Intensive Care Management of COVID-19

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Updated May 2, 2020 (version 8.1)

WHAT HAS CHANGED IN THIS UPDATE COMPARED TO VERSION 7.2?

- ***HFNC:*** Based on local experience, national guidelines, and review of both published and unpublished experience, we now reconfirm that a trial of HFNC is appropriate for patients not in distress. Patient status must be monitored closely, especially in the minutes/hours after HFNC initiation, and consideration given to intubation for patients with progressive deterioration or requiring >60% FiO2.
- ***Treatment trials:*** Trials of hydroxychloroquine (systemwide), tocilizumab (Dixie/LDS), sarulimab (IMC), and convalescent plasma (systemwide) now available.
- ***Remdesivir:*** With promising, unpublished but reliable data from NIH placebo-controlled RCT and "top line" results from Gilead-sponsored open-label trial, FDA approved "emergency use authorization" for this drug on May 1. However, as of May 1, drug not yet available — look for updates regarding availability and treatment criteria.
- ***Repeat testing/clearance:*** Standardized protocols are under development. For now, must discuss with ID/infection control any decision about changing isolation status. Because negative tests from a deep respiratory specimen may be helpful in "clearing" precautions, however, suggest repeat SARS-CoV-2 PCR x1 just prior to extubation for patients who have been intubated >2 weeks.
- ***Hyperlinks:*** Additional links (e.g. proning protocol & checklist), which should now be functional in this version.

WHAT HAS CHANGED IN THIS UPDATE COMPARED TO VERSION 6.5?

- ***PEEP strategy:*** Individualize selection of normal vs high PEEP ventilation strategy. Consider normal-PEEP strategy for intubated patients who have normal/high pulmonary compliance despite a low P/F ratio. For patients with typical ARDS (low compliance), low threshold for high-PEEP strategy, especially if P/F ratio ≤129.
- *DVT prophylaxis:* Recommend enoxaparin 30 mg q12h for DVT prophylaxis in patients with CrCl >30 & platelets >50.

Recommendations apply to three groups of patients (please reference current guidelines for additional descriptions):

1) *Confirmed COVID-19 case*
2) *Person Under Investigation (PUI) with "high risk*:" Patient planned for SARS-CoV-2 testing or awaiting test results and who clinician believes has a "high" risk of having COVID-19.
3) *"Other" risk:* Includes (1) PUI patients with SARS-CoV-2 testing pending but who have "low risk" of COVID-19 based on clinician judgement and (2) patients with syndromes consistent with COVID-19 still undergoing workup to determine need for SARS-CoV-2 testing.

Recommendations below supplement standard ICU care. Key recommendations are marked with an asterisk (*). Evidence and recommendations regarding the care of patients with potential, suspected, or confirmed COVID-19 is expected to evolve very rapidly in coming months. Clinicians treating COVID-19 patients should review CDC's updated recommendations frequently and consult with ICU leadership and/or infectious disease specialists as needed.

Issue	COVID-19 suspicion			Recommendation
	Confirmed COVID-19	High-risk PUI	Other risk	
GENERAL CARE, STAFFING, & PPE				
Goals of care	X	X	X	Immediate goals of care discussion; repeat as needed with changes in status.
	X	X	X	Use "informed assent" approach to DNR/DNI decisions as appropriate.
Level of care	X	X	X	Level of care is dictated by patient clinical condition.
	X	X	X	Low ICU admission/transfer threshold if risk for severe COVID, deteriorating.
	X			If P/F ratio <130 & not responding to other Tx, see ECMO referral criteria.
Room placement*	X	X	X	Standard room with door closed.
	COVID+ *All* PUI			Negative pressure room if available and patient is unstable, has impending respiratory failure, or ongoing or impending aerosolizing procedures.
	X			Cohort COVID-19 patients in accord with surge plan.
PPE*	X	X	X	Airborne (PAPR) plus gown/gloves for any aerosolizing procedure. If N95 used, add full face shield.
	COVID+ / *all* PUI		X	Gown, gloves, procedural mask, & eye shield if no aerosolizing procedure.
	X	X	X	If possible: dedicated safety officer monitors/assists all PPE donning/doffing.
	X	X	X	Wear gown outside PAPR. Ensure glove cuffs extend over gown cuffs.
	X	X	X	Post PPE donning/doffing instruction both inside and outside room.
	X	X	X	Ensure hand sanitizer dispenser is available inside patient room near door.
	X	X	X	Provide a clean and a dirty PPE table for PAPR cleaning outside room.
Communication	X	X	X	Use whiteboard in airborne rooms aid communication.
Nursing ratio	X	X	X	Favor 1:1 nursing ratio if on airborne precautions and resources permit.
	X			Nurse ratio 2:1 OK if both patients COVID+ patients and acuity permits.
Staffing	X	X	X	Minimize number of clinical staff who enter patient room.
	X	X	X	Staff must sign in daily.
	X	X	X	No students. Consider appropriateness of resident/fellow involvement.
Cardiac arrest (see modified ACLS algorithm)	X	X	X	Request/announce Code Blue events as "Code Blue Special."
	X	X	X	Limit team in room to 5-6. Stage others outside. Use telecritical care.
	X	X	X	Intubate ASAP after first rhythm check (± shock). **Hold CPR for intubation.**
Family and patient support	X	X	X	No visitors.
	X	X	X	Identify strategy for family communication & patient emotional support.
Telemedicine	X	X	X	Early involvement to reduce HCW exposure & optimize resource use.
Physical therapy	X	X	X	Standard care. No ambulation outside room.
Patient transport outside room	X	X	X	Necessity should be confirmed by attending physician prior to transport.
	X	X	X	Non-intubated patients should wear a face mask during transport.
	X	X	X	Intubated patients should be transported on the ventilator (no BMV).
	X	X	X	No transport on BIPAP or HFNC. OK for up to 15 L/min non-rebreather mask.
Personal clothing & equipment	X	X	X	Use only disposable stethoscope.
	X	X	X	Clean communication devices (e.g. phone) often with germicidal wipes.
	X	X	X	During shift, wear scrubs only. Change to clean clothes before leaving hospital.
CLINICAL EVALUATION				
Bedside imaging & testing	X	X	X	Consider utility of bedside & other imaging/diagnostic studies in context of personnel exposure and potential for equipment contamination.
	X	X	X	No "automatic" daily CXR.
	X	X	X	Very carefully clean any equipment (e.g. ultrasound) brought into room.
Procedures & bronchoscopy	X	X	X	Incorporate HCW exposure when considering risk/benefit of potential aerosol-generating diagnostic procedures, particularly bronchoscopy.
	X	X	X	When bronchoscopy needed, (rare), use disposable bronchoscope.

Issue	COVID-19 suspicion			Recommendation
	Confirmed COVID-19	High-risk PUI	Other risk	
CT scans	X	X	X	Routine or serial CT scans unnecessary. See CT findings summary.
Laboratory testing		X		Expeditiously submit specimens for COVID-19 testing.
		X	X	Send RFA PCR panel, CBC/diff (lymph count), CRP, LDH, CK.
	X			Possible prognostication aids: CRP, ferritin, IL-6 (expensive sendout), D-dimer.
	X	X	X	Low procalcitonin does not rule out bacterial pneumonia and elevated level does not rule out COVID-19 (or other viral pneumonia).
	X	X	X	Consider arterial line to aid ABGs/labs with less staff exposure. Otherwise, maintain PIVO IV and have nurse draw labs.
	X	X	X	If frequent ABGs, In-room iStat (e.g. unused OR device) may ↓ room traffic.
RESPIRATORY SUPPORT FOR NON-INTUBATED PATIENTS*				
Method of oxygenation support*	X	X	X	Monitor oxygen trajectory carefully.
	X	X	X	**A trial of HFNC (40-50L, goal FiO2 ≤60%) is appropriate in stable, non-distressed hypoxic patients. Reassess all patients on HFNC frequently.**
	X	X	X	Up to NRB 15L/min OK for transport.
	X	X	X	Avoid NIPPV. NIPPV trial may be warranted if patient would have clear reason for NIPPV in absence of COVID-19 rule out (e.g. COPD exacerbation).
	X	X	X	HFNC and NIPPV require airborne precautions in negative pressure room.
Self proning	X	X	X	Consider self-proning in awake patients on higher FiO2 (*anecdotal data only*)
Timing of endotracheal intubation*	X	X	X	**Use lower threshold to intubate.**
	X	X		**Reassess need for intubation frequently in patients on >60% FiO2.**
	X	X		Proceed with early intubation if deteriorating respiratory, hemodynamic , or mental status to avoid increased patient & HCW risk of emergent procedure.
	X	X	X	Consider patient-specific risks for harm from intubation or invasive ventilation (e.g. pulm HTN) when selecting intubation threshold.
INTUBATION*				
Staff, location, & PPE*	X	X	X	Intubation by most experienced available operator (options will vary).
	X	X	X	Perform intubation in negative pressure room. If going to OR, intubate in negative pressure room first before transport to OR.
	X	X	X	Minimize number of staff in the room but consider having a qualified backup physician nearby (or via telemedicine) to assist and aid global overview.
	X	X	X	Wear PAPR, gown, and [long] gloves that extend over gown cuffs.
Technique	X	X	X	Use RSI approach. Avoid BVM.
Induction agents	X	X	X	Etomidate (0.3-0.4 mg/kg) + roc (1-1.2 mg/kg) to aid rapid onset, avoid cough.
Preparation & preoxygenation*	X	X	X	Maximize pre-oxygenation with NC, simple face mask, or non-rebreather.
				Avoid preoxygenation with BVM and especially NIPPV if possible. • **If unavoidable, preoxygenate with HFNC in neg pressure/airborne room.** • **If BVM unavoidable during intubation, use small tidal volumes, two-person technique to achieve tight mask seal, and ensure filter in place.**
	X	X	X	Apply apneic oxygenation with 6L NC or HFNC.
	X	X	X	Perform pre-intubation timeout. Identify 1st to 4th-line intubation equipment.
Equipment	X	X	X	**Use video laryngoscopy with independent screen (e.g GlideScope).**
	X	X	X	Keep backup equipment and extra supplies outside the room.
	X	X	X	**Ensure BVM & vent have appropriate filter.**
	X	X	X	Ensure cleaning/transport protocol followed for reusable dirty equipment.
Circuit disconnects	X	X		Minimize disconnects, consider safely clamping ETT for disconnects.

Issue	COVID-19 suspicion			Recommendation
	Confirmed COVID-19	High-risk PUI	Other risk	
VENTILATOR MANAGEMENT				
Ventilator management	X	X	X	Initiate all patients *immediately* on lung protective/low-tidal volume ventilation via Intermountain computerized ventilator protocols.
PEEP strategy	X	X	X	For most patients, use high PEEP ladder if P/F ratio <130.
	X	X		Consider normal PEEP ladder (even if ↓↓ P/F ratio) if compliance high.
Neuromuscular blockade	X	X	X	*Routine* neuromuscular blockade is not recommended. Individual patients may benefit from bolus or infusion non-depolarizing paralytic.
Proning (see IHC proning protocol and checklist)	X	X	X	Consider early proning for patients with P/F ratio <130.
	X	X	X	Use manual proning, not Rotaprone bed.
	X	X	X	Usual proning protocol (16-18 hr/day prone)
	X	X	X	Consider risk/benefit of continued proning cycles at least daily.
APRV	X	X	X	APRV is not recommended.
HFOV	X	X	X	High-frequency oscillatory ventilation (HFOV) is contraindicated.
ECMO	X	X	X	ECMO evaluation: call TCC (outside IMC) or ECMO doc on call (at IMC). Consider risk/benefit ratio including staff exposure, transfer, unclear benefit.
	X	X	X	See COVID-19 ECMO criteria; criteria may vary with COVID-19 patient volume.
	X	X	X	If possible, obtain TTE prior to ECMO candidacy evaluation.
	X	X	X	Perform cannulation and ECMO in TICU negative pressure room
	X	X	X	ECMO team will reevaluate likely utility of continued ECMO periodically.
Tracheotomy	X			Prolonged invasive ventilation not uncommon, but avoid early trach.
COVID-19 retesting	X			If intubated >2 weeks, consider repeat COVID PCR (mini-BAL) pre-extubation.
				Consult ID/infection control for any decision on downgrading isolation status.
Sedation	X	X	X	Ensure adequate sedation with RASS goal 0 to -2 to reduce anxiety and ventilator dysynchrony requiring increased RN interactions.
Home CPAP	X	X	X	Consider patient-specific benefit of CPAP vs COVID aerosolization risk. If using CPAP, must use airborne precautions in negative pressure room.
FLUID/VOLUME MANAGEMENT				
Fluid resuscitation	X	X	X	Use multimodal assessment strategy to guide judicious fluid resuscitation if hypotensive or clinically volume depleted.
Maintenance fluid	X	X	X	Avoid maintenance IV fluid.
Diuresis	X	X	X	Diuresis per FACCT-Lite strategy if off pressors >12h & not already "dry."
PHARMACOLOGIC TREATMENT				
Treatment of bacterial pneumonia	X	X	X	Imaging appearance, symptoms, or exam findings consistent with bacterial PNA should be treated with ceftriaxone and azithromycin or, if DRIP ≥3-4, vancomycin plus cefepime plus azithromycin x5-7 days.
	X			Consider stopping empiric antibiotics after 48-72 hours if (1) cultures & urinary antigens negative; (2) no neutrophilia/bandemia; (3) no purulent sputum; (4) lobar pneumonia absent; (5) procalcitonin <0.25 (optional)
Systemic steroids	X			Contraindicated as specific COVID-19 Rx (↑ viral shedding, possible harm).
Stress-dose steroids	X	X	X	Clinician discretion for refractory hypotension
DVT prophylaxis	X	X	X	Possible ↑↑ DVT risk. Ensure VTE prophylaxis: enoxaparin 40 mg daily or 30 mg q12h, SQH 5000 units q8h if CrCl <30, or SCDs if platelets <30.
Bronchodilators	X	X		Prefer high-dose MDI + spacer (e.g. 8 puffs) for non-intubated patients.
Antiviral therapy*	X			See attached medication chart in consultation with infectious disease
• **Remdesivir**	X			See Intermountain treatment guide.
• **Other drugs**	X			Consider RCT, refer to Intermountain off-label treatment guide.

Potential targeted pharmacologic treatment for COVID-19

Updated May 1, 2020

Betacoronaviruses — SARS, MERS, and the COVID-19 agent SARS-CoV-2 — are enveloped positive-sense single-stranded RNA viruses, and several potential therapies target the virus's RNA-dependent RNA polymerase. SARS-CoV-2 entry into cells begins by binding the ACE2 receptor on target cells (type 2 pneumocytes) by the viral S-spike protein followed by S-protein cleavage by cellular proteases and endocytosis, explaining why SARS-CoV-2 causes a primary viral pneumonia and interest in HIV protease inhibitors for treatment. Other therapies focus on modulation of the immune response.`

As of May 1, 2020: No specific therapies are currently recommended by U.S. guidelines. While evidence regarding COVID-19 therapy is expected to evolve very rapidly, at present, off-label use of some drugs and treatment guidelines from China and Italy are almost entirely unsupported by evidence in humans. If possible, off-label treatments should occur as part of a clinical trial (NIH/WHO/CDC/FDA/Intermountain recommendation).

- **Clinicians treating COVID-19 patients should review Intermountain's updated recommendations frequently.**
- **Information about COVID-19 clinical trials enrolling at Intermountain is available here.**

Based on Chinese and Italian treatment guidelines and reported experience, preclinical data, and published data on MERS/SARS, three off-label and one unapproved drug are currently of greatest interest for COVID-19. *Consideration of potential adverse effects/contraindications is critical given very limited evidence for any targeted therapy.*

- Remdesivir: broad-spectrum antiviral that failed as Ebola treatment. An underpowered trial from China only had trend toward benefit but NIH-sponsored trial showed benefit. FDA approved an emergency use authorization on May 1 and Intermountain is working actively to obtain supply.
- [Hydroxy]chloroquine: Possibly impairs viral cell entry. Poor quality data so far include two small negative RCTs, a highly suspect viral clearance study; and a flawed VA observational study. **RCTs comparing HCQ to azithro or placebo underway at all Intermountain hospitals.**
- IL-6R antagonists: Monoclonal antibodies to IL-6 receptor, may help if SARS-CoV-2 triggers a "cytokine release syndrome"-like response. Weak data from tiny case series. **RCTs of sarulimab at IMC, tocilizumab at Dixie/LDS.**
- Convalescent plasma: Donor antibodies bind/inactivate virus. Case series only. **Open-label trial systemwide.**
- Lopinavir/ritonavir (Kaletra): SHORTAGE. HIV protease inhibitor, may inhibit viral entry into cell but negative RCT in 199 COVID-19 patients (? trend toward benefit). Substantial side effects & drug interactions.

Table 1. Selected/key agents currently considered or under study for treatment of COVID-19 (updated April 9, 2020)

Agent	Proposed mechanism in coronavirus treatment	Evidence	Available in U.S.	Consider use? (See IHC guidance)
Remdesivir	Nucleotide analog, inhibits RNA-dependent RNA polymerase	In vitro data. Unpublished reports suggest efficacy.	Extended use program?	**If available.**
Systemic corticosteroids	Suppress inflammation	No benefit, longer viral shedding in MERS. Lower *unadjusted* risk in small cohort study.	Y	CDC/WHO recommend against if no other indication. *May change.* Stress-dose hydrocortisone for septic shock per usual practice.
Hydroxychloroquine	Immune modulation? Acidify endosomes?	In vitro. Weak prelim data.	Y	**RCT available systemwide.**
Chloroquine	Anti-malarial. See HCQ.	See hydroxychloroquine	Y	Shortage. Prefer HCQ.
Sarilumab	IL-6 receptor antagonist. Inhibit "cytokine-release syndrome"	Untested. Major RCT in progress	Y	**RCT at IMC.** Avoid if confirmed other infection
Tocilizumab	IL-6 receptor antagonist. Inhibit "cytokine-release syndrome"-like response triggered by SARS-CoV-2	Small case series. Major RCT in progress.	Y	**RCT at LDS & Dixie.** Outside LDS/Dixie/IMC, consider w/ID input if, intubated and "CRS." Avoid if confirmed other infection.
Convalescent plasma	Neutralizing antibodies	Tiny case series x1	Evolving	**Ongoing trial systemwide.**

Agent	Proposed mechanism in coronavirus treatment	Evidence	Available in U.S.	Consider use? (See IHC guidance)
Therapeutic heparin or LMWH	Prevent/treat microthrombi or PE from *postulated* hypercoagulable state induced by COVID-19	None	Y	Use as specific treatment for all COVID-19 patients not currently recommended. Treat confirmed or clinical diagnosis of PE as usual.
Tissue plasminogen activator (tPA)	Break down microthrombi? Cleavage of viral S protein?	None	Y	N
Vitamin C	Anti-inflammator/anti-oxidant (?). No specific mech for COVID-19	CITRIS-ALI with potential mortality benefit in ARDS	Y	+/- consider at clinician discretion. **RCT at IHC possibly in May.**
Macrolide antibiotic	Macrolide antibiotic, possible anti-inflammatory activity	None in coronavirus. Benefit in CAP.	N	Can include azithromycin in CAP regimen if giving antibiotics.
Lopinavir/ritonavir (Kaletra)	Boosted protease inhibitor	In Chinese & Italian guidelines. Small RCT neg.	Y	Probably not. Also: shortage.
Zinc lozenges	Unclear	Shorter symptom duration in regular coronaviruses	Y	Y (see IHC information)
Chloroquine	Anti-malarial. See HCQ.	See hydroxychloroquine	Y	See hydroxychloroquine
IVIg	Neutralizing antibodies	None	Y	N
Nebulized alpha interferon	Induction of immune response	In Chinese guidelines; neg benefit in MERS	Y	N
Ribavirin	Induction of immune response	None. Option for COVID-19 in Chinese guidelines.	Y	N
Eculizumab (Solaris)	mAb against C5. Inhibit inflammatory response	None	Y	N
Nitazoxanide	Anti-parasitic with potential broad anti-viral properties	None in coronaviruses. RCTs underway.	Y	N
Camostat mesylate	Inhibits TMPRSS2 protease involved in viral membrane fusion	In vitro.	N	N
Umifenovir (Arbidol)	"Broad spectrum" antiviral in use in Russia & China >25 years, ?inhibits membrane fusion	Commonly part of COVID-19 treatment in China	N	N
Normacopan	Inhibits LTA4 and C5 pathways	None	N	N
Baricitinib Rulxolitinib	JAK-2 inhibitors, may inhibit endocytosis of viral particle	None (purely speculative)	Y	N
Adalimumab	mAb against TNFalpha.	None (purely speculative)	Y	N
Hemofiltration	Removal of cytokines	Negative trials in sepsis.	?	N
Mesenchymal stem cells	Unclear	Phase I data	N	N
Darunavir/cobicistat	Boosted protease inhibitor	None	Y	N
Danoprivir/ritonavir	Boosted protease inhibitor	None	N	N
Azvudine Emtricitabine/tenofovir	HIV NRTIs. No reason these should work for COVID-19	None	N	N
Favipiravir	Inhibits RNA-dep RNA polymerase	Use in Japan and ?China	N	N
Stool transplantation	Immune modulation	None	Y	N
Thalidomide	Immune modulation	None	Y	N
Fingolimod	MS immune modulation	None	Y	N
Bevacizumab	VEGF inhib; unclear for COVID-19	None	Y	N
Anti PD-1 antibody	Immunomodulation	None	N	N
Thymosin	Immunomodulation	None	N	N
Pirfenidone	Antifibrotic; unclear in COVID-19	None	Y	N
Ebastine	Second generation antihistamine	None	N	N
Dornase alfa neb	Mucolytic	None	Y	N
Bromhexine	Mucolytic	None	N	Alternative mucolytic if patient clinical findings merit otherwise.
Trad. Chinese meds	Unclear	None	N	N

Summary of CT Findings in COVID-19

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Updated March 30, 2020

Numerous case reports and case series describing imaging generally and CT findings in COVID-19 patients have been published. CT findings are not perfectly specific, but CT may identify findings that support or findings that are inconsistent with COVID-19. *Imaging findings may be absent in early disease.* However, CT should generally not be used for diagnosis and definitely not for serial monitoring.

American College of Radiology recommendation: "CT should be used sparingly and reserved for hospitalized, symptomatic patients with specific clinical indications for CT."

	Zhao (AJR)	Shi (Lancet ID)	Pan (Radiology)	Chung (Radiology)	Bernheim (Radiology)
Patients	101	81	82	21	121
Distribution (general)					
Peripheral dominant	87%	54%	61%	33%	52%
Peripheral or diffuse	99%	89%	95%	??	100%
Central dominant	1%	12%	0%	NR	0%
Bilateral	82%	79%	70%	76%	60%
Consolidation pattern					
GGOs alone	22%	65%	NR	57%	41%
GGOs with or without consolidation	86%	79%	73%	86%	75%
Consolidation only	14%	17%	NR	0%	3%
Mediastinal lymphadenopathy	1%	6%	0%	0%	0%
Pleural effusion	13%	5%	NR	0%	1%
Cavitation	NR	NR	NR	0%	0%

- Items in green tend would be suggestive but are not truly specific for COVID-19
- Items in orange appear to be inconsistent with COVID-19.
- Additional patterns/findings that were difficult to translate to tabular form:
  - Micronodules generally and centrilobular or bronchovascular distributions are not typical
  - Single or multiple purely solid nodules are not typical.

Findings tend to progress over days from mild, patchy GGO's to consolidation and more extensive parenchymal involvement, peaking typically at day 10 of symptoms. Fibrous streaks and features of organizing pneumonia then appear as patients begin to recover. In critically ill patients, findings of diffuse alveolar damage are most typical.

Evidence and recommendations for the evaluation of potential, suspected, or confirmed COVID-19 will evolve rapidly. Clinicians should review current guidelines and consult radiology leadership or infectious disease as needed.

References

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