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## INTRODUCTION

A novel coronavirus was identified in late 2019 as the cause of a cluster of pneumonia cases in Wuhan, China. It has since rapidly spread resulting in a pandemic. The World Health Organization designated the disease term COVID-19 (ie, Coronavirus Disease 2019) [1]. The virus that causes COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The major morbidity and mortality from COVID-19 is largely due to acute viral pneumonitis that evolves to acute respiratory distress syndrome (ARDS).

This topic will discuss the epidemiology, clinical features, and management of patients who become critically ill due to COVID-19. Other aspects of COVID-19, and other coronavirus-related diseases (severe acute respiratory syndrome [SARS] and Middle East respiratory syndrome [MERS]), are discussed separately. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention" and "Coronaviruses" and "Severe acute respiratory syndrome (SARS)" and "Middle East respiratory syndrome coronavirus: Virology, pathogenesis, and epidemiology".)

## GUIDELINES AND HOSPITAL POLICIES

The advice in this topic is based upon data derived from the management of patients with acute respiratory distress syndrome, emerging retrospective data in patients with COVID-19, expert opinion, and anecdotal observations of clinicians treating patients with COVID-19 in China, Italy, and Washington state (USA), where the large outbreaks have occurred. Guidelines have been issued by several societies and organizations including the Society of Critical Care Medicine, the Chinese Thoracic Society, the Australian and New Zealand Intensive Care Society (ANZICS), the World Health Organization and by the United States Centers for Disease Control and Prevention and National Institutes of Health [2-7]. (See "Society guideline links: Coronavirus disease 2019 (COVID-19) – International and government guidelines for general care".)

Learning from regions that have dealt with the overwhelming burden of COVID-19 to date, it is essential that all hospitals and health systems develop task forces to manage patients admitted with this disorder. This involves, but is not limited to, designating COVID-19-specific intensive care units (ICUs) and ICU teams, creating back up and expanded staffing schedules, utilizing detailed protocols for infection prevention and medical management, accessing research trials for patients with COVID-19, ensuring adequate personal protection equipment (PPE) supplies and training, forecasting demand, and prioritizing diagnostic lab testing.

## EPIDEMIOLOGY

Reports suggest that among those infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), up to 20 percent develop severe disease requiring hospitalization [8-15]. Although rates vary, among those who are hospitalized, up to one-quarter need intensive care unit (ICU) admission, representing approximately 5 to 8 percent of the total infected population. Differences in the rates of ICU admission may relate to cultural differences in practice and admission criteria for ICU as well as differences in predisposing factors such as age and comorbidities and testing availability in the populations served.

- **China** – In the Chinese cohorts, rates of ICU admission or severe illness ranged from 7 to 26 percent [9,10,15,16].

- **Italy** - Consistent with the range reported in China, preliminary reports from Italy suggest that the proportion of ICU admissions were between 5 and 12 percent of the total positive SARS-CoV-2 cases, and 16 percent of all hospitalized patients [17,18].

- **United States of America** – In an early study of 21 critically ill patients in Washington State, USA, 81 percent of patients with COVID-19 pneumonia were admitted to the ICU and 71 percent were mechanically ventilated [19]. However, this high rate likely reflects the older age of the population which largely came from a nursing home in the region. A larger analysis of 2449 patients reported hospitalization rates of 20 to 31 percent and ICU admission rates of 4.9 to 11.5 percent [20].

While three-quarters of critically ill patients were male in the Chinese cohorts, data are mixed with some reports suggesting an equal proportion of men and women [18,19] and other suggesting a male predominance [21,22].

## CLINICAL FEATURES IN CRITICALLY ILL PATIENTS

**Clinical features and complications** — General clinical features of COVID-19 patients and risk factors for progression are discussed separately (see "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Clinical features' and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Risk factors for severe illness'). Discussion here is limited to clinical features in those who are critically ill.

- **Rate of progression** – Retrospective studies of critically ill patients have suggested that among patients who develop critical illness, including acute respiratory distress syndrome (ARDS), onset of dyspnea is relatively late (median 6.5 days after symptom onset), but progression to ARDS can be swift thereafter (median 2.5 days after onset of dyspnea) [9,10,19,23,24].

- **Clinical features** – Among those who are critically ill, profound acute hypoxemic respiratory failure from ARDS is the dominant finding [8-10,19,21,22,24-28]. Hypercapnia is rare. Fevers tend to wax and wane during ICU admission. The need for mechanical ventilation in those who are critically ill is high ranging from 30 to 100 percent [9,19,21,22,25,28].

- **Length of stay** – Early clinical reports suggest that length of intensive care unit (ICU) stay appears to be long with many patients remaining intubated for one to two weeks or longer [22].

Reports from experts in the field suggest that many patients fail early attempts at weaning (eg, within the first week), although this does not appear to predict their eventual ability to wean and extubate. Only a small proportion of patients require tracheostomy. (See 'Extubation and weaning' below and 'Tracheostomy' below.)

- **Complications** – Common complications of COVID-19-related ARDS include acute kidney injury (AKI), elevated liver enzymes, and cardiac injury including cardiomyopathy, pericarditis, pericardial effusion, arrhythmia, and sudden cardiac death. As an example, in a single-center retrospective cohort from China of 52 critically ill patients with COVID-19, complications included AKI (29 percent; half of whom needed renal replacement therapy), liver dysfunction (29 percent), and cardiac injury (23 percent) [9].

  - Cardiac injury appears to be a late complication, developing after the respiratory illness improves. A high rate of cardiomyopathy was noted in a United States cohort (33 percent), and may relate to the older age in that population [19]. In another United States cohort in New York City, cardiac complications among mechanically ventilated patients included atrial arrhythmias (18 percent), myocardial infarction (8 percent), and heart failure (2 percent) [27]. One case series reported five patients who developed acute cor pulmonale, most of which occurred in association with hemodynamic instability or cardiac arrest [29]. All cases were thought to be most likely due to pulmonary embolism (PE), although a definitive diagnosis of PE was confirmed in only one case. Cardiac complications of COVID-19 are discussed in detail elsewhere. (See "Coronavirus disease 2019 (COVID-19): Myocardial injury" and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease" and "Coronavirus disease 2019 (COVID-19): Myocardial infarction and other coronary artery disease issues".)

  - Sepsis, shock, and multi-organ failure do occur but appear to be less common when compared with non-COVID-19-related ARDS. The need for vasoactive agents is variable, although a significant proportion need vasopressor support for hypotension (often due to sedation medications or cardiac dysfunction). In the cohort study from Wuhan, China, 35 percent of 52 patients received vasoactive agents [9]. In contrast, in the case series from New York City, 95 percent of the 130 patients who received mechanical ventilation required vasopressor support; the reasons for this were not specified [27].

  - As above, acute kidney injury is common among critically ill patients with COVID-19, and many require renal replacement therapy. This is discussed in detail elsewhere. (See "Coronavirus disease 2019 (COVID-19): Issues related to kidney disease and hypertension", section on 'Acute kidney injury'.)

- Data on the risk of secondary bacterial pneumonia are limited, but it does not appear to be a major feature of COVID-19. In a cohort of intubated patients from China, hospital-acquired pneumonia, in many cases with resistant pathogens, was reported in 12 percent [9]. This finding may be related to the high use of glucocorticoids for ARDS management in China. Further data are needed to elucidate the rate of superinfection in other countries.

- Lung compliance is high compared with other etiologies of ARDS and the rate of barotrauma appears to be low with only 2 percent developing pneumothorax, compared with 25 percent of those with severe acute respiratory syndrome coronavirus (SARS-CoV) [9,30]. There are limited data describing the lung pathology in patients with COVID-19. Case reports from post mortem cases and patients undergoing biopsy for another reason suggest a wide variation from mononuclear inflammation to diffuse alveolar damage, classic of ARDS [31,32]. (See "Acute respiratory distress syndrome: Epidemiology, pathophysiology, pathology, and etiology in adults", section on 'Pathologic stages'.)

- Neurologic complications in critically ill patients are common, especially delirium or encephalopathy which manifests with prominent agitation and confusion along with corticospinal tract signs (hyperreflexia). Consistent with this, intensivists have observed that sedation requirements are high in this population, particularly immediately after intubation. In one series of 58 patients with COVID-19-related ARDS, delirium/encephalopathy was present in approximately two-thirds of patients [33]. In addition, three of 13 patients who had brain MRI had an acute ischemic stroke; eight MRI studies demonstrated leptomeningeal enhancement. Cerebrospinal fluid (CSF) in seven patients was acellular and only one had elevated CSF protein; PCR assays of CSF were negative for the virus. It is unclear whether the neurologic complications noted in this and other reports are due to critical illness, medication effects, or represent more direct effects of cytokines or the SARS-CoV-2 virus [33-35]. Encephalitis, while reported, is rare [36]. Similarly, Guillain-Barré-barre syndrome following SARS-CoV-2 virus infection has also been described in a small case series [37].

- COVID-coagulopathy is common in this population with some patients developing abnormal coagulation profiles and others developing thrombosis. These features are discussed separately. (See "Coronavirus disease 2019 (COVID-19): Hypercoagulability".)

- **Laboratory** – Laboratory findings in critically ill patients (eg leukopenia, lymphopenia, leukocytosis, elevated D-dimer, lactate dehydrogenase, and ferritin, normal or low procalcitonin) are initially modest and similar to those with milder illness, although the procalcitonin level may be more elevated and lymphopenia more profound in critically ill patients [8,10,26]. (See "Cytokine release syndrome (CRS)" and "Coronavirus disease 2019

(COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Laboratory findings' and "Procalcitonin use in lower respiratory tract infections" and "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults", section on 'IL-6 pathway inhibitors'.)

Some patients with severe COVID-19 have laboratory evidence of an exuberant inflammatory response, similar to cytokine release syndrome (CRS), with persistent fevers, elevated inflammatory markers (eg, D-dimer, ferritin, interleukin-6), and elevated proinflammatory cytokines; these laboratory abnormalities have been associated with poor prognosis [38]. Clinical trials of anti-IL-6 agents for the treatment of COVID-19 are in progress. Further details regarding CRS are provided separately. (See "Cytokine release syndrome (CRS)" and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Laboratory findings' and "Procalcitonin use in lower respiratory tract infections" and "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults", section on 'IL-6 pathway inhibitors'.)

The presence of antiphospholipid antibodies has also been described; however, they are mostly of the IgA subclass, and the clinical significance is unclear [39]. Abnormal coagulation parameters which are commonly seen in COVID-19 patients (eg, elevated D-dimer, prolonged prothrombin time) are also discussed separately. (See "Coronavirus disease 2019 (COVID-19): Hypercoagulability" and "Diagnosis of antiphospholipid syndrome".)

- **Imaging** – Typical imaging findings do not appear to be different in mild or severe cases of COVID-19 (eg, ground-glass opacification with or without consolidative abnormalities, consistent with viral pneumonia, minimal or no pleural effusions) [9,40,41]. While imaging with chest computed tomography (CT) was commonly performed in Chinese cohorts, we prefer to avoid its use, unless necessary; if chest CT is used as a diagnostic tool, its use must be balanced with the risk to other patients and healthcare workers during the process of patient transport and time spent in the CT room. Characteristic findings on bedside lung ultrasound include thickening of the pleural line and B lines supporting alveolar consolidation. Pleural effusions are unusual [42]. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Imaging findings'.)

**Pathology** — There are a paucity of data describing lung pathology of COVID-19 pneumonia in critically ill patients. Most autopsy reports describe hyaline membrane changes and microvessel thrombosis suggestive of early ARDS (ie, exudative and proliferative phases of diffuse alveolar damage [DAD]) [32,43-48]. Other findings include bacterial pneumonia (isolated or superimposed on DAD) and viral pneumonitis [44,48]. Less common findings include acute fibrinous organizing pneumonia (AFOP; in the late stages) [49], amyloid deposition (heart and lung), and rarely alveolar

hemorrhage and vasculitis [48]. (See "Interpretation of lung biopsy results in interstitial lung disease", section on 'Diffuse alveolar damage'.)

Evidence of pulmonary thrombosis and thromboembolism has been reported in autopsy series [44,48,50]. (See "Coronavirus disease 2019 (COVID-19): Hypercoagulability", section on 'Clinical features'.)

Distant organ involvement has also been seen with the demonstration of virus in organs other than the lung and, in some cases, acute tubular necrosis and a generalized thrombotic microangiopathy in the kidney [44,48]. (See "Coronavirus disease 2019 (COVID-19): Issues related to kidney disease and hypertension".)

**Risk factors for progression** — Age appears to be the major risk factor that predicts progression to ARDS [12,19,20,25]. Comorbidities, high fever (≥39°C), history of smoking, and select laboratory features also predict progression and death from COVID-19. Importantly, adults of any age may develop severe disease and experience adverse outcomes, especially those with comorbidities. Further details regarding the risk of disease progression are provided separately. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Risk factors for severe illness'.)

## RESPIRATORY CARE OF THE NONINTUBATED PATIENT

Specific aspects of respiratory care relevant to deteriorating patients with COVID-19 before admission to the intensive care unit (ICU) are discussed here (table 1). These include oxygenation with low flow and high-flow systems, noninvasive ventilation and the administration of nebulized medications. For hospitalized patients who develop progressive symptoms, early admission to the ICU is prudent when feasible.

**Self-proning** — Some experts are encouraging that the hospitalized patient spend as much time as is feasible and safe in the prone position while receiving oxygen; the rationale for this approach is based upon limited direct evidence [51,52] and anecdotal observations in the field as well as indirect evidence of its efficacy in ventilated patients. (See 'Prone ventilation' below and 'Monitoring on noninvasive modalities' below.)

**Oxygenation targets** — The World Health Organization (WHO) suggests titrating oxygen to a target peripheral oxygen saturation ($SpO_2$) of ≥90 percent. For most critically ill patients, we prefer the lowest possible fraction of inspired oxygen ($FiO_2$) necessary to meet oxygenation goals, ideally targeting a $SpO_2$ between 90 and 96 percent, if feasible. However, some patients may warrant a lower target (eg, patients with a concomitant acute hypercapnic respiratory failure from chronic

obstructive pulmonary disease [COPD]) and others may warrant a higher target (eg, pregnancy). (See "Overview of initiating invasive mechanical ventilation in adults in the intensive care unit", section on 'Fraction of inspired oxygen'.)

**Low flow oxygen** — For patients with COVID-19, supplemental oxygenation with a low flow system via nasal cannula is appropriate (ie, up to 6 L/min). Although the degree of micro-organism aerosolization at low flow rates is unknown, it is reasonable to surmise that it is minimal.

Higher flows of oxygen may be administered using a simple face mask, venturi face mask, or nonrebreather mask (eg, up to 10 to 20 L/minute), but as flow increases, the risk of dispersion also increases, augmenting the contamination of the surrounding environment and staff.

Many experts have patients who wear nasal cannula also wear a droplet mask, especially during transport or when staff are in the room. Data to support this practice are largely non-peer-reviewed or derived from simulation experiments but make practical sense as a maneuver to reduce the infectious risk associated with potential aerosolization [53-55]. Additional information on the provision of low flow oxygen is provided separately. (See "Continuous oxygen delivery systems for the acute care of infants, children, and adults".)

**Patients with higher oxygen requirements** — As patients progress, higher amounts of oxygen are needed. Options at this point in **non**-COVID-19 patients are high-flow oxygen via nasal cannulae (HFNC) or the initiation of noninvasive ventilation (NIV). However, in patients with COVID-19, this decision is **controversial** and subject to **ongoing debate** [56,57]. Despite this controversy, both modalities have been used variably. In retrospective cohorts, rates for HFNC use ranged from 14 to 63 percent while 11 to 56 percent were treated with NIV [9,22,25,28]. While, there are no prospective data describing whether these modalities were successful at avoiding intubation, one retrospective study described the highest level of respiratory support in hospitalized COVID-19 patients was noninvasive modalities (HFNC and NIV) in 5.4 percent of patients and invasive ventilation in 30 percent [28].

**Deciding on a modality (noninvasive or invasive ventilation)** — We believe that the decision to initiate noninvasive modalities, HFNC or NIV, should be made by balancing the risks and benefits to the patient, the risk of exposure to healthcare workers, and best use of resources; this approach should be reassessed as new data become available. We encourage the development of hospital protocols and a multidisciplinary approach, which includes respiratory therapy staff, to facilitate this decision. In patients with COVID-19 who have acute hypoxemic respiratory failure and higher oxygen needs than low flow oxygen can provide, we suggest that noninvasive modalities, may be used **selectively** rather than proceeding directly to intubation (eg, a younger patient without comorbidities who can tolerate nasal cannulae). On the other hand, some patients may warrant

avoidance of HFNC and may benefit from proceeding directly to early intubation (eg, elderly or confused patient with comorbidities and several risk factors for progression).

Some experts advocate the avoidance of both modalities (ie, proceeding to early intubation if escalating beyond 6 L/min with continued hypoxemia or increased work of breathing). This is predicated on an increased risk of aerosolization and high likelihood that patients who need these modalities will ultimately, rapidly deteriorate and require mechanical ventilation (eg, within one to three days). This approach may be reasonable when resources are available. However, using this as an absolute rule may result in an excess of unnecessary intubations and place an undue load on ventilator demand as the disease surges. In addition, this is particularly problematic for patients under investigation (eg, COVID-19 testing pending), patients who have chronic nocturnal NIV requirements, patients with chronic respiratory failure who have high baseline oxygen requirements, and patients with do-not-intubate status but who might benefit otherwise from NIV or HFNC. Ultimately, these recommendations may change with time depending on the case load of COVID-19 patients in a given location.

**Oxygen via high flow nasal cannula versus noninvasive ventilation** — Among the noninvasive modalities, we prefer HFNC. Our preference for HFNC is based upon limited and inconsistent data, which, on balance, favor HFNC compared with NIV in patients with non-COVID-19-related acute hypoxemic respiratory failure, the details of which are provided separately (see "Heated and humidified high-flow nasal oxygen in adults: Practical considerations and potential applications", section on 'Medical patients with severe hypoxemic respiratory failure'). In addition, limited data suggest a high failure rate of NIV in patients with Middle East Respiratory Syndrome (MERS) [58] and other causes of acute respiratory distress syndrome (ARDS) (see "Noninvasive ventilation in adults with acute respiratory failure: Benefits and contraindications", section on 'Hypoxemic nonhypercapnic respiratory failure NOT due to ACPE'). However, NIV may be appropriate in patients with indications that have proven efficacy; these include patients with acute hypercapnic respiratory failure from an acute exacerbation of chronic obstructive pulmonary disease (AECOPD), patients with acute cardiogenic pulmonary edema, and patients with sleep disordered breathing (eg, obstructive sleep apnea or obesity hypoventilation). These data are provided separately. (See "Noninvasive ventilation in adults with acute respiratory failure: Benefits and contraindications", section on 'Patients likely to benefit'.)

**Monitoring on noninvasive modalities** — If HFNC or NIV is administered, vigilant monitoring of patients is warranted for progression with frequent clinical and arterial blood gas evaluation every one to two hours to ensure efficacy **and** safe ventilation (eg, frequent coughing may not be “safe”). We advocate a low threshold to intubate such patients, particularly if they show any signs of rapid progression. (See 'Timing' below.)

Although unproven, some experts, including us, provide HFNC (or NIV) while the patient is in the prone position. Limited evidence from case reports in non-COVID patients with acute respiratory distress syndrome and anecdotal evidence suggest feasibility and improvement in oxygenation in some patients [51,59,60]. Similarly, preliminary evidence supports improvements in oxygenation parameters in patients with COVID-19 receiving NIV or HFNC [61,62]. For example, in a retrospective study, 12 out of 15 COVID-19 patients treated with NIV and pronation (median total of two cycles, three hours) experienced an improvement in the peripheral oxygen saturation while the remainder either stabilized or deteriorated [61]. In another prospective study of 24 COVID-19 patients with hypoxemic respiratory failure, a third of whom were on oxygen flow of four liters or more (including HFNC), 15 patients (63 percent) could tolerate prone positioning for more than three hours [62]. Among those who tolerated prone positioning, six (40 percent) experienced improvements in oxygenation during prone positioning but in three of those improvement was not sustained upon resupination. It remains unclear whether pronation averts intubation, accelerates recovery, or reduces mortality. Future data are warranted to identify the optimal indications for and duration of pronation, and assessment of response.

Technical details regarding application of HFNC and NIV are provided separately. (See "Heated and humidified high-flow nasal oxygen in adults: Practical considerations and potential applications" and "Noninvasive ventilation in adults with acute respiratory failure: Practical aspects of initiation" and "Noninvasive ventilation in adults with acute respiratory failure: Benefits and contraindications".)

**Precautions for noninvasive modalities** — HFNC and NIV are considered aerosol generating procedures. Thus, when HFNC or NIV is used, airborne in addition to standard precautions should be undertaken (ie, airborne infection isolation room [also known as a negative pressure room], full personal protective equipment). (See "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings", section on 'Patients with suspected or confirmed COVID-19'.)

- HFNC – We advocate additionally placing a surgical or N95 mask on the patient during HFNC when healthcare workers are in the room, but the value of this practice is unknown [3]. Additional precautions for HFNC that have potential to reduce risk include starting at and using the lowest effective flow rate (eg, 20 L/minute and 0.4 $FiO_2$). Inhaled medications or gases (eg, epoprostenol, nitric oxide bronchodilators) should be avoided during HFNC.

- NIV – If NIV is initiated, a full-face mask rather than a nasal or oronasal mask is preferred to minimize particle dispersion. The mask should preferably have a good seal and **not** have an anti-asphyxiation valve or port. Use of a helmet has been proposed for delivering NIV to patients with COVID-19 [63]. However, experience is limited with this delivery method, especially in the United States. If NIV is used, dual limb circuitry with a filter on the expiratory

limb on a critical care ventilator may decrease dispersion compared with single limb circuitry on portable devices, although data to support this are lacking. We also suggest starting with continuous positive airway pressure (CPAP) using the lowest effective pressures (eg, 5 to 10 cm $H_2O$).

There are few data regarding aerosolization during HFNC and NIV. In a normal lung simulation study, dispersion of air during exhalation increased with increasing HFNC flow from 65 mm (at 10 L/minute) to 172 mm (at 60 L/minute) mostly along the sagittal plane (ie, above the nostrils) [64]. Similar distances were found when CPAP was delivered via nasal pillows (up to 332 mm with CPAP 20 cm $H_2O$). However, there was no significant leakage noted when CPAP was administered via an oronasal mask with good seal (picture 1 and picture 2). Air leak increased when connections on any device were loose. Dispersion seemed to be reduced when the simulator simulated injured lung.

**Nebulized medications (spontaneously breathing patients)** — Nebulizers are associated with aerosolization and potentially increase the risk of SARS-CoV-2 transmission. In patients with suspected or documented COVID-19, nebulized bronchodilator therapy should be reserved for acute bronchospasm (eg, in the setting of asthma or chronic obstructive pulmonary disease [COPD] exacerbation). Otherwise, nebulized therapy should generally be avoided, in particular for indications without a clear evidence-base; however some uses (eg, hypertonic saline for cystic fibrosis) may need to be individualized. Metered dose inhalers (MDIs) with spacer devices should be used instead of nebulizers for management of chronic conditions (eg, asthma or COPD controller therapy). Patients can use their own MDIs if the hospital does not have them on formulary.

If nebulized therapy is used, patients should be in an airborne infection isolation room, and healthcare workers should use contact and airborne precautions with appropriate personal protection equipment (PPE); this includes a N95 mask with goggles and face shield or equivalent (eg, powered air-purifying respirator [PAPR] mask]) as well as gloves and gown. All non-essential personnel should leave the room during nebulization. Some experts also suggest not re-entering the room for two to three hours following nebulizer administration. (See "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings".)

**Other** — Potential for transmission of SARS-CoV-2 should inform the use of other interventions in patients with documented or suspected COVID-19:

- It is prudent to minimize the following:
    - Positive airway devices for chronic nocturnal ventilation support
    - Chest physical therapy or oscillatory devices
    - Oral or airway suctioning

- Sputum induction should be avoided
- Bronchoscopy should be avoided in spontaneously breathing patients and limited to therapeutic indications (eg, life-threatening hemoptysis, central airway stenosis)

If any of these therapies are performed, similar PPE to that described for nebulizer therapy should be used. (See 'Nebulized medications (spontaneously breathing patients)' above and "Flexible bronchoscopy in adults: Overview".)

## THE DECISION TO INTUBATE

**Timing** — Timing of intubation in this population is challenging. Most patients with acute respiratory distress syndrome (ARDS) due to COVID-19 will warrant intubation and mechanical ventilation. Delaying intubation until the patient acutely decompensates is potentially harmful to the patient and healthcare workers and is not advised. For patients with escalating oxygen requirements, we monitor clinical and gas exchange parameters every one to two hours and have a **low** threshold to intubate patients with the following:

- Rapid progression over hours
- Lack of improvement on >40 L/minute of high flow oxygen and a fraction of inspired oxygen ($FiO_2$) >0.6
- Evolving hypercapnia, increasing work of breathing, increasing tidal volume, worsening mental status
- Hemodynamic instability or multiorgan failure

Most experts with experience managing COVID-19 patients suggest “early” intubation. However, the definition of what constitutes “early” is unclear. Use of noninvasive means are traditionally used to avoid intubation. However, their use is subject to controversy in patients with COVID-19 (see 'Patients with higher oxygen requirements' above). Clinicians should communicate closely and regularly about the potential for intubation in patients that are being followed and treated noninvasively so that the transition for intubation can be smooth and rapid once it has been identified that the patient needs intubation.

**Precautions** — Intubation is the highest risk procedure for droplet dispersion in patients with COVID-19 [56,65]. The following discussion is suitable for patients outside the operating room (eg, intensive care unit [ICU] and emergency department) (table 2).

- We are proponents of the development of intubation kits and intubation checklists for performing rapid sequence intubation (RSI) in this population (figure 1).

- Attention should be paid to donning full contact and airborne personal protective equipment (PPE) (figure 2 and figure 3) [56]. Appropriate PPE includes a fit-tested disposable N95 respirator mask (picture 3), with eye protection or a powered air-purifying respirator (PAPR), also known as an isolation suit (picture 4 and picture 5). Also included are gown, caps and beard covers, protective footwear, neck covering, and gloves (using the double glove technique). (See "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings".)

- Intubation should be performed in an airborne infection isolation room, if possible.

- Intubation should be performed by the most qualified individual (eg, anesthesiologist) since delayed intubation with multiple attempts may prolong dispersion and place the patient at risk of a respiratory arrest.

- Anecdotally, most experts suggest optimizing preoxygenation with nonaerosol-generating means (eg, avoidance of high flow oxygen delivered via nasal cannula) and intubation using video laryngoscopy. In patients previously on high flow oxygen, some experts switch to 100 percent nonrebreather masks for preoxygenation.

- When manual bag mask ventilation (BMV) is needed, switching the mask to a supraglottic device for manual bagging is appropriate. When feasible, BMV should be minimized before and after intubation, and a bacterial/viral high efficiency hydrophobic filter should be placed between the facemask and breathing circuit or resuscitation bag. Having a pre-prepared bag-mask with filter attached in every room with a COVID-19 patient is prudent. Using a two-person technique for an adequate face mask seal is also suggested.

- Clamping the endotracheal tube (ETT) for connections and disconnections is appropriate (eg, capnography testing following intubation), only if the patient is NOT spontaneously breathing.

- The ventilator and ventilator circuitry should be ready in advance with preplanned settings already entered so that as soon as the ETT is placed and confirmed with capnography, it can be connected directly to the ETT without additional manual bagging. In addition, if feasible, in-line suction devices and in-line adapters for bronchoscopy should be prepared and attached to the ventilator tubing in advance in order to avoid unnecessary disconnection for their placement at a later point in time. The expiratory limb on the ventilator should have a HEPA filter to decrease contamination of the ventilator and environment and protect staff when changing limb circuitry.

- To minimize exposure, bundling intubation with other procedures is appropriate as is bundling the chest radiograph for ETT and central venous catheter placement.

- Doffing should follow strict procedure and some experts also advocate for the use of viricidal wipes for areas of exposed skin during intubation (eg, neck) (figure 3).

New proposals are emerging for novel barrier protections for intubation. In one such pilot study, manually performing intubation inside a transparent box was described ("aerosol box") [66]. The box was designed so that it could be placed over a patient's head allowing intubation to be performed through two circular ports on the cephalad side of the box. In a simulation experiment, cough was approximated using a latex balloon and fluorescent dye. Use of the box was associated with significant reduction in aerosol deposition to the individual performing intubation, their PPE clothing, and the surrounding environment, when compared with the same simulation without the box. While proposed as an adjunct to protection, restriction of hand movements may be encountered during airway manipulation that would necessitate abandoning the procedure and the simulation may not accurately mimic the aerosolization behavior of virus particles. Such devices are not yet commercially available.

Detailed guidance regarding intubation in the operating room, optimal personal protective equipment, and procedural details regarding intubation itself are discussed separately. (See "Coronavirus disease 2019 (COVID-19): Anesthetic concerns, including airway management and infection control" and "Safety in the operating room", section on 'COVID-19' and "Direct laryngoscopy and endotracheal intubation in adults" and "Rapid sequence intubation for adults outside the operating room" and "The decision to intubate" and "Induction agents for rapid sequence intubation in adults outside the operating room" and "Neuromuscular blocking agents (NMBAs) for rapid sequence intubation in adults outside of the operating room".)

## VENTILATOR MANAGEMENT OF ACUTE RESPIRATORY DISTRESS SYNDROME

Most patients with COVID-19 who are mechanically ventilated appear to have acute respiratory distress syndrome (ARDS). Accurate data on duration of ventilation are limited but suggest prolonged mechanical ventilation for two weeks or more (table 1). All of the steps discussed below should proceed as resources allow.

Whether different phases of COVID-19 pneumonitis require different ventilatory strategies is unclear. One school of thought is that in the early phase of COVID-19, severe hypoxemia is associated with high compliance and low alveolar recruitability (atypical ARDS), while in the later phase, severe hypoxemia is associated with low lung compliance and high recruitability (classic ARDS) [67,68]. However, this hypothesis, remains unproven and optimal ventilatory strategies

based upon it are unclear. Until further data are available, we prefer a strategy that promotes lung protection as outlined in the sections below.

**Low tidal volume ventilation (LTVV)** — As for all patients with ARDS, patients with COVID-19 pneumonia who develop ARDS requiring mechanical ventilation should receive LTVV targeting ≤6 mL/kg predicted body weight (PBW; range 4 to 8 mL/kg PBW (table 3 and table 4)). We typically use a volume-limited assist control mode, beginning with a tidal volume of 6 mL/kg PBW, which targets a plateau pressure (Pplat) ≤30 cm $H_2O$, and applies positive end-expiratory pressure (PEEP) according to the strategy outlined in the table (table 5). This approach is based upon several randomized trials and meta-analyses that have reported improved mortality from LTVV in patients with ARDS. The experience among Chinese, Italian, and United States cohorts is that this approach is also beneficial in this population. Modifications to or deviations from this mechanical ventilation strategy may be required in the setting of severe hypercapnia or ventilator dyssynchrony (figure 4). (See "Ventilator management strategies for adults with acute respiratory distress syndrome", section on 'Patients who are not improving or deteriorating'.)

Anecdotal reports suggest that the COVID-19 ARDS phenotype is one of severe hypoxemia that is responsive to high PEEP with relatively high lung compliance such that Pplat ≤30 cm $H_2O$ is not difficult to achieve. As a consequence, we and other clinicians have a low threshold to start with higher than usual levels of PEEP (eg, 10 to 15 cm $H_2O$).

Expanded details on LTVV and other ventilator strategies in ARDS are provided separately. (See "Ventilator management strategies for adults with acute respiratory distress syndrome".)

We believe that oxygenation goals in critically ill patients with COVID-19 should be similar to those in nonventilated patients (ie, peripheral oxygen saturation between 90 and 96 percent (see 'Oxygenation targets' above)). However, in patents with COVID-19, some experts use a higher peripheral oxygen saturation ($SpO_2$) goal [7]. The rationale for this approach is that it may reduce the frequency of ventilator adjustments that require staff entry into the room, thereby reducing the risk to healthcare staff, although data are lacking to support it.

Reflecting the practice of LTVV, one retrospective Italian cohort reported that the median level of PEEP was 14 cm $H_2O$ (interquartile range [IQR] 12 to 16 cm $H_2O$) [22]. Ninety percent of patients required an $FiO_2$ >0.5, and the median $PaO_2/FiO_2$ ratio was 160 (IQR, 114 to 220).

**Failure of low tidal volume ventilation** — For patients with COVID-19 that fail to achieve adequate oxygenation with LTVV, we agree with other experts in the field who have chosen prone ventilation as the preferred next step. For its application, we use similar criteria to those in non-COVD-19 patients (ie, partial arterial pressure of oxygen/fraction of inspired oxygen [$PaO_2$:$FiO_2$] ratio <150 mmHg, a $FiO_2$ ≥0.6, and PEEP ≥5 cm $H_2O$; excessively high airway pressures; or

recalcitrant hypoxemia), although some experts use a higher $PaO_2$:$FiO_2$ ratio, given the good response seen in this population.

**Prone ventilation** — Our preference for using prone ventilation is based on its known efficacy in patients with ARDS as well as limited and anecdotal observations of intensivists in the field who have noted that unlike patients who had severe acute respiratory syndrome coronavirus (SARS-CoV), patients with COVID-19-related ARDS respond well to this maneuver [69]. Those who are experienced in ventilating patients with COVID-19-related ARDS also promote ventilating patients prone for as long as is feasible without prematurely returning the patient to the supine position (ie, 12 to 16 hours prone per day) and to perform the maneuver at change of shift when sufficient staff are available. The utmost care should be taken to avoid ventilator disconnections during proning and the number of personnel should be limited to that required for turning. This video which describes the prone procedure is freely available. Additional details regarding the efficacy, contraindications (table 6) and application (table 7) of prone ventilation are provided separately. (See "Prone ventilation for adult patients with acute respiratory distress syndrome" and "Ventilator management strategies for adults with acute respiratory distress syndrome", section on 'Ventilator strategies to maximize alveolar recruitment'.)

The good response to prone positioning may be due to preserved lung compliance in this population compared with patients who develop ARDS from other etiologies. Lung compliance is the change in lung volume for a given pressure. It can be measured using the following equations: lung compliance (C) = change in lung volume (V) / change in transpulmonary pressure (alveolar pressure [Palv] – pleural pressure [Ppl]); static lung compliance = tidal volume / Pplat – PEEP. The normal lung compliance is approximately 200 mL/cm $H_2O$ and in general compliance >50 mL/cm $H_2O$ has been noted by clinicians who have experienced ventilating patients with COVID-19.

Optimal timing and criteria for discontinuing prone ventilation is unclear and should be performed on an individualized basis. It is not unreasonable to use criteria similar to that in studies that have shown benefit in non-COVID-related ARDS (eg $PaO_2$:$FiO_2$ ≥150 mmHg, $FiO_2$ ≤0.6, PEEP ≤10 cm $H_2O$) maintained for at least four hours after the end of the last prone session) [70].

**Additional options** — Additional options for patients in whom prone ventilation **fails** include the following:

- Recruitment and high PEEP – Recruitment maneuvers and high PEEP strategies (table 8) may be performed to address severe hypoxemia; data supporting their use in non COVID-19-related ARDS is described separately. (See "Ventilator management strategies for adults with acute respiratory distress syndrome", section on 'Ventilator strategies to maximize alveolar recruitment'.)

- Pulmonary vasodilators – Pulmonary vasodilators may improve ventilation-perfusion mismatch in those with severe hypoxemia and may be particularly helpful in those with hypoxemia from an acute pulmonary arterial hypertension crisis. The two most commonly used agents are inhaled nitric oxide (NO) and inhaled prostacyclin, which are administered as a continuous inhalation. Inhaled vasodilators should only be administered through a closed system and require skilled personnel for their use. Potential risks and challenges with COVID-19 patients include aerosolization and clogging of bacterial/viral filters used in ventilator circuits when these medications are being administered. Inhaled NO may be preferred since it is associated with a lower need to change filters with resultant reduction in the risk to the respiratory healthcare provider. Further details regarding their use are described separately. (See "Acute respiratory distress syndrome: Supportive care and oxygenation in adults", section on 'Nitric oxide' and "Acute respiratory distress syndrome: Supportive care and oxygenation in adults", section on 'Prostacyclin' and "Inhaled nitric oxide in adults: Biology and indications for use", section on 'Acute hypoxemic respiratory failure'.)

- Neuromuscular blocking agents (NMBAs) – NMBAs may be reserved for patients with refractory hypoxemia or ventilator dyssynchrony. We do not favor their routine use in any patient with ARDS since data on outcomes are conflicting. (See "Acute respiratory distress syndrome: Supportive care and oxygenation in adults", section on 'Paralysis (neuromuscular blockade)' and "Neuromuscular blocking agents in critically ill patients: Use, agent selection, administration, and adverse effects".)

- Extracorporeal membrane oxygenation (ECMO) – While the World Health Organization suggests ECMO as a rescue strategy, we only use it in those who fail prone ventilation and the other evidence-based medical strategies listed above. In addition, ECMO is not universally available. As many hospitals choose to cohort patients in COVID-19-only intensive care units (ICUs), there may also be the challenge of delivering ECMO in ICUs that do not routinely care for ECMO patients; this would require the recruitment of additional specialized nursing and perfusionist staff. ECMO can also reduce the lymphocyte count and raise the interleukin-6 level, thereby interfering with the interpretation of these laboratory results [71]. (See "Extracorporeal membrane oxygenation (ECMO) in adults".)

Use of rescue strategies has varied among centers. In a single-center retrospective cohort of 52 critically ill patients with COVID-19 in Wuhan, China, approximately 12 percent received prone ventilation and 12 percent received ECMO [9]. In contrast, in the original cohort of 138 hospitalized patients with COVID-19, of the 17 patients who required invasive mechanical ventilation, 24 percent were treated with ECMO. Similarly, in an Italian cohort, only 1 percent of critically ill patients received ECMO [22].

**Additional ventilator precautions** — We recommend tight seals for all ventilator circuitry and equipment. For patients who have a tracheostomy, similar recommendations apply. Although the efficacy is unproven, some experts suggest placing the ventilator and intravenous (IV) line monitors outside the room, when feasible (eg, through a wall port). This allows frequent ventilator adjustments while simultaneously decreasing the risk of exposure to staff; although the efficacy of such maneuvers is unproven.

It is prudent to avoid unnecessary disconnection with the endotracheal tube (ETT) in ventilated patients with COVID-19 in order to avoid derecruitment and unnecessary exposure of virus to the environment. For example, in-line suction devices and in-line adapters for bronchoscopy are preferred, if resources allow. If disconnection is necessary (eg, during transfer when portable ventilators are used or manual bagging), the ETT should be temporarily clamped during disconnection and unclamped after reconnection. This is considered an aerosolizing procedure in which case an airborne infection isolation room is preferable but is not always feasible.

Other infection precautions include use of dual limb ventilator circuitry with filters placed at the exhalation outlets as well as heat moisture exchange (HME) systems rather than heated humification of single limb circuits. HME should be placed between the exhalation port and the ETT (figure 5 and figure 6). (See "The ventilator circuit".)

It is particularly important to adhere to the standard practice of maintaining the ETT cuff pressure between 25 and 30 cm $H_2O$ so that a tight seal exists between the cuff and the tracheal wall. (See "Complications of the endotracheal tube following initial placement: Prevention and management in adult intensive care unit patients", section on 'Maintain optimal cuff pressure'.)

All ventilators should have appropriate filters in place and agreed upon filter change schedule (eg, every six hours). The ventilator should be wiped down after every filter change.

Although an airborne isolation room is ideal, if not feasible, patients can be ventilated in a non-isolation room but need to be transported to an airborne isolation room when aerosol generating procedures take place (eg, extubation, bronchoscopy). Having a protocol in place for transport is prudent.

## INTERVENTIONS

Ventilated patients require frequent evaluation and develop complications that require intervention. Details relevant to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection are included in this section and mostly relate to infectious precautions.

In a biodistribution study of 1070 specimens obtained from 205 patients with COVID-19 pneumonia, bronchoalveolar lavage fluid specimens showed the highest positive rates (93 percent), followed by sputum (72 percent), nasal swabs (63 percent), fibrobronchoscope brush biopsy (46 percent), pharyngeal swabs (32 percent), feces (29 percent), and blood (1 percent). No urine specimens tested positive [72]. These data demonstrate that SARS-CoV-2 may be detected in several specimens, although the reported rates in this study may have been determined by the severity of illness of the individual tested.

In a systematic review of 10 retrospective cohort studies which evaluated transmission of severe acute respiratory syndrome coronavirus (SARS-CoV) to healthcare workers, endotracheal intubation had the highest risk (odds ratio [OR] 6.6, 95% CI 2.3-18.9), followed by noninvasive ventilation (OR 3.1, 95% CI 1.4-6.8), tracheostomy (OR 4.2, 95% CI 1.5-11.5), and bag-mask ventilation [73]. Other procedures were associated with a lower or insignificant risk of transmission but it is not known whether they can be applied to SARS-CoV-2. For example, duration of close contact during aerosolizing procedures and precautions used were not described.

**Collection of respiratory specimens in the intubated patient** — Some intubated patients require upper or lower respiratory tract sampling for diagnostic purposes (eg, diagnosis of COVID-19 or ventilator-associated pneumonia [VAP]). Technically, nasopharyngeal and oropharyngeal swabs do not have to be taken under airborne precautions. However, we prefer to obtain naso-and oropharyngeal swabs and tracheal aspirates under airborne precautions in the intensive care unit (ICU). Nonbronchoscopic alveolar lavage (“mini-BAL”) may also be performed as an alternative to bronchoscopy, although experience in this procedure is not universal among ICUs. If mini-BAL is performed for the diagnosis of COVID-19, use of smaller aliquots of lavage fluid is prudent (eg, three 10 mL aliquots to obtain 2 to 3 mL of fluid). (See "Clinical presentation and diagnostic evaluation of ventilator-associated pneumonia", section on 'Invasive respiratory sampling'.)

**Bronchoscopy** — We agree with the American Association for Bronchology and Interventional Pulmonology (AABIP) that bronchoscopy should have a limited role for the diagnosis of COVID-19 and should only be performed for this indication when upper respiratory samples are negative (ie, nasopharyngeal and oropharyngeal swabs, tracheal aspirates, or non-bronchoscopic bronchoalveolar lavage) and the suspicion remains high. Bronchoscopy may also be performed when another diagnosis is being considered and a bronchoscopic sample would change management (eg, suspected *Pneumocystis jirovecii* in an immunosuppressed patient) or when therapeutic bronchoscopy is indicated (eg, life-threatening hemoptysis or airway stenosis).

Bronchoscopy is an aerosol-generating procedure and should only be performed when necessary and likely to change management. Bronchoscopy through an established airway (eg, endotracheal tube [ETT]) likely carries less risk than bronchoscopy in a spontaneously breathing patient. In

patients with COVID-19, bronchoscopy should be performed in an airborne infection isolation room. Airborne precautions and personal protective equipment (PPE) should be donned before entering the room. Using PPE similar to that described for intubation is appropriate. (See 'The decision to intubate' above and "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings".)

Using ETTs with inline adapters for bronchoscopy is ideal to prevent disconnection from the ventilator and aerosolization. If bronchoscopy is needed for the diagnosis of COVID-19 pneumonia, then we suggest small aliquots of 10 mL to obtain 2 to 3 mL of lavage fluid placed in a sterile leak-proof container. Clamping suction tubing or turning off suction after the sample has been obtained before disconnecting the sample from the device is also prudent. Specimens should be in a double zip-locked sealed plastic bag, handled with the usual precautions, and labelled clearly as “COVID-19.”

We prefer the use of disposable bronchoscopes, although these are not universally available. For nondisposable equipment, we recommend cleaning the suction channels with standard cleaning solutions typically used for highly infectious material. We also suggest covering or sealing any vessel containing the bronchoscope during transport after use and wiping down the transport cart and bronchoscope display tower before leaving the room. Wipe down solution should be hydrogen peroxide or equivalent and should be left wet on all surfaces for at least one minute.

**Extubation and weaning** — Patients are often ready for extubation while they remain infectious, and because extubation is frequently associated with some coughing, it is considered an aerosol-generating procedure. Similar to intubation, we encourage the use of extubation protocols and check lists specific to each institution.

- **Weaning** – Readiness for extubation should follow standard practice of performing spontaneous breathing trials (SBT). However, COVID-specific approaches include the following:
    - Equipment – We suggest using closed systems and not using a T-piece trial for SBTs.
    - SBTs – To reduce the risk of reintubation following extubation, we prefer a higher degree of readiness in patients with COVID-19. This practice varies and may include higher criteria for passing an SBT. For example, some experts use lower pressure support ventilation [PSV] parameters (eg, 0 to 5 cm $H_2O$) rather than the typical 7 cm $H_2O$ during the trial while others promote SBT for longer periods (eg, two to four hours rather than the typical two hours). The rationale for altered criteria is based upon the observation that patients with COVID-19 are intubated for longer periods than non-COVID-patients [22] and anecdotal evidence that suggests a high volume of secretions and airway edema; all of

these factors place the patient at high risk of post extubation respiratory failure requiring reintubation. In addition, we prefer extubating patients directly to low-flow oxygen rather than high flow oxygen delivered via nasal cannulae (HFNC) or noninvasive ventilation (NIV), which may risk virus aerosolization. (See "Weaning from mechanical ventilation: Readiness testing" and "Methods of weaning from mechanical ventilation", section on 'Spontaneous breathing trial' and "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings".)

Cuff leak test – Whether the cuff leak test (CLT) should be performed routinely prior to extubation is unclear. However, its performance may be guided by clinical suspicion for upper airway edema (eg, fluid overload) or the presence of risk factors for post extubation stridor (eg, prolonged intubation ≥6 days, age >80 years, large endotracheal tube, traumatic intubation). Performing the cuff leak test should be weighed against the potential risk of aerosolization, and similar to extubation, it should be preferentially done in an airborne isolation room. In our institution, we routinely administer glucocorticoids (eg, methylprednisolone 20 mg intravenously every four hours for a total of four doses) to most patients with COVID-19 before extubation and only extubate those in whom the CLT is positive after glucocorticoids. We base this practice upon the high rate of airway edema noted in our population but understand that practice may vary depending upon the population served. (See "Extubation management in the adult intensive care unit", section on 'Cuff leak'.)

- **Extubation** – We prefer to perform extubation in an airborne isolation room. Respiratory therapists and others in the room during extubation should adhere to airborne precautions including N95 masks with eye protection or equivalent. In general, only two people are needed and extra staff outside the room should be available to help with additional equipment. Some experts use medications to decrease coughing (eg, lidocaine via ETT, low-dose opioid bolus, dexmedetomidine, remifentanil if available), although data to support the routine use of anti-tussives are limited. In the ICU, close communication with a clinician experienced in intubation regarding the occurrence of extubation in a COVID-19 patient is prudent, in case rapid reintubation is needed, particularly for patients pre-designated as having a difficult airway.

  Both low-flow and high-flow oxygen systems should be set up and readily available. We drape the patient's chest and face with a plastic cover to provide barrier protection between the patient and the operator (eg, a plastic poncho). We typically put the ventilator in standby mode (or switch off) immediately prior to extubation. After balloon deflation, extra care should be taken during extubation to keep the inline suction catheter engaged during cuff deflation and to have another handheld suction catheter available for the removal of pharyngeal and oral sections. The endotracheal tube should be removed as smoothly as is feasible during

inspiration, and disposed of into a biohazard plastic bag bundled together with the ventilator tubing, the plastic drape, and tape/ETT holders, and inline suction catheter. The bag is sealed and disposed of immediately. Further details regarding extubation are provided separately. (See "Extubation management in the adult intensive care unit", section on 'Extubation equipment and technique'.)

- **Post-extubation care** – The patient is monitored following the procedure. The threshold to reintubate patients with postextubation respiratory failure should be low. Postextubation care should support the application of supplemental oxygen at the lowest fraction of inspired oxygen ($FiO_2$) possible, preferably via low flow nasal canula. Because patients are often extubated while they remain infectious, we would advise adhering to a similar approach to oxygen delivery as before intubation. (See "Extubation management in the adult intensive care unit", section on 'Postextubation management' and 'Oxygenation targets' above.)

The procedure for palliative extubation should be similar except care following extubation also includes palliative medication and cessation of neuromuscular blockade.

Precautions for extubation in the OR are provided separately. (See "Safety in the operating room", section on 'COVID-19'.)

**Tracheostomy** — Reports from experts in the field suggest that many patients fail early attempts at weaning (eg, within the first week), although this does not appear to predict their eventual ability to wean and extubate. However, some patients require tracheostomy (in our experience <10 percent of ICU admissions).

- **Indications** – Indications appear to be similar to non-COVID patients (eg, failed extubation, secretion management, airway edema, neurological impairment such as that which impairs airway protection).

- **Timing** – The optimal timing for tracheostomy is unknown in COVID-19 patients. In non-COVID patients, changes in practice have led to most intensivists performing tracheostomy around day 7 to 10 following initial intubation. Although most intensivists perform tracheostomy approximately 7 to 10 days following initial intubation in patients without COVID-19, it seems reasonable to defer tracheostomy in patients with COVID-19 beyond this time frame. COVID-19 patients appear to require mechanical ventilation longer than other patients (eg, two to three weeks), but can still be successfully extubated after this point.

- **Procedure** – Tracheostomy is considered a high risk procedure for aerosolization.

    - Both open and percutaneous tracheostomy procedures are acceptable in COVID patients.

- The exact procedure should be determined in advance and at the discretion of the operator with the minimum number of personnel.
- To minimize cough, neuromuscular blockade is prudent.
- It is preferable that the procedure be done at the bedside in an airborne isolation room. The operator should wear appropriate PPE similar to other aerosol generating procedures. The tracheostomy tube should have the syringe attached for immediate balloon inflation once inserted. In addition, adapters with inline suction catheters attached is also appropriate. (See 'Precautions' above and "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings".)
- Procedures such as open suctioning, dressing changes, inner cannula care, and tracheostomy changes are also considered as aerosol-generating. Thus, post tracheostomy care should also occur in an airborne isolation room, if feasible (if not, consider a portable HEPA-filtration unit).

Novel barrier protections for performing tracheostomy have been proposed. In one report, tracheostomy was performed under an aerosol-reduction cover with a high-efficiency particulate air filtration unit placed close to the surgical field [74]. However, no description of aerosol deposition was provided.

- **Prolonged weaning** – Tracheostomy collar trials can be safely done in an airborne isolation room with resumption of ventilation and a closed loop system following the trial. However, some institutions use a portable HEPA filter to generate negative pressure in a room or use closed systems and dual limb circuitry with a HEPA filter attached to the exhalation limb to minimize environmental contamination. A surgical mask over the tracheostomy itself may also theoretically limit droplet spread.

  Once a patient can breathe for 24 hours on a tracheostomy collar (or similar), they can undergo trials of a speaking valve and “capping” with the balloon deflated. Placing a speaking valve and capping would be considered aerosol generating so airborne precautions are warranted. However, once a speaking valve is in place or the tracheostomy is capped, aerosolization is less of a consideration and is the equivalent of a patient with a cough and on low flow oxygen and the patients may wear a mask over their nose and mouth.

  Decannulation is considered an aerosol-generating procedure, and provided the patient remains infectious, all the usual airborne precautions should be taken.

- **Repeat testing** – Some institutions perform repeat SARS-CoV-2 testing to determine when to discontinue infection control precautions and inform resource allocation. Whether tracheal or

nasopharyngeal swabs should be used for this purpose is uncertain. If patients are tested and have a positive test, we continue precautions until two tests collected 24 hours apart are negative; however, it remains uncertain whether viral RNA detection during recovery reflects transmissible infection. (See 'Precautions' above and "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings" and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Viral shedding and period of infectivity'.) .

Further details regarding tracheostomy are provided separately. (See "Overview of tracheostomy".)

**Cardiopulmonary resuscitation** — In the event of a cardiac arrest, cardiopulmonary resuscitation (CPR) should proceed with all members of the team wearing appropriate PPE. Practicing a test run of a COVID-19 patient cardiac arrest is prudent. Bag-mask ventilation should be avoided (if feasible); the ventilator can be used instead to deliver a respiratory rate of 10 breaths per minute (bpm). Guidance for advanced cardiac life support and CPR in patients who are prone and cannot be returned to the supine position is provided separately. (See "Advanced cardiac life support (ACLS) in adults" and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease" and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease", section on 'Patients requiring cardiopulmonary resuscitation (CPR)' and "Basic life support (BLS) in adults".)

**Other interventions** — Guidance is lacking regarding other procedures commonly performed in the ICU. Many intubated patients have routine indications for central venous and arterial access for monitoring and for vasoactive drug infusion. Grouping standard procedures such as central venous catheter and arterial lines immediately following intubation is appropriate to minimize the frequency of exposure. The transmission risk of blood is unknown but likely to be low [72].

Significant pleural effusions and barotrauma appear to be unusual as a manifestation of COVID-19. In general, emergently indicated procedures and interventions should be performed as indicated, with appropriate infectious precautions. (See 'Clinical features in critically ill patients' above and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Clinical manifestations' and "Safety in the operating room", section on 'COVID-19'.)

Transfer of COVID-19 patients should be limited to necessary trips (eg, imaging for a diagnosis that would change management, travel to an airborne isolation room for high risk aerosol-generating procedures such as intubation and extubation).

## SUPPORTIVE CARE

General supportive care of the critically ill patient with COVID-19 pneumonia is similar to that in patients with acute respiratory distress syndrome (ARDS) due to other causes and is discussed in detail separately. Select issues pertinent to COVID-19 are discussed in the sections below. (See "Acute respiratory distress syndrome: Supportive care and oxygenation in adults", section on 'Supportive care'.)

**Routine measures** — The supportive care of mechanically ventilated patients that also apply to patients with COVID-19 are provided in several linked topics. However, potential differences that may pertain to COVID-19 patients are discussed in this section:

**Venous thromboembolism prevention** — We agree with the American Society of Hematology and the Society of Critical Care Medicine that routine pharmacologic venous thromboembolism (VTE) prophylaxis is warranted, preferably with low molecular weight heparin (LMWH; eg, enoxaparin 40 mg SC once daily), unless there is a contraindication (eg, bleeding, severe thrombocytopenia). (See "Prevention of venous thromboembolic disease in acutely ill hospitalized medical adults".)

Because the risk of VTE appears to be higher than usual in this population, use of more aggressive VTE prophylaxis in the form of increased intensity of a pharmacologic agent (eg, enoxaparin 0.5 mg/kg every 12 hours, unfractionated heparin 7500 units every eight hours) and/or the addition of a mechanical device is prudent. Markedly elevated D-dimer levels, which correlate with a poor prognosis, are used by some experts to guide intensification of anticoagulation (eg, >6 times the upper limit of normal). For patients with a creatinine clearance <30 mL/minute, enoxaparin should be reduced to 30 mg daily or changed to unfractionated heparin depending on the severity of kidney impairment and patient weight. Fondaparinux is appropriate in those with heparin-induced thrombocytopenia.

We believe that administering therapeutic anticoagulation (as a form of prophylaxis) may be assessed on an individual basis. However the indications for therapeutic anticoagulation, outside of documented VTE, are unclear but may include those with presumed VTE (eg, sudden unexplained deterioration in oxygenation or hemodynamic instability, acute cor pulmonale) and clotting of vascular devices (eg, venous, arterial devices, and hemodialysis devices).

Detailed descriptions of the VTE risk and management of COVID-19 patients with hypercoagulability are provided separately. (See "Coronavirus disease 2019 (COVID-19): Hypercoagulability".)

**Sedation and analgesia** — Anecdotal evidence suggests that requirements for sedation and analgesia appear high in mechanically ventilated patients with COVID-19 and that heavy use of sedatives and analgesic medication is required for ventilator synchrony. In our practice, we target a

Richmond Agitation-Sedation Scale (RASS (table 9)) of -1 to -2 (or similar on a different scoring system), and in patients with ventilator dyssynchrony, a RASS of -2 to -3. RASS of -4 to -5 are targeted in those with severe dyssynchrony and those requiring neuromuscular blockade. For those requiring intravenous (IV) infusions, propofol and fentanyl are generally the preferred agents. However, shortages of sedatives may influence the choice of agent. We also quickly transition to oral medications, provided that fluid resuscitation is adequate (eg, oxycodone, hydromorphone, lorazepam, diazepam). Further details regarding indications, daily awakening, protocols, and dosing are provided separately. (See "Sedative-analgesic medications in critically ill adults: Selection, initiation, maintenance, and withdrawal" and "Sedative-analgesic medications in critically ill adults: Properties, dosage regimens, and adverse effects" and "Pain control in the critically ill adult patient".)

**Others** — Other supportive measures are included here.

- **Nutritional support** – The same principles of nutrition in non COVID-19 critically ill patients should be applied to critically-ill COVID-19 patients. We are not proponents of extra protein supplementation, vitamin C or D supplementation, or trace element supplementation over and above the usual recommended daily doses. (See "Nutrition support in critically ill patients: An overview" and "Nutrition support in critically ill patients: Enteral nutrition" and "Nutrition support in critically ill patients: Parenteral nutrition".)
- **Glucose control**. (See "Glycemic control and intensive insulin therapy in critical illness".)
- **Stress ulcer prophylaxis**. (See "Stress ulcers in the intensive care unit: Diagnosis, management, and prevention" and "Management of stress ulcers".)
- **Hemodynamic monitoring**. (See "Pulmonary artery catheterization: Indications, contraindications, and complications in adults" and "Pulmonary artery catheterization: Interpretation of hemodynamic values and waveforms in adults" and "Novel tools for hemodynamic monitoring in critically ill patients with shock".)
- **Fever management**. (See "Fever in the intensive care unit", section on 'Outcomes'.)
- **Early physical therapy**. (See "Post-intensive care syndrome (PICS)", section on 'Prevention and treatment'.)
- **Ventilator-associated pneumonia precautions**. (See "Risk factors and prevention of hospital-acquired and ventilator-associated pneumonia in adults".)

**Monitoring for complications** — Critically ill patients with COVID-19 should be followed routinely for the development of complications associated with critical illness from COVID-19 or

extrapulmonary manifestations of SARS-CoV-2 infection. Only essential personnel should enter the rooms of infected patients when performing daily examinations, care, and procedures.

Common complications include acute kidney injury, mild transaminitis, cardiomyopathy, pericarditis, pericardial effusions, arrhythmias, sudden cardiac death, and superinfection (eg, ventilator-associated pneumonia [VAP]) (see 'Clinical features and complications' above). We suggest that daily laboratory studies include complete blood count with differential, chemistries, liver function and coagulation studies, arterial blood gases, ferritin level, D-dimer level, and lactate dehydrogenase. Serial measurement of cardiac troponins and a low threshold transthoracic echocardiogram may be helpful to evaluate for suspected cardiac injury.

Daily chest radiographs are not recommended routinely for mechanically ventilated patients with or without COVID-19. In patients with COVID-19 who are mechanically ventilated, chest radiographs should only be performed when there is an indication (eg, catheter- or endotracheal tube [ETT]-placement or a relevant clinical change). Chest computed tomography and other imaging should be limited to those in whom testing would change management. This rationale is based upon the increased risk of viral shedding with procedures that require transfer out of the intensive care unit (ICU). (See "Complications of the endotracheal tube following initial placement: Prevention and management in adult intensive care unit patients", section on 'Reassessment of position'.)

**Fluid and electrolytes management** — Unless patients have sepsis or volume depletion from high fever or gastrointestinal losses, we prefer conservative fluid management typical of that advised for patients with ARDS. (See "Acute respiratory distress syndrome: Supportive care and oxygenation in adults", section on 'Fluid management' and "Evaluation and management of suspected sepsis and septic shock in adults", section on 'Intravenous fluids (first three hours)' and "Treatment of severe hypovolemia or hypovolemic shock in adults".)

The management of patients who present with septic shock due to COVID-19 is similar to that in patients with septic shock from other causes. (See "Evaluation and management of suspected sepsis and septic shock in adults".)

**Glucocorticoids** — We agree with the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) that glucocorticoids should **not** be routinely administered to patients with COVID-19, unless there is a separate evidence-based indication (eg, asthma or chronic obstructive lung disease exacerbation, refractory septic shock, and adrenal insufficiency). However, their administration in **critically ill** patients with COVID-19-related ARDS is **controversial**. Based on data suggesting potential benefit of glucocorticoids in patients with all-cause ARDS, the Society of Critical Care Medicine (SCCM) provides a conditional, weak recommendation in favor of glucocorticoids in patients with COVID-19 who have severe ARDS (eg,

patients with a partial arterial pressure of oxygen/fraction of inspired oxygen [$PaO_2$:$FiO_2$] <100 mmHg). Although we also weakly recommend glucocorticoids in moderate to severe “all cause” ARDS (ie, non COVID-19-related ARDS) who fail low tidal volume ventilation, we do **not** suggest administering them routinely in the setting of COVID-19 and ARDS (see "Acute respiratory distress syndrome: Supportive care and oxygenation in adults", section on 'Glucocorticoids'). The rationale for not administering glucocorticoids in this population is that the data supporting any benefit did not include a sufficient proportion of patients with viral pneumonia to inform safety (eg, patients with severe acute respiratory syndrome [SARS], Middle East Respiratory syndrome [MERS], or influenza); this is especially important since data in patients with ARDS due to viral pneumonia were conflicting and some suggested harm [75-78].

If clinicians choose to administer glucocorticoids, the SCCM suggests that they should begin within the first 14 days, doses should be low, and courses should be short (eg, intravenous dexamethasone 20 mg IV once daily for five days, then 10 mg once daily for five days).

Data in COVID-19 patients are limited to a single retrospective Chinese cohort, where methylprednisolone administration reduced the risk of death in patients with COVID-19 compared with patients who did not receive methylprednisolone (hazard ratio [HR] 0.38; 95% CI 0.2-0.71) [25]. However, these data are fundamentally flawed and new data gathered prospectively should shed light on this controversial issue. (See "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults", section on 'Limited role of glucocorticoids'.)

As noted above, management of patients who present with shock due to COVID-19 is similar to that in patients with septic shock from other causes (see 'Fluid and electrolytes management' above). Low dose glucocorticoids are not routinely advised for septic shock. In the setting of COVID-19 and shock, we reserve low dose glucocorticoids (eg, hydrocortisone 200 to 400 mg/day in divided doses) for selected patients with refractory shock, in accordance with guidelines [7]. Low dose glucocorticoids are not routinely advised for non-refractory septic shock. The use of glucocorticoids in septic shock is discussed separately. (See "Glucocorticoid therapy in septic shock in adults", section on 'Administration'.)

**Nebulized medication** — Nebulization is considered an aerosol-generating procedure. For patients with COVID-19 who are intubated and require bronchodilators for an evidence-based indication (eg, acute bronchospasm from asthma or chronic obstructive lung disease exacerbation), we prefer the use of in-line metered dose inhalers (MDIs; ie, pressurized inhalers) rather than administration via a standard jet or vibrating mesh nebulizer due to the lower risk of aerosolization associated with MDIs [79,80].

For medications that can only be administered via a nebulizer, consideration should be given to stopping the medication if it is not essential for acute care (eg, inhaled colistin for patients with bronchiectasis) or using an MDI alternative, if available on formulary (eg, tobramycin capsule inhaler). Consideration should be given to the patient using their own supply if MDIs are not on formulary.

Placement of a filter at the expiratory port of the ventilation circuit during nebulization is prudent to minimize aerosolization into the room. Ideally, patients who require nebulizers, should be in an airborne infection isolation room. Only the healthcare staff necessary for nebulizer administration (eg, respiratory therapists or nurse) should be in the room for the initiation of the procedure and airborne precautions similar to those for intubation should be taken. (See 'The decision to intubate' above and "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings".)

**Investigational COVID-19 agents** — Several investigational agents have been proposed and individual institutions should work with their pharmacists and clinical researchers to enroll patients in clinical trials. We suggest the development of protocols by individual ICUs for the off-label use of investigational agents. This area is rapidly evolving and is discussed in detail separately. (See "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults", section on 'COVID-19-specific therapy'.)

**Management of co-infections and comorbidities** — Critically ill patients with COVID-19 who are intubated are at risk for developing VAP and other infections typical of all critically ill and/or intubated patients (eg, central line or urinary tract infections). When treating co-infections, potential drug interactions with any investigational COVID-19 agent should be assessed. Infectious disease experts should be involved early in the management of COVID-19 patients who are critically ill. Further details regarding management of chronic medications including nonsteroidal anti-inflammatories and angiotensin receptor inhibitors are provided separately. (See "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults", section on 'Uncertainty about NSAID use' and "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults", section on 'Managing chronic medications'.)

## SPECIAL POPULATIONS

There are no specific recommendations for pregnant women who are critically-ill with COVID-19 pneumonia. Management should be similar to uninfected patients. Issues regarding transmission and risk of acquiring SARS-CoV-2 in pregnant women is described separately. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention",

section on 'Pregnant and breastfeeding women' and "Critical illness during pregnancy and the peripartum period" and "Acute respiratory failure during pregnancy and the peripartum period" and "Coronavirus disease 2019 (COVID-19): Pregnancy issues".)

In patients with sickle cell disease who are critically-ill with COVID-19 in whom acute chest syndrome is contributing to their illness, consideration of early exchange transfusions and surveillance for the development of acute pulmonary hypertension is prudent [81]. (See "Acute chest syndrome in adults with sickle cell disease", section on 'COVID-19'.)

Issues that arise for other populations are provided in the following links:

- Renal issues (see "Coronavirus disease 2019 (COVID-19): Issues related to kidney disease and hypertension")
- Cardiac issues (see "Coronavirus disease 2019 (COVID-19): Myocardial infarction and other coronary artery disease issues" and "Coronavirus disease 2019 (COVID-19): Arrhythmias and conduction system disease" and "Coronavirus disease 2019 (COVID-19): Myocardial injury")
- Airway management and operating room issues (see "Coronavirus disease 2019 (COVID-19): Anesthetic concerns, including airway management and infection control")
- Cancer care (see "Coronavirus disease 2019 (COVID-19): Cancer care during the pandemic")

## PROGNOSIS

**Mortality** — Early data are emerging describing outcomes from COVID-19 in critically ill patients who develop acute respiratory distress syndrome (ARDS) [2,8-10,21,22,24-26]. Mortality appears lower than that in patients with severe acute respiratory syndrome (SARS-CoV) or Middle East respiratory syndrome (MERS). The mortality from COVID-19 appears driven by the presence of severe ARDS, and is approximately 50 percent (range 16 to 78 percent).

- In a single-center retrospective cohort of 52 critically ill Chinese patients with COVID-19, 62 percent had died by 28 days with a median duration of only seven days from intensive care unit (ICU) admission to death [9]. Among the 20 patients who survived, three remained on mechanical ventilation, three were receiving noninvasive mechanical ventilation or high flow oxygen via nasal cannulae (HFNC), and six were receiving low flow oxygen.
- In a retrospective cohort of 201 Chinese patients with COVID-19, the mortality was 52 percent among those who developed ARDS [25]. Among those who received mechanical ventilation, 66 percent died, 21 percent were discharged and 13 percent remained hospitalized.

- In a preliminary study of 21 critically ill patients in the United States, by day 5, 67 percent of critically ill patients had died, 24 percent remained critically ill, and 9.5 percent were discharged from the ICU [19].

- In an Italian cohort of 1591 patients, the ICU morality was 26 percent, but a significant proportion remained in the ICU at the time of the publication, which may have underestimated the true mortality [22].

Higher mortality was initially reported in males compared with females but this may have been due to the predominance of males affected with COVID-19 in the Chinese cohorts [8-10,25,26]; a similar difference has been noted in the preliminary reports from Italy but not from Washington state, USA [18,19].

**Risk factors for death** — Across countries, the consistent major risk factor associated with death in critically ill patients with COVID-19 is older age [9,10,17,20,22,24,25,82,83]. In two Chinese retrospective cohorts, death from ARDS was more likely to occur in those of older age ≥64 years (hazard ratio [HR] 6.17; 95% 3.26-11.67) [9,25]. Preliminary reports from Italy and the United States are reporting similar outcomes [17,18,20]. Other risk factors associated with death among critically ill patients include the following [9,10,17,20,22,24,25,84]:

- The development of ARDS, particularly severe ARDS, and the need for mechanical ventilation

- Comorbidities (eg, chronic cardiac and pulmonary conditions, hypertension, diabetes, chronic kidney disease)

- Markers of inflammation or coagulation (eg, D-dimer level >1 microg/mL admission, elevated fibrin degradation products, prolonged activated partial thromboplastin and prothrombin times)

- Select laboratory studies (eg, worsening lymphopenia, neutrophilia)

The rapidity of symptom progression does not appear to predict a worse outcome [9]

While high fever was associated with a higher likelihood of developing ARDS (HR 1.77; 95% CI 1.11-2.84), it appears to be associated with a lower likelihood of death (HR 0.41; 95% CI 0.21-0.82) [9,25], a phenomenon that has been noted previously in some critically ill patients. (See "Fever in the intensive care unit", section on 'Outcomes'.)

Further details on the risk factors associated with severe disease are provided separately. (See 'Risk factors for progression' above.)

**Long term sequelae** — The percentage of patients that require long term care is unreported. Similarly, the incidence of critical care neuromyopathy is not yet documented. In our experience the

rate may be higher than usual due to the prolonged nature of intubation in COVID-19 patients and higher use of neuromuscular blockade and sedatives, with or without concurrent glucocorticoid administration. (See "Neuromuscular weakness related to critical illness".)

The incidence of post-intensive care unit syndrome (PICS) is also unknown in COVID-19 patients. Nonetheless, patients should be followed and treated for PICS which involves nutritional, physical, psychological, and occupational therapy. (See "Post-intensive care syndrome (PICS)".)

## END OF LIFE ISSUES

In a public health emergency, values other than autonomy predominate. Like any critical illness, severe illness due to COVID-19 carries the potential of significant psychosocial distress to patients, families, and surrogates. In addition, unique aspects of COVID-19 and its management portend greater trauma including anxiety and stigma surrounding a novel pathogen and high-level isolation precautions including visitation limitation or prohibition including at the end of life. High levels of patient, family, and surrogate psychosocial distress should be anticipated and combatted with clear communication strategies and early palliative care involvement. Even if in-person visitation is not allowed due to public health care concerns, hospitals should promote internet based visual communication such as video communication between clinicians, families, and isolated patients.

Discussing end-of-life wishes with patients and their family should occur early in the course of management, including potentially even before diagnosis, especially in light of the poor outcomes for elderly patients with comorbidities who develop acute respiratory distress syndrome (ARDS) and require mechanical ventilation. Consultation with the palliative care teams and ethic experts should also be done to assist families in decision-making and assist clinicians with contentious issues or disagreement that may arise.

Due to the unique aspects to addressing needs of patient and families in this pandemic, several online resources are available for clinicians to use when having COVID-19 specific discussions with patients and families. They provide helpful language and strategies for conversations about a range of issues including, but not limited to, triaging, discussing goals of care, resource allocation, and grieving including:

- VIITALtalk
- Center to Advance Palliative Care
- National Coalition for Hospice an Palliative Care

Further principles regarding ethical issues in the intensive care unit (ICU) and advance care planning are discussed separately. (See "Ethics in the intensive care unit: Responding to requests

for potentially inappropriate therapies in adults" and "Ethics in the intensive care unit: Informed consent" and "Withholding and withdrawing ventilatory support in adults in the intensive care unit" and "Communication in the ICU: Holding a family meeting" and "Palliative care: Issues in the intensive care unit in adults" and "Advance care planning and advance directives", section on 'COVID-19 resources'.)

## DISCHARGE AND LONG TERM CARE

For patients who extubate successfully and can be safely discharged home, routine community precautions apply. For patients who require a tracheostomy or are deconditioned from critical illness, transfer to a long term acute care (LTAC) facility is typical. However, there is no guidance on whether or when patients should be re-tested. Many, but not all, LTACs require two negative SARS-CoV-2 RT-PCR tests performed 24 hours apart before accepting a patient with COVID-19. If positive testing delays transfer to an LTAC, continued infection control precautions are advised, and rehab and weaning should begin at the acute care facility. Discontinuation of infection control precautions is discussed elsewhere. (See "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings", section on 'Discontinuation of precautions'.)

Outcomes in patients who require long term care are unknown. Treatment of patients who require admission to an LTAC should be similar to non-COVID patients. Particular attention should be paid to continuing venous thromboembolism prophylaxis until the acute illness fully resolves or the patient become mobile, although the efficacy of this approach is unknown. Duration of therapeutic anticoagulation should be guided by the indication; for example, a minimum of three months for documented or presumed VTE is appropriate while shorter durations are reasonable for device thrombosis. (See "Coronavirus disease 2019 (COVID-19): Hypercoagulability".)

The management of patients who require long term mechanical ventilation is discussed separately. (See "Management and prognosis of patients requiring prolonged mechanical ventilation".)

## SURGE CAPACITY AND SCARCE RESOURCE ALLOCATION

COVID-19 is a global pandemic and has placed significant increases in demand for acute and critical care services on hospitals in many regions. This has necessitated operations maneuvers to increase capacity to be able to provide care for more patients, for more higher acuity patients requiring intensive care unit (ICU) admission and mechanical ventilation, and for patients with special isolation requirements. Surge capacity may be achieved by maximizing resources across three domains:

- Care spaces (ie, beds)
- Staff
- Physical equipment

In the COVID-19 pandemic, this has included expanding ICU care into non-ICU spaces, utilizing non-critical care trained staff to participate in delivering critical care, and innovative approaches to obtain, conserve, and increase the efficiency of physical equipment including personal protective equipment (PPE; eg, repeat use of N95 masks) and mechanical ventilators (eg, double ventilation, repurposing operating room ventilators). As an example, some experts have published preliminary data to highlight the use of one ventilator for use in multiple patients [85]. However, this maneuver was designed for a disaster setting where one might reasonably expect that several patients might need life support at similar levels. Use of this measure as a life-saving measure in patients with COVID-19 could be complicated if patients are not matched well in terms of their ventilator settings. Potential use of anesthesia ventilators for longer-term mechanical ventilation is provided separately. (See "Coronavirus disease 2019 (COVID-19): Intensive care ventilation with anesthesia machines".)

In some instances, such as in Italy, despite mobilizing to surge capacity, demand for care has still outpaced supply such that overt rationing has occurred [86]. All hospitals facing the potential of an acute surge event due to COVID-19 or another insult should have a process to approach the allocation of scarce resources such as ICU beds and mechanical ventilators. Most individual states in the United States have guidance documents which can be adapted for local institutions [87]. General principles that guide and underpin scarce resource allocation policies include:

- Maximization of lives saved and/or life-years saved
- Transparency
- Stakeholder and public input
- Separation between the clinical team and the triage process (eg, ethics committees for difficult triage decisions)
- Robust palliative care and supportive measures for patients who are not provided with critical care resources

## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Coronavirus disease 2019 (COVID-19) – International and government guidelines for general care" and "Society guideline links: Coronavirus disease 2019 (COVID-19) – Guidelines for specialty care" and "Society guideline links: Coronavirus disease 2019 (COVID-19) – Resources for patients".)

## INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Coronavirus disease 2019 (COVID-19) overview (The Basics)")

## SUMMARY AND RECOMMENDATIONS

- Among patients hospitalized with coronavirus disease 2019 (COVID-19), up to one-quarter require intensive care unit (ICU) admission. (See 'Introduction' above and 'Epidemiology' above.)
- Profound hypoxemic respiratory failure from acute respiratory distress syndrome (ARDS) is the dominant finding in critically ill patients. Common complications include acute kidney injury (AKI), elevated liver enzymes, and the late development of cardiac injury, including sudden cardiac death. Sepsis, shock, and multi-organ failure are less common. (See 'Clinical features in critically ill patients' above.)
- For most critically ill patients with COVID-19, we prefer the lowest possible fraction of inspired oxygen ($FiO_2$) necessary to meet oxygenation goals, ideally targeting a peripheral oxygen saturation between 90 and 96 percent. (See 'Respiratory care of the nonintubated patient' above and 'Oxygenation targets' above and 'Low flow oxygen' above.)
    - The use of high-flow oxygen via nasal cannulae (HFNC) and noninvasive ventilation (NIV) is **controversial** based on infection control concerns and the frequent need for mechanical ventilation despite these measures. The decision to initiate noninvasive modalities requires balancing the risks and benefits to the patient, the risk of exposure to healthcare workers,

and best use of resources; this approach should be reassessed as new data becomes available. (See 'Patients with higher oxygen requirements' above.)

- In patients with COVID-19 who have acute hypoxemic respiratory failure and higher oxygen needs than low flow oxygen can provide, we suggest selective use of noninvasive measures rather than routinely proceeding directly to intubation (**Grade 2C**). As an example we might trial HFNC in younger patients without comorbidities who can tolerate nasal cannulae. In contrast, we may proceed directly to early intubation in patients at higher risk (eg, elderly patients and patients with comorbidities or risk factors for progression).

- Among the noninvasive modalities we suggest HFNC rather than NIV (**Grade 2C**). Our preference for HFNC is based upon limited and inconsistent data, which, on balance, favors HFNC compared with NIV in HFNC in patients with non-COVID-19-related acute hypoxemic respiratory failure. NIV via a full face mask (with a good seal) may be appropriate in patients with indications that have proven efficacy including acute hypercapnic respiratory failure from an acute exacerbation of chronic obstructive pulmonary disease, acute cardiogenic pulmonary edema, and sleep disordered breathing. (See "Heated and humidified high-flow nasal oxygen in adults: Practical considerations and potential applications", section on 'Medical patients with severe hypoxemic respiratory failure' and "Noninvasive ventilation in adults with acute respiratory failure: Benefits and contraindications", section on 'Patients likely to benefit'.).

- For patients with COVID-19 who receive HFNC or NIV, vigilant monitoring is warranted for progression with frequent clinical and arterial blood gas evaluation every one to two hours to ensure efficacy **and** safe ventilation. The threshold to intubate such patients should be low. Attempting prone positioning is also appropriate.

- For critically ill patients with COVID-19, intubation should **not** be delayed until the patient acutely decompensates since this is potentially harmful to both the patient and healthcare workers. We have a low threshold to intubate those who have (see 'Timing' above):

  - Rapid progression over a few hours
  - Failure to improve despite HFNC >40 L/min and $FiO_2$ >0.6
  - Development of hypercapnia
  - Hemodynamic instability or multiorgan failure

- Intubation is a high risk procedure for aerosol dispersion in patients with COVID-19 and attention should be paid to donning full personal protective equipment (PPE) with airborne precautions (figure 2 and figure 3) as well using equipment that minimizes dispersion (eg, video

laryngoscopy) and the development of protocols for the procedure (eg, check lists) (table 2 and figure 1). (See 'Precautions' above and "Safety in the operating room", section on 'COVID-19'.)

- We use low tidal volume ventilation (LTVV) targeting ≤6 mL/kg predicted body weight (PBW) (range 4 to 8 mL/kg PBW (table 3 and table 4)) that targets a plateau pressure ≤30 cm $H_2O$ and applies positive end-expiratory pressure (PEEP) according to the strategy outlined in the table (table 5). For patients with COVID-19 who fail LTVV, prone ventilation is the preferred next step (table 7 and table 6). (See 'Ventilator management of acute respiratory distress syndrome' above and "Ventilator management strategies for adults with acute respiratory distress syndrome" and "Prone ventilation for adult patients with acute respiratory distress syndrome" and "Extracorporeal membrane oxygenation (ECMO) in adults".)

- Several procedures, including the collection of respiratory specimens, bronchoscopy, extubation, tracheostomy, and cardiopulmonary resuscitation are aerosol-generating and should be avoided or minimized, if possible. All procedures should be grouped when possible. (See 'Interventions' above.)

- Patients with COVID-19 pneumonia who are mechanically ventilated for ARDS should receive the usual daily surveillance, and supportive care including conservative fluid management (unless patients have sepsis or volume depletion) (table 1). Measurement of surveillance cardiac troponins and a low threshold to perform transthoracic echocardiography is appropriate for the early detection of cardiac injury. (See 'Supportive care' above and 'Monitoring for complications' above.)

    - In critically ill patients with COVID-19-induced ARDS who do not have a specific indication (eg, acute bronchospasm or refractory septic shock), we suggest **not** administering glucocorticoids (**Grade 2C**). The rationale for not administering glucocorticoids in this population is that the data supporting any benefit in the non-COVD-19 population did not include a sufficient proportion of patients with viral pneumonia to inform safety and that data in patients with ARDS due to viral pneumonia (eg, severe acute respiratory syndrome [SARS], Middle East respiratory syndrome [MERS], influenza) suggested harm. (See "Acute respiratory distress syndrome: Supportive care and oxygenation in adults", section on 'Glucocorticoids'.)

    - For acute bronchodilation, we prefer the use of in-line metered dose inhalers (MDIs) rather than administration via a standard jet or vibrating mesh nebulizer due to the lower risk of aerosolization associated with MDIs. Individual institutions should work with their pharmacy regarding compassionate use of investigational medications and trial enrollment. We suggest the development of protocols by individual ICUs for the off-label use of

investigational agents. (See 'Nebulized medication' above and "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults", section on 'COVID-19-specific therapy'.)

- For patients with COVID-19 who develop ARDS, the prognosis is poor with mortality ranging from 52 to 67 percent. The highest rates of death occur in those ≥64 years. (See 'Prognosis' above.)
- A greater level of anxiety and trauma among patients and families should be anticipated and combatted with clear communication strategies and early palliative care involvement. Precautions should continue if the patient continues to test positive for COVID-19 before discharge to a long term acute care facility. (See 'End of life issues' above and 'Discharge and long term care' above.)
- Several measures should be adopted to accommodate a surge in COVID-19 cases including included expanding ICU care into non-ICU spaces, utilizing non-critical care trained staff to participate in delivering critical care, and innovative approaches to obtain, conserve, and increase the efficiency of physical equipment (eg, personal protective equipment and mechanical ventilators). (See 'Surge capacity and scarce resource allocation' above.)



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