

## WHAT IS COVID-19?

Coronavirus disease 2019 (COVID-19) is a respiratory illness that can spread from person to person. Patients with COVID-19 have experienced mild to severe respiratory illness, including fever, cough and shortness of breath. The virus that causes COVID-19 is a novel (new) coronavirus. It is not the same as other types of coronaviruses that commonly circulate among people and cause mild illness, like the common cold. Approximately 5% of patients infected with COVID-19 will require ICU level of care<sup>1</sup>. While the mortality rate among ALL infected patients is in the range of 0.5% - 4%, patients requiring hospitalization it is 5-15% and for those who require ICU 22-62%<sup>2</sup>.

## HOW DOES COVID-19 SPREAD?

The virus that causes COVID-19 is thought to spread mainly from person-to-person, between people who are in close contact with one another (within about 6 feet) through respiratory droplets when an infected person coughs or sneezes. It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes, but this is not thought to be the main way the virus spreads.

## BACKGROUND INFORMATION ON TREATMENT

Recommendations for the treatment of patients with COVID-19, the disease caused by the SARS-CoV-2 virus, are evolving. This document is designed to update healthcare staff working in intensive care units (ICU) on current recommendations and is based on published guidelines, as well as expert opinion and feedback from critical care units caring for COVID-19 patients.

Different regions of the world are reporting different case fatality rates and ICU utilization. This variation may be explained by different SARS-CoV-2 strains or differences in testing and reporting. We have learned that being older (median age ~60 years) or having comorbid conditions (~40%) such as diabetes or cardiac disease increases probability of ICU admission.<sup>i</sup>

We have learned that being older (median age ~60 years) or having comorbid conditions (~40%) such as diabetes or cardiac disease increases probability of ICU admission. The most common reason for requiring ICU is respiratory support with approximately 2/3 of these patients meeting ARDS criteria. Septic shock and organ dysfunction (particularly AKI) appear in significant proportion of patients with COVID-19 and are associated with increasing mortality<sup>3</sup>. Septic shock and organ dysfunction (particularly acute kidney injury) appear in some patients with COVID-19 and are associated with increasing mortality. Renal failure occurs in approximately 7% of ICU patients and portends a poor prognosis. Cardiac arrhythmias can also occur as well as evidence of acute cardiac injury (troponins are often elevated). Below is the typical evolution of disease after exposure (although times may be variable):

<sup>1</sup> Wu Z, et al. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. JAMA. Published online February 24, 2020. Doi: 10.1001/jama.2020.2648

<sup>2</sup> Wang D, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. Published online February 7, 2020. Doi:10.1001/jama.2020.1585

<sup>3</sup> Murthy S, et al. Care for critically ill patient with COVID-19. JAMA 2020. Published online March 11,2020. Doi: 10.1001/jama.2020.3633

- 6 days= dyspnea
- 8 days= hospital admission
- 10 days= ICU admission/intubation

## ICU MANAGEMENT OF PATIENTS

ICU management of patients with COVID-19 is similar to management of patients with other viral pneumonias with a few important considerations which are subject to updates by the CDC - <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>

- Admit COVID-19 patients to private rooms if available.
- Cohort COVID-19 patients and providers as possible to minimize use of PPE and prevent spread
- Restrict visitors to areas with COVID-19 patients
- Use droplet face masks for staff during assessment and transfer of symptomatic patients
- Wear airborne isolation precautions including eye-protection while caring for patients during aerosol-generating procedures (intubation, bronchoscopy, open-suctioning of airways); These procedures should take place in negative airflow areas
- Avoid use of high-flow nasal oxygen or non-invasive ventilation due to risk of aerosolization of the virus; consider early intubation to “close the circuit”
- Favor meter dosed inhalers over nebulizers for intubated patients to keep circuit closed
- Require education on proper use of personal protective equipment (PPE) for all staff
- ARDS from COVID-19 does not typically cause the severe reduction in compliance seen by other causes for ARDS
- Bronchoscopy should only be utilized if necessary and NOT to diagnose COVID-19
- Consider risks and benefits of steroids in patients who develop ARDS; more information is available at <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184>
- Lymphopenia is common and a neutrophil/lymphocyte ratio > 3 may suggest a worse prognosis<sup>4</sup>.

COVID-19 does not cause typical acute respiratory distress syndrome (ARDS):

- COVID doesn't appear to cause substantially reduced lung compliance (which is generally a hallmark finding of ARDS).
- The predominant problem might be one or more of the following:
  - Atelectasis (alveolar collapse).
  - Drowning of the alveoli by fluid.
- Any strategy to increase the mean airway pressure will treat atelectasis (e.g. APRV or conventional ARDSnet ventilation using a high-PEEP strategy).
- If *drowning* of the alveoli is a significant issue, proning may facilitate drainage of secretions. APRV may also be useful to facilitate airway clearance (rapid dumping breaths create expiratory airflow that can facilitate secretion clearance).

Conventional ARDSnet ventilation:

- Tidal volumes should be targeted to a lung-protective range (6 cc/kg ideal body weight).
- High PEEPs should be utilized.

<sup>4</sup> Liu J, et al. Neutrophil-to-lymphocyte ratio predicts severe illness patients with 2019 novel Coronavirus in the early stage. Pre-print. Doi: 10.1101/2020.02.10.20021584

## Airway pressure release ventilation (APRV):

- Early APRV could be very useful for these patients (i.e. used as the initial ventilator mode, rather than a salvage mode). APRV may be well suited to the pathophysiology of COVID, because it provides a high mean airway pressure and facilitates secretion clearance.
- More information on APRV can be found here <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2732103/>.
- A reasonable starting place is generally:
  - P-high: 30-35 cm (higher if more profound hypoxemia)
  - P-low: zero
  - T-high: 5 seconds
  - T-low: 0.5 seconds (titrate based on flow rates; consider reduction if tidal volume >8 cc/kg)
- Improvement in oxygenation seen with APRV often takes several hours as lung tissue gradually recruits.
- APRV initiation can cause hemodynamic shifts, so pay careful attention to blood pressure during initiation.
- True failure to respond to APRV within 12-24 hours (e.g. with  $\text{PaO}_2/\text{FiO}_2 < 100-150$ ) would be a strong argument to move towards prone ventilation. However, when started early APRV may be more likely to succeed – thereby avoiding the need for proning.

## Permissive hypercapnia:

- Regardless of the ventilator mode, permissive hypercapnia may be useful. The safe extent of permissive hypercapnia is unknown, but as long as hemodynamics are adequate a pH of >7.1 or >7.15 may be tolerable (hypercapnia is preferred over lung-injurious ventilation).
  - Slow administration of IV bicarbonate is an acceptable strategy to improve pH while simultaneously continuing lung-protective ventilation. Targeting a mildly elevated serum bicarbonate (e.g. 28-30 mEq/L) can facilitate safe ventilation with low tidal volumes.

## Proning:

- Prior to consideration of proning, optimization on the ventilator for 12-24 is generally preferable.
- For failure to respond to initial ventilator optimization (e.g. with persistent  $\text{PaO}_2/\text{FiO}_2$  below 150 mm), prone ventilation should be considered.
- Reports from COVID patient use describe proning as extremely effective.
  - This makes sense, because proning is expected to be effective for basilar lung recruitment and secretion clearance (which seem to be the primary problems with these patients).
  - The question is whether the same effect could be achieved more easily using APRV. Proning is very labor-intensive and will require consumption of lots of personal protective equipment (since multiple providers will need to turn the patient repeatedly). If the same effect can be achieved with APRV, that could be an easier solution (especially at centers which lack extensive experience with proning).

## ANTIVIRAL AND IMMUNOMODULATORY THERAPIES

To date, there are no specific recommendations for antiviral or immunomodulatory therapies. Several antivirals such as remdesivir and lopinavir/ritonavir are undergoing clinical trials, as well as other agents such as vitamin C and the anti-ILC tocilizumab.

## FURTHER INFORMATION

The worst-case scenario for ICU patients is progression to the acute respiratory distress syndrome (ARDS). Use lung-protective ventilation strategies and conservative fluid management. Consider empiric antibiotics for concomitant bacterial pneumonia. Treat with prone positioning for  $\text{PaO}_2:\text{FiO}_2 < 150$  and utilize ECMO as resources allow. Facilities should ensure an allocation plan in the event ventilators or rooms become scarce. Continue to work with local and state planners for contingency planning in the event of breach of surge capacity.

## ADDITIONAL INFORMATION

Questions about COVID-19 may be directed to the ISDH COVID-19 Call Center at the toll-free number 877-826-0011 (available 8 a.m. to midnight).

Additional information and resources for COVID-19 are available at the links below.

- ISDH COVID-19 webpage: <https://coronavirus.in.gov>
- CDC COVID-19 webpage: <https://www.cdc.gov/coronavirus>

<sup>1</sup><https://jamanetwork.com/journals/jama/fullarticle/2761044>