INFOLETTER 6 – COVID-19

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Content overview

Initial ELSO Guidance Document - ECMO for COVID-19 Patients with Severe Cardiopulmonary Failure

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Journal: ASAIO *Published Online: March 30, 2020*

Authors from: USA, the Netherlands, Australia, Czech Republic, Colombia, India

The **Extracorporeal Life Support Organization** (ELSO) and all of the ELSO worldwide chapters have prepared this document to describe when and how to use extracorporeal membrane oxygenation (ECMO) in COVID-19 patients. It is a **consensus guideline** intended for experienced ECMO centers. ECMO **can be lifesaving** in patients with severe forms of ARDS or refractory cardiocirculatory compromise. Initial experience in Japan and South Korea with ECMO in >50 COVID-19 cases **has had survivors**, with many still receiving treatment. The Society of Critical Care Medicine has promulgated guidelines for the management of COVID-19 patients and recommends the use of ECMO **when conventional management fails**. Due to the intensive hospital resource utilization, substantial staff training, and multidisciplinary needs associated with starting an ECMO program, **ELSO recommends against starting new ECMO centers for the sole purpose of treating patients with COVID-19**. A list of experienced ECMO centers is provided on the ELSO website. During the COVID-19 surge, it is reasonable to concentrate those patients with the greatest chance of benefit from receiving ECMO in a hospital where an experienced ECMO team is available.

ECMO **indications, access, and management** are described in the ELSO Guidance for Adult Respiratory and Cardiac failure on the ELSO web site (https://www.elso.org/default.aspx). ECMO is indicated in patients who have a high risk of mortality. There are several ways to measure mortality risk in ARDS. All include **PaO2/FiO2 below 100**, despite and after optimal care. For adult respiratory failure, the recently published EOLIA trial contains three indications that define severe ARDS where ECMO may be useful. When patients meet indications, ECMO **should be initiated immediately** in an experienced center, and not days later. Because the use of ECMO for COVID-19 is occurring during a pandemic which can overwhelm hospital resources, unique considerations for ECMO in COVID-19 patients are:

Should ECMO be considered for COVID-19 patients? This is a case by case decision that should be reassessed regularly. If the hospital must commit all resources to other patients, then ECMO should not be considered until the resources stabilize. If the hospital feels that ECMO can be safely provided, then it should be offered. The use of ECMO in patients with a combination of advanced age, multiple co-morbidities, or multiple organ failure should be rare.

Should ECMO during CPR (E-CPR) be considered for COVID-19 patients? Due to the complexity associated with doing E-CPR, centers who do not currently provide this, should not initiate programs during times of limited resources. Inexperienced ECMO centers should consider whether to continue. **At experienced centers, E-CPR may be considered for in-hospital cardiac arrest** depending on resource availability. However, in patients with COVID-19, the **potential for cross-contamination** of staff and the use of personal protective equipment (PPE) by multiple practitioners when in short supply, should be considered in the risk-to-benefit ratio of performing E-CPR. Initiating E-CPR in patients with multiple co-morbidities or multiple organ failure should be rare.

Should ECMO be considered for traditional indications during the COVID-19 pandemic? Understanding hospital resource limitations as above, standard ECMO should continue when that is possibly related to overall hospital resources.

When ECMO is used: What patients are the highest priority? Younger patients with minor or no co-morbidities are the highest priority while resources are limited. Health care workers are a high priority. It should be acknowledged that this is a dynamic prioritization. As resources change, priorities should shift based on what can be safely done in the hospital-specific setting.

What patients should be excluded? Standard contraindications apply: terminal disease, severe central nervous system damage, Do Not Resuscitate status, or advanced directives refusing such therapy. Exclusions for COVID-19 during limited resources are hospital or region-specific. Because prognosis is worse with co-morbidity and age, patients with significant co-morbidities should be excluded and older age should be considered when balancing resource availability with the potential to improve outcomes. Because prognosis is worse with time on invasive mechanical ventilation, **patients on mechanical ventilation greater than 7 days** should be generally excluded. Renal failure is not an exclusion.

What protective measures for the team should be used? Standard COVID-19 precautions as recommended by WHO and national health organizations should be used. There are currently no special precautions recommended for blood contact.

What is the definition of futility for termination? Not all patients will improve with ECMO support. As is standard with usual ECMO care, clinicians should be continuously evaluating when ECMO no longer provides a positive benefit: risk ratio and should at that point return to conventional management regardless of how long the patient has been on ECMO. During times of limited resources, this becomes especially important and while the definition will be hospital or region-specific, **observing no lung or cardiac recovery after approximately 21 days** on ECMO can be considered futile, and the patient can be returned to conventional management. (Note: for situations where withdrawal of life-sustaining therapies is not an option, this change of management does not constitute withdrawal.)

What is the incidence of cardiac failure and how is it managed? As in any patient, cardiac failure is defined as sustained hypotension despite other management. Failure is confirmed and measured by physiologic parameters and echocardiography. **VA access is indicated,** perhaps in the form of V-VA. Therefore, timely echocardiographic assessment in the presence of any clinical suspicion of cardiac dysfunction or sign of circulatory compromise should be undertaken.

For ELSO member centers, when you use ECMO for COVID-19, **please enter your patient in the Registry at the time they go on** (and later when discharged). Early registry entry allows ELSO to be able to provide member centers with the **real-time and up-to-date** outcomes and complication data. **Centers that are using ECMO and are not ELSO members are encouraged to join ELSO and enter COVID-19 cases. The membership fee is waived during this pandemic.**

Extracorporeal Membrane Oxygenation for Coronavirus Disease 2019 in Shanghai, China

https://journals.lww.com/asaiojournal/Abstract/onlinefirst/Extracorporeal_Membrane_Oxygenation_for.98540.aspx

Journal: ASAIO *Published Online: March 30, 2020*

Authors from: China

In this article, the authors focused on indications and management of ECMO treatment in COVID-19 with respect to the clinical guidelines and local practice. They also shared their experience so far: **Eight COVID-19 patients have received ECMO** in Shanghai with 7 with VV ECMO support and 1 VA ECMO during cardiopulmonary resuscitation. As of March 25, 2020, 4 patients died (50% mortality), **three patients (37.5%) were successfully weaned** off ECMO after 22, 40 days and 47 days support respectively, **but remain on mechanical ventilation**. One patient is still on VV ECMO with mechanical ventilation. The PaO2/FiO2 ratio before ECMO initiation was between 54 to 76 and all were well below 100. The duration of mechanical ventilation before ECMO ranged from 4-21 days. Except for the one emergent VA ECMO during cardiopulmonary resuscitation, other patients were on ECMO support for between 18 to 47 days. In conclusion, ensuring effective, timely, and safe ECMO support in COVID-19 is key to improving clinical outcomes. ECMO support might be an integral part of the critical care provided for COVID-19 patients in centers with advanced ECMO expertise.

ECMO has been used clinically in Shanghai for nearly 19 years. **Diffuse pulmonary edema and hyaline membrane formation** are the main pathological features in COVID-19 patients. Hypoxia can progress rapidly, and optimal mechanical ventilation might not be enough to correct for patients in critical status. Traditional ECMO indications, or the standards as adopted in the EOLIA study, may lead to prolonged hypoxia and multiple organ failure in these patients. Therefore, **the authors recommend the early establishment of ECMO** when mechanical ventilation is insufficient to correct hypoxia in COVID-19 patients. Their indications are consistent with the latest version of the Chinese COVID-19 Guidelines. More data on the mechanism of death and disease are required to determine **whether ECMO is appropriate to offer to COVID-19 patients**. However, it appears that the damage and duration of lung injuries in COVID19 are extensive and **prolonged ECMO support might be required** as shown in the present study. In conclusion, ensuring effective, timely, and safe ECMO support in COVID-19 is key to improving clinical outcomes. ECMO support might be an integral part of the critical care provided for COVID-19 patients in centers with advanced ECMO expertise.

The Variety of Cardiovascular Presentations of COVID-19

https://www.ahajournals.org/doi/pdf/10.1161/CIRCULATIONAHA.120.047164

Journal: Circulation *Published Online: April 3, 2020*

Authors from: USA

There is increasing awareness of the **cardiovascular manifestations of COVID-19** and the adverse impact that cardiovascular involvement has on prognosis. Discriminating between a cardiac or respiratory etiology of symptoms can be challenging since each may present predominantly with

dyspnea. It is also critical to recognize when **cardiac and pulmonary involvements coexist**. In this paper, the authors present four cases (Chest pain and ST elevation in a 64 y/o woman resulting in a diagnosis of a cardiogenic shock, IABP was utilized; Cardiogenic shock rescued by VAV ECMO in a 38 y/o man; Decompensated heart failure in a 64 y/o woman treated with conventional management; Uncomplicated COVID-19 in a 51 y/o male heart transplant recipient on chronic immunosuppression), that illustrate a variety of cardiovascular presentations of COVID19 infection. In addition to discussing the basic clinical physiology, they also discuss clinical decision making in the current environment, while considering resource allocation and the welfare of health care professionals.

In patients presenting with **what appears to be a typical cardiac syndrome, COVID-19 infection should be in the differential** during the current pandemic, even in the absence of fever or cough. One should have a **low threshold to assess for cardiogenic shock** in the setting of acute systolic heart failure related to COVID. If inotropic support fails in these patients, **the authors consider IABP** as the first line mechanical circulatory support device because it requires the least maintenance from medical support staff. When patients on VV ECMO for respiratory support develop superimposed cardiogenic shock, the **addition of an arterial conduit** at relatively low blood flow rates may provide the necessary circulatory support without inducing LV distension. Their experience confirms that rescue of patients even with profound cardiogenic or mixed shock may be possible with temporary hemodynamic support at centers with the availability of such devices. COVID-19 infection can cause **decompensation of underlying heart failure** and may lead to mixed shock. Invasive hemodynamic monitoring, if feasible, may be helpful to manage the cardiac component of shock in such cases. Medications that prolong the QT interval are being considered for COVID-19 patients and may require closer monitoring in patients with underlying structural heart disease. The heart transplant recipient exhibited similar symptoms of COVID-19 infection as compared to the general population. For those transplant patients requiring hospitalization, **how to alter the anti-metabolite and immunosuppression regimens remains uncertain**. Furthermore, the COVID-19 pandemic creates a challenge for the management of heart failure patients on the heart transplant waitlist, forcing physicians to balance the risks of delaying transplant with the risks of donor infection and uncertainty regarding the impact of post-transplant immunosuppression protocols.

COVID-19 pandemic and cardiac imaging: EACVI recommendations on precautions, indications, prioritization, and protection for patients and healthcare personnel

https://academic.oup.com/ehjcimaging/advance-article/doi/10.1093/ehjci/jeaa072/5815408
Journal: European Heart Journal - Cardiovascular Imaging Published Online: April 3, 2020
Authors from: Norway, Belgium, Italy, Romania, France, Portugal, Germany, UK...

The scope of these EACVI recommendations is to summarize the challenges and possible solutions in cardiac imaging during the pandemic. In particular, the full-text provides specific indications and recommendations on **how to perform an echocardiogram** during the pandemic whilst safeguarding both patient and staff. Commentary is given on patients with known or acute

cardiac disease. Some of the recommendations relating to the appropriate use of imaging modalities in the COVID-19 pandemic **must be considered only as expert advice** due to the lack of evidence-based scientific data and the rapidly changing global situation.

Key points:

Important considerations in patients with suspected or confirmed COVID-19

- Cardiac imaging should be performed if appropriate and only if it is likely to substantially change patient management or be lifesaving
- Use the imaging modality with the best capability to meet the request, but consider also the safety of medical staff regarding exposure
- Elective non-urgent and routine follow-up exams may be postponed or even canceled

Risks of contamination in patients with suspected or confirmed COVID-19 include

- Possible/significant risk of infection for professionals (technicians, physicians, nurses, other personnel)
- Possible/significant risk of contamination of equipment and facilities
- Risk of widespread contamination due to the transportation of critically ill or high-risk patients—the echo machine should be brought to the patient
- Prolonged duration of a cardiac imaging study will increase the likelihood of contamination

Advice for cardiac imaging

- Echocardiography should not routinely be performed in patients with COVID-19 disease
- A range of different cardiovascular manifestations can be found in COVID-19 which may require cardiac imaging, including a bedside echocardiographic study
- A focused cardiac ultrasound study (FoCUS) is recommended to reduce the duration of exposure
- The risk of contamination of equipment and personnel is very high during TOE—consider repeat TTE, CT scan, or CMR as alternatives
- Chest CT is frequently used to confirm COVID-19 pneumonia and might provide possible synergies and opportunities of cardiac imaging
- Coronary CT angiography can exclude or confirm an acute coronary syndrome in COVID-19 pneumonia where elevated troponins are common
    - LV function can be assessed by LV angiogram in patients with acute coronary syndromes during the invasive revascularization procedure
    - Positive troponins and myocardial dysfunction or severe arrhythmia suggestive of Tako-tsubo or myocarditis may be an indication for acute CMR if of vital importance for treatment, and a patient can be safely transferred for imaging
    - Indications for fetal echocardiography remain the same as outside the COVID-19 pandemic

SARS-CoV-2, COVID-19 and inherited arrhythmia syndromes

https://www.heartrhythmjournal.com/article/S1547-5271(20)30285-X/pdf

Journal: Heart Rhytm *Published Online: March 28, 2020*

Authors from: Italy, Spain, Germany, UK, the Netherlands…

Currently, there is no proven effective therapy against the virus, and the impact on other diseases including inherited arrhythmia syndromes is uncertain. **Arrhythmogenic effects of COVID-19** can be expected, potentially contributing to the disease outcome. This may be of importance for patients with an increased risk for cardiac arrhythmias, either secondary to acquired conditions or co-morbidities or consequent to inherited syndromes. Management of patients with inherited arrhythmia syndromes such as **Long QT syndrome, Brugada syndrome, Short QT syndrome and Catecholaminergic Polymorphic Ventricular Tachycardia** in the setting of the COVID-19 pandemic may prove particularly challenging. Depending on the inherited defect involved, these patients may be susceptible to pro-arrhythmic effects of COVID-19-related issues such as fever, stress, electrolyte disturbances and use of antiviral drugs. The authors describe the potential COVID-19 associated risks and therapeutic considerations for patients with distinct inherited arrhythmia syndromes and provide recommendations, pending local possibilities, for their monitoring and management during this pandemic.

Key considerations:

Long QT:

- QTc-interval monitoring when using (hydroxy)chloroquine in COVID-19 patients
- QTc-interval monitoring when using or combining anti-viral drugs in COVID-19 patients
- QTc-interval monitoring in patients with known LQTS acquired QT-prolongation or conditions associated with acquired QT-prolongation (e.g. use of other QT-prolonging drugs, structural heart disease, bradycardia <50/min, liver, and renal disease)
- When QTc is above 500msec, we advise consultation with a cardiologist (“QT-specialist”) for guidance (which might, e.g., result in intensified monitoring, raising potassium levels, and/or discontinuation of one or more QT-prolonging drugs)
- Patients with acquired LQTS or patients using a combination of QT-prolonging drugs should have a high serum potassium level. Avoiding hypokalemia is not enough and the adagium should be "serum potassium of 5 is better than 4."

Brugada syndrome:

- All patients with Brugada syndrome should self-treat with paracetamol/acetaminophen immediately if they develop signs of fever and self-isolate.
- Patients without an ICD who are at higher risk due to fever include a. sodium channel disease with or without a type 1 ECG pattern, b. children and young adults (under 26 years old) and the elderly (over 70 years) with Brugada syndrome; and c. all patients with a spontaneous type 1 Brugada pattern and/or cardiac syncope.
- If these higher-risk patients develop a high fever (>38.5C) despite paracetamol treatment, they will need to attend the emergency department. The emergency department must be

forewarned to allow assessment by staff with suitable protective equipment. Assessment should include an ECG and monitoring for arrhythmia. If an ECG shows the type 1 Brugada ECG pattern, then the patient will need to be observed until fever and/or the ECG pattern resolves. If all ECGs show no sign of the type 1 ECG pattern, then they can go home to self-isolate.

- Patients who are not part of the higher risk group and have a drug-induced type 1 ECG pattern, no symptoms of syncope and no sign of a spontaneous type 1 pattern at any other time are at the lowest risk and can afford to self-isolate at home. The risk of visiting the emergency department and contracting COVID-19 is likely to outweigh the risk of an LTE. Attendance to the hospital should then be dictated by other clinical features, such as palpitations or (pre-)syncope, etc. The same advice holds for patients with an ICD. Management in the hospital should include monitoring of ECG abnormalities and arrhythmia, as well as efforts to reduce the body temperature (with antipyretic drugs, preferably paracetamol/acetaminophen, or eventually ibuprofen). More generally, BrS patients, in particular those with a pathogenic or likely pathogenic variant in SCN5A, are advised to self-isolate in their private environment.

Short QT syndrome:
The authors do not believe that there is a particular concern when SQTS patients are infected with SARS-CoV-2.

A Practical Approach to the Management of Cancer Patients During the Novel Coronavirus Disease 2019 (COVID-19) Pandemic: An International Collaborative Group

https://theoncologist.onlinelibrary.wiley.com/doi/pdf/10.1634/theoncologist.2020-0213
Journal: The Oncologist *Published Online: March 26, 2020*
Authors from: USA, Canada, UK, UAE, Taiwan, China…

Many cancer patients frequently visit the hospital for treatment and disease surveillance. They may be **immunocompromised** due to the underlying malignancy or anticancer therapy and are at higher risk of developing infections. Several factors increase the risk of infection, and cancer patients commonly have multiple risk factors. Cancer patients appear to have an estimated **twofold increased risk of contracting SARS-CoV-2** than the general population. With the WHO declaring the novel coronavirus outbreak a pandemic, there is an urgent need to address the impact of such a pandemic on cancer patients. This includes changes to resource allocation, clinical care, and the consent process during a pandemic. Currently and due to limited data, there are no international guidelines to address the management of cancer patients in any infectious pandemic. In this review, the **potential challenges associated with managing cancer patients during the COVID-19 infection pandemic** will be addressed, with suggestions of some practical approaches.

Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: Information for healthcare professionals

https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1002/ijgo.13156
Journal: International Journal of Gynaecology and Obstetrics Published Online: April 4, 2020
Authors from: China, Denmark, Canada, Burkina Faso, India, Australia, Kenya, Portugal…

FIGO has issued the following guidance for the management of pregnant women at the four main settings of pregnancy: (1) ambulatory **antenatal care** in the outpatient clinics; (2) management in the setting of the **obstetrical triage**; (3) **intrapartum management**; and (4) **postpartum management and neonatal care**. They also provide guidance on the medical treatment of pregnant women with COVID-19 infection.

Key points:

- Pregnant women with confirmed COVID-19 infection should be managed by **designated tertiary hospitals** and should be counseled on the risk of adverse pregnancy outcome.
- **Negative pressure isolation rooms** should be set up for safe labor and delivery and neonatal care. This may not be possible in many low-resource settings but all possible attempts should be made for isolation and infection control.
- During the COVID-19 pandemic period, a detailed history regarding exposure relevant to COVID-19 and clinical manifestations should be acquired routinely from all pregnant women attending for routine care.
- **A Chest CT scan should be included in the work-up of** pregnant women with suspected/probable/confirmed COVID-19 infection.
- Suspected/probable cases should be **treated in isolation** and confirmed cases should be managed in a negative pressure isolation room. A woman with a confirmed infection who is critically ill should be admitted to a negative pressure isolation room in the ICU.
- Antenatal examination and delivery of pregnant women infected with COVID-19 should be carried out in a negative pressure isolation room in the labor ward. Human traffic around this room should be limited when it is occupied by an infected patient.
- All medical staff involved in the management of infected women should wear appropriate PPE as required.
- Management of COVID-19-infected pregnant women should be undertaken by a **multidisciplinary team** (obstetricians, maternal-fetal medicine subspecialists, intensivists, obstetric anesthetists, internal medicine or respiratory physicians, midwives, virologists, microbiologists, neonatologists, infectious disease specialists).
- **Timing and mode of delivery should be individualized, dependent mainly on the clinical status of the patient, gestational age, and fetal condition**
- At present, limited data suggest that there is **no evidence of vertical mother-to-baby transmission** in women who develop COVID-19 infection in late pregnancy.
- There is currently **insufficient evidence regarding the safety of breastfeeding** and the need for mother/baby separation. If the mother is severely or critically ill, the separation appears the best option, with **attempts to express breastmilk** to maintain milk production. If the

patient is **asymptomatic or mildly affected, breastfeeding and colocation (rooming-in) can be considered** by the mother in coordination with healthcare providers.

- Healthcare professionals engaged in obstetric care should be trained and fitted appropriately for respirators.

Breastfeeding and Coronavirus Disease-2019. Ad Interim Indications of the Italian Society of Neonatology Endorsed by the Union of European Neonatal & Perinatal Societies

https://onlinelibrary.wiley.com/doi/abs/10.1111/mcn.13010
Journal: Maternal and Child Nutrition *Published Online: April 3, 2020*
Authors from: Italy

Besides the possible consequences of COVID-19 infection on a pregnant woman and the fetus, a major concern is related to the potential effect on the neonatal outcome, the appropriate management of the mother-newborn dyad and finally the compatibility of maternal COVID-19 infection with breastfeeding. **The Italian Society on Neonatology** (SIN) after reviewing the limited scientific knowledge on the compatibility of breastfeeding in the COVID-19 positive mother and the available statements from Health Care Organizations, has issued the following indications that have been endorsed by the **Union of European Neonatal & Perinatal Societies** (UENPS). If a mother previously identified as COVID-19 positive or under investigation for COVID-19 **is asymptomatic or paucisymptomatic at delivery, rooming-in is feasible and direct breastfeeding is advisable**, under strict measures of infection control.
On the contrary, when a mother with COVID-19 is **too sick to care for the newborn, the neonate will be managed separately and fed fresh expressed breast milk, with no need to pasteurize** it, as human milk is not believed to be a vehicle of COVID-19. This guidance might be subject to change in the future when further knowledge will be acquired about the COVID-19 pandemic, the perinatal transmission of SARS-CoV-2 and clinical characteristics of cases of neonatal COVID-19.

No Evidence of Rapid Antiviral Clearance or Clinical Benefit with the Combination of Hydroxychloroquine and Azithromycin in Patients with Severe COVID-19 Infection

https://www.sciencedirect.com/science/article/pii/S0399077X20300858?via%3Dihub
Journal: Médecine et Maladies Infectieuses *Published Online: March 30, 2020*
Authors from: France

Chloroquine analogs have been shown to inhibit the acidification of endosomes and to exhibit **in vitro a non-specific antiviral activity** at high micromolar concentration against COVID-19. In their study, Gautret et al. reported a 100% viral clearance in nasopharyngeal swabs in 6 patients after 5 and 6 days of the combination of hydroxychloroquine and azithromycin.
This rate of viral clearance was lower with hydroxychloroquine alone (57.1%) and was only 12.5% in patients who did not receive hydroxychloroquine. The authors of the present study performed a **prospective study virologic and clinical outcomes of 11 (7 were men, mean age 58.7 yrs)**

consecutive patients received **hydroxychloroquine** and **azithromycin** using the same dosing regimen reported by Gautret et al. Eight patients had significant comorbidities associated with poor outcomes (obesity: 2; solid cancer: 3; hematological cancer: 2; HIV-infection: 1). Initially, 10/11 had a fever and received nasal oxygen therapy. **Within 5 days, one patient died, two were transferred to the ICU**. In one patient, hydroxychloroquine and azithromycin were discontinued after 4 days because of a **prolongation of the QT interval** from 405 ms before treatment to 460 and 470 ms under the combination. Repeated nasopharyngeal swabs in 10 patients (not done in the patient who died) using a qualitative PCR assay **were still positive for SARS-CoV2 RNA in 8/10 patients at days 5 to 6 after treatment initiation.** These virologic results stand in contrast with those reported by Gautret et al. and cast doubts about the strong antiviral efficacy of this combination. Furthermore, in their report Gautret et al also reported one death and three transfers to the ICU among the 26 patients who received hydroxychloroquine, also underlining the poor clinical outcome with this combination. In addition, a recent study from China in individuals with COVID-19 found no difference in the rate of virologic clearance at 7 days with or without 5 days of hydroxychloroquine, and no difference in clinical outcomes (duration of hospitalization, temperature normalization, radiological progression). In summary, despite a reported antiviral activity of chloroquine against COVID-19 in vitro, the authors **found no evidence of a strong antiviral activity or clinical benefit of the combination of hydroxychloroquine and azithromycin** for the treatment of our hospitalized patients with severe COVID-19. Ongoing RCTs will provide more data.

Gargle lavage as a safe and sensitive alternative to swab samples to diagnose COVID-19: a case report in Japan

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa377/5815296
Journal: Clinical Infectious Diseases *Published Online: April 2, 2020*
Authors from: Japan

The diagnosis of COVID-19 requires upper or lower respiratory samples. However, up to 80% of the patients do not have a productive cough. To protect healthcare workers during sampling for diagnosis, the US CDC **recommends not inducing cough to collect sputum samples**, but rather the collection of nasopharyngeal and/or oropharyngeal swabs, or nasopharyngeal wash/aspirate or nasal aspirate. Nasal swabs are reported to have higher viral titers than throat swabs; accordingly, nasopharyngeal swabs are the preferred samples in Japan. However, nasopharyngeal and oropharyngeal **swabs cause discomfort** to patients and can potentially increase the risk of direct exposure of healthcare workers by provoking coughing. Moreover, the **sensitivity for virus detection is low with these swabs**; the viral load is reportedly higher in sputum samples. In this article, the authors report **a case in which gargle lavage samples yielded a positive PCR result**. A 55-year-old man came to our hospital with a clinical and epidemiological history suggestive of COVID-19. CT-scan revealed patchy ground-glass opacities. Oropharyngeal swabs and gargle lavage (using 10 mL of normal saline) were collected because he did not produce sputum. Samples were positive for COVID-19 by RT-PCR. Additional gargle lavage samples and oropharyngeal swabs were collected and tested on Days 8 and 9 and found to be positive, with a **slightly higher amount**

of viral genome in the gargle lavage sample. His PCR became negative on Day 16 and 19, and discharged on Day 19. For other respiratory pathogens, gargle lavage samples have been reported to be more sensitive than throat swabs. **Gargle lavage can be done by patients themselves without putting healthcare professionals at increased risk**.

A novel treatment approach to the novel coronavirus: an argument for the use of therapeutic plasma exchange for fulminant COVID-19

https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-2836-4
Journal: Critical Care *Published Online: April 2, 2020*
Authors from: USA

Chinese authorities have reported success in treating COVID-19 with convalescent plasma. The authors of the present study propose therapeutic plasma exchange (TPE)as a possible treatment for a **fulminant disease with a cytokine storm**. TPE uniquely offers a benefit on multiple levels by **removing inflammatory cytokines, stabilizing endothelial membranes, and resetting the hypercoagulable state**. An in-depth review is beyond the scope of this editorial, but some rationale is mentioned. Busund and colleagues showed a tendency toward improved mortality with adjunct TPE in adult patients with sepsis and multiple organ failure in the sole, adult-only randomized controlled trial on this subject while a **meta-analysis** by Rimmer showed **mortality benefit** in adult patients as well. Drawing from this data, Patel and colleagues utilized TPE during the 2009 H1N1 influenza A outbreak in three pediatric patients presenting in a similar fashion to those seen with fulminant COVID-19 today. All three patients developed ARDS with a hemodynamic compromise that continued to deteriorate despite standard care and rescue therapy for ARDS including inhaled nitric oxide (3/3) and veno-venous ECMO (1/3). Predicted mortality was high, but **all three had a full recovery** from their illness after receiving rescue TPE. Others have reported successful outcomes, feasibility, and safety of TPE for sepsis, but **none have investigated specifically in pneumonia/ARDS.** The authors of the present editorial recently conducted a retrospective clinical trial, in which the **patients receiving adjunct TPE were propensity-matched to patients with similar illness** who received standard of care alone. All patients required ≥ 2 vasopressors and all patients receiving TPE required mechanical ventilator support. Nearly half of the patients in both groups (39/80) presented with pneumonia as the primary source of infection and **subgroup analysis showed the mortality benefit** with TPE in these patients (47.8% mortality vs. 81.3% mortality, $p = 0.05$). Further evaluation is needed.

Proposal of a low-dose, long-pitch, dual-source chest CT protocol on third-generation dual-source CT using a tin filter for spectral shaping at 100 kVp for CoronaVirus Disease 2019 (COVID-19) patients: a feasibility study

https://link.springer.com/article/10.1007%2Fs11547-020-01179-x
Journal: La Radiologica Medica *Published Online: April 1, 2020*
Authors from: Italy

Patients with COVID-19 undergoing chest CT on **third-generation dual-source CT** (DSCT) were included. The imaging protocol included a **dual-energy acquisition** (HD-DECT, 90/150Sn kVp) and **fast, low-dose, long-pitch CT, dual-source scan** at 100Sn kVp (LDCT). Subjective (Likert Scales) and objective (**signal-to-noise and contrast-to-noise ratios**, SNR and CNR) analyses were performed; radiation dose and acquisition times were recorded. Nonparametric tests were used. The **median radiation dose was lower for LDCT than HD-DECT** (Effective dose, ED: 0.28 mSv vs. 3.28 mSv, p = 0.016). LDCT had a median acquisition time of 0.62 s (vs 2.02 s, p = 0.016). SNR and CNR were significantly different in several thoracic structures between HD-DECT and LDCT, with the exception of lung parenchyma. The qualitative analysis demonstrated a **significant reduction in motion artifacts** with **comparable diagnostic reliability** between HD-DECT and LDCT. **Ultra-low-dose, dual-source, fast CT protocol provides highly diagnostic images for COVID-19 with the potential for reduction in dose and motion artifacts.**

Severe Acute Respiratory Syndrome Coronavirus 2 RNA Detected in Blood Donations

https://wwwnc.cdc.gov/eid/article/26/7/20-0839_article
Journal: Emerging Infectious Diseases *Published Online: April 3, 2020*
Authors from: China

Wuhan Blood Center began screening for SARS-CoV-2 RNA on January 25, 2020. They screened donations in real-time (n=2430) and retrospectively (n=4995) and found **plasma samples positive for viral RNA from 4 asymptomatic donors.** Samples from these donors were further tested for specific IgG and IgM against SARS-CoV-2 by ELISA; results were negative, indicating the possibility of infection in the early stage and the need to follow-up with these donors.

Microneedle array delivered recombinant coronavirus vaccines: Immunogenicity and rapid translational development

https://www.thelancet.com/pdfs/journals/ebiom/PIIS2352-3964(20)30118-3.pdf
Journal: EBioMedicine *Published Online: April 2, 2020*
Authors from: USA, the Netherlands

Safe vaccines that rapidly induce **potent and long-lasting virus-specific immune responses** against recent causative agents of coronaviruses outbreaks are urgently needed. The coronavirus

spike (S) protein, a characteristic structural component of the viral envelope, is considered a key target for vaccines for the prevention of coronavirus infection.
The authors of the present study first **generated codon-optimized MERS-S1 subunit vaccines** fused with a foldon trimerization domain to mimic the native viral structure. In variant constructs, they engineered immune stimulants (RS09 or flagellin, as TLR4 or TLR5 agonists, respectively) into this trimeric design. They comprehensively tested the pre-clinical immunogenicity of MERS-CoV vaccines in mice when delivered subcutaneously by traditional needle injection, or intracutaneously by dissolving microneedle arrays (MNAs) by evaluating virus-specific IgG antibodies in the serum of vaccinated mice by ELISA and using virus neutralization assays. Driven by the urgent need for COVID-19 vaccines, **they utilized this strategy to rapidly develop MNA SARS-CoV-2 subunit vaccines and tested their pre-clinical immunogenicity in vivo** by exploiting our substantial experience with MNA MERS-CoV vaccines.In the article, they describe the development of MNA delivered MERS-CoV vaccines and their pre-clinical immunogenicity. Specifically, **MNA delivered MERS-S1 subunit vaccines elicited strong and long-lasting antigen-specific antibody responses**. Building on our ongoing efforts to develop MERS-CoV vaccines, promising immunogenicity of MNA-delivered MERS-CoV vaccines, and their experience with MNA fabrication and delivery, including clinical trials, they rapidly designed and **produced clinically-translatable MNA SARS-CoV-2 subunit vaccines within 4 weeks** of the identification of the SARS-CoV-2 S1 sequence. Most importantly, these MNA delivered SARS-CoV-2 S1 subunit vaccines **elicited potent antigen-specific antibody responses that were evident beginning 2 weeks after immunization**. MNA delivery of coronaviruses-S1 subunit vaccines is a promising immunization strategy against coronavirus infection.

The use of high-flow nasal oxygen in COVID-19

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Journal: Anaesthesia *Published Online: April 4, 2020*
Authors from: Ireland

The use of **high-flow nasal oxygen** (HFNO) in COVID-19 is the subject of much debate, relating to the benefits and harms that may result in patients and healthcare workers alike. The position of HFNO in the various guidelines is controversial. Joint guidance issued by the Faculty of Intensive Care Medicine, Intensive Care Society, Association of Anaesthetists and Royal College of Anaesthetists from the UK states that "**HFNO or similar devices should be avoided**," remarking that there is "no survival benefit compared to conventional oxygen therapy, and the risk of environmental viral contamination may be higher". The WHO recommends that HFNO **should only be used in selected patients with hypoxaemic respiratory failure**. The guideline lists hypercapnia, hemodynamic instability, multi-organ failure and abnormal mental status as scenarios that render it generally inappropriate for use. It recommends that patients are cared for in a monitored setting and by experienced personnel capable of performing tracheal intubation in the event of acute deterioration or failure to improve after a short trial ("about 1 hour"). The COVID-19 guidelines of the Australian and New Zealand Intensive Care Society (ANZICS) state that HFNO is a "**recommended therapy**" for hypoxia associated with COVID-19 illness, **as long as staff is wearing**

optimal PPE. The COVID-19 guidelines of the Surviving Sepsis Campaign recommend **using HFNO over conventional oxygen therapy in patients with acute hypoxemic respiratory failure despite conventional oxygen therapy**. An additional recommendation is made that HFNO is used over NIV in these patients.

The evidence-base for the understanding of **aerosolization** with HFNO is sparse and it is even worse for the evaluation of **the risk of transmission**. However, one systematic review suggested that during the SARS outbreaks, healthcare workers exposed to HFNO were not at increased risk of transmission, based on the low quality of evidence. Whilst the HFNO flow rate appears to influence aerosol spread, this **does not inherently mean that flow rates should be reduced** as a safety measure. Statistically significant increases in spread might not necessarily indicate a linear increase in clinical risk. Furthermore, it is well-demonstrated that some HFNO benefits are determined by flow rate, such as positive airway pressure generation.

Prone positioning is a widely used therapy in ARDS and COVID-19. Whilst mechanical ventilation is typically undertaken as a prelude to proning, it is not a pre-requisite. For a **proning of the awake patient**, HFNO may be a more practical and comfortable alternative than NIV, though the use of both has been described. Early use of HFNO and of awake prone positioning has been speculated by some clinicians as a cause for the reduced mortality from COVID-19 observed in Jiangsu Province compared to Hubei Province in China.

Clear plastic drapes may be effective at limiting aerosolization and droplet spray during extubation: implications for COVID-19

https://link.springer.com/article/10.1007%2Fs12630-020-01649-w

Journal: Canadian Journal of Anesthesia *Published Online: April 3, 2020*

Authors from: Canada

Aerosol-generating medical procedures (AGMP) in patients with COVID-19 pose a high risk of transmission of the illness to clinical staff, especially in the setting of global shortages of PPE. During AGMP, such as **intubation or extubation**, contamination of surfaces with virus-loaded droplets may also occur. The authors of the present study performed a series of experiments utilizing a coughing mannequin for an assessment of whether clear plastic drapes were effective in containing aerosolization during extubation. The authors showed that the **use of low-cost barriers (clear plastic drapes) was able to significantly limit aerosolization and droplet spray.** The inexpensive and simple method of using clear drapes during extubation (and possibly intubation) of COVID-19 patients may be considered by frontline staff and infection control specialists as an additional precaution to PPE. Modifications of the clear plastics can be adapted for surgical procedures that may be AGMPs. Limitations of this work include its low-fidelity design and use of a larger particle (fluorescent Glo-Germ in UV lit environment) that may not reflect the true spread of a virus-like SARS-CoV-2. It is particularly important that the staff takes care **not to generate further aerosols when removing the drapes**. The authors also recommend using the three-panel draping as opposed to the single-drape technique. Further studies will be needed to further refine this model and its findings.

Potential impact of contaminated bronchoscopes on novel coronavirus disease (COVID-19) patients

https://www.cambridge.org/core/services/aop-cambridge-core/content/view/FD72AC3CD8D143DFB1498296F034FD2A/S0899823X20001026a.pdf/potential_impact_of_contaminated_bronchoscopes_on_novel_coronavirus_disease_covid19_patients.pdf

Journal: Infection Control & Hospital Epidemiology *Published Online: April 2, 2020*
Authors from: USA

Critically ill patients with COVID-19 may require **therapeutic bronchoscopy** or sample collection via **bronchoalveolar lavage** (BAL). Results of BAL assays are used to make clinical decisions that may impact outcomes. Clinicians have reported that COVID-19 patients had bacterial and fungal pulmonary **coinfections** with potential pathogens including Escherichia, Salmonella, Pseudomonas, and Stenotrophomonas, which is associated with significantly higher mortality rates.
Ofstead et al. have conducted **prospective studies that evaluated the effectiveness of bronchoscope reprocessing** in five hospitals in the United States. Microbial growth was detected on 65.7% of 35 bronchoscopes. 28.6% of the bronchoscopes harbored high-concern organisms or actionable levels of microbial growth (>100 CFU). Several breaches on multiple levels were identified. There is currently an urgent need to reduce the number of patients requiring hospitalization or intensive care, in part because of shortages of ventilators and personal protective equipment. Given the **high bronchoscope contamination rates found during routine use in previous studies**, the possibility of bronchoscopy-associated transmission of COVID-19 or other pathogens that could cause secondary infections must be considered. Theoretically, high-level disinfection should eliminate these risks when bronchoscopes are well-maintained and reprocessed according to manufacturer instructions and professional guidelines. However, **even during normal patient loads, practices are frequently substandard**, and pathogens are commonly present on patient-ready endoscopes. The use of **sterile, disposable bronchoscopes** would substantially reduce the risks for patients and reprocessing personnel, and this **approach has been recommended by the American Association for Bronchology and Interventional Pulmonology.** However, single-use bronchoscopes are not universally available and may **not be sufficient for advanced bronchoscopy**. When **reusable bronchoscopes** must be used, they should be **segregated from gastrointestinal endoscopes** and **sterilized rather than relying on high-level disinfection**.

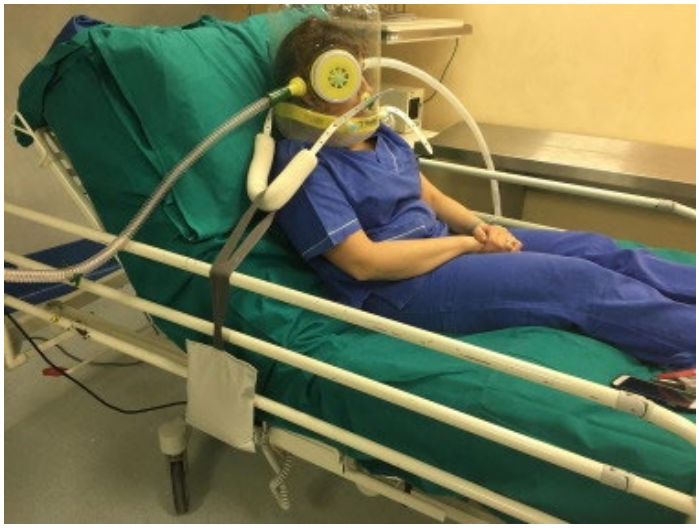
The "helmet bundle" in COVID-19 patients undergoing non invasive ventilation

https://www.sciencedirect.com/science/article/pii/S0964339720300628?via%3Dihub
Journal: Intensive and Critical Care Nursing *Published Online: April 2, 2020*
Authors from: Italy

Substantial **exposure to exhaled air** occurs within one meter from patients receiving noninvasive ventilation (NIV) via face-mask. Large air leaks affect the efficacy of NIV and should be avoided, whereas small air leaks can be compensated for by ventilators designed for NIV and are usually

tolerated. Recently Cabrini et al suggested the use of the **helmet device for Continuous Airway Pressure (CPAP)** and Pressure Support Ventilation (PSV) to limit the virus spread into the ambient air. The number of available ICU beds during the COVID-2019 outbreak is less than the total number of COVID-19 patients requiring NIV or CPAP. In order to prevent ICU admission, **the use of helmets in general wards could be implemented**. The Helmet is a reusable single patient interface, made of a clear plastic hood on a hard-plastic ring with a multi-size silicon-polyvinyl chloride soft collar, to fit a wide range of necks' dimensions. With this device, the patient's exhalate can be filtered by applying a high-efficiency particulate (HEPA) filter at the helmet outlet. There are several challenges regarding the use of the helmet. In the present article, the authors concentrate on **practical tips for improving the patient's comfort.**

The gas airflow generates turbulence and consequently noise. They suggest the use of a **Heat and Moisture Exchanger (HME) filter on the helmet gas inspiratory limb**. Basically, the inner filter membrane works like an engine exhaust muffler, resulting in a significant noise reduction inside the helmet. The choice of fixing a system to anchor the helmet during CPAP significantly affects patient comfort. The authors suggest **avoiding armpit straps during helmet CPAP**, as they can cause pain and device-related pressure ulcers. On the contrary, the counterweights system seems to be the best approach to minimize the risks of pressure sores and pain during this treatment. **Active humidification** during high flow Helmet-CPAP is required. The problem is more prevalent with Venturi systems with a high inspiratory oxygen fraction and when only medical gases are employed. The modern active heated humidifiers, through NIV software, are able to deliver an absolute humidity above 10 mgH2O/L. The use of an active humidifier set at 26 °C, with a temperature gradient increasing towards the patient (+2°/28° at the helmet gas inlet port) improves absolute and relative humidity inside the helmet, while avoiding under-humidification in healthy subjects. These settings provide a proportional amount of water for the helmet inner temperature, due to a rising of temperature inside the hosing line and a reduction in moisture build-up before the helmet inlet. If an HME filter is used as a noise reduction system, it must be placed between the medical gas source and the heater chamber inlet.



Estimates of the severity of coronavirus disease 2019: a model-based analysis

https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30243-7.pdf
Journal: The Lancet Infectious Diseases *Published Online: March 30, 2020*
Authors from: UK

In the face of rapidly changing data, the estimates of a **case fatality ratio of COVID-19 differ substantially in magnitude**. The authors of the present study aimed to provide robust estimates, accounting for censoring and ascertainment biases. They collected **individual-case data for patients who died from COVID-19** in Hubei, China (reported by national and provincial health commissions to Feb 8, 2020), and for cases outside of mainland China (from government or ministry of health websites and media reports for 37 countries, as well as Hong Kong and Macau, until Feb 25, 2020). Using data on 24 deaths that occurred in mainland China and 165 recoveries outside of China, they estimated **the mean duration from onset of symptoms to death to be 17.8 days** and **to hospital discharge to be 24.7 days**. In all laboratory-confirmed and clinically diagnosed cases from mainland China (n=70117), they estimated a **crude case fatality ratio (adjusted for censoring) of 3.67%**. However, after further adjusting for demography and under-ascertainment, they obtained the **best estimate of the case fatality ratio in China of 1.38%**, with substantially **higher ratios in older age** groups (0.32% in those aged <60 years vs 6.4% in those aged ≥60 years), up to 13.4% in those aged 80 years or older. Estimates of case fatality ratio from international cases stratified by age were consistent with those from China. The estimated **overall infection fatality ratio for China was 0.66%**, with an increasing profile with age. Similarly, estimates of the **proportion of infected individuals likely to be hospitalized increased with age up to a maximum of 18.4%** in those aged 80 years or older.

Liver Impairment in COVID-19 Patients: A Retrospective Analysis of 115 Cases From a Single Center in Wuhan City, China

https://pubmed.ncbi.nlm.nih.gov/32239796/?from_term=covid+19&from_sort=date&from_page=16&from_pos=2
Journal: Liver International *Published Online: April 2, 2020*
Authors from: China

This **retrospective, single-center study** was **conducted on 115 confirmed cases** of COVID-19 in Wuhan. Liver function and related indexes were analyzed to evaluate its relationship with disease progression. Part of the patients presented with varying degrees of abnormality in liver function indexes. However, **the levels of ALT, AST, TBIL, GGT and LDH in COVID-19 patients were not significantly different in comparison with hospitalized community-acquired pneumonia patients**, and the levels of albumin were even significantly higher. Levels of ALT, AST, TBIL, LDH, and INR showed statistically significant elevation in severe COVID-19 cases compared with that in mild cases. However, the **clinical significance of the elevation is unremarkable**. The majority of severe COVID-19 patients showed a significant decrease in albumin levels that continued throughout the progress of the illness. Most of the liver function indexes in COVID-19 patients were **correlated**

with CRP and neutrophil-to-lymphocyte ratio (NLR). Logistic regression analysis further identified NLR as the independent risk factor for severe COVID-19, as well as age.

Neutrophil-to-Lymphocyte ratio and Lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis

https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25819
Journal: Journal of Medical Virology *Published Online: April 3, 2020*
Author from: Mexico

Accumulated evidence suggests that a **subgroup of patients with severe COVID-19** could have a **dysregulation of the immune response** that allows the development of **viral hyperinflammation.** Thus, all patients with severe COVID-19 should be screened for hyper inflammation using laboratory parameters in order to improve mortality. **The Neutrophil-to-Lymphocyte ratio** (NLR) and **Lymphocyte-to-C-reactive protein ratio** (LCR) are established inflammation markers that reflect systemic inflammatory response, and both are available in almost all laboratories. A meta-analysis of six Chinese studies was performed to investigate whether NLR and LCR values can help predict clinical severity in patients with COVID-19. A total of 828 patients was included, 407 with severe disease. **The NLR values were found to increase significantly in COVID-19 patients with severe disease** (SMD=2.404, 95% CI=0.98 to 3.82), **while LCR values were decreased significantly** (SMD= -0.912, 95% CI= -1.275 to -0.550).

Clinical course of COVID-19 in a series of patients with chronic arthritis treated with immunosuppressive targeted therapies

https://ard.bmj.com/content/early/2020/04/01/annrheumdis-2020-217424
Journal: Annals of the Rheumatic Diseases *Published Online: April 2, 2020*
Authors from: Italy

The recent outbreak of COVID-19 represents a source of concern for the management of patients with **inflammatory rheumatic diseases**. Since the first reports of COVID-19 in Italy, the authors have circulated a survey with 2-week follow-up contact to patients with chronic arthritis treated with **biological disease-modifying antirheumatic drugs** (bDMARDs) or **targeted synthetic disease-modifying antirheumatic drugs** (tsDMARDs) followed up at a biological outpatient clinic in Pavia, Lombardy. No patient refused to participate.
During the first month, information from **320 patients** was collected (female 68%, mean age 55±14 years) treated with bDMARDs or tsDMARDs (57% with rheumatoid arthritis, 43% with spondyloarthritis, 52% treated with tumor necrosis factor inhibitors, 40% with other bDMARDs and 8% with tsDMARDs). **Four patients were confirmed cases of COVID-19** identified through rhinopharyngeal swabs. Another **four patients reported symptoms** that were highly suggestive of COVID-19. **Five additional patients with reported certain contacts** remained asymptomatic at the end of the 2-week observation period. All patients with confirmed COVID-19 received at least one

antibiotic course, and the hospitalized patient also received antiviral therapy and hydroxychloroquine. Overall, five patients were on previous stable treatment with hydroxychloroquine. **All patients with symptoms of infection temporarily withdrew the bDMARD or tsDMARD** at the time of symptom onset. To date, there have been no significant relapses of the rheumatic disease. **None of the patients with a confirmed diagnosis of COVID-19 or with a highly suggestive clinical picture developed severe respiratory complications or died.** Only one patient, aged 65, required admission to hospital and low-flow oxygen supplementation for a few days. The findings do not allow any conclusions on the incidence rate of SARS-CoV-2 infection in patients with rheumatic diseases, nor on the overall outcome of immunocompromised patients affected by COVID-19. A high level of vigilance and strict follow-up should be maintained on these patients. However, the preliminary experience shows that **patients with chronic arthritis treated with bDMARDs or tsDMARDs do not seem to be at increased risk of respiratory or life-threatening complications from SARS-CoV-2 compared with the general population.** These findings are not surprising as the severe respiratory complications caused by coronaviruses are thought to be driven by the **aberrant inflammatory and cytokine response** perpetuated by the host immune system. During different coronavirus outbreaks, such as SARS and MERS, there has been no increased mortality reported in patients undergoing immunosuppression for organ transplantation, cancer or autoimmune diseases. Accordingly, among 700 patients admitted for severe COVID-19 at the Pavia hospital, none was receiving bDMARDs or tsDMARDs.

Uneventful course in IBD patients during SARS-CoV-2 outbreak in northern Italy

https://www.gastrojournal.org/article/S0016-5085(20)30445-5/pdf?referrer=https%3A%2F%2Fpubmed.ncbi.nlm.nih.gov%2F32247695%2F%3Ffrom_term%3Dcovid%2B19%26from_sort%3Ddate%26from_page%3D8%26from_pos%3D4

Journal: Gastroenterology *Published Online: March 26, 2020*
Authors from: Italy

This observational study included all 522 pediatric (n=59, age 7-18 yrs) and adult IBD patients followed in the tertiary referral center in Bergamo. All patients were recommended not to modify their treatment regimen (59% salicylates only, 22% thiopurines, methotrexate, steroids or other immunosuppressants, 16 % biologic treatment with Infliximab, Adalimumab, Vedolizumab, Ustekinumab or Golimumab). No case of COVID-19 was reported in the cohort, and in particular, **no patient was admitted to hospital with SARS-CoV-2 proven infection**.
Based on the epidemiological model extrapolating data from Wuhan, it can be estimated that among the IBD cohort there should have been 21 infected patients. Systemic inflammation is a crucial target for the treatment of COVID-19 pneumonia, even though salicylates haven't been tested as a modifying agent. However, a recent report seems to suggest an **important role of a cytokine cascade** in the development of COVID-19 acute respiratory distress. This speculation supports the theory that **patients on immunosuppressive treatment could be at lower risk of developing complicated SARS-CoV-2 complications.** These findings warrant further investigation.

Tocilizumab, an anti-IL6 receptor antibody, to treat Covid-19-related respiratory failure: a case report

https://www.annalsofoncology.org/article/S0923-7534(20)36387-0/pdf
Journal: Annals of Oncology *Published Online: March 27, 2020*
Authors from: France

Preliminary data suggest that IL-6 may be a potentially actionable target cytokine to treat COVID-19-related ARDS and cytokine storm. The authors report the case of a patient with respiratory failure linked to COVID-19 who had a **rapid favorable outcome after two infusions of the anti-interleukin 6 receptor inhibitor tocilizumab**. This suggests that anti-IL6 receptor inhibitor treatment could decrease the risk of progression by mitigating the cytokine storm in the lungs with COVID-19. The current indications for tocilizumab are rheumatoid arthritis, juvenile arthritis, giant cell arteritis, and -- more recently-- **cytokine release syndromes associated with chimeric antigen receptor T cell therapies.**
A 42-year-old male recently diagnosed with metastatic renal cell carcinoma had been hospitalized for clinical symptoms suggestive of COVID19, which was confirmed by RT-PCR. Chest CT revealed bilateral patchy ground-glass opacities. Antiviral therapy lopinavir-ritonavir use (400mg-100mg orally) was begun at D7 and maintained for 5 days, according to local guidelines. On day 8, sudden dyspnea and saturation drop required oxygen supplementation increase to 6 l/min, without the need for artificial ventilation. He **received two doses of tocilizumab**, at 8 mg/kg intravenously for each dose, 8 hours apart, with good tolerability. Thereafter, he **experienced clinical improvement, rapidly afebrile and gradually decreased oxygen consumption**. This was fully discontinued on day 12. Chest CT on day 12 confirmed improvement by showing partial regression of the pulmonary infiltrates and ground-glass appearance. C-reactive protein in the blood, a surrogate marker of cytokine storm, decreased from 225 mg/L to 33 mg/L in 4 days. No major change was observed in circulating lymphocytic subpopulations after tocilizumab, and the percentage of CD4 + CD25 + lymphocytes was found high, before and after tocilizumab. The Patient ultimately clinically fully recovered from COVID-19 symptoms. More data for the use of tocilizumab in this clinical setting is needed, preferably from an RCT.

Emetine, Ipecac, Ipecac Alkaloids and Analogues as Potential Antiviral Agents for Coronaviruses

https://www.mdpi.com/1424-8247/13/3/51/htm
Journal: Pharmaceuticals *Published Online: March 21, 2020*
Authors from: Australia

This article presents the rationale for potentially using old drugs (**emetine, other ipecac alkaloids or analogues**) that have been used to treat amoebiasis in the treatment of COVID-19. Emetine had amongst the lowest reported half-maximal effective concentration (EC50) from over 290 agents screened for the MERS and SARS coronaviruses. While EC50 concentrations of emetine are achievable in the blood, studies show that concentrations of emetine can be almost **300 times higher in the lungs**. Furthermore, based on the relative EC50s of emetine towards the

coronaviruses compared with Entamoeba histolytica, emetine could be much more effective as an anti-coronavirus agent than it is against amoebiasis. This paper also discusses the **known side effects** of emetine and related compounds, how those side effects can be managed, and the optimal method of administration for the potential treatment of COVID-19. The emetic effects of ipecac syrup can be completely eliminated and nausea significantly reduced by the use of 5-HT3 antagonists, such as ondansetron. Given the serious and immediate threat that the COVID-19 coronavirus poses, our long history with emetine and the likely ability of emetine to reach therapeutic concentrations within the lungs, ipecac, emetine, and other analogues should be considered as potential treatment options, especially **if in vitro studies confirm viral sensitivity.**

Favipiravir: pharmacokinetics and concerns about clinical trials for 2019-nCoV Infection

https://ascpt.onlinelibrary.wiley.com/doi/epdf/10.1002/cpt.1844

Journal: Clinical Pharmacology and Therapeutics *Published Online: April 4, 2020*
Authors from: China

Favipavir is a **broad-spectrum antiviral drug approved in Japan for the treatment of influenza**. It competes with purine nucleosides and interferes with viral replication by incorporation into the virus RNA and thus potentially **inhibiting the RNA dependent RNA polymerase (RdRp)** of RNA viruses. Favipiravir is considered as one of the potential candidates for COVID-19, although in vitro and preclinical animal studies are not yet available. A clinical trial to evaluate the safety and efficacy of favipiravir in the treatment of COVID-19 (ChiCTR2000029600) was conducted in Shenzhen, with 80 patients recruited. The results showed that the 35 patients in the favipiravir arm demonstrated **significantly shorter viral clearance time** as compared with the 45 patients in the control arm (median 4 days vs. 11 days). The rate of improvement assessed by a chest X-ray was also higher in the favipiravir arm (91.43% versus 62%). Another multi-centered randomized clinical study (ChiCTR200030254) also showed effective control of COVID-19 by favipavir. For general patients with COVID-19, the seven-day clinical recovery rate increased from 55.86% to 71.43% with favipiravir treatment. For the general group of COVID-19 patients and patients with hypertension and/or diabetes, the time of fever reduction and cough relief in the favipiravir treatment group was also decreased significantly. Compassionate use of favipavir represents a possibility in treatment of COVID-19, based on its mechanism of action by inhibiting RdRp, as well as safety data in previous clinical studies. However, the exact efficacy of favipiravir has to be evaluated in further clinical trials.

Computational studies of drug repurposing and synergism of lopinavir, oseltamivir and ritonavir binding with SARS-CoV-2 Protease against COVID-19

https://www.tandfonline.com/doi/abs/10.1080/07391102.2020.1752802?journalCode=tbsd20
Journal: Journal of Biomolecular Structure and Dynamics *Published Online: April 6, 2020*
Authors from: India

Considering the emergency and urgency, the drug repurposing concept is being explored for COVID-19. Recently, the **combination of three known drugs, lopinavir, oseltamivir and ritonavir** has been proposed to control virulence to a great extent in COVID-19 affected patients within 48 hours. Hence, the authors tried to understand the **effect of synergism** of these drugs against the SARS-CoV-2 protease **using sequential docking studies**. As a result, a **combination** of three drugs showed **better binding energy** than **that of individual drugs**. Further, the complex was subjected to molecular dynamics simulations to get insights into the stability of the complex, considering the simultaneous interactions between three drugs and the protein. **The protein complexed with three drugs remained stable** during the simulations. Hence, these drugs can be explored further for drug repurposing against the successful inhibition of COVID-19.

Creating a Palliative Care Inpatient Response Plan for COVID19 – The UW Medicine Experience

https://www.jpsmjournal.com/article/S0885-3924(20)30176-7/pdf
Journal: Journal of Pain and Symptom Management *Published Online: March 30, 2020*
Authors from: USA

Significant numbers of patients are being admitted to the hospital with severe illness, often in the setting of advanced age and underlying co-morbidities. Therefore, **palliative care is an important part of the response to this pandemic**. University of Washington (UW) Medicine developed a **strategy to implement a palliative care response** for a multi-hospital healthcare system that incorporates conventional capacity, contingency capacity, and crisis capacity. The strategy was developed by their palliative care programs. This publication shares their multi-faceted strategy **in the emergency department, the intensive care units, and the acute care services.** The strategy focuses on key content areas including **identifying and addressing goals of care, addressing moderate and severe symptoms, and supporting family members**.

Strategy for Emergency Department (ED)	Conventional Capacity	Contingency Capacity	Crisis Capacity
1) ED can access onsite specialty palliative care 7 days/week from 9am to 6pm, by consult request. Additionally, palliative care telephonic coaching and support available 24 hours a day, 7 days/week	X		
2) Planned daily huddles with ED to address increased need for palliative care **Palliative Care Intervention:** - Consults for patients with poor prognosis and at risk of intubation or resuscitation prioritized - Patients admitted to the hospital followed daily through check-in with primary team - Support for implementing DNR orders using informed assent or based on medical futility when appropriate - Chart review results and brief or full consults documented in the EHR		X	X
3) Embed a palliative care specialist in ED to assist & address high volumes of patients and **screen patients based on following criteria:** ▪ COVID-19+/PUI with respiratory distress ▪ Multi-morbidity, severity of illness, & high oxygen requirement ▪ Clinical status: symptom burden, frailty (using Clinical Frailty Scale[10]), baseline functional status ▪ Code status: DNAR/DNI, DNAR-intubation ok, & Full code with high intubation risk Based on screening the following will happen: 1. meet or call with family/legal surrogate to address GOC and code status 2. coach ED team on GOC and code status discussion 3. assist with documentation of discussions and transitions of care After hours Palliative Care on-call provider can assist with telephone support and coaching.		X	X

Abbreviations for tables: ED – Emergency department; DNR – do not resuscitate; PUI – person under investigation; ARDS – acute respiratory distress syndrome; GOC – goals of care; ICU – intensive care unit; GIP – general inpatient; EHR – electronic health record.

	Conventional Capacity	Contingency Capacity	Crisis Capacity
Intensive Care Unit (ICU) – Non-COVID-19 Units 1) ICU can access onsite specialty palliative care 7 days/week from 9am to 6pm, by consult request. Additionally, palliative care telephonic coaching available 24 hours a day, 7 days/week	X		
2) Daily huddle with key ICUs to assess confirmed COVID-19+ for unmet palliative care needs or needs exceeding ICU team's capacity, prioritizing: I. Lack clear GOC or full code by default II. GOC or code status not aligned with prognosis III. End of life or moderate/severe symptom needs IV. Family needing high levels of support **Palliative care intervention:** - Assist through coaching or brief or full consultation		X	X
3) Follow Contingency Capacity approach regarding interaction and reasons for intervention and modify as follows. **Palliative care intervention:** I. Invoke coaching or brief consultation, document critical content II. Lead symptom assessment and management including medication ordering III. Assist with transitions of care (i.e. withdrawing life support, GIP hospice, discharge on hospice) when applicable IV. Support for implementing DNR orders based on medical appropriateness or scarce resource allocation models			X
ICU – COVID-19 Units 1) Palliative Care will embed palliative care specialist in COVID-19 ICUs during daytime hours to assist & address: i. goals of care and code status discussions with family/legal surrogate ii. coach ICU providers with complex GOC discussions iii. assist with documentation of transitions in goals of care, transitions in site of care (i.e. GIP hospice, discharge with hospice) iv. support for implementing DNR orders based on medical appropriateness or approved scarce resource allocation models, including DNR based on informed assent or based on medical futility when appropriate After hours Palliative Care on-call provider can assist with telephone support and coaching		X	X