used for psoriasis could actually be beneficial.

Cardiology

STEMI Care and COVID-19: The Value Proposition of Pharmacoinvasive Therapy.

Bainey KR, Bates ER, Armstrong PW.
Circ Cardiovasc Qual Outcomes
2020 Apr 27; PMID: 32339038

Level of Evidence: 5 - Expert opinion
Type of Article: Letter to the Editor

BLUF: One of the most important factors to consider when treating a STEMI is the first-medical-contact-to-device time. While percutaneous coronary intervention (PCI) is the preferred reperfusion strategy when available, fibrinolytic therapy and pharmacoinvasive strategy can be used effectively and may help mitigate some of the challenges caused by COVID-19 in treating STEMI patients.

Summary: The COVID-19 pandemic has dramatically altered the treatment approach for patients with ST-elevation myocardial infarction (STEMI). Patients may be hesitant to access the emergency medical system or risk hospital exposure to COVID-19, emergency department evaluations are prolonged with additional screening for COVID-19, and transfer to the catheterization laboratory is complicated by possible staff exposure and delays caused by PPE use. **Fibrinolytic therapy and pharmacoinvasive strategy have shown to be efficacious when delivered in a timely manner, and require less personnel and avoid time-to-treatment delays when compared to percutaneous coronary intervention (PCI)**. These techniques are currently being used even at hospitals with PCI capabilities, and can be used effectively **especially in low-risk STEMI patients (TIMI score ≤5).**

COVID-19 and cardiovascular disease: What we know, what we think we know, and what we need to know.

Dhawan R, Gundry RL, Brett-Major DM, Mahr C, Thiele GM, Lindsey ML, Anderson DR.Dhawan R,
J Mol Cell Cardiol
2020 April 24; PMID: 32339565
Level of Evidence: 5 Expert Opinion
Type of Article: Letter

Summary: Currently, there is an urgent need for additional research on COVID-19 to help mitigate its global impact and improve the outcomes of patients. From what we know, COVID-19 is highly susceptible to specific age-groups and co-morbidities such as cardiovascular diseases. Individuals in this population who are taking ACE inhibitors (ACEi) and Angiotensin II receptor blockers (ARB) are thought to be at an increased risk for COVID-19 infection due to upregulation of ACE2 receptors. On the other hand, ACEi may limit the inflammatory response from COVID-19 infection and protect from ARDS development. A suggestion of a robust CD4+ T cell response may allude to a better prognosis for patients infected with the virus, however, the kinetics and effectiveness of specific immunological responses with COVID-19 severity still remains unclear.

A treatment strategy for acute myocardial infarction and personal protection for medical staff during the COVID-19 epidemic: the Chinese experience.

Han Y
Eur Heart J
2020 Apr 27; PMID: 32338764
Level of Evidence: 5- Expert opinion
Type of Article: Guideline

Summary excerpt: "Guidance on the treatment strategy of acute myocardial infarction (AMI) and personal protection for medical staff during the COVID-19 epidemic was released by the Chest Pain Center Committee, Medical Quality Control Center of Cardiovascular Diseases in Liaoning province, China,[1] which received great attention from cardiologists, with >30,000 online viewings at the time of writing. The guideline is briefly outlined."

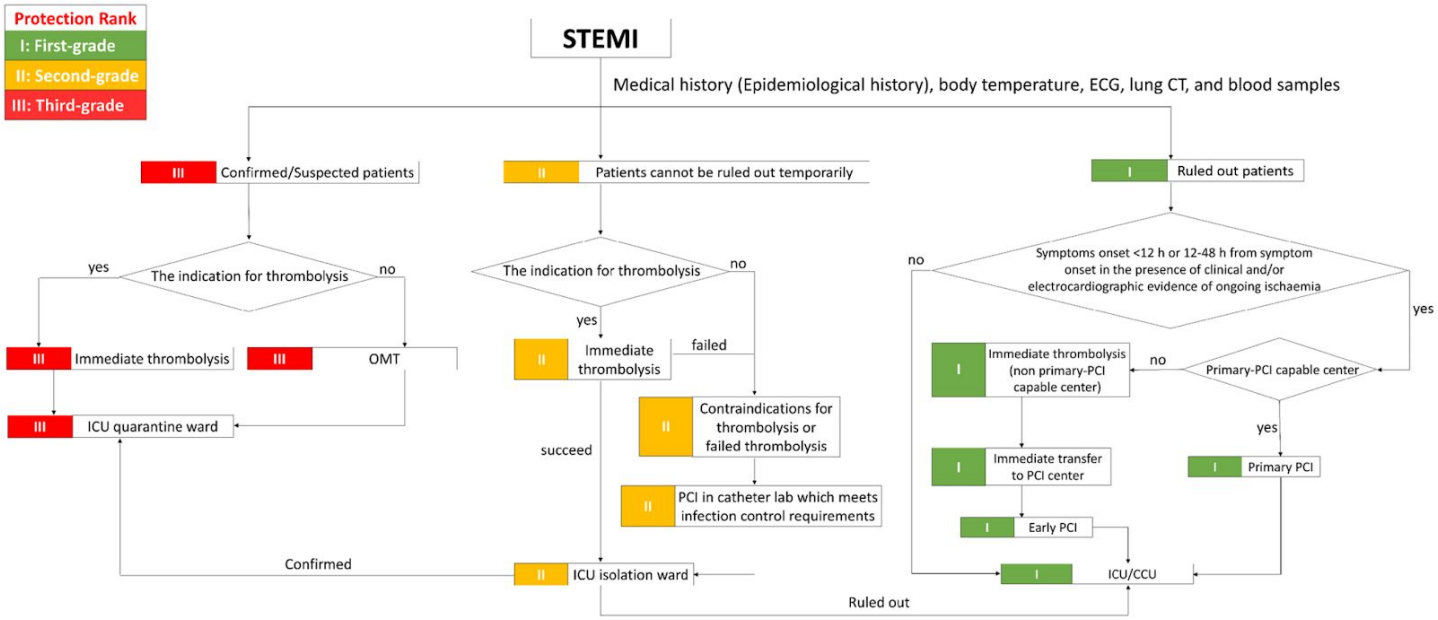


Fig 1. Algorithm for management of STEMI. CCU, coronary care unit; ECG, electrocardiogram; ICU, intensive care unit; PCI, percutaneous coronary intervention; OMT, optimized medical treatment; STEMI, ST-segment elevation myocardial infarction

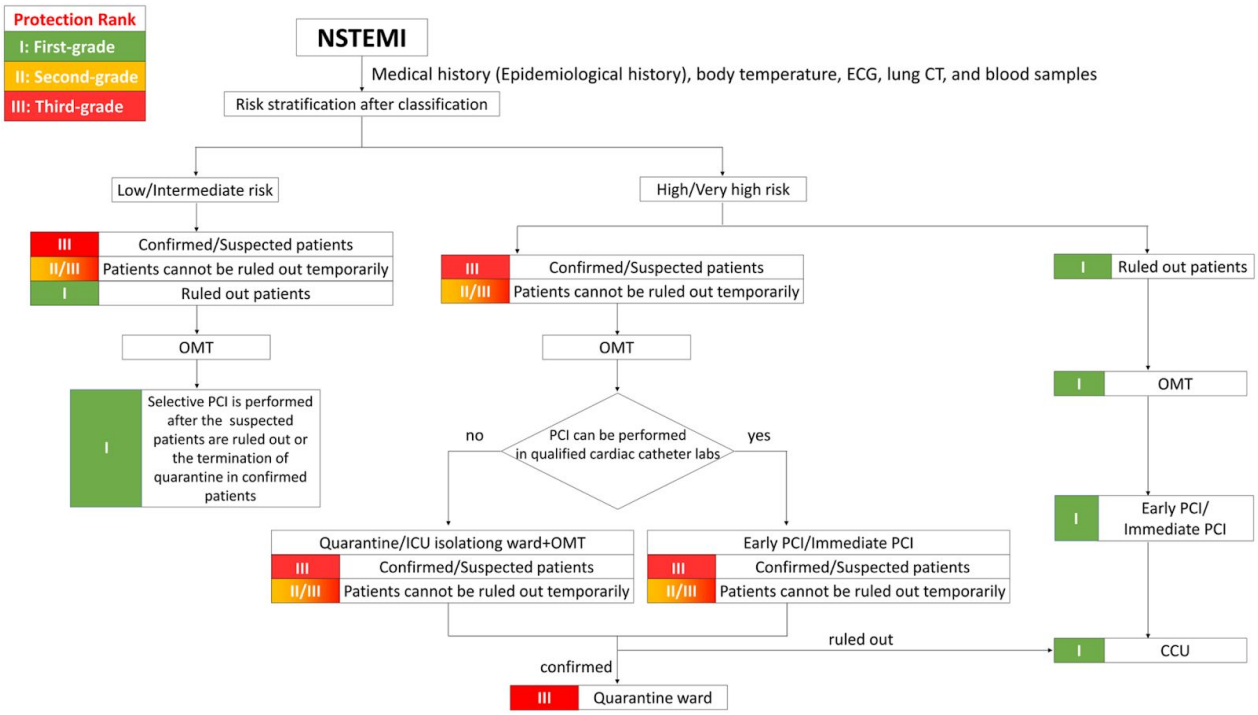


Fig 2. Algorithm for management of NSTEMI. ECG, electrocardiogram; ICU, intensive care unit; PCI, percutaneous coronary intervention; NSTEMI, non-ST-segment elevation myocardial infarction; OMT, optimized medical treatment.

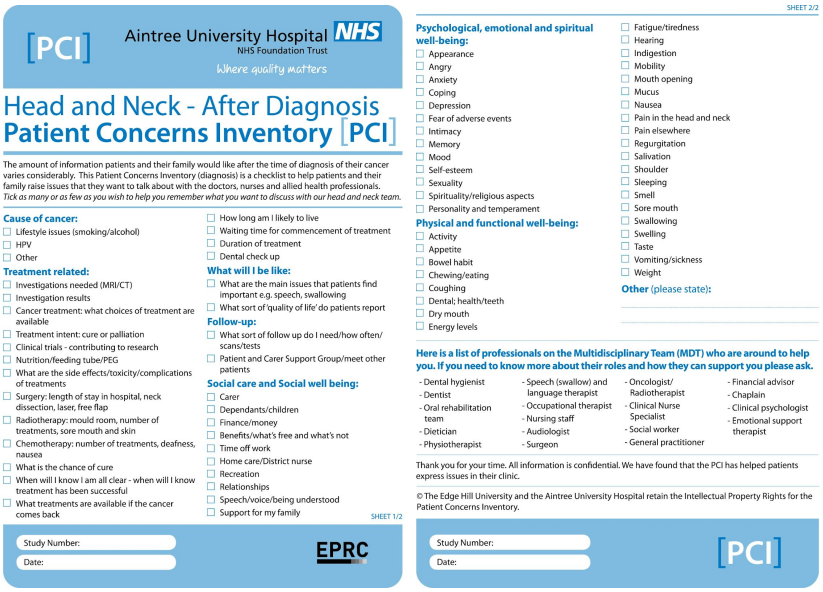
Why Fibrinolytic Therapy for STEMI in The COVID-19 Pandemic is Not Your New Best Friend.
Kirtane, Ajay J; Bangalore, Sripal
Circ Cardiovasc Qual Outcomes
2020 Apr 27; PMID: 32339025
Level of Evidence: 5 - Expert Opinion
Type of Article: Comment
BLUF: As directors of two major cardiac catheterization laboratories in New York City, the authors refute recent discussion of fibrinolytic therapy (FT) as a preferred approach compared to percutaneous coronary intervention (PCI) for STEMI during the COVID-19 pandemic and establish that with the use of full PPE for all STEMI cases, **PCI remains the best option for reperfusion in suspected STEMI.**

Abstract:
The COVID-19 pandemic has strained global health care systems in ways that simply could not have been imagined just several months ago. Writing from the heart of New York City - the unfortunate new epicenter of this pandemic - we have been confronted with this new reality head-on. As directors of two major academic cardiac catheterization laboratories in the city, we both have had to operationalize logistical planning of physician and staff redeployments as well as modification of our respective hospital units including conversion of large portions of the catheterization laboratory into COVID-19 intensive care units in order to deal with the surge of COVID-19 patients within the hospital.

Endocrinology
COVID-19 and diabetes: is metformin a friend or foe?
Ursini F, Ciaffi J, Paola Landini M, Meliconi R
Diabetes Res Clin Pract
2020 Apr 24; PMID: 32339534
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summary: Previous research has suggested an epidemiological link between diabetes and COVID-19. Studies have also found that human ACE2 (angiotensin converting enzyme 2) represents the docking site used by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) for invading target cells. This letter speculates that metformin, when co-treated with angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, may theoretically increase ACE2 availability in the respiratory tract thus promoting SARS-CoV2 infection.

Hematology and Oncology
The After Diagnosis Head and Neck cancer-specific Patient Concerns Inventory (HaNC-AD) as a pre-treatment preparation aid during the COVID-19 pandemic.
Kanatas A, Rogers SN
Eur Arch Otorhinolaryngol
2020 Apr 27; PMID: 32338298
Level of Evidence: 5 - Expert Opinion
Type of Article: Communication
BLUF: Authors describe the use of the Head and Neck cancer-specific Patient Concerns Inventory (HaNC-AD PCI, Appendix 1) in telephone consultations due to the COVID-19 pandemic following diagnosis of a head and neck cancer and prior to treatment. Based on experience, authors have found this to be a useful tool in allowing the patient time to consider and reflect on aspects of their care, express concerns, understand the treatment, and provide informed consent.

Abstract: The coronavirus disease 2019 pandemic has resulted in new challenges for clinicians, head and neck cancer (HNC) patients and carers. There is evidence that the current crisis is **affecting the management of HNC patients**. Most healthcare systems have introduced remote consultations to decrease the risk of coronavirus infection to patients, carers and clinicians. At present, **HNC patients may be anxious and due to logistical issues, may not be adequately prepared for their treatment**. To ensure that patients have a thorough understanding of their treatment and expected outcome during the current COVID-19 crisis there may be merit in the use of the HaNC-AD PCI.



[PCI] Aintree University Hospital NHS
NHS Foundation Trust
Where quality matters

Head and Neck - After Diagnosis Patient Concerns Inventory [PCI]

The amount of information patients and their family would like after the time of diagnosis of their cancer varies considerably. This Patient Concerns Inventory (diagnosis) is a checklist to help patients and their family raise issues that they want to talk about with the doctors, nurses and allied health professionals.
Tick as many or as few as you wish to help you remember what you want to discuss with our head and neck team.

Cause of cancer:
- ☐ Lifestyle issues (smoking/alcohol)
- ☐ HPV
- ☐ Other

Treatment related:
- ☐ Investigations needed (MRI/CT)
- ☐ Investigation results
- ☐ Cancer treatment: what choices of treatment are available
- ☐ Treatment intent: cure or palliation
- ☐ Clinical trials - contributing to research
- ☐ Nutrition/feeding tube/PEG
- ☐ What are the side effects/toxicity/complications of treatments
- ☐ Surgery: length of stay in hospital, neck dissection, laser, free flap
- ☐ Radiotherapy: mould room, number of treatments, sore mouth and skin
- ☐ Chemotherapy: number of treatments, deafness, nausea
- ☐ What is the chance of cure
- ☐ When will I know I am all clear - when will I know treatment has been successful
- ☐ What treatments are available if the cancer comes back
- ☐ How long am I likely to live
- ☐ Waiting time for commencement of treatment
- ☐ Duration of treatment
- ☐ Dental check up

What will I be like:
- ☐ What are the main issues that patients find important e.g. speech, swallowing
- ☐ What sort of 'quality of life' do patients report

Follow-up:
- ☐ What sort of follow up do I need/how often/ scans/tests
- ☐ Patient and Carer Support Group/meet other patients

Social care and Social well being:
- ☐ Carer
- ☐ Dependants/children
- ☐ Finance/money
- ☐ Benefits/what's free and what's not
- ☐ Time off work
- ☐ Home care/District nurse
- ☐ Recreation
- ☐ Relationships
- ☐ Speech/voice/being understood
- ☐ Support for my family

SHEET 1/2

Study Number:
Date:
EPRC

SHEET 2/2

Psychological, emotional and spiritual well-being:
- ☐ Appearance
- ☐ Angry
- ☐ Anxiety
- ☐ Coping
- ☐ Depression
- ☐ Fear of adverse events
- ☐ Intimacy
- ☐ Memory
- ☐ Mood
- ☐ Self-esteem
- ☐ Sexuality
- ☐ Spirituality/religious aspects
- ☐ Personality and temperament

Physical and functional well-being:
- ☐ Activity
- ☐ Appetite
- ☐ Bowel habit
- ☐ Chewing/eating
- ☐ Coughing
- ☐ Dental; health/teeth
- ☐ Dry mouth
- ☐ Energy levels
- ☐ Fatigue/tiredness
- ☐ Hearing
- ☐ Indigestion
- ☐ Mobility
- ☐ Mouth opening
- ☐ Mucus
- ☐ Nausea
- ☐ Pain in the head and neck
- ☐ Pain elsewhere
- ☐ Regurgitation
- ☐ Salivation
- ☐ Shoulder
- ☐ Sleeping
- ☐ Smell
- ☐ Sore mouth
- ☐ Swallowing
- ☐ Swelling
- ☐ Taste
- ☐ Vomiting/sickness
- ☐ Weight

Other (please state):

Here is a list of professionals on the Multidisciplinary Team (MDT) who are around to help you. If you need to know more about their roles and how they can support you please ask.

- Dental hygienist
- Dentist
- Oral rehabilitation team
- Dietician
- Physiotherapist
- Speech (swallow) and language therapist
- Occupational therapist
- Nursing staff
- Audiologist
- Surgeon
- Oncologist/ Radiotherapist
- Clinical Nurse Specialist
- Social worker
- General practitioner
- Financial advisor
- Chaplain
- Clinical psychologist
- Emotional support therapist

Thank you for your time. All information is confidential. We have found that the PCI has helped patients express issues in their clinic.

© The Edge Hill University and the Aintree University Hospital retain the Intellectual Property Rights for the Patient Concerns Inventory.

Study Number:
Date:
[PCI]

Appendix 1. The (HaNC-AD PCI) as used in telephone consultations following a diagnosis of head and neck cancer.

Surgical Subspecialties

General Surgery

[Perioperative Considerations During Emergency General Surgery in the Era of COVID-19: A U.S. Experience.]

Orthopoulos G, Fernandez GL, Dahle JL, Casey E, Jabbour N.
J Laparoendosc Adv Surg Tech A.
2020 Apr 27; PMID: 32339074
Level of Evidence: 5 – Expert Opinion
Type of Article: Opinion

Summary: The authors share considerations made for their perioperative protocols to ensure patient and healthcare worker safety. Considerations include thorough briefing and coordination between patient care teams, appropriate use of PPE and negative pressure rooms, and judicious use of high-speed energy or high-amplitude large-plume generating smoke devices during surgery.

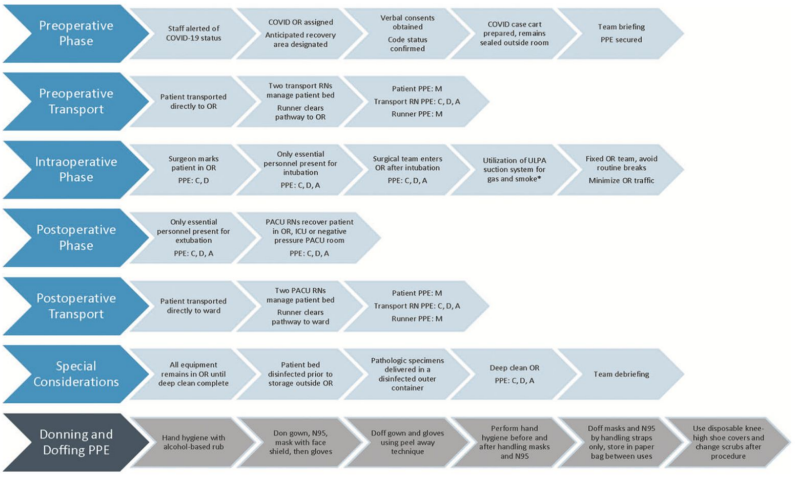


FIG. 1. Perioperative protocol phases. *If laparoscopic, ULPA. A, aerosol precautions (N95 mask or PAPR); C, contact precautions (gown, gloves); D, droplet precautions (mask with face shield); M, simple face mask; PPE, personal protective equipment; ULPA, ultra low particulate air suction system.

[COVID-19 a Short-Term Challenge, Telewound a Lifetime Change.]

Douglas Queen, Keith Harding
Int Wound J.
2020 Apr 27; PMID: 32339442
Level of Evidence: 5 - Expert Opinion
Type of Article: Editorial

Summary: The COVID-19 pandemic, and the social distancing requirements that come with it, have forced healthcare providers to implement telehealth measures to ensure proper medical follow-up. Queen and Harding posit that a similar sentiment can be applied to wound care. Innovations like telewound can be adopted to provide remote assessment, diagnosis, and follow-up for patients with wounds.

Otolaryngology

Guidelines of clinical practice for the management of swallowing disorders and recent dysphonia in the context of the COVID-19 pandemic.

Mattei A, Amy de la Bretèque B, Crestani S, Crevier-Buchman L, Galant C, Hans S, Julien-Laferrière A, Lagier A, Lobryeau C, Marmouset F, Robert D, Woisard V, Giovanni A; French Society of Otorhinolaryngology, Head, Neck Surgery (SFORL); French Society of Phoniatrics, Laryngology (SFPL).
Eur Ann Otorhinolaryngol Head Neck Dis.
2020 Apr 20, PMID: 32332004
Level of Evidence: 5 - Expert Opinion
Article Type: Commentary

BLUF: The French Society of Phoniatrics and Laryngology recommend that patients with swallowing disorders may be assessed if it is an emergency and only in a hospital setting. Additionally, flexible endoscopic assessments are not recommended due to risk of droplet exposure and protection must be worn during video fluoroscopic exam, nasogastric insertion and removal. Laryngologist may examine recent dysphonia with proper PPE.

Abstract:
Procedures putting healthcare workers in close contact with the airway are particularly at risk of contamination by the SARS-Cov-2 virus, especially when exposed to sputum, coughing, or a tracheostomy. In the current pandemic phase, all patients should be considered as potentially infected. Thus, the level of precaution recommended for the caregivers depends more on the type of procedure than on the patient's proved or suspected COVID-19 status. Procedures that are particularly at high risk of contamination are clinical and flexible endoscopic pharyngo-laryngological evaluation, and probably also video fluoroscopic swallowing exams. Voice rehabilitation should not be considered urgent at this time. Therefore, recommendations presented here mainly concern the management of swallowing disorders, which can sometimes be dangerous for the patient, and recent dysphonia. In cases where they are considered possible and useful, teleconsultations should be preferred to face-to-face assessments or rehabilitation sessions. The latter must be maintained only in few selected situations, after team discussions or in accordance with the guidelines provided by health authorities.

Topical preparations to reduce SARS-CoV-2 aerosolization in head and neck mucosal surgery.

Parhar HS, Tasche K, Brody RM, Weinstein GS, O'Malley BW Jr, Shanti RM, Newman JG.Parhar HS, et al.
Head Neck.
2020 Apr 25, PMID: 32333619
Level of Evidence: 5 - Expert Opinion
Article Type: Literature Review

BLUF: A database review conducted using PubMed/Medline for topical agents used against coronaviruses found the use of Povidone-iodine has potential of reducing viral load of SARS-CoV2 aerosolization, suggesting its use can decrease the risk of transmission when performing upper airway mucosal surgery.

Abstract:
Aim**:** The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has put health care workers at risk when exposed to aerosolized viral particles during upper airway mucosal surgery. The objective of this review was to discuss topical preparations that could be utilized preoperatively to help to decrease viral load and potentially reduce the risks of viral transmission.
Methods**:** A PubMed/MEDLINE database review of articles was performed querying topical preparations with virucidal activity against coronaviruses.
Results**:** Povidone-iodine (PVP-I) solutions ranging from 0.23% to 7% have been found to demonstrate highly effective virucidal activity against a broad range of viruses including several coronaviruses responsible for recent epidemics including SARS-CoV-1 and MERS-CoV.
Conclusions**:** While specific evidence regarding SARS-CoV-2 is lacking, PVP-I-based preparations have been successfully demonstrated to reduce viral loads of coronaviruses. They are relatively safe to use in the upper airway and may reduce risk of SARS-CoV-2 aerosolization during upper airway mucosal surgery.

Thyroid surgery during COVID-19 pandemic: Principles and philosophies.

Shaha AR.
Head Neck.
2020 Apr 27; PMID: 32338793
Level of Evidence: 5 - Expert Opinion
Article Type: Editorial

BLUF: The author presents major decision-making issues regarding thyroid surgery during the COVID-19 pandemic and offers recommendations for these issues.

Summary: The author proposes recommendations for main decision-making issues in thyroid surgery during COVID-19. These recommendations for specific issues are summarized below:

- **Anaplastic thyroid cancer**
  - Consider extent of disease and cross-sectional imaging for decisions concerning surgery.
  - Utilize BRAF based therapies and external radiation therapy.
  - Utilize ultrasound guided core biopsy and immunohistochemistry to confirm diagnosis of an unresectable tumor.
  - Avoid elective tracheostomies unless necessary (i.e. if patient is having acute airway distress).
- **Medullary thyroid cancer**
  - Consider extent of disease with calcitonin, CEA, ultrasound, and cross-sectional imaging in decision-making for surgery.
  - If the disease appears to be limited with calcitonin levels under 400, monitor patient for a few months.
- **Locally aggressive thyroid cancer**
  - Consider extent of disease and its involvement to the central compartment vital organs (i.e. recurrent laryngeal nerve, trachea, esophagus, etc.).
    - Cross-sectional imaging will help determine involvement.
    - Decision on surgery timing will be different if preoperative FNA shows poorly differentiated thyroid cancer.

        - The goal is to delay surgery, if possible, while avoiding compromise to total surgical resection and involvement of central compartment organs.
    - Follow hospital guidelines and use proper protection for patients needing fiberoptic evaluation.
- **Large primary tumors and bulky nodal disease**
    - Review history of the presence of tumor and the duration of the nodal metastasis in determining timing for surgery.
        - Cross-sectional imaging will help determine proximity of the tumor to vital structures.
- **Low and intermediate risk thyroid carcinomas**
    - Surgery can be delayed for about 3 to 6 months.
    - Repeat ultrasound may be done in 3 to 4 months.
- **Microcarcinomas**
    - Surgery can be delayed for these patients.
    - Encourage patients to remain under active surveillance or deferred intervention.
    - Ultrasound may be used for exact location and determining need for active intervention.
- **Recurrent thyroid carcinoma**
    - Observe for an extended period of time with repeat imaging studies in 4 to 6 months.
    - Consider surgery if the tumor is plastered against the trachea.
    - Consider alternate treatment choices like alcohol injection and radio frequency ablation for localized nodal recurrences.
- **Indeterminate thyroid nodules**
    - These patients can be monitored.
    - If small tumors are BRAF or TERT positive, still may monitor for a period of time before surgery.
- **Large goiters**
    - Surgery can be avoided, even with tracheal deviation and mild compression.
    - Consider intervention if there is rapid progression, major compression symptoms, or impending acute airway issues.
- **Benign thyroid conditions**
    - Manage as per usual guidelines.
    - Consultations may be done virtually.
    - Guidelines recommended by ATA for FNAs of incidental thyroid nodules should be applied.
    - Avoid FNA on smaller, non-suspicious nodules.

Transplant Surgery

Severe COVID-19 in a renal transplant recipient: A focus on pharmacokinetics.

Meziyerh S, Zwart TC, van Etten RW, Janson JA, van Gelder T, Alwayn IPJ, de Fijter JW, Reinders MEJ, Moes DJAR, de Vries APJ.
Am J Transplant
2020 Apr 26; PMID: 32337790
Level of Evidence: 4 - Case Report
Type of Article: Case Report

BLUF: This case report describes a COVID-19 positive, solid organ transplant recipient whose clinical course was complicated by extreme overexposure to the transplant rejection medication everolimus following co-administration of chloroquine and lopinavir/ritonavir therapy highlighting the importance of improved drug-drug interaction awareness during the COVID pandemic.

Abstract: The current Coronavirus Disease 2019 (COVID-19) pandemic requires extra attention for immunocompromised patients, including solid organ transplant recipients. We report on a case of a 35-year old renal transplant recipient who suffered from a severe COVID-19 pneumonia. The clinical course was c**omplicated by extreme over-exposure to the mammalian target of rapamycin inhibitor everolimus,** following co-administration of chloroquine and lopinavir/ritonavir therapy. The case is illustrative for dilemmas that transplant professionals may face in the absence of evidence-based COVID-19 therapy and concurrent pressure for exploration of experimental pharmacological treatment options. However, the risk-benefit balance of experimental or off-label therapy may be weighed differently in organ transplant recipients than in otherwise healthy COVID19 patients, owing to their immunocompromised status and potential drug interactions with immunosuppressive therapy. **With this case-report, we aimed to achieve increased awareness and improved management of drug-drug interactions associated with the various treatment options for COVID-19 in renal transplant patients.**

High-Immunological Risk Living Donor Renal Transplant during the COVID-19 Outbreak: Uncertainties and Ethical Dilemmas.

Ho QY, Chung SJ, Gan VHL, Ng LG, Tan BH, Kee TYS.Ho QY
Am J Transplant
2020 April 26; PMID: 32337825
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter

BLUF: In the midst of a global pandemic the considerations of transplantation bring up uncertainties such as severity, impact of COVID-19, recovery time and treatment options. In addition, ethical dilemmas to proceed or defer transplantation could affect both the patients and healthcare providers.

Summary: We describe the challenges of performing a high-immunological risk living donor renal transplant during the COVID-19 outbreak. A 42-year-old lady with end-stage renal disease from lupus nephritis had failed peritoneal dialysis due to pleuro-peritoneal leak, failed vascular access creation due to early thrombosis and had recurrent dialysis catheter malfunction. The transplant from her husband was ABO-incompatible and had positive B cell flow crossmatch with multiple donor-specific antibodies. Neither alternative donors nor paired exchange candidates were available. Priority access to deceased donors is limited and unpredictable.

OBGYN

Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis.

Ferrazzi E, Frigerio L, Savasi V, Vergani P, Prefumo F, Barresi S, Bianchi S, Ciriello E, Facchinetti F, Gervasi MT, Iurlaro E, Kustermann A, Mangili G, Mosca F, Patanè L, Spazzini D, Spinillo A, Trojano G, Vignali M, Villa A, Zuccotti G, Parazzini F, Cetin I.
BJOG
2020 Apr 27; PMID: 32339382

Level of Evidence: 4 - Case Series
Type of Article: Research
BLUF: This retrospective study looked at 42 patients who had COVID-19 diagnosed shortly before or after delivering at one of twelve hospitals in Italy in March. Three of the neonates had positive COVID-19 tests; two were delivered vaginally and one was delivered by c-section. Based on this data, intrapartum COVID-19 transmission cannot be ruled out, but risk of transmission associated with vaginal delivery appears low. COVID-19 also does not appear to be associated with more severe disease in pregnant patients nor does it seem to increase the risk of spontaneous preterm delivery.

Summary: This retrospective study assesses the relationship between mode of delivery and neonatal outcomes in patients with COVID-19 infection confirmed within the 36 hours before or after delivery. All of the patients received care in between March 1st and 20th at one of twelve hospitals in Italy. Of the 42 patients enrolled in this study, 18 underwent cesarean section (10/18 due to worsening COVID-19 symptoms). Findings included:

- Fever as the most common maternal symptom; most of the cases were moderate or mild, with four admissions to critical care and seven requiring oxygen support
- Spontaneous preterm birth in 5/24 vaginally delivered cases and preterm delivery in 6/18 cases delivered by c-section
- Two cases of neonates with 5min APGAR scores of less than seven; both were preterm
- Ten cases where breastfeeding was allowed, with patients wearing surgical masks; two of the newborns that breastfed had positive COVID-19 tests and both were to mothers that were diagnosed after delivery and therefore did not wear a mask when breastfeeding prior to their diagnosis; the neonates were tested only after their mothers were diagnosed
- One neonate who did not breastfed had an initially equivocal test for COVID-19 in the hours after birth but a positive test three days later, with early gastrointestinal symptoms and later development of respiratory symptoms; they were born vaginally but immediately separated from their mother due to severe postpartum hemorrhage

The authors conclude their data does not rule out the possibility of intrapartum transmission of COVID-19, though the risk associated with vaginal delivery appears low. The data also suggests that COVID-19 does not increase the risk of spontaneous preterm delivery and has a less severe course in pregnant patients as compared to SARS and MERS.

Psychiatry

Access to evidence-based care for eating disorders during the COVID-19 crisis.

Weissman RS, Bauer S, Thomas JJ.Weissman RS, et al.
Int J Eat Disord.
2020 Apr 27; PMID: 32338400
Level of Evidence: 5- Expert Opinion
Type of Article: Letter
Summarizing excerpt: The authors explore ways COVID-19 has impacted individuals with eating disorders. They provide resources for this community which includes “original research or systematic reviews on obstacles to health services use and strategies to improve access to care; technological tools to provide or enhance interventions; patients' and clinicians' attitudes or perspectives on using digital tools for clinical care; and factors influencing therapeutic alliance.”

Abstract: The COVID-19 pandemic has forced an abrupt change in the delivery of clinical services, including for individuals with an eating disorder. We present this Virtual Issue as a resource for the eating disorder community to showcase research published in the International Journal of Eating Disorders that provides information on effective strategies to help address the challenges arising from COVID-19-related disruptions. Articles included describe original research or systematic reviews on obstacles to health services use and strategies to improve access to care; technological tools to provide or enhance interventions; patients' and clinicians' attitudes or perspectives on using digital tools for clinical care; factors influencing therapeutic alliance; and ideas for improving reach and uptake of digital interventions. We hope that readers will find ways to observe and record their own experiences during this global crisis; the experiences of people at risk for developing or exhibiting an eating disorder; and the experiences of those who care for people with an eating disorder. These lived experiences will be invaluable in formulating hypotheses for future studies in service of advancing the understanding of eating disorders and improving interventions and policies for reducing the burden of suffering attributable to eating disorders.

R&D: Diagnosis & Treatments

Current Diagnostics

Classification of COVID-19 patients from chest CT images using multi-objective differential evolution-based convolutional neural networks.

Singh D, Kumar V, Vaishali, Kaur M.
Eur J Clin Microbiol Infect Dis.
2020 Apr 27. PMID: 32337662
Level of Evidence: 5 - Mechanism-based reasoning
Type of Article: Research

BLUF: The authors tested a novel deep learning method, multi-objective differential evolution (MODE)-based convolutional neural network (CNN), for classifying patients as either COVID-19 infected or not, based on lung CT scans. They found their method to outperform other modelling schemes such artificial neural networks (ANN) and adaptive neuro-fuzzy inference systems (ANFIS).

Abstract:
Early classification of 2019 novel coronavirus disease (COVID-19) is essential for disease cure and control. Compared with reverse-transcription polymerase chain reaction (RT-PCR), chest computed tomography (CT) imaging may be a significantly more trustworthy, useful, and rapid technique to classify and evaluate COVID-19, specifically in the epidemic region. Almost all hospitals have CT imaging machines; therefore, the chest CT images can be utilized for early classification of COVID-19 patients. However, the chest CT-based COVID-19 classification involves a radiology expert and considerable time, which is valuable when COVID-19 infection is growing at rapid rate. Therefore, an **automated analysis of chest CT images is desirable** to save the medical professionals' precious time. In this paper, a **convolutional neural networks (CNN) is used to classify the COVID-19-infected patients as infected (+ve) or not (-ve).** Additionally, the initial parameters of CNN are tuned using multi-objective differential evolution (MODE). Extensive experiments are performed by considering the proposed and the competitive machine learning techniques on the chest CT images. Extensive analysis shows that the **proposed model can classify the chest CT images at a good accuracy rate**.

COVID-19 and chest CT: do not put the sensitivity value in the isolation room and look beyond the numbers.

Adams HJA, Kwee TC, Kwee RM.Adams HJA, et al.
Radiology.
2020 Apr 27; PMID: 32339083
Level of Evidence: 5 - Expert opinion
Type of Article: Letter

BLUF: Adams HJA et al. raised concerns with the conclusions reported by Kim et al. and question whether any conclusions about sensitivity and specificity for chest CT in COVID-19 can be made given the limited data available.

Summary: Adams HJA et al. questions whether the conclusions are supported by the data in a recent study. "Kim et al. reported chest CT to have a high pooled sensitivity of 94% (95% confidence interval: 91%-96%), but a low specificity of 37% (95% confidence interval 26%-50%). **However, we believe that there is no convincing evidence yet that chest CT achieves such a high sensitivity in diagnosing COVID-19 in clinical practice."** The main concern is the **lack of non-diseased controls in 58 of 63 studies included,** which Adams HJA et al. believe should have excluded these studies from the analysis based on the criteria set forth by Kim et al.

Developments in diagnostics

Clinical role of lung ultrasound for the diagnosis and monitoring of COVID-19 pneumonia in pregnant women.

Buonsenso D, Raffaelli F, Tamburrini E, Biasucci DG, Salvi S, Smargiassi A, Inchingolo R, Scambia G, Lanzone A, Testa AC, Moro F.Buonsenso D, et al.
Ultrasound Obstet Gynecol.
2020 Apr 26; PMID: 32337795
Level of Evidence: 4- Case Series
Article Type: Research

BLUF: This case series of four pregnant, COVID-19 positive women found that lung ultrasound (LUS) is more sensitive than chest x-ray at detecting COVID-19, making it an valid alternative tool for monitoring lung involvement and assisting treatment decisions.

Abstract: Lung ultrasound has recently been suggested by the Chinese Critical Care Ultrasound Study Group and Italian Academy of Thoracic Ultrasound as an accurate tool to detect lung involvement during COVID-19. Although chest Computer Tomography (CT) represents the gold standard to assess lung involvement, with a specificity even superior to the nasal/pharyngeal swab for diagnosis, lung ultrasound examination can be a valid alternative to CT scan, with some advantages, particularly desirable for pregnant women. Indeed, ultrasound can be performed directly at bed side by a single operator, reducing the risk of spreading the outbreak among health professionals, as well as it is a radiation free exam making to be easier monitoring those patients who require serial exams. In the present study, we reported **four cases of pregnant women affected by COVID-19** infection who have been monitoring with lung ultrasound examination. **All patients showed ultrasound features indicative of COVID-19 pneumonia at admission**: **irregular pleural lines and vertical artifacts (B-lines) were observed in all four cases, whereas patchy areas of white lung in two cases. LUS was more sensitive than chest X-ray in detecting COVID-19.** Three patients had resolution of lung pathology at ultrasound after 96 h of admission. Two pregnancies are ongoing, whereas two patients had cesarean delivery with no fetal complications. PCR testing of both cord blood and newborn swabs were negative in both cases.

The Use of Digital Health in the Detection and Management of COVID-19.

Alwashmi MF
Int J Environ Res Public Health
2020 Apr 23; PMID: 32340107
Level of Evidence: 5- Expert opinion
Type of Article: Commentary

BLUF: A detailed review of available and theoretical technological innovations that could be harnessed against COVID-19 or future infectious disease outbreaks. Possible digital health innovations include:

- Digital triage and provider consultations in addition to drone-delivered test kits and smartphone apps allowing patients have results interpreted wirelessly

- Remote monitoring technologies wirelessly connected in patient homes such as thermometers that would allow continuous monitoring of body temperature
- Contact tracing measures using artificial intelligence, GPS and bluetooth on smartphones to track and identify exposed individuals

Abstract:
Digital health is uniquely positioned to enhance the way we detect and manage infectious diseases. This commentary explores the potential of implementing digital technologies that can be used at different stages of the COVID-19 outbreak, including data-driven disease surveillance, screening, triage, diagnosis, and monitoring. Methods that could potentially reduce the exposure of healthcare providers to the virus are also discussed.

Developments in Treatments

Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Clinical Trial

Borba MGS, Val FFA, Sampaio VS, et al.; CloroCovid-19 Team
JAMA Netw Open
2020 Apr 1; PMID: 32339248
Level of Evidence: 2 – Randomized Control Trial
Type of Article: Research

BLUF: This article presents an intention-to-treat analysis of a **Brazilian, single-center, randomized control trial** studying the **effect of two doses of chloroquine diphosphate (CQ)** as adjuvant therapy (high-dose, 600mg PO b.i.d. for 10 days vs low-dose, 150mg PO b.i.d. for 4 days) in **inpatients with suspected or confirmed COVID-19 (n=81)** being treated with ceftriaxone, azithromycin, and oseltamivir. **The high-dose group** had a **higher incidence of QTcF elongation (7/37 vs 4/36) and lethality (16/41 vs 6/40)** at day 13 without significant differences in endpoint viral load, prompting the authors to **recommend against this study's high-dose regimen**, though the **low statistical power prevented conclusions on overall CQ safety or efficacy**.

Abstract:
Importance: There is no specific antiviral therapy recommended for coronavirus disease 2019 (COVID-19). In vitro studies indicate that the antiviral effect of chloroquine diphosphate (CQ) requires a high concentration of the drug.
Objective: To evaluate the **safety and efficacy of 2 CQ dosages** in patients with severe COVID-19.
Design, setting, and participants: This **parallel, double-masked, randomized, phase IIb clinical trial with 81 adult patients** who were **hospitalized** with severe acute respiratory syndrome coronavirus 2 **(SARS-CoV-2) infection** was conducted from March 23 to April 5, 2020, at a tertiary care facility in Manaus, Brazilian Amazon.
Interventions: Patients were allocated to receive **high-dosage CQ** (ie, 600 mg CQ twice daily for 10 days) **or low-dosage** CQ (ie, 450 mg twice daily on day 1 and once daily for 4 days).
Main outcomes and measures: Primary outcome was reduction in lethality by at least 50% in the high-dosage group compared with the low-dosage group. Data presented here refer primarily to safety and lethality outcomes during treatment on day 13. Secondary end points included participant clinical status, laboratory examinations, and electrocardiogram results. Outcomes will be presented to day 28. Viral respiratory secretion RNA detection was performed on days 0 and 4.
Results: Out of a predefined sample size of 440 patients, 81 were enrolled (41 [50.6%] to high-dosage group and 40 [49.4%] to low-dosage group). Enrolled patients had a mean (SD) age of 51.1 (13.9) years, and most (60 [75.3%]) were men. Older age (mean [SD] age, 54.7 [13.7] years vs 47.4 [13.3] years) and more heart disease (5 of 28 [17.9%] vs 0) were seen in the high-dose group. Viral RNA was detected in 31 of 40 (77.5%) and 31 of 41 (75.6%) patients in the low-dosage and high-dosage groups, respectively. **Lethality** until day 13 was **39.0% in the high-dosage group** (16 of 41) and **15.0% in the low-dosage group** (6 of 40). The **high-dosage group** presented **more** instance [*sic]* of **QTc interval greater than 500 milliseconds** (7 of 37 [18.9%]) compared with the low-dosage group (4 of 36 [11.1%]). Respiratory secretion at day 4 was negative in only 6 of 27 patients (22.2%).
Conclusions and relevance: The preliminary findings of this study suggest that the **higher CQ dosage should not be recommended for critically ill patients with COVID-19** because of its potential safety hazards, especially when taken concurrently with azithromycin and oseltamivir. These findings cannot be extrapolated to patients with nonsevere COVID-19.

COVID-19, Pulmonary Mast Cells, Cytokine Storms, and Beneficial Actions of Luteolin

Theoharides TC
Biofactors
2020 Apr 27; PMID: 32339387
Level of Evidence: 5 – Expert Opinion
Type of Article: Letter

Summary: The author, an **immunologist** at Tufts and **investor in the company marketing luteolin** as an herbal supplement, **makes a case for the flavonoid luteolin** as a **potential anti-inflammatory to treat COVID-19**. The author cites its **binding to SARS-CoV-2 spike protein**, its role in **inhibiting mast cells and pro-inflammatory** responses, and *in silico* studies suggesting strong affinity for the spike protein as evidence for potential use as an anti-SARS-CoV-2 therapeutic. Their enthusiasm is measured by sourcing and administration concerns to avoid allergic reactions.

The Role of Adipocytes and Adipocyte-Like Cells in the Severity of COVID-19 Infections

Kruglikov, I. L., & Scherer, P. E.
Obesity
2020 Apr 27; PMID: 32339391
Level of Evidence: 5 – Expert Opinion
Type of Article: Commentary

BLUF: The authors propose thiazolidinediones, PPARy agonists which stabilize inactive fibroblasts, may serve to reduce the development of pulmonary fibrosis in patients with COVID-19.

Abstract:
Coronavirus disease-2019 (COVID-19), caused by the highly pathogenic virus SARS-CoV-2, demonstrates high morbidity and mortality caused by development of a severe acute respiratory syndrome connected with extensive pulmonary fibrosis (PF). In this perspective, we argue that **adipocytes and adipocyte-like cells, such as pulmonary lipofibroblasts, may play an important role in the pathogenic response to COVID-19.**

Expression of angiotensin-converting enzyme 2 (ACE2 - the functional receptor for SARS-CoV) - is upregulated in adipocytes of obese and diabetic patients, which turns adipose tissue into a potential target and viral reservoir. This may explain why obesity and diabetes are potential comorbidities for COVID-19 infections. Similar to the recently established adipocyte-myofibroblast transition (AMT), pulmonary lipofibroblasts located in the alveolar interstitium and closely related to classical adipocytes, demonstrate the ability to transdifferentiate into myofibroblasts that play an integral part of PF. This may significantly increase the severity of the local response to COVID-19 in the lung. To reduce the severity and mortality with COVID-19, we propose to probe for the clinical response to thiazolidinediones (TZDs), PPARγ agonists, that are the well-known anti-diabetic drugs. TZDs are able to stabilize lipofibroblasts in their "inactive" state, preventing the transition to myofibroblasts and thereby reducing the development of pulmonary fibrosis and stimulating its resolution.

Kallikrein-kinin blockade in patients with COVID-19 to prevent acute respiratory distress syndrome.
van de Veerdonk FL, Netea MG, van Deuren M, van der Meer JW, de Mast Q, Brüggemann RJ, van der Hoeven H.van de Veerdonk FL, et al.
eLife
2020 Apr 27; PMID: 32338605
Level of Evidence: 5 – Expert Opinion
Article Type: Editorial
Summary: Authors discuss pathophysiology of COVID-19 and call for research into a hypothesis that bradykinin drives pulmonary edema and could be treated by monoclonal antibodies, and that further inflammation would respond to inhibiting the IL-1/IL-6 pathway.

Mental Health & Resilience Needs

COVID-19's Impact on Healthcare Workforce

Response to and Recovery from the COVID-19 Pandemic: What Will It Take?
Morganstein JC, West JC, Schimmels J, Benedek DM.
Psychiatry
2020 Apr 27; PMID: 32338584
Level of Evidence: 5 - Expert Opinion
Type of Article: Commentary
Summary: The well-being of healthcare personnel is profoundly affected by the fear and uncertainty surrounding outbreaks. It is important that these health care workers feel protected and like they can trust and respect that their organization is looking out for them. Organizations should work to mitigate these mental health effects by preparing first responders for the psychological impact of traumatic events, promoting social connectedness through activities such as group check-ins after shifts, promoting self-care, and normalizing reactions to stress.

Medical personnel, COVID-19 and emotional impact.
Joob B, Wiwanitkit V.Joob B, et al.
Psychiatry Res.
2020 Apr 12; PMID: 32335465
Level of Evidence: 6- No Evidence Cited
Type of Article: Commentary
Summarizing excerpt: "The COVID-19 pandemic has posed an extreme threat to global health and become a leading cause of death worldwide. Loss, as a more encompassing theme, interweaves many aspects of people's life in this challenging time. Failure to address the pressing needs of those experiencing loss and grief may result in poor mental and physical health. **Recognizing the uniqueness of each individual and their loss and grief will provide opportunities to develop tailored strategies that facilitate functional adaptation to loss and promote mental health and wellbeing in this crisis**."

Preserving mental health and resilience in frontline healthcare workers during COVID-19.
Santarone K, McKenney M, Elkbuli A.Santarone K, et al.
Am J Emerg Med.
2020 Apr 24; PMID: 32336584
Level of Evidence: 5 - Expert Opinion
Type of Article: Letter
Summarizing excerpt: "Efforts must be made to allow physicians to seek help if needed without stigma or repercussion. Psychological support should be made available in a variety of methods so that the physician has the freedom to choose an approach that works best. Emphasis should be placed on individualized emotional support plans, as psychological care is not one-size-fits-all…Physician well being should be one of our highest priority, as public health and vitality is theirs."

Impact on Public Mental Health

Is Returning to Work during the COVID-19 Pandemic Stressful? A Study on Immediate Mental Health Status and Psychoneuroimmunity Prevention Measures of Chinese Workforce.
Tan W, Hao F, McIntyre RS, Jiang L, Jiang X, Zhang L, et al.
Brain Behav Immun.
2020 Apr 23; PMID: 32335200
Level of Evidence: 4 - Cross-sectional review
Type of Article: Research
BLUF: The authors of this study found using an online questionnaire in China that only 10.8% of respondents met the diagnosis of post-traumatic stress disorder (PTSD) after returning to work during the COVID-19 pandemic. The respondents reported a low prevalence of anxiety (3.8%), depression (3.7%), stress (1.5%) and insomnia (2.3%).

Abstract: This study aimed to quantify the immediate psychological effects and psychoneuroimmunity prevention measures of a workforce returning to work during the COVID-19 epidemic. Workforce returning to work was invited to complete an online questionnaire regarding their attitude toward the COVID-19 epidemic and return-to-work along with psychological parameters including the Impact of Event Scale-Revised, Depression, Anxiety, Stress Scale- 21 (DASS-21) and Insomnia Severity Index (ISI). Psychoneuroimmunity prevention measures include precautions at personal and organization levels. From 673 valid questionnaires, we found that 10.8% of respondents met the diagnosis of post-traumatic stress disorder (PTSD) after returning to work. The respondents reported a low prevalence of anxiety (3.8%), depression (3.7%), stress (1.5%) and insomnia (2.3%). There were no significant differences in the severity of psychiatric symptoms between workers/technicians and executives/managers. >95% reported psychoneuroimmunity prevention measures including good ventilation in the workplace and wore a face mask as protective. Factors that were associated with the severity of psychiatric symptoms in the workforce were marital status, presence of physical symptom, poor physical health and viewing return to work as a health hazard ($p < 0.05$). In contrast, personal psychoneuroimmunity prevention measures including hand hygiene and wearing face masks as well as organizational measures including significant improvement of workplace hygiene and concerns from the company were associated with less severe psychiatric symptoms ($p < 0.05$). Contrary to expectations, returning to work had not caused a high level of psychiatric symptoms in the workforce. The low prevalence of psychiatric symptoms could be due to confidence instilled by psychoneuroimmunity prevention measures before the resumption of work. Our findings would provide information for other countries during the COVID-19 pandemic.

Focus on Mental Health During the Coronavirus (COVID-19) Pandemic: Applying Learnings from the Past Outbreaks.
Shah K, Kamrai D, Mekala H, Mann B, Desai K, Patel RS
2020 Mar 25; Cureus
PMID: 32337131
Level of Evidence: 5- Expert Opinion
Type of Article: Review

BLUF: This review of the literature assesses the psychological impact of previous infectious disease outbreaks, such as MERS, SARS, and Ebola and found evidence of psycholgical harm to both healthcare workers and the general public, including PTSD, depression, and increased suicide during past outbreaks. The authors suggest the general public should avoid excessive media coverage of the pandemic, maintain a healthy lifestyle, and reach out to others. For healthcare workers, the authors outline five steps to support mental health: 1) access to a psychiatric treatment team, 2) clear and consistent information regarding Covid-19, 3) promotion of telepsychiatry, 4) timely behavioral therapy to those who need it, and 5) research and clinical trials on antiviral prophylactic treatment.

Abstract: The 2019 novel coronavirus (COVID-19) has gained global attention after it originated from China at the end of 2019, and later turned into pandemic as it affected about 118,000 in 114 countries by March 11, 2020. By March 13, 2020, it was declared a national emergency in the United States as the number of COVID-19 cases, and the death toll rose exponentially. To contain the spread of the disease, the world scientist community came together. However, the unpreparedness of the nations, even with the advanced medical sciences and resources, has failed to address the mental health aspect amongst the public, as all efforts are focused on understanding the epidemiology, clinical features, transmission patterns, and management of COVID-19 pneumonia. **Our efforts in this review are to evaluate and study similar outbreaks from the past to understand its adverse impact on mental health, implement adequate steps to tackle and provide a background to physicians and healthcare workers at the time of such outbreaks to apply psychological first aid.**

Resources

Interactive web-based graphs of novel coronavirus COVID-19 cases and deaths per population by country.
Idogawa, Masashi; Tange, Shoichiro; Nakase, Hiroshi; Tokino, Takashi
Clin Infect Dis
2020 Apr 27; PMID: 32339228
Level of Evidence: 5 - Expert Opinion
Type of Article: Correspondence
BLUF: This is an introduction to the Transition of New Coronavirus COVID-19 Cases and Deaths per Population by Country website (linked below); this site draws data from the European Centre for Disease Prevention and Control, World Health Organization situation reports, and population data of the United Nations, in order to provide a transition of the COVID-19 situation over time and give a visual portrayal of the trends of COVID-19 between countries.
Website link: https://web.sapmed.ac.jp/canmol/coronavirus/index_e.html

Abstract: An accurate grasp of COVID-19 situation is considered highly important. The website we launched provides **graphs of COVID-19 cases and deaths per one million population over time including trajectory analysis**, and one can easily grasp the COVID-19 trend and adequately compare the situation between countries through this interactive graph system.

Covid-19 treatment update: follow the scientific evidence.
Becker RC.
J Thromb Thrombolysis.
2020 Apr 27; PMID: 32338320
Level of Evidence: 5 - Expert opinion
Type of Article: Letter
Summarizing Excerpt: "The following Covid-19 treatment update is dedicated to pharmacologic therapies, their mechanism(s) of potential benefit, safety considerations and optimal study design for planned and ongoing clinical trials. The focus is on chloroquine and hydroxychloroquine- two oral drugs that have been available and used widely for the prevention and treatment of malaria and in the management of autoimmune diseases."

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