COVID-19: SEDATION-VENTILATION LIBERATION OF COVID+ PATIENTS

A Rapid Guidance Summary from the Penn Medicine Center for Evidence-based Practice
Last updated May 6, 2020 12:00 pm All links rechecked April 27th unless otherwise noted.

Key questions answered in this summary

- How should sedatives be dosed?
- What fluid resuscitation approach should be taken with ventilated patients?
- How often should spontaneous breathing tests be attempted?
- What are the criteria to begin a spontaneous breathing test?
- What is the protocol for a spontaneous breathing test?

Summary of major recommendations

- Minimizing continuous sedation and instead favoring bolused sedation to targeted endpoints reduces number of days of mechanical ventilation.
- Patients with ARDS should receive minimal fluid resuscitation.
- Ventilator weaning tests should be attempted daily upon improvement of respiratory status.
- Ventilator weaning protocol should follow a low PEEP lung-protective guide from ARDSnet (see Appendix A).
- Some identified medical centers recommend NG or NJ enteral access prior to extubation in patients intubated for more than 48 hrs (†)

Public health agency and professional society guidelines on continuous sedation

Source	Recommendations
NIH April 21	The Panel recommends using, as needed, intermittent boluses of neuromuscular blocking agents (NMBA), or continuous NMBA infusion, to facilitate protective lung ventilation (moderate-strength recommendation based on expert opinion).
DoD April 13	In patients with moderate-severe ARDS (PaO_2/FiO_2 < 150), neuromuscular blockade by continuous infusion **should not** be routinely used, but may be considered in the setting of worsening hypoxia or hypercapnia and in situations where the patient's respiratory drive cannot be managed with sedation alone resulting in ventilator dyssynchrony and lung derecruitment… [To reduce days of invasive mechanical ventilation] minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions.
WHO April 11	The goal is to reach the sedation target with the lowest possible sedative medication to minimize toxicity… Continuous infusions of benzodiazepines should be avoided when at all possible to reduce the risks of oversedation, prolonged days of IMV and delirium… **In patients with moderate-severe ARDS (PaO_2/FiO_2 < 150), neuromuscular blockade by continuous infusion should not be routinely used**… Continuous neuromuscular blockade may still be considered in patients with ARDS, both adults and children, in certain situations: ventilator dyssynchrony despite sedation, such that tidal volume limitation cannot be reliably achieved; or refractory hypoxaemia or hypercapnia.
Surviving Sepsis March 28	For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, we suggest using, as needed, intermittent boluses of neuromuscular blocking agents (NMBA), over continuous NMBA infusion, to facilitate protective lung ventilation.

†–CORRECTED May 12: the initial version of this report read "extubated for more than 48 hrs."

Medical center guidance on continuous sedation

Source	Policy
Brigham April 15	1. Following Rapid Sequence Intubation, ensure analgesia/sedation is started as paralytics may still be active (assume 60 minutes for Rocuronium, 10 minutes for succinylcholine), target sedatives to a **RASS score -2 to -3** 2. After paralytics are worn off, assess patient synchrony with the ventilator (e.g., signs of breath-stacking, double triggering, other ventilator alarms) 3. If synchronous, lighten sedation to the lowest level that maintains synchrony, ideally **RASS score 0 to -1.** 4. If not synchronous, escalate sedation as needed to achieve synchrony regardless of RASS 5. If patient remains dyssynchronous despite deep sedation (RASS -4 to -5), initiate continuous paralytic 6. Target sedation to RASS - 4 to -5 and BIS 40 to 60 (before initiating paralytic) 7. Titrate neuromuscular blockade to ventilator synchrony
Penn Medicine April 14	A goal for RASS and BPS for each patient should be established and documented. **Patients with ARDS resulting in ventilator asynchrony despite ventilator adjustments may require lower RASS goals of -2 to -3. If ventilator asynchrony persists despite RASS goal of -2 to -3, a RASS goal of -4 to -5 should be attempted. If ventilator asynchrony persists, consider neuromuscular blockage with a RASS goal of -4 to -5.** Dosing and monitoring of neuromuscular blockade should done in accordance with the UPHS Guideline for Use of Neuromuscular Blocking Agents in the ICU… Neuromuscular blockade is only required in the presence of ventilator dyssynchrony and deep sedation (RASS -4 to -5)… Intermittent dosing may be preferred over continuous infusion.
MGH April 5	For mechanically ventilated patients with COVID-19 and moderate-to-severe ARDS we suggest using as needed intermittent boluses of [neuromuscular blocking agents] over continuous infusions to facilitate lung protective ventilation and prone positioning. In the event of persistent ventilator dyssynchrony requiring > 3 bolus doses in 2 hours or persistently high plateau pressures, we suggest using a continuous [neuromuscular blocking agent] with re-evaluation every 24-48 hours.

Public health agency and professional society guidelines on fluid resuscitation

Source	Recommendations
NIH April 21	For mechanically ventilated adults with COVID-19 and ARDS: the panel recommends a conservative fluid strategy over a liberal fluid strategy (moderate-strength recommendation based on evidence from non-randomized studies).
DoD April 13	Aggressive fluid resuscitation may worsen oxygenation and outcomes in both children and adults, so in the absence of shock, fluid boluses should be minimized.
Surviving Sepsis March 28	For mechanically ventilated adults with COVID-19 and ARDS, we ***suggest*** using a conservative fluid strategy over a liberal fluid strategy.
WHO March 19	Use conservative fluid management in patients with [Severe Acute Respiratory Infection] when there is no evidence of shock.

Public health agency and professional society guidelines on frequency of and criteria for spontaneous breathing tests

Source	Recommendations
WHO April 11	Use a daily coordinated spontaneous breathing trial (SBT) protocol to liberate patients from mechanical ventilation as soon as possible as this improves patient outcomes… Daily screen for SBT readiness: spontaneous breathing efforts, resolving/stable disease, $SpO_2 \geq 90\%$ on $FiO_2 \leq 0.50$ and PEEP ≤ 8 cm H_2O, pH > 7.3 and minute ventilation ≤ 15 L/min, no significant vasopressor use, no active myocardial ischemia, no elevated ICP.
DoD April 13	[To reduce days of invasive mechanical ventilation] use weaning protocols that include daily assessment of readiness to breathe spontaneously.

Medical center guidance on frequency of and criteria for spontaneous breathing tests

Source	Policy
Brigham April 15	All patients with improving or stable respiratory disease should be considered for weaning from sedation and mechanical ventilation when they meet the following criteria: … $FiO_2 \leq 50\%$, PEEP ≤ 10 with $SpO_2 > 92\%$; Hemodynamically stable (minimal to no vasopressor requirements to maintain target MAPs). Assess patient readiness for weaning at least once daily.
MGH April 5	… should an extubation fail, it will result in an additional aerosol generating procedure, which put the intubation team at risk. As a consequence, we recommend a cautious approach to vent weaning and spontaneous breathing trials. We recommend that the switch from volume control to pressure support not occur until the patient has a P:F safely above 200 with a PEEP of 8 or less. We recommend a P:F threshold of 230. In the absence of obesity, PEEP should be weaned to 5 cm H_2O before a spontaneous breathing trial is appropriate.

Public health agency and professional society guidelines on spontaneous breathing test protocols

Source	Recommendations
DoD April 13	Target an *ARDSnet lung-protective strategy* (**4-8 mL/kg ideal body weight**), and lower inspiratory pressures (**plateau pressure <30 cm H_2O**). Start with 6 mL/kg [predicted] body weight tidal volume and titrate to as high as 8 mL/kg as long as the lungs are compliant. In patients with moderate to severe ARDS, suggest titrating to a higher PEEP as tolerated… In younger children, maximal PEEP setting is 15 cm H_2O as higher PEEP can result in decreased cardiac output. Permissive hypercapnia ensuring adequate hemodynamics and a pH > 7.15 may be tolderated.
WHO April 11	Low level of pressure support: (PS 5-7 cm H_2O and CPAP of 5 cm H_2O) or Low level of CPAP alone: (CPAP at 5 cm H_2O). [see Appendix B for algorithm]

Medical center guidance on spontaneous breathing test protocols

Source	Policy
MGH April 5	A spontaneous breathing trial should consist of a period of 2 hours on 0/0. Once the spontaneous breathing trial is passed, extubation is appropriate.
Brigham April 15	A daily spontaneous awakening trial, consisting of temporary cessation of sedatives until a RASS [Richmond Agitation-Sedation Scale] of 0 [alert and calm, spontaneously pays attention to caregiver] is achieved, is to be considered for all patients who meet the following criteria: … supine position, continuous paralytics discontinued for a minimum of 6 hours prior to spontaneous awakening trial and has evidence of spontaneous motor and/or train of fours is 4/4 for neurostimulator test, hemodynamically stable (defined as HR < 120, MAP > 65, and vasopressor requirement of levophed gtt < 10 µg/min), $SpO_2 > 92\%$ or $PaO_2 > 75$ with an $FiO_2 \leq 50\%$ and PEEP ≤ 10 (and most recent PpI < 30). A daily spontaneous breathing trial is considered for all patients who meet the requirements for a daily spontaneous awakening trial. [A] spontaneous breathing trial consists of Pressure Support ventilation mode with a PS = 5 and PEEP = 5. Spontaneous breathing trial discontinued if the patient develops: evidence of increased work of breathing with RR > 30, hypoxia (SpO2 < 92%), hemodynamic instability, rapid shallow breathing index = RR/Tidal Volume > 105. Terminate all spontaneous breathing trials after 30 minutes and return to prior VC settings if patients are deemed not ready to extubate… Extubation should be considered if patients meet the following criteria: breathing spontaneously, RASS 0 to -1, able to follow commands, intact cough and able to protect airway, require airway suctioning for secretions < q2h. Other considerations include: FiO2 < 40% at the time of extubation, optimization of volume status prior to extubation.

Medical center guidance on extubation

Source	Policy
Yale April 20	Extubations: Extubate to nasal cannula (less than 5L or use 100% NRB with blender) – similar precautions as for intubation (cannot give racemic epinephrine so if concern about airway (no cuff leak or difficult intubation) give steroids and repeat the next day. Recommend placement of NJ tube prior to extubation.
Brigham April 15	Place NG tube prior to extubation for patients intubated for > 48 hrs. Patients should have an NG tube placed prior to extubation given the frequency of swallowing issues post-extubation in these patients and delayed clearance for swallowing due to challenges obtaining video swallow/FEES (fiber-optic) in COVID patients. NGT placement after extubation is also challenging and high-risk for clinicians on floor services. Exceptions (e.g. in young patients who are A/Ox3) must be discussed by attending. Prior to extubation, remove OG tube replace with an NG tube. Regular NG tubes have the advantage of being able to put to suction and be used for bolused feeds. However, if the team anticipates long-term enteral access, consider small bore feeding tube (more challenging to palce given need for two-step chest xray or bronchoscopy to confirm placement.

Other guidance for mechanical ventilator management

Source	Recommendations
Nebraska April 20	PEEP decrease may be made when: After 24 hours stability, if FiO_2 is maintained 0.1 from prior value with PEEP wean, revert back to prior PEEP. The LRCP will re-check the Pplat and driving pressure prior to and after each change in PEEP. If the Pplat is >30 cm H_2O and driving pressure >15 cm H_2O, decrease the Vt by 1 mL/kg. If the patient is already at the minimum Vt (4 mL/kg) and unable achieve the desired PEEP as outlined in the table, contact the ordering provider.
Yale April 20	Low Tidal Volume Ventilation (ARDSnet Protocol). ARDSnet Low PEEP protocol should be considered as standard, High PEEP protocol can be considered in a subset of patients who are PEEP responsive.
WHO April 11	Intubation and invasive mechanical ventilation are indicated in most patients with ARDS and hypoxaemic respiratory failure. Lung protective ventilation (LPV) reduced mortality in patients with ARDS. LPV means: delivering low tidal volumes (TV) (target 6 mL/kg ideal body weight or less); achieving low plateau airway pressure (Pplat) (target Pplat ≤ 30 cm H_2O; and use of moderate positive end-expiratory pressure (PEEP) to recruit lung.
DoD April 13	For intubated patients with ARDS and a PaO2/FiO2 ration < 150, recommend early proning… Start with 6 mL/kg [predicted] body weight tidal volume and titrate as needed. In patients with moderate to severe ARDS, suggest higher PEEP instead of lower PEEP… Permissive hypercapnia ensuring adequate hemodynamics and a pH > 7.15 may be tolerated.

About this report

A Rapid Guidance Summary is a focused synopsis of recommendations from selected guideline issuers and health care systems, intended to provide guidance to Penn Medicine providers and administrators during times when latest guidance is urgently needed. It is not based on a complete systematic review of the evidence. Please see the CEP web site (http://www.uphs.upenn.edu/cep) for further details on the methods for developing these reports.

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Appendix A. ARDSnet protocol summary

NIH NHLBI ARDS Clinical Network

Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

1. $PaO_2/FIO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
   Males = 50 + 2.3 [height (inches) - 60]
   Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode
3. Set ventilator settings to achieve initial V_T = 8 ml/kg PBW
4. Reduce V_T by 1 ml/kg at intervals ≤ 2 hours until V_T = 6ml/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: PaO_2 55-80 mmHg or SpO_2 88-95%

Use a minimum PEEP of 5 cm H_2O. Consider use of incremental FIO_2/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher FiO2

FIO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FIO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO2

FIO_2	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FIO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

PLATEAU PRESSURE GOAL: ≤ 30 cm H_2O

Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.

If Pplat > 30 cm H_2O: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).

If Pplat < 25 cm H_2O and V_T < 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H_2O or V_T = 6 ml/kg.

If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H_2O.

pH GOAL: 7.30-7.45

Acidosis Management: (pH < 7.30)

If pH 7.15-7.30: Increase RR until pH > 7.30 or $PaCO_2$ < 25 (Maximum set RR = 35),

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If pH < 7.15: Increase RR to 35.

If pH remains < 7.15, V_T may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).

May give $NaHCO_3$

Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

I: E RATIO GOAL: Recommend that duration of inspiration be ≤ duration of expiration.

PART II: WEANING

A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:

1. $FIO_2 \leq 0.40$ and PEEP ≤ 8 OR $FIO_2 \leq 0.50$ and PEEP ≤ 5.
2. PEEP and $FIO_2 \leq$ values of previous day).
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mmHg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

B. SPONTANEOUS BREATHING TRIAL (SBT);

If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with $FIO2 \leq 0.5$ and PEEP ≤ 5:

1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H_2O with PS ≤ 5
2. Assess for tolerance as below for up to two hours.
   - a. $SpO_2 \geq 90\%$ and/or $PaO_2 \geq 60$ mmHg
   - b. Spontaneous $V_T \geq 4$ ml/kg PBW
   - c. RR ≤ 35/min
   - d. pH ≥ 7.3
   - e. No respiratory distress (distress= 2 or more)
     - HR > 120% of baseline
     - Marked accessory muscle use
     - Abdominal paradox
     - Diaphoresis
     - Marked dyspnea
3. If tolerated for at least 30 minutes, consider extubation.
4. If not tolerated resume pre-weaning settings.

Definition of UNASSISTED BREATHING

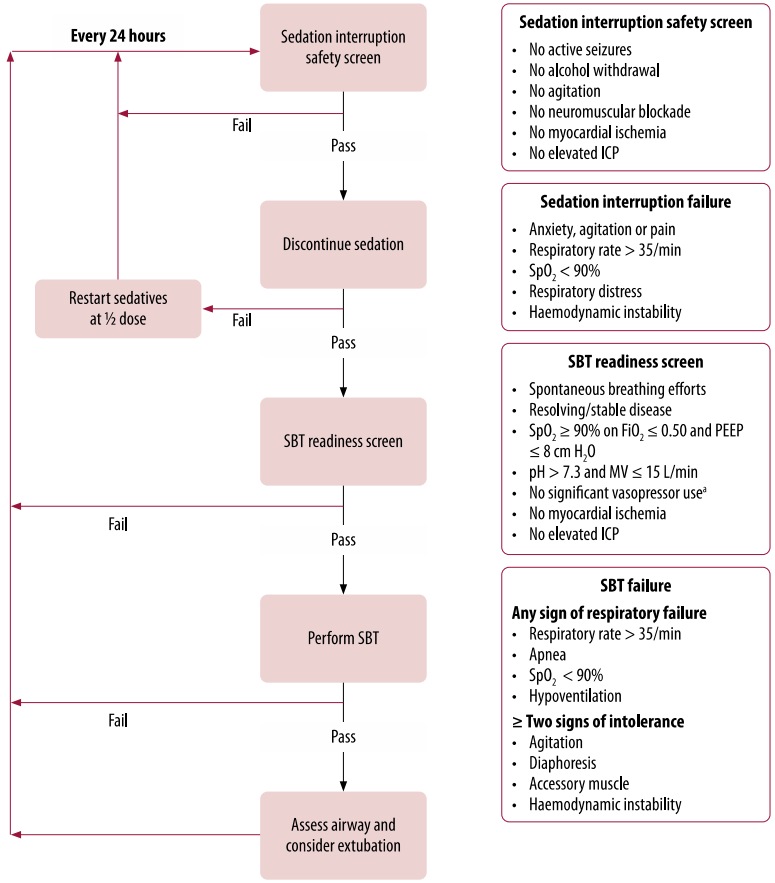
(Different from the spontaneous breathing criteria as PS is not allowed)

1. Extubated with face mask, nasal prong oxygen, or room air, OR
2. T-tube breathing, OR
3. Tracheostomy mask breathing, OR
4. CPAP less than or equal to 5 cm H_2O **without pressure support or IMV assistance.**

Appendix B. WHO Spontaneous Breathing Test Algorithms

11.1 Algorithm for coordinating daily sedation interruption with daily SBT

Consider using an algorithmic framework to systematically assess if your patient is ready to have their sedation interrupted and be liberated from the ventilator. This is adapted from the *Awakening and Breathing Controlled trial* (Girard et al, 2008) and can be adapted to your ICU.



Sedation interruption safety screen
- No active seizures
- No alcohol withdrawal
- No agitation
- No neuromuscular blockade
- No myocardial ischemia
- No elevated ICP

Sedation interruption failure
- Anxiety, agitation or pain
- Respiratory rate > 35/min
- SpO_2 < 90%
- Respiratory distress
- Haemodynamic instability

SBT readiness screen
- Spontaneous breathing efforts
- Resolving/stable disease
- $SpO_2 \geq 90\%$ on $FiO_2 \leq 0.50$ and PEEP ≤ 8 cm H_2O
- pH > 7.3 and MV ≤ 15 L/min
- No significant vasopressor use[a]
- No myocardial ischemia
- No elevated ICP

SBT failure

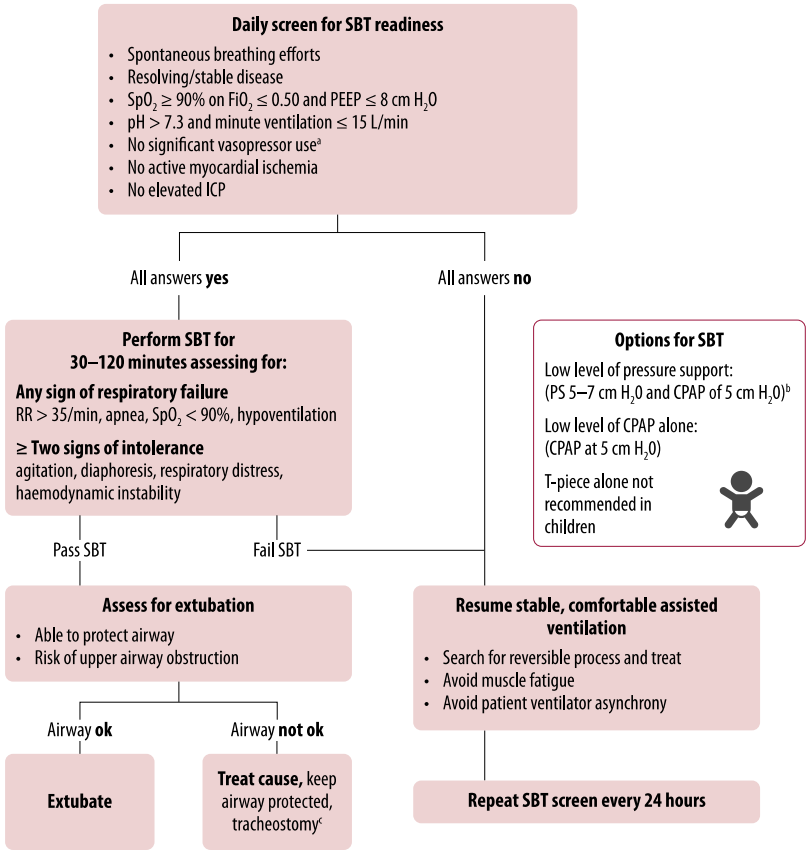
Any sign of respiratory failure
- Respiratory rate > 35/min
- Apnea
- SpO_2 < 90%
- Hypoventilation

≥ Two signs of intolerance
- Agitation
- Diaphoresis
- Accessory muscle
- Haemodynamic instability

Notes:
[a] Dopamine ≤ 5 ug/kg/min or equivalent;
ICP – intracranial pressure; MV – mechanical ventilation.

11.2 Algorithm for liberating patient from invasive mechanical ventilation

Consider using an algorithmic framework to systematically assess if your patient is ready to be liberated from the ventilator. This is adapted from the review article entitled *Discontinuing mechanical ventilatory support* (MacIntyre, 2007).



Notes:
[a] Dopamine ≤ 5 ug/kg/min or equivalent;
[b] PS in children may be higher (10 cm H_2O) given increased resistance in ETT;
[c] Consider tracheostomy based on local practice.