Welcome to the University of Utah’s review course of critical care management, especially as it pertains to the non-ICU trained anesthesiologist’s management of critically ill COVID-19 patients.

The course will be broken down by organ systems affected by the virus, and the clinical management of subsequent problems that may arise. The material in the course is based on established non-COVID-19 critical care guidelines, current knowledge, accepted interventions, and recommendations of care tailored for COVID-19 patients, as well as institutional guidelines and videos where applicable. There are supplementary video learning tools provided through the Society of Critical Care Medicine (https://covid19.sccm.org/nonicu.htm). Please take a moment now to fill out a quick registration form in order to access those modules. The material contained in this course will be updated frequently, and as new developments arise.

Chapter 1: Epidemiology and personal protection
   1) What we know about COVID-19
   2) Proper use of PPE

Chapter 2: Shock in COVID-19
   1) What is shock?
   2) Types of shock
   3) Considerations for shock in COVID-19
   4) Fluid resuscitation in COVID-19
   5) Pressor support
   6) Monitoring
   7) Early antibiotic treatment
   8) Coinfection
   9) Steroid use

Chapter 3: Respiratory
   1) Respiratory characteristics and presentation of COVID-19
   2) Non-invasive management of hypoxemia
   3) Indications for intubation
   4) Intubation guidelines
   5) ARDS and COVID-19
   6) Mechanical Ventilation for ARDS
   7) Commonly encountered problems with mechanical ventilation in ARDS
   8) Invasive management of oxygenation
   9) Invasive management of oxygenation
   10) Proning
   11) Role of VV ECMO in COVID-19

Chapter 4: Cardiac
   1) Initial workup
   2) Acute coronary syndrome
3) Arrythmias
4) Myocarditis
5) Heart failure
6) Management of cardiac arrest

Chapter 5: Thrombotic Considerations
   1) Hypercoagulability
   2) DIC

Chapter 6: Investigational Interventions/Therapies

Chapter 7: Renal Considerations
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   2) Acute on Chronic Kidney Injury
   3) Medications
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Chapter 8: Hepatic Considerations
   1) Incidence of Hepatic Dysfunction
   2) Clinical Significance

Chapter 9: Special Considerations for the Anesthesiologist
   1) ASA Guidance on Utilizing OR Vents as ICU Vents
   2) ASA Joint Statement on Multiple Patients per Ventilator
Chapter 1: Epidemiology and Personal Protection

What do we know?

Proper use of PPE

Information in this section may change quickly. While every effort will be made to maintain the most up to date information, if there are questions please review primary sources such as through the CDC, WHO. If there are institutional questions regarding policy, please discuss with the COVID administrator.

What do we know?

1) Type of virus:

Enveloped RNA virus that is classified as a betacoronavirus, closely related to the SARS-CoV and MERS CoV. A mutation in the S glycoprotein found on the envelope is thought to have made the virus transmissible to humans sometime in late 2019. COVID-19 is believed to utilize the ACE2 receptor as a mode of entry into human cells, which may explain the proclivity of the virus to primarily infect the lower respiratory tract, where ACE2 receptors are present in large numbers in alveolar type II cells\(^1\). Alveolar type II cells are primarily responsible for secretion of surfactant, which helps to maintain patent alveoli.

2) Viral transmission:

Primarily believed to be respiratory droplets, which are most commonly spread within 6 feet of contact. However, some patients have had evidence of the virus in blood and stools, which may explain other modes of transmission\(^2\).

3) Virus stability:

a) Incubation period has a median of 5-6 days, where the carrier is asymptomatic but may be shedding virus. That period’s range has been documented from 1-14 days, with one case thought to have had an incubation period of up to 24 days\(^3\).

b) Surface stability in one experiment where particles of COVID-19 were aerosolized showed that the virus remained viable in the air over the 3-hour duration of the experiment. Viable virus was detected on copper surfaces up to 4 hours, on cardboard up to 24 hours, and plastic and stainless steel for up to 72 hours\(^4\).

4) Disinfection\(^5\):

a) The CDC recommends that contaminated surfaces be cleaned with soap and water prior to disinfection

b) Disinfection with a diluted bleach solution or with cleaners with >70% alcohol content is currently recommended

c) Contaminated laundry/linens/scrubs should be removed, not shaken, and washed on the warmest setting possible

d) Alcohol based hand sanitizer should have alcohol content of 60-95%

5) Clinical presentation:

a) Most common presenting complaints are fever (>37.5°C), cough, chest tightness, and dyspnea. Based on early reports from China, ground glass opacity was the most common radiologic finding
in severe disease (with no abnormalities seen in a majority of mild cases). Lymphocytopenia (<1500 cells/ml) was present in 83% of patients

b) 37% of critically ill COVID-19 patients have had elevations in AST/ALT, 36% had thrombocytopenia and 34% had leukopenia

6) Morbidity and mortality rates:
   a) The most recently reported data from the CDC states that 20-30% of patients admitted to the hospital with severe disease have required ICU admission and respiratory support. Of those, 14-64% received HFNC and 47-71% received mechanical ventilation.
   b) Among hospitalized patients with pneumonia and no ICU admission requirement, the mortality rate is reported to be 4-15%.
   c) Those with ICU needs, mortality rate is reported to be 49%.
   d) The overall case fatality rate is reported to be 2.3% in the initial infections seen in China. Per the CDC, this rate was generated from hospitalized patients and likely doesn’t include those with mild illness in the community, and may in fact be lower.

7) Role of ACE inhibitors and ARBs

a) Given the known mechanism of cellular entry via ACE2 receptors, and a correlation seen with patients with worse cardiovascular disease, hypertension and diabetes, there has been concern about the role that ACE inhibitors and ARBs could play in higher risk of severe illness with COVID-19 infection
   i) In mice, ACE2 receptor expression is upregulated in those treated with ACEi/ARBs
   ii) ACE2 receptors are primarily concentrated in the pulmonary endothelium, kidneys, heart, blood vessels and gut

b) Liu et al noted that serum angiotensin II levels were significantly higher in those with higher viral load and increased severity of lung injury (those patients were not on ACEi/ARBs)
Angiotensin II is known to induce vasoconstriction (concern for pulmonary vasoconstriction) and alter oxidative damage pathways.

c) There are several studies that showed a positive correlation between ACEi/ARB use in those with ARDS with either reduced risk of pneumonia or improved survival.

i) Upregulation of ACE2 may exert anti-inflammatory and antioxidative effects.

d) Despite reports that there was a correlation between those on ACEi/ARBs and more severe disease, there is no current clinical evidence to support this.

e) All professional societies who have issued statements regarding these medications indicated that they should be continued unless clinically indicated otherwise.

### Proper use of PPE

1) Proper use of PPE is essential in the care and treatment of our patients, as it protects others and ourselves from exposure.

   a) Current best practice guidelines state that PPE for aerosolizing procedures (bronchoscopy, endoscopy, intubation, open oropharyngeal suctioning, administration of nebulized medications, bag-mask ventilation, use of non-invasive positive pressure ventilation (NIPPV), disconnection of patient from ventilator, performance of surgical airway, CPR) should include N95 or PAPR mask, gown, gloves, and protective eye wear.

   b) For all other aspects of patient care, a normal surgical mask, gown, gloves, protective eye wear, and frequent hand hygiene are thought to be sufficient in preventing transmission.

2) The official CDC guidance for donning and doffing\(^\text{10}\) is the University of Utah’s official donning and doffing guideline, and should be reviewed frequently.

   a) Our specific guidelines (University of Utah sign in required):


       [https://pulse.utah.edu/site/ipac/Pages/PPE.aspx](https://pulse.utah.edu/site/ipac/Pages/PPE.aspx)

3) Most infectious transmissions when PPE is in use occur in the process of doffing, often as a result of improper donning procedures, especially from improper gown tying\(^\text{11}\).

4) For video reference, Mount Sinai Health System demonstrates proper technique [here](https://www.youtube.com/watch?v=Qg98GJGJg0).

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Chapter 2: Shock in COVID-19 Patients

Definition of shock
Types of shock
Considerations for shock in COVID-19
Fluid resuscitation
Vasopressors
Monitoring
Early antibiotic treatment
Coinfection
Steroid use

Primary resources for this section:

- SCCM Diagnosis and Management of Shock
- Principles and Management of Sepsis and Septic Shock: Wake Forest, Dr Vivek Jha
  https://www.youtube.com/watch?v=kizYxOPm6yU

Please also refer to the full guidelines Surviving Sepsis Campaign\(^1\) and the revised WHO Guidelines for Clinical Management of COVID-19\(^2\). The findings relevant to shock are summarized and contrasted below.
Definition of shock

As described in the WHO guidelines for clinical management of COVID-19, shock is defined by MAP <65mmHg despite adequate fluid resuscitation and evidence of end-organ damage as described by serum lactate >2mmol/L, with vasopressors required to keep MAP >65mmHg

Types of shock

<table>
<thead>
<tr>
<th>Physiologic variable</th>
<th>Preload (R)</th>
<th>Preload (L)</th>
<th>Pump function</th>
<th>Afterload</th>
<th>Tissue perfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical measurement</td>
<td>RAP/CVP</td>
<td>PCWP/LVEDP</td>
<td>Cardiac output/index</td>
<td>SVR/TPR</td>
<td>MvO2</td>
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<tr>
<td>Hypovolemic</td>
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<tr>
<td>- Hemorrhagic</td>
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<td>- Burns</td>
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<td>- Pancreatitis (3rd spacing)</td>
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<td>- Anaphylaxis</td>
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<td>Cardiogenic</td>
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<tr>
<td>LV Dysfunction</td>
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<td>RVMI</td>
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<tr>
<td>- RCA occlusion</td>
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<tr>
<td>- Inferior and RV MI</td>
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<tr>
<td>- Isolated RV dysfunction</td>
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<tr>
<td>Obstructive</td>
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<tr>
<td>Pulmonary Vascular</td>
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<td>- PE</td>
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<td>- Sévere PH</td>
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<td>Mechanical</td>
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<tr>
<td>- Pericardial tamponade</td>
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<td>- Tension pneumothorax</td>
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<tr>
<td>- Constrictive pericarditis</td>
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<tr>
<td>- Restrictive cardiomyopathy</td>
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</table>


COVID-19 and shock

1) Incidence of shock in COVID-19 patients requiring ICU care estimated to be 20-25%, although reported as high as 70% in some retrospective studies
2) Appears to be distributive shock most commonly – speculation about cytokine mediated but cardiogenic shock and sepsis from superimposed bacterial infection are also being reported. Superimposed infection was present in 16% in one retrospective analysis from China, and was associated with a significant increase in mortality
3) Cytokine storm has been proposed as a contributor of the pathology seen in severely ill COVID-19 patients
a) Cytokine storm: “A hyperinflammatory state that is characterized by fulminant multi-organ failure and elevation of cytokine levels”
b) The SCCM revised sepsis guidelines acknowledge cytokine storm as a possible mechanism of severe disease development, however do not endorse any treatments based on this theory (immune modulators) at this time

**Fluid resuscitation**

Watch this video for an excellent review of evaluation of volume status: [https://www.youtube.com/watch?time_continue=28&v=hPobftCnOBA&feature=emb_logo](https://www.youtube.com/watch?time_continue=28&v=hPobftCnOBA&feature=emb_logo)

1) **Surviving Sepsis Campaign:**
   a. Guidance of fluid administration beyond initial resuscitation by dynamic parameters (passive leg raise, fluid challenges with serial stroke volume measurements, variations in systolic pressure, pulse pressure, IVC size or stroke volume variation)—suggestion, weak evidence, based on non-COVID19 research
   b. For acute resuscitation of COVID19 patients with shock, a conservative over a liberal fluid resuscitation strategy should be employed—weak recommendation, very low-quality evidence (based on assumption that critically ill COVID19 patients will likely develop ARDS)
   c. For acute resuscitation, crystalloids are recommended over colloids—strong recommendation, moderate quality evidence, based on non-COVID patient evidence
   d. For acute resuscitation, buffered/balanced crystalloids (those containing bicarbonate, or bicarbonate precursor such as acetate, lactate, etc) are recommended over unbalanced crystalloids (0.9% NS) - weak recommendation, moderate quality of evidence, based on non-COVID patient evidence
   e. For acute resuscitation, it is not recommended to use hydroxyethyl starches, gelatins, dextrans—strong, weak and weak recommendations respectively, based on non-COVID patient evidence
   f. For acute resuscitation, it is not recommended to use albumin for initial resuscitation—weak recommendation, moderate quality evidence, based on non-COVID patient evidence

2) **WHO:**
   a. 250-500ml rapid bolus of crystalloids in first 15-30 minutes, reassess after each bolus
   b. Monitor for signs of fluid overload (JVD, crackles in lung fields, pulmonary edema on imaging), be ready for intubation if this becomes apparent
   c. Consider dynamic indices of volume responsiveness (passive leg raise, fluid challenges with serial stroke volume measurements, or variations in systolic pressure, pulse pressure, inferior vena cava size, or stroke volume in response to changes in intrathoracic pressure during mechanical ventilation)
   d. Do not use hypotonic crystalloids, starches, gelatins for resuscitation

**Vasopressors**

1) **Surviving Sepsis Campaign:**
   a. For adults with COVID19 and shock, it is suggested to use norepinephrine as the first line vasoactive agent, or use vasopressin or epinephrine if norepinephrine is not
available – weak recommendation, low quality of evidence, based on non-COVID patient evidence
b. Dopamine is not recommended as a first line vasoactive agent if norepinephrine is not available – strong recommendation, high quality of evidence, based on non-COVID patient evidence
c. If a second-line agent is needed for low MAPs despite adequate titration of norepinephrine or first line agent, it is suggested to use vasopressin – weak recommendation, low quality of evidence
d. In patients with evidence of cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine, it is suggested to add dobutamine over increasing norepinephrine – weak recommendation, very low-quality evidence, based on non-COVID patient evidence
e. For refractory shock, it is suggested to use low-dose corticosteroid therapy (200mg/day) over no corticosteroid therapy – weak recommendation, low quality of evidence, based on non-COVID patient evidence
f. Target MAP 60-65mmHg

2) WHO:
   a. Utilize vasopressors when shock persists after fluid resuscitation
   b. Target MAP >= 65mmHg
   c. Can administer through large bore peripheral IV if central access not available, close observation for extravasation employed
   d. Norepinephrine first line; epinephrine, vasopressin second line
   e. Do not routinely give systemic steroids for treatment of viral pneumonia

Monitoring

   1) Monitoring is not specifically addressed in either of these documents
      a) Arterial line and central line/CVP monitoring may be considered with acknowledgement of typical risks and benefits, as well as prolonged exposure of proceduralist to patient
      b) Anecdotally, central access may become a priority if the patient is likely to need prone positioning to improve oxygenation

Early antibiotics

   1) Strongly recommended to initiate within 1 hour of ICU admission as part of the original surviving sepsis campaign (please see the University of Utah’s “Preferred Empiric Antibiotics” resource in the Pulse folder).
      a. Surviving Sepsis Campaign:
         i. In critically ill patients with MERS, 18% had bacterial and 5% viral co-infections
         ii. Empiric antibiotics are recommended over no antibiotics in the critically ill COVID19 patient with respiratory failure with daily assessment for de-escalation–weak recommendation, low quality of evidence (rationale is that bacterial co-infection may exist), based on non-COVID patient evidence
      b. WHO:
         i. Give empiric antimicrobials to treat all potential causes of SARI and sepsis within 1 hour of initial patient assessment
1. *Please refer to the University of Utah Antibiotic Guidance available on pulse for specific recommendations
2. *Vancomycin/zosyn likely to be first line – utilize [Drip score calculator](#) to assess for likelihood of presence of drug resistant pneumonia and again refer to hospital antibiotic guidelines if likely
   ii. Neuraminidase inhibitor should be considered in those at risk for influenza
   iii. De-escalate on the basis of microbiology results and clinical judgment

**Coinfection**

1. Do not forget that on presentation, these patients will have undifferentiated shock – meaning you won’t know the cause of their shock
   a. Coinfection with other respiratory viral illnesses, such as influenza or RSV, as well as bacterial pneumonia has been documented
   b. Always assess for other sources of infection based on history, physical and labs
   c. Assess for severity of end organ damage
      i. Place foley – monitor UOP
      ii. Initial lab evaluation: CMP, CBC with special attention towards lactate, electrolytes and white count
      iii. Workup to determine source of infection/shock:
         1. COVID-19 PCR
         2. Respiratory viral panel (including influenza)
         3. Urinalysis w/ reflex culture
         4. Chest x-ray
         5. Blood culture x 2
         6. Sputum culture (if able to be safely obtained)
         7. Troponin
         8. Serum lactate and/or ABG
         9. Consider ScVO2 if central access available
         10. Consider utility of TTE (POCUS can help assess overall cardiac function, and be part of assessing volume status—see Chapter 5)
   d. Continue with periodic surveillance as management changes are employed

**Use of Steroids**

1) WHO
   a. Do not routinely give systemic steroids for treatment of viral pneumonia

2) SCCM
   a. For refractory shock, it is suggested to use low-dose corticosteroid therapy (200mg hydrocortisone IV/day – given as 50mg q6h at the University of Utah) over no corticosteroid therapy – *weak recommendation, low quality of evidence, based on non-COVID patient evidence*

3) Special consideration must be given to those who are on chronic steroids

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Chapter 3: Respiratory Considerations

The bulk of the review materials are contained in this chapter, so pull up a chair and stay awhile!

Respiratory characteristics and presentation of COVID-19
Non-invasive management of hypoxemia
When to intubate
Intubation
ARDS
Invasive management of oxygenation
Invasive management of ventilation
Proning
VV ECMO

The building blocks of this section will again be provided by the SCCM videos of ICU Care for the Non-ICU Physician. Please view these first:

- Diagnosis and Management of Acute Respiratory Failure:
- Mechanical Ventilation 1:
  https://covid19.sccm.org/Presentations/Mechanical-Ventilation1/story_html5.html?lms=1
- Mechanical Ventilation 2:

Additional resources:

- NEJM Proning Example: https://www.youtube.com/watch?v=E_6jT9R7WJs
- ARDSNet Full Mechanical Ventilation Protocol:
**Respiratory characteristics and presentation of COVID-19**

1) COVID-19 causes a severe acute respiratory illness (SARI) that has been described as an interstitial pneumonia with progression to ARDS
   a) There have been several clinical reports that comment on relatively higher lung compliance, and therefore lower ventilator pressure requirements in patients with severe COVID-19 requiring mechanical ventilation vs classic ARDS patients
2) Postmortem histologic samples show interstitial mononuclear infiltrates, fibromyxoid exudates, desquamated pneumocytes, pulmonary edema, and hyaline membrane formation
3) Clinically, rapid progression of pulmonary disease and requirement for invasive mechanical ventilation has been described
   a) There have been two distinct sequences of COVID-19 detected
   b) L type was responsible for 96% of cases in Wuhan China
   c) S type has been found in 38% of cases outside Wuhan, and may be associated with less severe disease manifestations, with more potential for rapid spread
4) Interestingly, there is a lower reported prevalence of those with pre-existing pulmonary diseases diagnosed with COVID-19 both in China and Italy
   a) One theory is that the treatments used for maintenance of chronic respiratory illnesses, especially inhaled corticosteroids, may either reduce the risk of symptoms, the display of symptoms, or even suppress viral replication
5) An example of a clinical timeline:
**Non-invasive management of hypoxemia**

Goal SpO₂ 92-96% (some ARDS protocols have lower limit 90%)

1) Use of inhalers are preferred over nebulized medications
   a) Increased risk of aerosolization with nebulizers
2) NC: 1-6LPM (max fiO₂ 0.44)
3) Venturi mask/simple face mask: 5-8 LPM (max fiO₂ 0.55)
4) Nonrebreather: 6-10 LPM (max fiO₂ up to 1.0)
5) High Flow Nasal Cannula (HFNC): Up to 60 LPM (max fiO₂ 1.0)
   a) Heated and humidified
   b) Increases FRC due to increased PEEP at high flows
   c) Titratable oxygen content versus flows depending on patient needs
   d) WHO supports the use of HFNC in COVID-19 patients⁵
      i) Based on previously published literature, not likely to increase aerosolization/virus spread
      ii) May reduce the need for intubation
      iii) Should not be used in those with altered mental status, worsening hypercapnia, hemodynamic instability or multiorgan failure
6) Non-invasive positive pressure ventilation (NIPPV): BIPAP/CPAP (variable fiO₂)
   a) WHO and SCCM Support a trial of NIPPV if the patient does not imminently require intubation
   b) *The MICU at the University of Utah is currently discouraging use of NIPPV, unless a patient is admitted with NIPPV already in use
   c) Considerations:
      i) These devices are considered to be aerosol generating and should be used judiciously
      ii) Appropriate precautions and PPE should be employed (negative pressure room, isolation)
      iii) No evidence that NIPPV reduces rate of intubation for ARDS patients
When to intubate

1) RR > 35
2) paO2 <60mmHg on fio2 0.60
3) paCO2 >55mmHg (in those without chronic lung disease)
4) Hemodynamically unstable
5) Inability to protect airway
6) Combative
7) Obvious signs of respiratory fatigue
8) *Special consideration should be given to COVID-19 patients – earlier intubation in a more controlled setting is favored to minimize exposure to team members
   a) Page Anesthesia Airway Team
   b) This decision should be made within a reasonable timeframe of escalating care and no signs of improvement – one hospital in China recommends intubation after 2h trial of HFNC
   c) Clinical judgement and knowledge of resources and triage protocols should also be considered

Intubation

University of Utah Department of Anesthesia Guidelines for Intubation:
1) Discussion with primary team regarding other comorbidities
2) Use clear, closed loop communication throughout
3) Ensure equipment available in room:
   a) Ventilator with expiratory limb HEPA filter
   b) Ambu bag
   c) Oxygen supply
   d) Suction with Yankauer
   e) Stethoscope
4) Proper donning PPE
5) Bring necessary equipment and drugs into room
   a) Clinical judgement in drug selection depending on patients hemodynamic status and other comorbidities
   b) Glidescope Go/DL
   c) ETT and appropriate stylet
   d) Syringe to inflate cuff
   e) HEPA filter
   f) Calorimetric CO2 detector (not necessary if capnograph to be used)
6) Airway assessment – get additional tools as necessary
7) Have closed suction system ready
8) Rapid sequence induction
   a) Ensure paralysis to avoid coughing
   b) Avoid positive pressure ventilation if possible
   c) Given pathology, patients may desaturate rapidly
   d) If PPV required, two-hand mask with HEPA filter just distal to mask at all times to minimize droplet spread
9) Use video laryngoscope if possible
   a) Avoid awake airways → coughing
   b) Know where your surgical airway kit is, and how to use it

ARDs
1) SARI in COVID-19: Often described as ARDS due to diffuse lung injury and difficulty with oxygenation, however one key difference clinically has been the absence of high ventilator pressures in COVID-19 patients
2) How is ARDS defined?

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

<table>
<thead>
<tr>
<th>Acute Respiratory Distress Syndrome</th>
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<tbody>
<tr>
<td><strong>Timing</strong></td>
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<tr>
<td><strong>Chest imaging</strong></td>
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<td><strong>Origin of edema</strong></td>
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<tr>
<td><strong>Oxygenation</strong></td>
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</tbody>
</table>

Possible ultrasonographic findings at lung examination. 0: Normal aeration with normal sliding, with A-lines pattern; 1: Multiple B-lines but separated by at least 5 mm; 2: Multiple, coalescent, not well-separated B-lines; 3: Lung consolidation, hyperechoic area with air bronchogram. Numbers on the left side of each ultrasound image represent the depth (in cm)

b) Ultrasound findings in COVID-19

i) Some reports with patchy areas of B lines, abnormally hyperechoic pleura

ii) May have more clinical utility when there is concern for pneumothorax

iii) More education on performing and interpreting lung ultrasound – remember that this imaging is tricky, and requires previous practice with acquisition and interpretation – when in doubt consult Anesthesia Echo Team

(1) https://echo.anesthesia.med.utah.edu/lung-ultrasound-water/

(2) https://echo.anesthesia.med.utah.edu/basic-lung-ultrasound/
Mechanical Ventilation for ARDS

Goals of mechanical ventilation in ARDS/ALI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Goal</th>
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<tbody>
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<td>PaO₂</td>
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<tr>
<td>Plateau Pressure</td>
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<tr>
<td>Tidal volume</td>
<td>6ml/kg predicted body weight</td>
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<td>pH</td>
<td>&gt; 7.15</td>
</tr>
</tbody>
</table>


1) Choose any ventilator setting
2) Initial tidal volume: Vt 8cc/kg PBW, reduce by 1ml/kg/hr until goal Vt = 6ml/kg
3) Rate: Try to set at baseline rate present prior to intubation, not >35
4) PEEP: Initially 5
   a. WHO and SCCM recommend higher PEEP strategy in patients with moderate to severe ARDS
   b. Increase by 2-3cm H₂O every 15-30 minutes
Commonly encountered problems with mechanical ventilation in ARDS

*Please see University of Utah Anesthesiology Simulator video for orientation ICU ventilator and troubleshooting common scenarios: [https://medicine.utah.edu/anesthesiology/covid-19.php](https://medicine.utah.edu/anesthesiology/covid-19.php)

1) Elevated ventilator pressures (*have been encountered less in COVID-19 than in traditional ARDS)
   a. What is Plateau Pressure (Pplat)?
      i. It is a measure of static compliance; reflects pressure in the small airways and alveoli
   b. What causes elevation in Pplat?
      i. Non-compliant lung
         1. Pneumothorax
         2. ARDS
         3. Pulmonary edema
         4. Pneumonia
   c. Initial interventions for elevated Pplat
      i. Prolonged elevation in Pplat is associated with barotrauma
      ii. Goal Pplat in ARDS <30cm H2O
iii. If life-threatening hemodynamic instability, disconnect patient from ventilator and ventilate with Ambu bag
iv. Decrease Vt by 1ml/kg to a minimum of 4ml/kg (this may need to be accompanied by increase in RR to maintain physiologic pH)

d. What is Peak Inspiratory Pressure (PIP)?
i. A measure of dynamic compliance, and is determined by airway resistance in the tubing or the large airways of the lungs
e. What causes isolated elevation in PIP (when Pplat is relatively normal)?
i. Mucous plugging
ii. Mainstem intubation
iii. Endobronchial intubation
iv. Bronchospasm
v. Other occlusion of ETT tip

2) Patient-ventilator dyssynchrony
a. Patient sedation: RASS goal initially -2 to -3, titrate deeper if oxygenation/ventilation problems encountered

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Combative</td>
<td>Overly combative, violent, immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes tube(s) or catheter(s); aggressive</td>
</tr>
</tbody>
</table>
i. Consider bolus paralytics if lung protective ventilation is not feasible
   1. Both WHO and SCCM advise against continuous infusion of NMB
   2. Although there is evidence of liver and kidney injury in critically ill COVID-19 patients, succinylcholine and rocuronium still ok for use with the typical considerations (prolonged immobility, history of paralysis from spinal cord injury/stroke, burns, acute hyperkalemia for succinylcholine)
   3. *The MICU at University of Utah has published a protocol for cisatracurium infusion, to be used as a last resort in difficult to oxygenate/ventilate ARDS cases:
      b. For an excellent summary of infusions used for sedation, pain control and paralysis, please see the following document prepared by the University of Michigan Critical Care Collaborative Network:

3) Auto-PEEP
   a. Occurs when there is not enough time for complete exhalation, and next breath delivered on top of those volumes → hyperinflation, causing increased pressure at end-exhalation
   b. More likely to occur in patients with pre-existing obstructive lung disease (COPD, asthma) and superimposed ARDS
   c. May be a cause of increased work of breathing/patient-ventilator dyssynchrony, barotrauma, hemodynamic instability
   d. Management
      i. If life-threatening hemodynamic instability, disconnect patient from ventilator to allow full exhalation
      ii. Decrease I:E (either by decreasing respiratory rate or the ventilator setting)
iii. Consider increasing inspiratory flows to 60-100L/min to decrease inspiratory time and allow more time for exhalation

**Invasive Management of Oxygenation**

Commonly accepted goals: SpO2 88-95% or PaO2 55-80 mmHg

1) Adjustments of PEEP and FiO2 meet these goals
2) Oxygen toxicity is to be avoided (hyperoxic acute lung injury, or HALI) and is associated with significant increase in mortality
3) Decrease FiO2 to <0.75 when possible to prevent HALI
4) Recruitment maneuvers
   a) In a recent meta-analysis including 3,025 patients, recruitment maneuvers have not shown overall mortality benefit in ARDS, but may reduce hospital length of stay, and may improve oxygenation on third ventilator day
   b) Risk of barotrauma in unaffected alveoli

**Invasive Management of Ventilation**

Employment of the above strategies to change minute ventilation (MV) to target a physiologic pH:

1) Increasing rate
2) Increasing tidal volume (up to 8cc/kg PBW, ideally 6cc/kg)
3) Goal pH 7.30-7.45 – ventilation is titrated based on this and not paCO2
   a) If acidotic beyond this range, increase MV by increasing rate first, then increasing Vt if acidosis still present
4) Permissive hypercapnia
   a) Generally accepted when ventilation is difficult
   b) No clear mortality benefit\textsuperscript{11}
   c) Goal is to keep pH in physiologic range, ideally 7.30-7.45 – some goals are lower (>7.15)
   d) Consequences of hypercapnia must be considered (increased pulmonary vascular resistance/potentiation of hypoxic vasoconstriction, increased RV workload, decreased effectiveness of pressors)
      i) If pulmonary hypertension complicated by RV dysfunction/failure encountered, consider therapies for decreasing PVR (see Ch 4, Cardiac)
         (1) University of Utah’s Inhaled Epoprostenol Protocol: https://pulse.utah.edu/policies/Lists/Policies/DispForm.aspx?ID=3029

Proning

The official University of Utah proning protocol can be found here: https://pulse.utah.edu/policies/Lists/Policies/DispForm.aspx?ID=11860

1) Key points
   a) Proning can be used in mechanically ventilated patients with severe hypoxic respiratory failure to optimize oxygenation
   b) University of Utah and other institutions have trialed prone positioning for patients who are \textit{not} mechanically ventilated, but receiving HFNC or NIPPV
   c) Most studied in patients with ARDS where short lived improvements in oxygenation are common (70%) and sometimes dramatic (e.g.Gattinoni et al, 2001). Some patients have no effect and others have a long-lasting effect, persisting well after rolling supine again.
   d) 2013 PROSEVA trial found a marked mortality benefit in patients with severe ARDS (i.e., P/F ratio <150)
   e) Proning is very resource intensive from a personnel standpoint and may not be feasible if staffing is strained by an overwhelming surge of patients, which may also increase utilization of limited PPE supplies.
2) Physiologic Effects

**Prone Position in ARDS**

![Images of lung densities in supine and prone positions](image)

**Fig. 4.** Differences in the distribution of lung densities in a patient with ARDS on a computed tomography scan between supine position (top) and prone position (bottom). A. Image taken at end expiration in the supine position. B. Image taken at end inspiration in the supine position. Images C and D were taken from the same lung volumes in the prone position. Note the improved aeration in the dorsal lungs both at end expiration and end inspiration in the prone position compared with the supine position. From Reference 118, with permission.

a) Supine position
   i) Reduction in VC
   ii) Reduction FRC

b) Prone position
   i) Optimization of V/Q matching (increased blood flow to the dependent lung)
   ii) Increase in FRC
   iii) Reduced atelectasis
   iv) Facilitates secretion drainage
   v) Less lung deformation in the prone position (increased homogeneity) → increased ventilation
   vi) Abdomen is less likely to distend when in prone position → increase in FRC
   vii) Heart sits against sternum (rather than left lung) → lung is less compressed
   viii) Decreased transpleural pressure gradient between dependent and non-dependent lung in the prone position
   ix) Plateau pressure is more uniformly distributed when prone → more uniform alveolar ventilation
   x) Recruitment maneuvers have been shown to be more effective in the prone position
   xi) Alterations in chest wall mechanics → allowing lungs to inflate at lower pressures

3) Indications
   a) Severe ARDS with life threatening, refractory hypoxemia

4) Contraindications
   a) Untrained staff
   b) Extreme obesity
   c) Hemodynamic instability
5) General Procedure Considerations

(see video from NEJM, PROSEVA trial, link at top of Chapter)

a) All lines including endotracheal tube should be sutured in place
b) Assemble sufficient trained staff to coordinate positioning safely
c) Provide padding and support for potential pressure areas (e.g., face, upper chest, pelvis, knees)
d) Turn patient prone
e) Abdomen should hang between two pillows/ supports
f) Duration varies among protocols (e.g., 6-16 hours a day for up to 10 days)

6) Complications

a) Decreased enteral nutrition
   i) Traditionally tube feeds are stopped when prone due to increased risk of aspiration
   ii) There is some evidence to support continuing TF while prone, however this will require clinical judgement in the individual patient\(^\text{12}\)
b) ETT obstruction or dislodgement
c) Increased intrabdominal pressure/ICP
d) Difficult to perform procedures or reintubate
e) Facial edema/pressure trauma

7) Evidence

There have been multiple conflicting RCTs but the weight of evidence now suggests prone ventilation is beneficial in selected severe ARDS patients:

a) Gattinoni et al 2001 was the original study showing improvement in oxygenation of most patients with ALI/ARDS by proning
b) Recent meta-analyses suggest a mortality benefit for patients with severe ARDS (PF ratio <100), with an NNT of 11
c) Subsequent to the above meta-analyses, the PROSEVA trial by Guerin et al 2013 showed a marked mortality benefit (NNT = 6) for prone ventilation in severe ARDS (28-day mortality 16% prone versus 32.8% supine)
d) Experienced teams are contributing to positive outcome with prone position

VV ECMO in COVID-19

1) This is an emerging body of literature
2) WHO supports its use as a management choice for persistently hypoxemic COVID-19 patients\(^2\)
3) Indications\(^13\)
   a) Inability to adequately oxygenate despite maximal ventilator management, paralysis, adherence to proning protocols and/or other adjuncts
      i) PaO2/fiO2 70-80mmHg
      ii) pH < 7.2
   b) Availability of an expert center that has clinical expertise in the use of ECMO
   c) Subjectively good chance for recovery – isolated respiratory disease
4) Contraindications – per U of Utah MICU guidelines
   a) Cardiogenic shock
   b) Mechanical ventilation >7 days
c) Significant comorbidities

d) Multiorgan failure

5) Considerations

a) Mortality benefits at this point are not clear
   i) One paper analyzed the overall mortality of COVID-19 VV ECMO patients (in publications up until April 1) found the pooled mortality rate to be 94.1%.

b) Consider palliative care consult prior to initiation of VV ECMO

c) Resource heavy intervention – with increasing demand this intervention may not be sustainable

d) Personnel exposure is theoretically higher, as nursing staff, intensivists, echocardiographers will likely be frequently in and out of patient’s room

6) More specific details regarding cannulation can be found in this review paper published in The Lancet 03/2020

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2 Xu et al. Pathological findings of COVID-19 associated with severe acute respiratory distress syndrome. The Lancet. 02/18/2020. DOI: https://doi.org/10.1016/S2213-2600(20)30076-X


4 Halpin et al. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? The Lancet. 04/03/2020. https://doi.org/10.1016/S2213-2600(20)30167-3


Chapter 4: Cardiac Considerations

Initial Workup

Acute Coronary Syndrome

Arrhythmias

Myocarditis

Heart Failure

Management of Cardiac Arrest

Cardiac dysfunction has been documented in several studies of COVID-19 patients, and may be associated with increased mortality. A Chinese retrospective study showed the incidence of cardiac injury (as defined by troponin-I >99% percentile from normal) to be 17% in survivors, and 59% in non-survivors. The Chinese Center for Disease Control released a large case series of COVID-19 patients, with an overall mortality rate of 2.3%, however with a mortality rate of 10.5% was noted in the subset of patients with underlying cardiovascular disease. Yet another study cites a statistically significant correlation between elevated troponin levels and incidence of ARDS, arrhythmia and death.

In those with pre-existing cardiac disease (known CAD, history of MI, systolic dysfunction, diastolic dysfunction, etc) it is easily reasoned that an imbalance in myocardial oxygen supply and demand result in injury. Additionally, acute inflammatory states such as those seen in patients with COVID-19 can result in coronary plaque rupture leading to myocardial injury. This has been previously documented in viral infections such as influenza and in acute inflammatory states.

Fulminant myocarditis has also been previously well-described as a result of viral infection, but current incidence and therapies in COVID-19 is currently unknown.

Primary resources to be read:

- Review of current cardiovascular findings in COVID-19
  https://jamanetwork.com/journals/jamacardiology/fullarticle/2763844
- RV Failure in ARDS
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5911554/

1. Initial Workup
   a) History
      i) Previous cardiac pathology, including systolic/diastolic dysfunction, CAD, MI, arrhythmia
      ii) Predisposing conditions for cardiac dysfunction: diabetes, hypertension
      iii) Medications (antihypertensives, antiarrythmics, anticoagulants)
      iv) Symptoms, including chest pain, pressure, nausea, vomiting, dyspnea, new edema (may be difficult to distinguish from pulmonary pathology)
   b) Chart review: Any reports of cardiac interventions (surgery, cath, stent placement), prior echo
   c) Physical
      i) Signs of new cardiac dysfunction (often specific but not sensitive, with decreased specificity in a patient with interstitial pneumonia)
         1) JVD
         2) Pulmonary crackles
         3) Edema
d) Tests
   i) EKG – daily is reasonable in COVID-19 patients at high risk for cardiac involvement
      (1) New arrhythmia
      (2) New focal ST segment depression or elevation – STEMI or NSTEMI
      (3) Diffuse ST segment elevation – pericarditis or myocarditis
      (4) PE – in 15-25% of patients with new PE, EKG will show prominent S wave in lead I, and Q wave with inverted T wave in lead III
   
   ii) Troponin- to be done serially if first is elevated (suggest q6h), otherwise consider daily in ICU patients
   iii) BNP – may have a role in following progression of severe disease – increasing pro-BNP levels throughout hospitalization associated with increased mortality
   iv) CXR – evaluation for cardiomegaly, pulmonary edema
   v) BMP – assess for electrolyte abnormalities
   vi) Magnesium
   vii) Echo
      (1) TTE preferred if suspicion of cardiac dysfunction is high
      (2) Can help direct management when there is persistent shock
      (3) Not to be ordered routinely on COVID-19 patients

2. Acute Coronary Syndrome
   a) May be difficult to distinguish from other cardiopulmonary disease manifestations of COVID-19 infection – know your patient and understand their pre-test probability for having underlying CAD which may predispose them to new ACS in the stressful setting of an acute viral infection
      i) In limited reports from China, the prevalence of pre-existing cardiovascular disease in patients with COVID-19 requiring hospitalization ranged from 15-40%
   b) New EKG abnormalities
   c) Rapid increase in troponin – may indicate myocardial infarction
   d) Echo that shows new wall motion abnormalities
   e) If suspicion is high or there are questions – consult cardiology
   f) Coronary angiography may be necessary, but comes with risks of transport and exposure
3. **Arrhythmias**
   a) Unknown incidence with COVID-19
   b) Likely due to new or exacerbated heart disease, acidemia, hypoxemia
   c) Management per ACLS guidelines

4. **Myocarditis**
   a) New myocarditis has been described in several autopsies done on COVID-19 patients that describe myocardial infiltration by inflammatory myocytes
   b) Has been described as a later finding in COVID-19, even after resolution of pulmonary pathology
   c) Possibility of causal reaction of COVID-19 utilizing ACE2 receptors for cell entry, however this has not been confirmed (see section below on Role of ACE2 Receptors)
   d) Non-COVID viral myocarditis
      i) Important cause of dilated cardiomyopathy
      ii) Diagnosis: histopathologic definitive (via biopsy) and cardiac MRI supportive – may not be feasible in COVID-19
      iii) Supportive findings
         1) Diffuse ST segment elevation
         2) New high-grade AV block
         3) TTE: Global hypokinesis with or without effusion
         4) Normal angiography
      iv) Treatment
         1) Supportive management of heart failure as below
         2) Treatment of viral illness
         3) Immunosuppressive therapies are not recommended

5. **Heart Failure**
   a) LV systolic and/or diastolic dysfunction
      i) Consider when there is persistent hypotension despite fluid resuscitation and adequate titration of pressors
         1) Aggressive fluid resuscitation in those with severe diastolic dysfunction can make pulmonary edema worse
      ii) Evidence on echocardiography with supportive signs (decreased cardiac index, increased PCWP)
      iii) Correct electrolytes, acidemia, hypoxemia which may contribute
      iv) Careful consideration of volume resuscitation
      v) Inotropic support
         1) As per WHO and SCCM guidelines, pressor treatment of shock thought to be from sepsis to include norepinephrine and vasopressin – this may add to increased SVR
         2) Consider addition of dobutamine and/or milrinone for inotropic support
vi) Consider diuresis when hemodynamic stability has been achieved

b) RV Systolic dysfunction
   i) Incidence 10-25% when ARDS is present: increased pulmonary vascular resistance driven by intrinsic disease, hypoxia, hypercapnia, effects of mechanical ventilation
   ii) Echocardiographic findings of RV dysfunction along with findings of elevated PA pressures, CVP are supportive
   iii) Careful fluid administration
   iv) Vasopressors and inotropes as above (norepinephrine and dobutamine)
   v) Consider adjuvant therapies: levosimendan, inhaled nitric oxide, inhaled epoprostenol
   vi) Consult cardiology

6. Management of cardiac arrest
   a) There is not currently an official University of Utah protocol for cardiac arrest
   b) Provider protection from exposure is first priority
      i) High risk for exposure during CPR
   c) Likely to be arrest due to hypoxia – establishing secure airway and fiO2 1.0 is second priority
      i) ACLS to be followed
Chapter 5: Thrombotic Considerations

Hypercoagulability

DIC

Primary resources:

- General resource for preventing venous thromboembolism (Johns Hopkins, not COVID specific):
  https://www.hopkinsmedicine.org/armstrong_institute/improvement_projects/infections_complications/VTE/
- DIC Review from NCBI
  https://www.ncbi.nlm.nih.gov/books/NBK441834/

1. Hypercoagulability
   a. Existing reports describe VTEs and PEs in COVID-19 patients\(^1\)
   b. Proposed mechanism is general inflammatory state caused by primary immune response to viral infection, coupled with hemostasis if ventilated or on other mechanical support
   c. Consider early initiation of LMHW
   d. Considerations:
      i. Active postop bleeding, or history of bleeding in the past 3 months (ulcer, intracranial within 1 year)
      ii. Advanced liver disease (INR >1.5) – doesn’t mean no anticoagulation is needed, but may be higher risk for hemorrhagic complications
      iii. Platelet count <50k or <100k and downtrending
      iv. History of HIT
      v. Presence of neuraxial catheters
      vi. Caution use of LMWH and heparin in those with acute renal dysfunction\(^2\)
         1. Consult your pharmacist for dose modifications
         2. Typical dose modifications:
            a. If CrCl > 30: Lovenox 40 mg SC daily
            b. If CrCl < 30 or AKI: Heparin 5000 units SC TID
   e. Intervention\(^3\):
      i. Low Risk: Minor surgery in mobile patients. Medical patients who are fully mobile. Observation patients with expected hospital stay <48 hours. No prophylaxis; reassess periodically, ambulate.
      ii. Moderate Risk: Most general, thoracic, open gynecologic, or urologic surgery patients. Medical patients, impaired mobility from baseline or acutely ill. UFH or LMWH prophylaxis
iii. High Risk: Hip or knee arthroplasty, hip fracture surgery, multiple major trauma, spinal cord injury or major spinal surgery, abdominal-pelvic surgery for cancer. Pneumatic compression device AND LMWH or other anticoagulant

2. DIC

a. Case reports exist of severe coagulopathy/DIC occurring in the course of COVID-19 and appear to be associated with a poor prognosis especially when PT, D-dimer and fibrin-degradation products were abnormal.

b. In another study, coagulopathy was defined by 3 second prolongation of PT or 5 second extension of aPTT. Within this study, coagulation was determined to be abnormal in 19% overall; 50% in non-survivors and 7% in survivors.

c. Median time to onset 4 days.

d. Labs
   i. PT/PTT
   ii. D-dimer
   iii. Fibrinogen and/or FDP
   iv. Consider periodic ROTEM if ongoing bleeding/interventions

e. Management
   i. Not bleeding: supportive care. Consider platelet transfusion if platelet count <30k
   ii. Bleeding: hold anticoagulation, administer blood products based on ROTEM, PRBCs if severe hemorrhage

1. Consider RiaSTAP, KCentra to limit volume given high risk for ARDS, cardiac dysfunction


Chapter 6: Investigational Interventions/Therapies

As of April 13, 2020, there are currently no CDC or FDA approved anti-viral or immunomodulating treatment options. Instead emphasis is placed on evidence-based supportive care and prevention of infection spread. Given that this is an area of study that will evolve rapidly, updates will be made periodically and as new evidence emerges. This section will be based on the current CDC and FDA guidelines and the investigational literature they provide. Studies in the US and worldwide are underway.

Primary resources:

- Considerations during a pandemic for off-label drug use and compassionate use: https://jamanetwork.com/journals/jama/fullarticle/2763802

1. Investigational interventions
   a. Remdesivir
      i. Inhibits viral replication through terminating RNA transcription
      ii. Demonstrates in vitro activity against COVID-19, and in vitro/in vivo activity against similar betacoronaviruses
      iii. Clinical trials are ongoing (can be accessed through CDC link above) including NIH sponsored randomized, double-blind, placebo controlled study examining remdesivir vs standard supportive therapy
      iv. Not currently FDA approved, and use outside of study setting must be obtained via compassionate use (reserved for pregnant women and children under 18)
   b. Chloroquine/hydroxychloroquine
      i. Both have demonstrated in-vitro activity against SARS-CoV and SARS-CoV-2 (COVID-19); hydroxychloroquine has relatively higher potency against COVID-19
      ii. No randomized RCTs to evaluate benefit
         1. One study with a small number of participants demonstrated decreased RNA viral load, unclear clinical benefit\(^1\)
         2. Another small study from France also endorses increased viral clearance with hydroxychloroquine, but had poor adherence to intervention, resulting in n= 6 receiving treatment\(^2\)
      iii. Toxicity: Please see figure below for toxicity considerations
      iv. Clinical trials are ongoing for both treatment and prevention of infection (can be accessed through CDC link above)
      v. CDC provided examples of dosing regimens (all are anecdotal)
         1. 400mg BID on day one, then daily for 5 days
         2. 400 mg BID on day one, then 200mg BID for 4 days
3. 600 mg BID on day one, then 400mg daily on days 2-5

c. Lopinavir/ritonavir
   i. Combination medication typically used for HIV therapy
   ii. Has shown reduced mortality when used to treat SARS-CoV-1 in retrospective observational studies – unclear significance when compared to SARS-CoV-2 (COVID-19)
   iii. An open-label RCT was done including 199 patients, which showed no difference in clinical improvement or improvement in time to discharge, as well as no difference in viral clearance or 28 day mortality
   iv. Additional RCTs are underway
   v. Toxicity: Please see chart below for toxicity considerations

d. Interferon-α and interferon-β
   i. Immunomodulatory agents aimed at modifying “cytokine storm” seen in some patients with severe illness
   ii. No current animal or human data that support effectiveness against COVID-19
   iii. Not currently recommended for treatment

e. Convalescent plasma and hyperimmune globulin (hyperimmune globulin is a biological product manufactured from convalescent plasma)
   i. Those who have recovered from COVID19 may have developed antibodies that may be effective for others in fighting the illness
   ii. In prior studies of severe viral illnesses, convalescent plasma was associated with a reduction in mortality in H1N1, as well as for patients with SARS or severe influenza
   iii. One uncontrolled case series showed clinical improvement in 5/5 patients with severe manifestations of COVID-19 after transfusion of convalescent plasma
   iv. Another prospective study of 10 severely ill patients diagnosed with COVID-19 were given convalescent plasma on average 16.5 days after onset of illness
      1. Measured levels of neutralizing antibody significantly
      2. Lymphocyte counts decreased, CRP decreased overall
      3. They report significantly improved clinical symptoms within 3 days, including oxyhemoglobin saturation
   v. Convalescent plasma is not an FDA approved treatment, however they have issued guidance regarding pathways for use of convalescent plasma, patient eligibility, collection of plasma (link at beginning of document)
**Table 1. Summary of Pharmacology for Select Proposed COVID-19 Treatments**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target</th>
<th>Adult dose/administration</th>
<th>Contraindications</th>
<th>Toxicities</th>
<th>Major drug-drug interactions</th>
<th>Special populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine (Plaquenil)</td>
<td></td>
<td>200 mg orally twice daily for 5 days then 200 mg daily</td>
<td>Hypersensitivity to chloroquine</td>
<td>None</td>
<td>None</td>
<td>May be used in pregnancy if benefit outweighs risks</td>
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<tr>
<td>Hydroxychloroquine (Plaquenil)</td>
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<td>400 mg PO daily (200 mg qid)</td>
<td>Hypersensitivity to hydroxychloroquine, 4-aminoquinoline compounds, or any component of the formulation</td>
<td>None</td>
<td>None</td>
<td>May be used in pregnancy if benefit outweighs risks</td>
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<tr>
<td>Lopinavir/ritonavir (Kaletra)</td>
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<td>400 mg PO twice daily</td>
<td>Hypersensitivity to lopinavir/ritonavir or any of the ingredients, including ritonavir</td>
<td>None</td>
<td>None</td>
<td>May be used in pregnancy if benefit outweighs risks</td>
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<tr>
<td>Umifenovir (Arbidol)</td>
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<td>200 mg orally twice daily</td>
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<td>None</td>
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<tr>
<td>Remdesivir (Veklury)</td>
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<td>200 mg IV by 1 h infusion, followed by 5 mg/h infusion for 10 days</td>
<td>None</td>
<td>None</td>
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<td>Favipiravir (T-705)</td>
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<td>150 mg PO twice daily</td>
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<tr>
<td>Adjuvant therapies</td>
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<td></td>
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<tr>
<td>Tolliformin (Actemra)</td>
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<td>8-10 mg/ml in cytokine storm</td>
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</table>

**Abbreviations:** ACE2, angiotensin-converting enzyme 2; AST, aspartate aminotransferase; C2L, chemokine (C-C motif) ligand 2; COVID-19, coronavirus disease 2019; CYP, cytochrome P450; G6PD, glucose 6-phosphate dehydrogenase; GFR, glomerular filtration rate; IV, intravenous; Pigs, pigs; USTIAL, U0126 glucocorticoid/transferase family member 1.


Chapter 7: Renal Considerations

Information in this section is obtained from the International Society of Nephrology, and supplemented where cited.

https://www.theisn.org/covid-19

1. Renal dysfunction in patients with previously healthy kidneys
   a. No evidence that renal dysfunction occurs in those with mild to moderate COVID-19 infection
   b. Incidence appears to be higher in those with critical illness caused by COVID-19
      i. ATN from shock, hypotension
      ii. Cytokine mediated from cytokine storm
      iii. Direct renal insult due to ACE2 receptors – unknown, but proposed
   c. 5 of 138 patients in one study showed signs of AKI, and 2 required CRRT

2. Acute on chronic renal dysfunction in COVID-19 positive patients
   a. Relationship between the two is unclear
      i. Immunosuppression (especially post-transplant) – higher risk for severe disease
      ii. Higher degree of community exposure (dialysis centers)
   b. Routine dialysis should be continued with appropriate precautions
   c. In hospitalized patients, suggest daily BMP to assess for electrolyte abnormalities and change in serum creatinine/creatinine clearance

3. Medications
   a. Continuation of ACE and ARBs is recommended
      i. Concern for upregulation of ACE2 receptors, which the virus utilizes for cell entry, in those who are one ACE/ARB
      ii. No evidence to support that patients are higher risk for severe disease who are on these medications

4. Indications for dialysis
   a. Intractable electrolyte abnormalities (especially K+)
   b. Methanol/salicylate poisoning
   c. Acidosis
   d. Uremia
   e. Therapy resistant fluid overload

Chapter 8: Hepatic Considerations

1) Incidence of Hepatic Dysfunction
   a. 51% of a cohort in Shanghai had new elevations in AST/ALT on admission
      i. 30% of those had known liver disease prior to COVID-19 infection
      ii. Correlated with higher fever, male gender, lower lymphocyte count –
           interpreted to be associated with more severe disease¹
   b. Patient cohort in Wuhan showed incidence of 43% acute liver injury²
   c. No reports of fulminant liver failure

2) Significance
   a. At this stage, unclear significance – no studies available have been able to
      address this specifically
   b. Possible impact of pre-existing liver disease, associated hypotension, direct viral
      effects and/or drug affects
      i. Caution may need to be employed when acute liver injury is present and
         treatment with lopinavir/ritonavir is planned – known to be hepatotoxic³

³ Sulkowski, M. Drug-induced liver injury associated with antiretroviral therapy that includes HIV-1 protease
Chapter 9: Special Considerations for the Anesthesiologist


Utility and preparation of anesthesia ventilators as ICU ventilators – ASA Guidance

1) Guidance from the ASA
   a. OR ventilators are first line backup in the case of shortages of ICU ventilators
      i. Temporary FDA approval
      ii. National estimate of full-feature ventilators: 62,000
      iii. Usable ventilators estimated at 200,000 when OR ventilators, older machines, and strategic national stockpile (SNS) machines included
   b. An anesthesia provider should be immediately available to manage the machine
   c. Scavenging is not necessary if HEPA filter placed appropriately
   d. Which ventilators should be used?
      i. Those able to best mimic SIMV + PS modalities
      ii. Those that use less oxygen – pneumatically driven vents consume more O2
   e. Utilizing inhaled agents for sedation is NOT recommended
   f. Monitoring of inspiratory oxygen content is mandatory as inspired oxygen content in a circle system can be significantly lower than the fresh gas concentration

2) Please see full guideline through the link above prior to utilizing an OR vent for ICU vent

Utilizing single ventilator for multiple patients – ASA Joint Statement

1) Statement in conjunction with SCCM, AARC, ASA, APSF, AACN, CHEST
2) Utilization of a single ventilator should NOT be done, as it is currently unable to be done safely with standard equipment
   a. ARDS ventilator management is complex, disease often non-homogenous even in a single patient
   b. Two patients unlikely to have same needs
      i. Risk for barotrauma/underventilation/hypoxemia
      ii. Spoke like arrangement of patients around a ventilator
1. Far from oxygen supply, suction
2. Higher risk for disease transmission
3. One patient spontaneously ventilating will set the rate for the remainder of the patients on that vent

c. In the event that the demand for ventilators has reached crisis levels, and triage is necessary, it is “better to purpose the ventilator to the patient most likely to benefit than fail to prevent, or even cause, the demise of multiple patients”

ENT Procedures

https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2764032

1) Non-urgent procedures should be delayed and/or limited depending on local disease burden
   a) For example, non urgent may include benign disease such as thyroid cancer, salivary gland cancer, and surveillance visits for patients with known head and neck cancers
2) Any appointments/procedures that are deemed necessary should have phone screening for new signs of aggressive disease progression (severe dysphagia, airway compromise that may need emergency room) and for symptoms of COVID-19
3) Any procedure of the aerodigestive tract is considered to be high risk for transmission of COVID-19
   a) If patient has known COVID-19, procedure should be done under all the typical precautions (negative pressure room, PAPR/N95, frequent hand hygiene, etc)
   b) It is strongly recommended that any patient requiring surgical intervention that will expose staff to nasal, mucosal, pharyngeal and pulmonary secretions to also utilize maximal PPE as above
      i) It is astutely observed that observed levels of community disease will not reflect the true prevalence
4) As such, please follow current intubation guidelines for the University of Utah for all ENT procedures at this time
Chapter 10: Nutrition Considerations

This section is adapted from the joint statement from the SCCM and ASPEN:

1) Nutritional assessments may not be able to be done in person
   a) Limit exposed personnel and use of PPE

2) When to start nutrition?
   a) Goals:
      i) Enteral nutrition within 24-36 hours of ICU admission or
      ii) Enteral nutrition within 12 hours of intubation
   b) May need to wait for GI symptoms in COVID-19 patients to recover (nausea, vomiting, diarrhea, abdominal discomfort)

3) Why is early enteral nutrition important?
   a) Statistically significantly lower mortality rate and lower rate of infection even with trophic feeds

4) When to not provide early nutrition
   a) Patient intolerance
   b) Escalating pressor requirement
   c) High pressure respiratory support in use (NIV, CPAP, PEEP)
      i) Concern for bowel ischemia
   d) Consideration of switching to earlier parenteral nutrition in COVID-19 patients may be necessary
      who anticipate long ICU stays, higher concern for ischemic bowel
      i) Overall rate of ischemic bowel is 0.3% in general, non-COVID clinical trials
      ii) Parenteral nutrition will limit personnel exposure by avoiding procedures involving
           placement and maintenance of an enteral access device

5) What nutrition and how?
   a) Enteral nutrition is preferred over parenteral nutrition
   b) 10-12Fr NG feeding tube
   c) Placement in stomach
      i) If feeds not tolerated, recommend prokinetic agent
      ii) Final strategy is post-pyloric placement of NG
      iii) Confirm placement by X-ray prior to feeding
   d) Continuous feeds preferred over bolus
   e) Place pump outside room if possible (less personnel exposure)
   f) Trophic feeds ramped to 15-20kcal/kg (actual body weight), with protein goal 1.2-2.0gm/kg/day
      as tolerated
      i) Indirect calorimetry may not be practical in the setting of COVID-19, and best
         recommendation is to continue to feed based on actual body weight.
   g) Standard high protein (>20% protein) polymeric isosmotic enteral formula should be used in the
      early acute phase of illness
      i) May consider fiber free if significant GI function becomes apparent
6) Monitoring
   a) Serum triglyceride levels – especially with concurrent use of propofol
   b) Phosphorous levels – refeeding syndrome
   c) Daily physical exam – special attention to abdomen
   d) Monitoring of passing of stool/gas

7) COVID-19 Patients requiring proning
   a) Recommended to continue enteral nutrition while prone
      i) Several studies show that prone position and feeding not associated with increased risk of aspiration
   b) Can consider risks and benefits of post-pyloric placement if necessary depending on clinical situation