PREFACE

Our goal is to bring to you what is known about the disease, how far we have come in understanding it, and the methods that have shown promise in taking care of our patients.

A previously unknown disease entity brought the world to its heels in early 2020, causing a pandemic outbreak worldwide. This new infection was initially diagnosed as a pneumonia of unknown cause that was detected in Wuhan, China and the first confirmed case was reported to WHO on December 31, 2019. The pathogen responsible for this infection is SARS-CoV-2, a novel coronavirus suspected to have arisen from animal reservoirs. Initial infections were linked to a live seafood and animal meat market in the region suggesting an initial animal-human spread followed by human-human transmission worldwide leading to the infection reaching pandemic proportions. On February 11, 2020 WHO termed the disease caused by this novel coronavirus as COVID-19 (Coronavirus disease 2019). Medical literature has been limited as this pandemic emerged, however a global effort to control and curb the infection along with active research being conducted has been able to provide us with valuable information to tackle this new disease. As of June 7, 2020, more than 6.9 million people have been infected, with over 400,000 deaths worldwide¹. The disease has a wide spectrum of severity with the sickest patients often requiring prolonged inpatient care, pushing healthcare delivery systems worldwide to the brink of a catastrophe.

This book is a collection of resources that we hope will be useful for physicians and other colleagues fighting COVID-19 on behalf of their patients. It aims to be updated, incorporating recent developments and research findings at Upstate University and from our colleagues worldwide. Through its current and subsequent iterations to this living document we strive to be able to provide an updated source of guidance for inpatient management in COVID-19.

This quick guide is provided to providers and others without charge and we hope it is shared with all who can use it. We ask two things: that the contents not be altered, and that any materials or of references used from this publication that Upstate Medical University and the primary authors are cited as the source.
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ACKNOWLEDGEMENTS

It is sometimes hard to imagine if our lives will go back to the way it was or if this is the new normal? None of us had ever imagined that we will witness a pandemic in our lifetime despite reading about the flu pandemic of 1918 and the fortunately contained SARS, MERS, and Ebola epidemic.

This pandemic has seen the entire medical community come together and share their knowledge pool to find a cure for this unforgiving illness. Similarly, this book is a combined effort from SUNY Upstate Medical University’s Department of Medicine with valuable contributions from the Division of Hospital medicine, Division of Pulmonary, Critical care and Sleep Medicine, Division of General Internal Medicine, Division of Infectious disease, and the vital and painstaking effort of our medical students from SUNY Upstate College of Medicine.

We hope these guidelines will help us achieve our mission “To improve the health of the communities we serve through education, biomedical research and patient care”.

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# Table of Contents

PREFACE ................................................................................................................. 2  
AUTHORS ............................................................................................................... 3  
ACKNOWLEDGEMENTS ..................................................................................... 4  
EPIDEMIOLOGY .................................................................................................... 10  
  VIROLOGY .......................................................................................................... 10  
  CHRONOLOGY OF COVID-19 ........................................................................ 10  
    Global data: ..................................................................................................... 11  
    New York State Data: .................................................................................... 11  
    Onondaga County Data: ................................................................................ 11  
  TRANSMISSION: .................................................................................................. 11  
    Source ........................................................................................................... 11  
    Modes of transmission ................................................................................... 11  
    Infectivity ....................................................................................................... 12  
    Incubation period ........................................................................................... 12  
    Serology ......................................................................................................... 12  
PATHOPHYSIOLOGY .............................................................................................. 13  
  LIFE CYCLE INSIDE HOST CELL ..................................................................... 13  
  ACTIVATION OF IMMUNE SYSTEM .................................................................. 13  
THROMBOSES ...................................................................................................... 14  
INFECTION CONTROL .......................................................................................... 15  
  INFECTION CONTROL PRECAUTIONS FOR ROUTINE CARE: ............... 15  
    ☐ Enhanced Airborne with eye precautions: ............................................... 15  
    ☐ Surgical mask for patient and standard precautions: ............................ 15  
  INFECTION CONTROL PRECAUTIONS FOR HIGH RISK CARE: ............. 15  
    Aerosol generating procedures: ................................................................. 15  
PAPR TRAINING/INFECTION CONTROL ............................................................ 16  
CRITICAL STRATEGIES TO PRESERVE PPE: .............................................. 16  
    Extended use PPE: ....................................................................................... 16  
    Mask Disinfection: ....................................................................................... 17  
    Single provider rule: .................................................................................... 17  
    Tele-Health visits: ....................................................................................... 17  
    Consultants: ................................................................................................. 17  
CODE BLUE GUIDELINES ...................................................................................... 17  

VERSION 1.2, Last Updated – June 7, 2020
Phenotype H (Late Stage, Typical ARDS) ......................................................................................... 43
MANAGEMENT OF RESPIRATORY FAILURE ............................................................................. 44
Systemic Corticosteroids .............................................................................................................. 44
Bronchodilator Therapy ................................................................................................................ 44
Awake prone positioning .............................................................................................................. 44
Supplemental Oxygen .................................................................................................................. 44
INTUBATION .................................................................................................................................. 46
Indications ..................................................................................................................................... 46
Preparation ..................................................................................................................................... 46
Preoxygenation .............................................................................................................................. 46
Sedation .......................................................................................................................................... 46
Placement (Intubation) ................................................................................................................... 47
Post-intubation management ......................................................................................................... 47
MECHANICAL VENTILATION ........................................................................................................ 48
Basics ............................................................................................................................................. 48
Initial Ventilator Settings ............................................................................................................... 48
Subsequent Tidal Volume adjustment ............................................................................................ 48
Additional ventilator adjustment .................................................................................................... 48
Airway Pressure Release Ventilation ............................................................................................. 50
Sedation/Analgesia/Paralysis ......................................................................................................... 50
Pain ................................................................................................................................................ 51
Delirium ......................................................................................................................................... 51
Tracheostomy ................................................................................................................................ 52
Weaning, Extubation and Liberation from Mechanical Ventilation ............................................ 53
Refractory Hypoxemia ................................................................................................................... 56
Extracorporeal Membrane Oxygenation (ECMO) .................................................................... 58
Ventilator-Induced Lung Injury (VILI) ........................................................................................ 59
Ventilator Associated Pneumonia (VAP) ..................................................................................... 59
SHOCK ............................................................................................................................................. 61
Septic Shock ................................................................................................................................. 62
Cardiogenic Shock ........................................................................................................................ 63
Cytokine Activation Syndrome/Cytokine Release Syndrome (CRS) ........................................... 64
DISCHARGE GUIDELINES ........................................................................................................... 65
COVID TRANSITION TEAM ........................................................................................................ 65
DISCONTINUATION OF TRANSMISSION-BASED PRECAUTIONS ........................................... 65
EPIDEMIOLOGY

Virology

- WHO designated the term COVID-19 for Coronavirus disease 2019 caused by SARS-CoV-2 (previously known as 2019-nCoV).²
- Genomic sequencing has indicated that SARS-CoV-2 is a β coronavirus, closely related to the SARS-CoV virus responsible for the SARS epidemic and distantly related to the MERS-CoV virus responsible for MERS epidemic.³
- SARS-CoV-2 was found to be 96% identical at the whole-genome level to a bat coronavirus.³
- Both SARS-CoV and SARS-CoV-2 use the same receptor for cell entry; the angiotensin-converting enzyme II (ACE2).
- There is a high degree of homologous RNA recombination during replication. RNA viruses typically make up emerging and re-emerging infections due to high mutation rates with environmental adaptation and rapid evolution.⁴
- Coronaviridae are known to cause infections in human, birds and mammals. They can lead to respiratory, enteric, hepatic and neurologic disease.

Chronology of COVID-19

- December 2019: A cluster of patients were admitted to hospitals in Wuhan, China with a diagnosis of pneumonia of unknown etiology. Patients were linked to a seafood and wet animal wholesale market in Wuhan
- January 7, 2020: China confirms cases are due to a novel coronavirus
- January 20, 2020: First case reported in the US Snohomish county, Washington state, patient returned from recent travel to China
- January 30, 2020: Total of 9976 cases reported in at least 21 countries, WHO declares a global health emergency
- February 11-12, 2020: COVID-19 officially named, around 44,000 total cases with about 400 outside of China
- February 2020: Italy emerges as major European epicenter of the disease
- February 29, 2020: US reports its first COVID-19 death
- March 13, 2020: Declared a national emergency in the US
- March 26, 2020: US has most confirmed cases with at least 81,000 and more than 1,000 deaths⁵
Global Data:
- Countries with the most reported confirmed cases of COVID-19 (as of June 4, 2020)\(^6\)
  - United State: 1,872,660
  - Brazil: 614,941
  - Russia: 440,538
- Worldwide case counts updated and published regularly by teams with the World Health Organization, John Hopkins University and others.

New York State Data:
- First reported case: March 1, 2020\(^7\)
- Total positive tests as of June 4, 2020: 375,133 (51% male and 48.4% female)
- NYS county with highest amount of reported cases: Queens with 62,542 cases

Onondaga County Data:
- First reported case: March 16, 2020\(^8\)
- Total positive tests as of June 4, 2020: 2,222 (60% female, 40% male)
- Age groups of 20-29 years old and 50-59 years old with highest incidence of cases

Transmission:

Source
- Genome sequencing shows that bats appear to be the primary source of this virus; however, it is unclear at this moment how the infection was transmitted to humans.\(^3\)

Modes of transmission
- Person-to-person is believed to primarily occur via direct contact or via droplets from infected individual, both symptomatic and asymptomatic.
- SARS-CoV-2 has also been detected from other sources like stool, blood, tears and semen however it is uncertain at this moment whether these sources are responsible for transmission.\(^9-11\)
- Transmission is primarily suspected to be via respiratory droplets, which usually do not travel more than 6 feet and tend to settle down rather than stay suspended midair.
- This has prompted worldwide social distancing measures and universal mask usage to reduce transmission.
Airborne transmission via aerosolized particles has not been clearly established. However the presence of SARS-CoV-2 in experimentally generated aerosols has been shown.\textsuperscript{12}

In a health-care setup, aerosolization can occur in several situations, hence using airborne transmission precautions is strongly advised.

**Infectivity**

- It is unknown how long an infected individual may remain infectious.
- Viral RNA levels from upper respiratory specimens are shown to be the highest around the onset of symptoms, however they have been detected before and after a clinical illness, if present.\textsuperscript{13-16}
- Viral RNA shedding does not always correlate with the infectivity of a virus and it is unknown if there is a threshold below which an individual is unlikely to be infectious.
- It is unknown how long the virus can live on surfaces, but other coronaviruses are known to live on surfaces for 6-9 days.\textsuperscript{17}
- However, the use of disinfectants has been shown to inactivate other coronaviruses.\textsuperscript{18}
- This makes environmental decontamination and infection control especially important in a home and health-care setup.
- As the world looks towards re-opening, measures are being taken globally to minimize and reduce transmission in our day to day lives.

**Incubation period**

- Incubation period for COVID-19 is believed to be up to 14 days. Most cases occur 4-5 days after exposure.\textsuperscript{19}

**Serology**

- Antibodies to the virus are produced after the infection, some of which are presumed to be protective.
- This has been evidenced by effectiveness of convalescent plasma donation in transmitting the neutralizing capabilities from recovered individuals.\textsuperscript{20}
- FDA has approved emergency authorization for antibody tests which may help to establish specific antibodies that confer a protective immunity.
- Serologic testing of those antibodies in the future may aid in vaccination and measuring protective immunity to SARS-CoV-2.
PATHOPHYSIOLOGY

- Coronaviruses are enveloped, positive-sense, single-stranded RNA viruses that infect a wide variety of hosts.21,22
- Four genera are largely known; α, β, γ, and δ which are based on the structure of their genome. α and β coronaviruses infect only mammals.23
- SARS-CoV-2 belongs to β coronaviruses, just as SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV).

**Life Cycle inside host cell**

- The virus completes its life cycle through five steps22
  - Attachment – Binds to the host receptors.
  - Penetration – Entry into host cells via membrane fusion or endocytosis, followed by release of viral content into the host.
  - Biosynthesis – Viral mRNA in the host nucleus initiates manufacturing of viral proteins.
  - Maturation – New viral particles are produced.
  - Release – Released from host cell into circulation

- Angiotensin converting enzyme 2 (ACE2) has been identified as a functional receptor for SARS-CoV.24 The expression of this receptor has been categorically seen to be high in the lung, heart, ileum, kidney and bladder.25
- Using ACE2 receptors which are highly expressed on the lung epithelial cells26–28, the virus begins destroying these cells, resulting in activation of innate immunity of the host.
- Antiviral therapies that may interfere with these steps may help in decreasing severity of infection and hastening recovery.

**Activation of Immune system**

- The main components of the Immune system are the **innate and adaptive** immunity.
  - Innate immunity includes the pulmonary macrophages, airway epithelium and dendritic cells.29
  - Adaptive Immunity - Innate immune cells fight against the virus till an adaptive immunity is involved.26
- The T cell responses are initiated by antigen presentation via macrophages and dendritic cells after they phagocytize the virus.
- The CD4+ cells activate the B cells to promote production of virus-specific antibodies, while CD8+ T cells directly participate in killing the viral-infected cells.26
- Patients with severe diseases are believed to be in a pro-inflammatory state with increased concentrations of cytokines such as Interleukin IL-6, IL-10, macrophages inflammatory proteins (MIP) and tumor necrosis factors (TNF)-alpha.\textsuperscript{26,30,31}
- IL-6 levels seem to correspond to the severity of the disease.\textsuperscript{26,22}
- IL-6 and IL-8 in turn attract more neutrophils to the area of infection (like the lungs, GI tract) leading to tissue injury. This is followed by injury secondary to cytotoxic CD8+ T cell-mediated injury as well.\textsuperscript{32}
- This promotes a cascade of increased inflammation induced injury to the host tissue in the setting of continued viral replication.

**Thromboses**
- There is an increased incidence of thrombotic events with COVID-19. The pathogenesis of this is not known.\textsuperscript{33–35}
- Elevated D-Dimer levels have been seen to be associated with higher mortality in COVID-19.\textsuperscript{36}
- Infection with COVID-19 is hypothesized to cause a disruption of the Virchow’s triad which places individuals at a high risk of thrombosis.\textsuperscript{37}

**Endothelial injury**
- Direct invasion by virus, invasive catheters, Systemic inflammatory response

**Stasis**
- Immobilization and hospitalization

**Hypercoagulable state**
- Due to imbalance between procoagulant and anticoagulant factors
INFECTION CONTROL

Infection Control precautions for Routine care:

- **Enhanced Airborne with eye precautions:**
  - Apply for all COVID-rule out and COVID-positive patients. This order comes up automatically if you enter ‘COVID’ into epic.
  - Appropriate personal protective equipment (PPE):
    - N95 with protective goggles or face shield (or PAPR), gloves, and gown.
    - For donning and doffing instructions, refer to Appendix 1.

- **Surgical mask for patient and standard precautions:**
  - For low-risk patients who are asymptomatic and being tested prior to discharge to a facility, surgical mask with standard precautions is appropriate.
  - To determine appropriate PPE for staff and patients, refer to Appendix 2.

Infection Control precautions for High risk care:

- It is important to minimize procedures that carry a risk of nebulization
  - Positive airway devices for chronic nocturnal ventilation support (call Pulmonary for clearance to use positive airway devices)
  - Chest PT
  - Oral or airway suctioning
  - Avoid sputum induction
  - Decrease use and frequency of nebulizers

**Aerosol generating procedures:**

- Intubation, vent circuit changes/leaks, bronchoscopy, suctioning, nebulized treatment, bag valve manual ventilation, disconnecting from vent, high flow nasal canula (HFNC), non-invasive positive pressure ventilation (NIPPV) which includes both continuous positive airway pressure (CPAP) and bilevel positive airway pressure
(BiPAP), tracheostomy placement and exchange, and cardiopulmonary resuscitation (CPR).
- Endotracheal intubation should be performed by the most experienced provider.
- Video laryngoscopy is preferred over direct laryngoscopy for first pass success.
- Any aerosol-generating procedures should optimally be performed in a negative pressure room with full PPE. Refer to Appendix 3 for current policy.
- MDI therapy is non-aerosolizing and doesn’t require enhanced PPE or private room. MDIs will be left in the room for all COVID-19 positive and R/O COVID-19 patients.
- For patients with a tracheostomy place an ear-loop mask over the trach collar. Ensure these are changed when excessively moistened. As these patients rely on humidification, Oxymasks should be used for transport.
- Pediatric patients requiring a neonatal circuit (<10kg) should be bagged with an infant HME. Door should be closed during procedure and this applies to any direct care staff.

For Respiratory Procedures Protocol kindly refer to Appendix 4

PAPR Training/Infection Control
- When coming on to service and needing PAPR training or to contact infection control, keep these numbers on you:
  - Days: call environmental health and safety at x45782
  - Nights/weekends: call university police to reach infection control x44000

Critical strategies to preserve PPE:

Extended use PPE:
- You can go between confirmed COVID rooms, as well as COVID and rule-out patients, wearing the same N95 and face shield/goggles or PAPR.
- You will doff your gown and gloves in the patient’s room and wash your hands before re-gowning for the next room.
- You should also wipe down the front of the hood or goggles/face shield (while still wearing it) with PDI wipes between rooms.
- Goggles, face shields, and PAPR hoods are reusable and should not be discarded unless compromised.
- When seeing a mix of COVID and COVID rule-out patients under extended PPE, you may consider seeing rule-out patients first and COVID patients last.

**Mask Disinfection:**
- In a preliminary investigation from the NIH, four methods of mask disinfection were examined: vaporized hydrogen peroxide, 70°C dry heat, ultraviolet light, and 70% ethanol spray.
- All four methods eliminated SARS-COV2 virus, but only hydrogen peroxide did not damage the integrity of the mask.
- NIH concluded that this is the preferred method and it is being used at Upstate.\(^{39}\)

**Single provider rule:**
- COVID-19 rule out and confirmed patients should be seen by a single provider from each team.
- Try to see stable patients only once per day.

**Tele-Health visits:**
- We are aiming to have an iPad available for within-room use for every COVID-confirmed and COVID-rule out patient.
- Please contact the charge nurse/nursing supervisor to arrange for an iPad if not already available.
- Please take advantage of video calls to decrease the use of PPE.

**Consultants:**
- Consultants who can complete their assessment without seeing the patient should do so.
- PT/OT/ST should be ordered only as critically necessary.

**CODE Blue Guidelines**
- Infection control guidelines are different for COVID positive and rule-out patients.
- Please refer to Upstate COVID policy **COV R-02**
- A simplified layout of the room for infection control is available in **Appendix 5**
Post-exposure prophylaxis for healthcare workers:
- Please contact Dr. Kristopher Paolino (PaolinoK@upstate.edu) if you have been exposed to a COVID-19 positive patient in the last 4 days without any gloves or mask (PPE) to enroll in the hydroxychloroquine trial.

Discontinuation of precautions for COVID-19 infection:
- Please follow the algorithm Appendix 6 to make decisions on removal of isolation precautions and movement of patients to non COVID units when able.
- The policy for discontinuation of precautions is dynamic and is frequently updated.
- Refer to policy COV D-04 on Upstate website for the latest on the same.
TESTING PROCEDURES

Approach to testing:
- Priority is testing of symptomatic inpatients and health care workers.
- Diagnosis of COVID-19 is based on RT-PCR testing of respiratory samples from upper respiratory (nasopharyngeal and oropharyngeal swabs), and from the lower respiratory tract whenever possible.
- Sputum induction should be avoided due to increased risk of aerosolization.
- If you disagree with a COVID test ordered by another physician, talk with them to understand their clinical reasoning.
- If the test was sent for Wadsworth PCR assay and you strongly believe that this was not indicated, you may have a window to cancel the test by calling the microbiology lab (315-464-4459).

Reverse Transcriptase PCR testing
- RT-PCR is the gold standard test for diagnosing acute respiratory infection from viral infections similar to SARS-CoV-2.
- Diagnosing COVID-19 is challenging due to its relatively long incubation period (approximately 2 weeks) with prolonged interval of viral shedding prior to symptom onset (approximately 5 days).
- RT-PCR assays performed on nasopharyngeal and throat specimens were positive only 65% and 70% of the time, respectively.
- A single negative swab from the upper airway does not rule out SARS-CoV-2 infection and repeat sampling in 24-48 hours is recommended if there is high clinical suspicion based on imaging findings.
- Lower respiratory tract specimens give higher diagnostic yield than upper respiratory specimens in patients with pneumonia, consistent with what was observed for SARS. For intubated patients, SCCM suggests obtaining lower respiratory tract samples in preference to upper.
Efficacy of Testing:
- The sensitivity and specificity of the RT-PCR-based assays are generally high. Thus, a single positive swab is confirmatory for the diagnosis of SARS COVID-19.
- However, they have low negative predictive value and thus a single negative swab from the upper airway does not rule out SARS-CoV-2 infection.  

Prolonged PCR Positivity:
- Based on multiple case studies, it is likely that cases of re-testing positive after resolution of symptoms and radiographic abnormalities and 2 negative RT-PCR tests are due to fluctuations in viral shedding, testing sample location/fluid-type, or delayed transfer of virus from the lower respiratory tract to the nose and throat by coughing, etc.  
- Multiple studies done in China showed that COVID-19 positive patients were RT-PCR positive for a median of 11-12 days but could range from 4-45 days. Early PCR conversion was associated with younger age, milder infection (non-ICU), and low levels of IL-6 and IL-10.  

Wadsworth PCR assay:
- This is the default assay. Turn-around time may be as short as 4 hours, but you should plan on up to 24 hours.
- The test is run in batches in order to preserve reagents, the micro lab will wait until they have enough specimens to run a full plate.
- Note that, as with all tests, there is the possibility of false negative results. We don’t know what that rate is. If you receive a negative result for a patient in whom you have a high suspicion for COVID-19, you should retest after contacting the COVID ID person on call.

Cepheid Rapid test:
- This test has a rapid turn-around time; 15-30 minutes from the time the specimen is received by the Downtown microbiology lab.

When is Rapid testing indicated?
The following patients may have COVID test ordered with priority of RAPID.

1. Symptomatic patients in the Adult ED who require admission and are not being automatically routed to COVID units. For example, patients coming from long term facilities are admitted to COVID units for isolation regardless of test results and priority testing is not indicated.
2. Select **symptomatic patients in the Pediatric ED** who require admission (ONLY if it changes bed assignment)

3. **Patients transferred to UUH/UCH** who have been assigned a bed on a specialty, non-COVID unit, subsequently found to be symptomatic on arrival, need to be tested, and the result may change their bed assignment

4. **Inpatients who become symptomatic** and would be moved to a COVID unit if positive result

5. **Transplant patients** who require testing

6. **Symptomatic homeless patients**

**Respiratory Viral Panel (RVP) and COVID Testing:**
- Note that previously the RVP and the COVID test were linked.
- Given the changes in the epidemiology of respiratory viruses in our community (i.e., decreasing RVP positivity and increasing COVID positivity), most of our adult admits could reasonably be tested for COVID alone, given appropriate acute symptoms.
- If an RVP is ordered, it will still automatically reflex to COVID testing if negative.

**Antibody Testing (SARS-CoV-2 IgG Assay):**
- IgG antibodies are a marker of a prior exposure to SARS-CoV-2 virus. Antibody tests designed by several commercial laboratories are now available. However there remains considerable variability between the assays and no clear correlation to protective immunity yet.
- IgG antibodies should not be used for diagnosis of acutely ill patients suspected of COVID-19.
- Patients should continue to follow strict physical distancing, hand hygiene, cough etiquette and universal masking rules regardless of their SARS-CoV-2 IgG antibody status.
- Studies in rhesus macaques suggest immunity following primary infection may protect against subsequent exposures.\(^{47}\)
- The test’s performance in clinical setting is currently unknown.
- According to the WHO, as of April 24th, 2020, no study has evaluated whether the presence of antibodies to SARS-CoV-2 creates immunity to subsequent infection by the virus in humans.\(^{48}\)
- Serologic testing is currently recommended for disease surveillance, monitoring infection progression, assessing an individual’s immune response, and identifying potential donors for convalescent plasma.
- It is not recommended for initial diagnosis or emergency triage due to the high rate of false negatives in early infection.
- The **timing of serologic testing** may be vital to its efficacy. Time from initial symptom onset is most well described to guide test interpretations.
  - 0-5 days may have low rates of seroconversion, leading to many false negative diagnoses.
  - IgM may increase after 5-10 days and fall after 30 days.
  - IgG may increase after 10 days and remains elevated.

**Efficacy of testing:**
- Sensitivity appears to increase with increased time from symptom onset (as low as 11% in the first 5 days of illness).
- Efficacy assessed against real-time reverse transcriptase polymerase chain reaction (RT-PCR) (current gold standard for diagnosis). Overall sensitivities range 68.6 – 88.7. Specificities range 90.6 – 100.49,50

**Abbott Architect SARS-CoV-2 IgG assay**
- The assay is approved for use under the FDA’s Emergency Use Authorization (EUA).
- Among 73 patients with confirmed COVID-19, all mounted detectable IgG antibodies 14 days or longer after the symptom onset.51
- Cross-reactivity with common cold coronaviruses is a possibility but remains low in this assay. Only 0.5% of individuals assumed to be negative for COVID-19 tested positive for SARS-CoV-2 IgG. 51
- If you send COVID IgG and discharge a patient while pending, Steve McClintick’s team will follow up with the results

**Limitations**
- This is not point-of-care test (POC).
- It is unknown if the presence of IgG antibodies will protect a person from future infection or disease.
- Symptomatic patients suspected to have COVID-19 should be tested using a molecular assay to detect SARS-CoV-2 RNA.
- Immunocompromised patients who have COVID-19 may have a delayed antibody response and produce levels of antibody which may not be detected by the assay.

Experimental diagnostics:

- There is an ongoing study to collect and analyze saliva for COVID-19 RNA to develop a rapid diagnostic method. The study is currently active on 6K and at Community Campus.
- COVID-19 confirmed and COVID-19 rule out patients get one saliva swab after providing informed consent; a subsequent saliva specimen is collected four days after admission for confirmed patients.
- Dr. Kristopher Paolino and Dr. Katie Anderson are helping coordinate. Please refer to them for any questions.
DOCUMENTATION

- COVID-19 specific smartphrases have been created on EPIC for appropriate documentation.
- A smartphrase for documentation of APNIC protocol is also available. (Proning of non-ventilated patients)
- To look up these smartphrases go to
  o Personalize > Smartphrase manager > User phrases > User: PANDA, SANCHIT [00119762] > Sharing > + Add me

COVID-19 Smartphrases

  o .COVID19HPI - H&P template
  o .COVID19PROGRESS - Progress note template
  o .COVID19VIRTUALVISIT - Virtual visit note for telehealth services
  o .COVID19ATTESTATION - Attending attestation for patient
  o .COVID19DCATTEST - Attending attestation for discharge summary

- Ensure appropriate documentation on the following categories to maintain continuity of care in H&P and progress notes
  o Assessment and associated problems
  o Oxygenation status
  o P/F ratio
    ▪ (PaO2/FiO2 in %) x 100
    ▪ Estimated PaO2 and FiO2 are available in the template
  o Volume status
  o Antibiotics used
  o Code Status

- We are working with IMT to share these smartphrases with all users. Until that step is complete, smartphrases need to be manually looked up and shared for use.

Discharge instruction Smartphrases

  o COVIDSELFQUARNOTICE
  o COVIDPLASMAPROJECT
  o COVID-19 specific discharge instructions are also available for lookup on Discharge instructions > Insert smarttext tab

Proning Protocol – APNIC Protocol

  o .APNICPROTOCOL – Document relevant details as per APNIC protocol prior to and then 2 hours after initiating proning protocol.

- For any questions/feedback regarding documentation please contact Dr. Sanchit Panda (PandaS@Upstate.edu)
ADMISSION GUIDELINES

- The criteria for admission are the same for any other. A positive test alone is not grounds for admission in an otherwise stable patient.
- Note that all COVID-confirmed patients (and rule-outs) should be admitted to INPATIENT status, not observation due to the pandemic.
- ED admissions should involve attending-to-attending sign-outs for all patients (not just COVID).

A stable patient with a positive or pending test can be discharged from the ED provided

1. Department of health is notified
2. The patient is provided with information on self-isolation for 14 days (or until pending test results are negative).
3. Patients discharged from the ED should be connected with the ‘COVID Transitions team’, to be followed for continued stability. To connect with them, look on Amion under ‘COVID-19 Transitions Clinic’.

When to suspect COVID-19 (as per WHO\textsuperscript{52})

Most common symptoms:
- Fever
- Dry cough
- Fatigue

Less common symptoms:
- Myalgias
- Sore throat
- Diarrhea
- Conjunctivitis
- Headache
- Loss of taste or smell
- A rash on skin, or discoloration of fingers or toes.

Serious symptoms:
- Shortness of breath or dyspnea
- Chest pain or pressure
- Acute neurological symptoms
On average it takes 5–6 days from when someone is infected with the virus for symptoms to show, however it can take up to 14 days.

**Admission criteria from ED:**
- Dyspnea (Clinically defined as the inability to speak in full sentences)
- Hypoxemia ≤ 93%
- COVID (or COVID rule out) patients with cardiac chest pain
- COVID (or COVID rule out) patients with new neurological signs and symptoms
- Sepsis
- ARDS
- Clinical judgment, in discussion with the admitting team.
- Consider not admitting COVID patients (or COVID rule-out) with mild symptoms based on CXR/CT findings or laboratory data (For example, abnormal laboratory findings considered routine for a COVID patient: LFTs elevation, leukopenia/lymphopenia).

- **Code status/ Advanced directives/ MOLST/ Health care proxy:** Must be discussed and verified with every patient on admission.

**Triage from outside hospitals:**
- Patients with a diagnosis of COVID-19 infection should be accepted for transfer only if they have needs that their hospital cannot provide - in compliance with EMTALA, not solely on the basis of being COVID positive.
- They should be managed at the requesting hospital unless transfer is required for specialized care (Note that the potential need for ICU level care, “risk of decompensation” does not merit transfer if the requesting hospital has an ICU).
- If there is a surge of patients, then COVID transfer team would be activated that will handle requests for transfers of COVID-19 infected individuals.
Special Populations and Isolation Policy:

- Patients from the below special population list if presenting to the ED, or directly admitted, should be considered to be at higher risk of developing COVID within the next 14 days.
  - Skilled nursing facilities
  - Assisted living facilities
  - Memory care facilities
  - Adult Group Homes
  - Group homes for adults with disabilities
  - Rehab facilities
  - DOCS/justice center/county jail patients
  - Homeless pts and Patients living in homeless shelters.

- These patients will be placed on COVID isolation in the ED and, if admitted, placed on 6K/7A 7U (if appropriate/eligible) and 3W, or an appropriate ICU if clinically indicated
- These patients are to be tested for COVID only if assessment reveals a concern for active infection
- Whether tested or not these patients are to remain in COVID isolation for at least 7 days
- Patients may be discharged at any point, when medically stable, there is no minimum required length of stay. Nursing homes may require negative PCR tests before accepting
- If they are afebrile and symptomatically improving 2 PCR tests can be sent 24 hours apart on day 6 and 7.
- If both are negative, they can be released from isolation, and can be discharged if clinically stable
- See policy COV D-04 (Appendix 6) for discontinuation of Isolation precautions for COVID
DIAGNOSTIC WORKUP

- Diagnostic workups include evaluation for signs of a multi organ failure.53
- Although the full relevance of every test is not known at the moment, abnormal values might work as a heralding sign for systemic damage.

LABORATORY TESTING:

- Initial workup on admission (for COVID-confirmed patients):54,55
  - CBC with diff, BMP, LFTs, LDH, CRP, IL-6, D-Dimer, Troponin, CPK, PT/INR, PTT, Fibrinogen, Procalcitonin, baseline EKG
  - If LFTs elevated
    - Acute Hepatitis panel, HIV
  - If AKI – UA, Urine Pr:Cr ratio
  - B-HCG for women of childbearing age
- Daily labs for stable floor patients:
  - CBC with diff, BMP
- Non-routine labs for stable floor patients (consider every other day):
  - LFTs, LDH, CRP, D-dimer, Troponin, CPK, pro-BNP, PT/INR, PTT
- Clinical worsening:
  - Hemodynamic instability, worsening hypoxia, new neurological symptoms
  - CBC with diff, BMP, LFTs, LDH, CRP, D-dimer, Troponin, CPK, Procalcitonin, pro-BNP, PT/INR, PTT, Fibrinogen, Ferritin, EKG, Arterial blood gas

IMAGING:

- CXR: On admission and if clinically worsening.
  - Portable CXR is the preferred modality for tracking disease process (including evolution of ARDS) in confirmed COVID-19.
- Contrast enhanced or Non-contrast chest CT:
  - Patients with confirmed COVID-19 do not need a CT Chest evaluation for ARDS.
- Patients may require CT Chest to evaluate for other pathology or causes of hypoxemia, e.g. pulmonary embolism.
- Additionally, COVID patients may decompensate quickly and it is preferable to minimize unnecessary transportation.

- **Transthoracic echocardiogram**: Obtain if elevated troponin, EKG changes, or suspicion for cardiogenic shock. Avoid routine TTE.

### Role of imaging in guiding decisions to discontinue isolation:

- Due to a concern about the potential false negative rate of the COVID tests, there is a role of imaging prior to discontinuing isolation in these patients.
- In patients with a **high suspicion for COVID-19 but a negative test**:
  - Begin with a portable CXR:
    - If negative, proceed to Non-contrast chest CT.
      - If negative, you may proceed with discontinuing isolation per your clinical judgement.
    - If either imaging is positive or your suspicion remains high, this may be additionally suggestive of COVID and continuing precautions should be discussed with ID.
  - Note that chest CT is not indicated as the primary modality for tracking clinical course for known COVID-19 including evolving ARDS and should not be used to motivate admission in otherwise clinically stable patients.

### BRONCHOSCOPY:

- Lower respiratory samples have higher yield, but given extensive exposure risk, upper respiratory samples via nasopharyngeal and oropharyngeal swabs are preferred for diagnosis for COVID-19.56
- Induced sputum is NOT recommended.
- Bronchoscopy is only recommended in intubated patients if
  - Upper respiratory samples are negative AND another diagnosis would significantly change clinical management.
- For example: PCP pneumonia in an immunocompromised patient, life-threatening hemoptysis, intractable mucus plugging, malignancy with endobronchial obstruction or airway stenosis.
- If bronchoscopy is to be performed, it is recommended to be in a negative pressure room with only essential staff present (Bronchoscopist, Nurse and Respiratory Therapist) and with Full PPE (N95 or PAPR, gloves, gown, face shield, head covers and shoe covers).
- The bronchoscope should be disposable (to avoid cross infection).
CLINICAL COURSE

TIMELINE

- Time from exposure to first symptoms (incubation): 4-14 days

- Median time from illness onset to:
  - Admission: 5-8 days
  - Sepsis: 9 days (7-13 days)
  - ARDS: 12 days (8-15 days)
  - ICU transfer: 12 days
  - Mechanical ventilation: 14.5 days
  - Acute cardiac injury: 15 days (10-17 days)


VERSION 1.2, Last Updated – June 7, 2020
- Secondary infection: 17 days (13-19 days)
- Death: 18.5 days (15-22 days)
- Discharge: 22 days

**SPECTRUM OF SEVERITY OF DISEASE**

- In a summary of 72,314 patients in China with COVID-19:61
  - 81%: mild symptoms
  - 14%: severe symptoms (hypoxemia or >50% lung involvement)
  - 5%: critical symptoms (Respiratory failure, shock, multiorgan dysfunction)
  - Overall Case fatality rate of 2.3%

**COMPLICATIONS**

- Complications include respiratory failure, ARDS, thromboembolic phenomena, inflammatory damage, AKI, DIC, secondary infections, acute cardiac injury, and heart failure
- Rare cases of acute necrotizing encephalopathy and encephalitis have been recently reported.

**Respiratory Complications**

- Acute lung Injury (ALI) and Acute respiratory distress syndrome (ARDS) are the major complications in patients with severe disease and can manifest shortly after the onset of dyspnea.
- Most patients with COVID-19 requiring ICU level of care will develop ARDS.
- In a study of 138 patients in Wuhan, ARDS developed in 20 percent with a median of eight days after the onset of symptoms; mechanical ventilation was implemented in 12.3 percent.62
- There are several anecdotal reports suggesting a rapid progression of hypoxemic respiratory failure (within 12-24 hours).
- Histologically, bilateral diffuse alveolar damage with cellular fibromyxoid exudates, desquamating pneumocytes, pulmonary edema, and hyaline membrane formation may be seen. 55

- Several hypotheses have been put forward to explain pulmonary injury in COVID-19. Primary pulmonary manifestations can be attributed to pulmonary endothelial damage and injury to alveolar type 2 cells.
  - Pulmonary endothelium - SARS-CoV-2 virus binds to the ACE2 receptor for cell entry, and infection may alter ACE/ACE2 pathways with resultant alteration in pulmonary vasculature and filling of alveolar spaces with fluid and debris.
  - Alveolar type 2 Cells – Injury to these cells may lead to loss of surfactant with resultant alveolar collapse.

**Cardiac complications**

- Cardiac complications can manifest as acute cardiac injury, cardiomyopathy, arrhythmias.
- A subset of patients can sustain significant acute cardiomyopathy with LVEF <30% and a component of cardiogenic shock. 62,63,64
- A fulminant myocarditis syndrome has been described as a complication presenting as chest pain, dyspnea, and hypotension with troponin elevation, EKG finding of STEMI, and ECHO showing decreased EF.
- This can occur after improvement of respiratory failure.

**Thromboembolic complications**

- Thromboembolic complications are being increasingly reported, with presentations from VTE and PE to acute strokes and limb ischemia.33–35,65,66
- Infection with COVID-19 is hypothesized to cause a disruption of the Virchow’s triad which places individuals at a high risk of thrombosis.37
Cytokine Storm Syndrome

- A hyperinflammatory state that is characterized by fulminant multi-organ failure and elevation of cytokine levels similar to hemophagocytic lymph-histiocytosis (HLH) syndrome.\textsuperscript{67}

Other Inflammatory complications

- A Multi-system inflammatory syndrome has been described in children with features similar to Kawasaki disease and Toxic shock syndrome. Case reports have described incidence of Guillain-Barré syndrome.\textsuperscript{68–70}
PROGNOSTIC FACTORS

Studies have shown the association of certain risk factors and a worse outcome with COVID-19.  

Patients with severe disease and following risk factors are at higher risk of development of ARDS: (Adapted from MGH COVID-19 guidelines)

**Epidemiologic:**
- Age > 65
- BMI > 30
- Chronic lung disease
- History of CKD
- DM with HbA1c > 7.6
- History of hypertension
- History of Cardiovascular disease
- Use of biologics
- History of transplant or other immunosuppression
- Uncontrolled HIV (Viremic or CD4 <200)

**Vitals:**
- Respiratory Rate > 24 breaths/min
- Heart Rate > 125 beats/min
- SpO2 ≤ 93% on ambient air
- PaO2/FiO2 < 300 mmHg

**Labs:**
- D-dimer > 1 ug/mL
- CK > twice upper limit of normal
- CRP > 100
- LDH > 245 U/L
- Ferritin > 500 ug/L
- Elevated troponin
- Admission absolute lymphocyte count < 0.8
GENERAL MANAGEMENT

- As per ID and NY state guidelines, we will not be offering experimental antiviral therapies outside of clinical trials. There are potential risks of providing immunosuppressive medications in COVID-infected patients that need to be carefully studied.

Early advanced care planning:
- Obtain HCP and discuss code status on admission. Educate the patient and family on disease course and prognosis. Palliative care is now available 7 days a week.

Oxygenation:

Goals
- Maintain adequate oxygenation
  - Target SpO2 92-96%
  - Target 88-94% in patients with oxygen dependent COPD
- Maintain stable work of breathing
  - Target respiratory rate < 24
  - Target normal respiratory effort (no signs of increased respiratory work)
- Ensure that when oximetry order is placed, this saturation target is listed.
- Oxygen supplementation can be provided on the medical floors via Nasal cannula or Oxymask
- High flow nasal cannula use is limited to MICU for now, due to high risk of deterioration in these patients and risk of aerosolization of virus.

Consult MICU if patient has
- SpO2 <92% on ≥ 6 L of oxygen or,
- PF ratio <200 or,
- Rapidly increasing oxygen requirements
Fluid resuscitation:
- Conservative fluid management is recommended to mitigate risk of progression to respiratory failure, exercise cautious hydration particularly after 3rd-4th liter bolus of initial resuscitation.
- Patients transferred from the ICU who were on pulmonary vasodilators such as inhaled nitrous oxide or inhaled epoprostenol should be monitored for development of heart failure, particularly right sided.

Antibiotics:
- Clinical reports indicate rate of bacterial superinfection is low (10-20%) but when present, does increase mortality risk. 73
- Most societies encourage empiric therapy, especially if the patient is worsening.
- Please utilize the antibiotic order set to determine best antibiotics for treatment.
- Antibiotics should be discontinued as soon as possible (within 48 hours) if:
  a. Clinical status is not deteriorating, cultures do not reveal a specific pathogen at 48 hours, and procalcitonin and WBC are relatively stable from 0 to 48 hours.
  b. Exercise clinical judgment and it should prevail over any specific lab value.
      Low procalcitonin levels might be suggestive of a non-bacterial cause, however procalcitonin levels may be elevated later in the course of the disease and do not indicate a bacterial super-infection. 74

Steroids:
- Avoid using empirically given potential harm unless there is another indication early in the disease.
- If profoundly hypoxic or in hyperinflammatory state (i.e., refractory septic shock, cardiac failure, ARDS, cytokine storm), may consider low to moderate dose steroids (0.5-1 mg/kg/day of solumedrol) as per a weak recommendation issued by Surviving Sepsis Campaign. 40
- There is controversy about inhaled steroids increasing viral shedding, however we feel that they can be given if indicated for another pathology as discussed above.
- Chronic steroids should not be discontinued, and stress dose steroids may be indicated in these patients.
**Home Inhaled Corticosteroids:**
- For asthma, continue usual dose
- For COPD with asthmatic component or clear prior benefit, continue ICS

**Inhaled medications:**
- Should be administered by metered dose inhaler rather than nebulization given the risk of nebulization causing aerosolization of virus.

**DVT pharmacologic prophylaxis:**
- COVID-19 infection places patients at increased risk for thromboembolism.
- Should be prescribed for all hospitalized patients unless contraindicated.
- Please use VTE prophylaxis order set to select appropriate pharmacologic therapy.

**LMWH and Heparin:**
- There is an increased incidence of VTE and related complications in COVID-19 with an increase in markers such as D-dimer, prothrombin time (PT) & activated partial thromboplastin time (aPTT) increasing the risk of VTE.\(^3\)\(^5\),\(^7\)\(^5\)
- Significantly elevated D-dimers were shown to be associated with the development of ARDS and increased mortality.\(^7\)\(^6\),\(^7\)\(^7\)
- Anticoagulant treatment using chemical VTE prophylaxis was found to decrease 28 day mortality in patients with D-dimer > 6x upper limit of normal.\(^7\)\(^8\)
- A subset of SARS-CoV-1 and COVID-19 patients displayed worsening hypoxic respiratory failure with rising D-dimers despite adequate thromboprophylaxis, suggesting the role of microthrombi in causing worsening of symptoms.\(^7\)\(^9\)–\(^8\)\(^1\)
- Dose escalation to an intermediate or full dose anticoagulation might be appropriate in this setting.
- There is also evidence for preference of LMWH as the primary choice of anticoagulation due to its anti-inflammatory effects.\(^8\)\(^2\)
- Upstate policy COV T-05 outlines the therapeutic anticoagulation protocols for patients at Upstate. It can be found in the **APPENDIX - 8**

**ACE inhibitor/ARB:**
- There is no convincing data supporting discontinuing home ACE-I/ARBs at this time. unless there is another indication for discontinuation (e.g. hypotension or AKI).\(^3\)
- Do not re-initiate ACE-I/ARB during acute phase of illness, it can be started after recovery for indications such as CHF, Cardiomyopathy, and CKD.

**NSAIDs/Acetaminophen:**

- Some anecdotal reports suggest that use could be causing clinical deterioration as SARS-CoV-2 binds to cells via ACE2, ACE2 upregulated by NSAIDs in animal models. ⁸³
- Acetaminophen is preferred agent for an antipyretic effect
- Avoid NSAIDs if possible, however can be used if clinically indicated. ⁸⁴,⁸⁵

**Statins:**

- Should be continued if patient is on it chronically.
- It is not recommended to initiate statins due to lack of clear evidence of benefit
- NIH recommends against using statins outside of a clinical trial
SPECIFIC THERAPY

Convalescent Plasma Therapy:

The potential benefits
1. Rapid decline and clearance of virus
2. Decrease in the cytokine storm seen in acute respiratory distress syndrome associated with severe COVID-19 infection
3. Improved morbidity and mortality
4. Decrease of time on ventilator with improved oxygenation
5. Decrease in total hospitalization days

The potential risks
1. Allergic reaction
2. Volume overload
3. Potential antibody enhancement of the virus

Eligible patients
- **Severe COVID-19**: Dyspnea, RR > 30/min, O2 sat < 93%, P/F ratio < 300, and/or lung infiltrates > 50% within 24-48 hours
- **Life-threatening disease**: respiratory failure, septic shock, multiorgan failure
- Must be able to provide informed consent

- If eligible, obtain informed consent to enroll in prospective Convalescent Plasma Trial at Upstate.
- Treat with 1 unit of convalescent plasma and this may be repeated once daily for a maximum of 3 doses
- Refer to **APPENDIX – 9** for further details. \(^{20,86}\)

Remdesivir:
- It is a RNA dependent RNA polymerase inhibitor \(^{87}\)
- Adaptive COVID-19 Treatment Trial (ACTT), sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) released an interim analysis indicating a 31% faster recovery time and survival benefit from 11.6% to 8.0%. \(^{88}\)
- FDA approved Remdesivir (RDV) for emergency use on May 1, 2020 for *hospitalized adults and children with suspected or confirmed COVID-19 with severe disease* \(^{89}\)
(SpO2 of 94% or lower on room air requiring supplemental oxygen, mechanical ventilation, or ECMO)
- Adverse effects include diarrhea, transaminitis, rash, renal impairment
- Currently its usage requires approval by Infectious Disease team

- **Criteria** for Remdesivir use at Upstate:
  - Proven COVID-19 disease defined by positive PCR within 7 days prior to therapy AND have been sick for < 10 days
  - AND have severe disease defined by at least 1 of the following:
    - SpO2 ≤ 93% on room air
    - Requiring supplemental oxygen
    - Requiring mechanical ventilation

- **Ineligible if:**
  - Patient is already improving on current therapy
  - Patient is expected by the clinical team to die in the immediate short-term and administration of RDV will unlikely change overall outcome
  - Patient has been on mechanical ventilation for >24 hours or is on ECMO
  - There is evidence of COVID-induced acute kidney injury
  - Patient has already received RDV in the past 6 months for any duration

- Contraindications: Hypersensitivity to RDV or ALT ≥ 5x upper limit of normal

**Tocilizumab:**
- Refer to section on Cytokine activation syndrome.
ICU CARE SUPPLEMENT

- This section will cover issues that are pertinent from a critical care aspect of COVID-19. There might be some overlap between the conditions discussed here and, in the sections, prior.
- **COVID-GRAM Critical Illness Risk Score** at the time of admission may be valuable in predicting a risk of development of critical illness.\(^{90,91}\)

**When to Consult MICU**

1. Respiratory failure
   a. If the patient needs \(O_2 \geq 6\) LPM to maintain \(\text{SpO}_2 > 92\%\) or \(\text{PaO}_2 > 65\).
   b. Rapid escalation of oxygen requirements
   c. Significant work of breathing
2. Hemodynamic instability after initial conservative fluid resuscitation
   a. \(\text{SBP} < 90\), Mean arterial pressure < 65, or Heart rate > 120.
3. Acidosis
   a. \(\text{ABG with pH} < 7.3\) or \(\text{PCO}_2 > 50\) (acute)
4. Persistent Lactic Acidosis > 2
5. Need for intensive nursing care
6. Severe comorbid illness / high risk for deterioration (Lymphopenia, Increasing CRP, Progression of infiltrates on CXR)
7. Multiorgan failure

**Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS)**

- ALI and ARDS are major complications in patients with severe disease and can manifest shortly after the onset of dyspnea.
- Most patients with COVID-19 requiring ICU level of care will develop ARDS.

**Berlin Definition of ARDS**

Establishes the diagnostic criteria
- Onset – Acute (Over 1 week or less)
- Bilateral opacities detected on CXR or Chest CT
- \(\text{PF ratio} <300\text{mmHg with a minimum of } 5\text{cm H2O PEEP (or CPAP)}\)
- Must not be fully explained by cardiac failure or fluid overload
Severity of ARDS and mortality

<table>
<thead>
<tr>
<th>Severity</th>
<th>PaO2/FiO2 (on PEEP/CPAP &gt;5)</th>
<th>All-cause mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>200-300</td>
<td>27 %</td>
</tr>
<tr>
<td>Moderate</td>
<td>100-200</td>
<td>32 %</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;100</td>
<td>45 %</td>
</tr>
</tbody>
</table>

H and L Phenotype Theory in COVID-19 Pneumonia

Phenotype L (Early Stage, Atypical ARDS)
- *Low elastance (i.e. high compliance)*
- *Low ventilation to perfusion ratio*
- *Low lung weight*
- *Low recruitability*
  - Hypoxemia with preserved CO₂ clearance
  - May present without dyspnea as the amount of air in the lungs is normal
  - Respond well to oxygen, pulmonary vasodilators, or early intubation
  - Have normal lung compliance, even post intubation, therefore they can tolerate higher tidal volumes than 6mL/kg
  - Worsening in the disease process occurs with increasing lung edema, inflammation, lung weight, and atelectasis. Patient will continue to compensate by increasing minute ventilation → increases intrathoracic pressure and lung permeability → patient self-induced lung injury (PSILI) → transitions L phenotype to the H phenotype.
  - **Goal**: decrease the work of breathing to prevent transitioning to the H phenotype

Phenotype H (Late Stage, Typical ARDS)
- *High elastance (i.e. low compliance)*
- *High right-to-left shunt*
- *High lung weight*
- *High recruitability*
  - Patients have low lung compliance and high elastance caused by edema
  - Treat as severe ARDS: higher PEEP, prone positioning, etc.
Management of Respiratory Failure

Systemic Corticosteroids
- Currently it is not recommended routinely for ARDS unless there are other indications as below. If treating another condition, use corticosteroids at a low dose for a short duration.92
  1. Asthma or COPD exacerbation.
  2. Shock with history of chronic steroid use (>10 mg prednisone daily).
  3. Shock requiring multiple pressors (>2) without a history of chronic steroid use.

Bronchodilator Therapy
- Non-intubated patient with COVID-19 or COVID-19 rule out
  - MDI + spacer is preferred over nebulization
  - Ask patients to bring home inhalers if MDI supply is limited

- Intubated patient with COVID-19 or COVID-19 rule out
  - Continue to use MDIs (4 puffs instead of 2 puffs)92

Awake prone positioning
- Order: “Adult COVID Prone Positioning IP” and inflammatory markers (CK, ferritin, D-dimer, LDH, CRP, and ESR) every other day.
- For further details on Awake proning, please refer to Appendix 7.

Supplemental Oxygen
  **High-Flow Nasal Cannula**
- It is a highly effective method of oxygen supplementation in patients with hypoxemic respiratory failure with intact mentation, intact airway, and minimal secretions.
- It should be avoided in patients with multi-organ failure, hypercapnia, and hemodynamic instability.
- Consider, if hypoxic (<92%) despite 8-10 L NC/oxymask.
- Due to larger diameter of tubing and humidification \( \rightarrow \) up to 100% FiO\(_2\) can be delivered at flow rates of up to 60L/min.
- It may reduce the requirement for intubation in some patients or allow pre-oxygenation without a bag valve mask prior to intubation.
- To reduce the risk of aerosolization, consider:
  - Placing a surgical mask over the cannula and face. Replace when moist.
  - Ideally the patient should be in a negative pressure room, but a private room may be usable.
  - Try to use the lowest effective flow rate and FiO\textsubscript{2} to keep SpO\textsubscript{2}>92%.
  - When possible, turn off flow before removal of the mask.

**Non-Invasive Ventilation**

- CPAP and BIPAP should be avoided on COVID-19 positive and rule-out patients. Any orders for either of these need to be cleared through Pulmonary via consult.
**Intubation**

**Indications**
- Respiratory distress (accessory muscle use, paradoxical abdominal breathing)
- Rapid progression of disease
- $\text{SpO}_2 < 90\%$ despite maximal supplemental oxygen
- Arterial pH $< 7.3$ with $\text{PaCO}_2 > 50$
- Worsening mentation
- Hemodynamic instability
- Multiorgan failure

**Preparation**
- Use a negative-pressure room for intubation whenever possible.
- Limit intubation team in room to 3 members: intubator, nurse or other clinician, respiratory therapist. If needed, a second intubator wearing PPE should remain outside the room to assist with anticipated difficult airways or as necessary.
- Use a plastic drape/cover to cover the patient to limit spread of aerosols.

**Preoxygenation**
- Preoxygenate the patient for 3 to 5 minutes with 100% $\text{O}_2$ using low or moderate flow rates (10 to 15 L/minute). Avoid Bag Mask Ventilation (BMV) if at all possible.
- 5 minutes of preoxygenation is preferred if circumstances permit.
- If the patient remains hypoxic ($\text{SpO}_2 < 93\%$), can use BMV with HEPA filter and PEEP valve. Hold the mask tightly on the patient’s face using 2-hand thenar technique, increase oxygen flow rate as needed, and have the patient breathe passively. Perform synchronized bag-assist ventilation only if required.
- Upright posture or reverse Trendelenburg positioning improves preoxygenation.

**Sedation**
- Sedation and paralysis with Neuro muscular blocking agents (N MBA) to prevent cough.
Placement (Intubation)
- Rapid sequence induction (RSI) is the technique of choice for intubation in COVID-19.
- Confirm placement with chest x-ray. Endotracheal tube (ETT) should be 2-5cm above the carina.
- ETT should be connected to the ventilator via a viral filter.

Post-intubation management
- Inflate cuff immediately following ETT placement and prior to initiating Positive pressure ventilation (PPV)
- Consider placing CVC and arterial lines together after intubation then obtain imaging to confirm placement.

Mechanical ventilation

Basics
- For education about basic ventilator management please refer to the following links:
  - Vent Basics for non-intensivists - Andrew Philip, MD, FACP, FCCP
    https://drive.google.com/file/d/1QgvczLYaTlpqGF_irrA646LBnGgs70g/view?usp=sharing
  - Mechanical Ventilations - Birendra Sah, MD, FCCP
    https://drive.google.com/file/d/1pvFaSCO9kteSxOjyrdUCoPcZAM3FpOPZ/view?usp=sharing

Initial Ventilator Settings
- Low tidal volume ventilation\(^{93,94}\)
  1. Set mode to volume-limited assist control mode (VAC)
  2. Target Tidal Volume (TV) - 6-8 mL/kg of ideal body weight (IBW)
  3. PEEP: PEEP of 10 to 15 cm H\(_2\)O to start.
  4. FiO\(_2\): Start with FiO\(_2\) 100% and titrate oxygen to target PaO\(_2\) 55 to 80 or SpO\(_2\) 90 to 96
  5. Plateau pressure (Pplat) <30 cm H\(_2\)O.
  6. Goal pH >7.20

Subsequent Tidal Volume adjustment
- GOAL - Pplat ≤30 cm H\(_2\)O
  - Check inspiratory Pplat with 0.5 second inspiratory pause at least every four hours and after each change in PEEP or tidal volume.
    - If Pplat >30 cm H\(_2\)O, decrease tidal volume in 1 mL/kg IBW decrements to 5 or 4 mL/kg IBW.
    - If Pplat <25 cm H\(_2\)O and tidal volume <6 mL/kg, increase tidal volume by 1 mL/kg IBW until Pplat >25 cm H\(_2\)O or tidal volume = 6 mL/kg.
  - If breath stacking (auto-PEEP) or severe dyspnea occurs, tidal volume may be increased to 7 or 8 mL/kg IBW if Pplat remains ≤30 cm H\(_2\)O.\(^{94}\)

Additional ventilator adjustment
Minute Ventilation = Respiratory Rate (RR) x Tidal Volume (TV)

**Tidal Volume**
- Initial TV 6-8 cc/kg IBW
- Permissive hypercapnia to achieve low TV, pH > 7.20

**Respiratory Rate**
- If pH > 7.45, ↓RR
- If pH 7.15 - 7.30, ↑RR until pH > 7.30, or PaCO₂ < 25 (max RR= 35 breaths/min)
- If pH < 7.15, ↑RR to 35 breaths/minute
- If pH still < 7.15, consider the following:
  - TV may be increased by 1 mL/kg until pH > 7.15 (until Pplat reaches 30 cm H₂O or TV reaches 8 cc/kg).
  - Deep sedation advancing to RASS -5 if needed and initiating paralysis.
  - If still no improvement, initiate prone ventilation (to improve V/Q mismatch and ventilation)
- New RR = current RR x current pCO₂ / target pCO₂

**Oxygenation**
- Titrate PEEP and FiO₂
- GOAL - PaO₂ > 75, SpO₂ 92%-96%,
- FiO₂: Titrate FiO₂ ≤ 60% to maintain goal
  - If patient desaturates increase FiO₂ to 100% and titrate down to goal.
- PEEP: Titrate with increments as per ARDSnet Table below with goal FiO₂< 60%

<table>
<thead>
<tr>
<th>OXYGENATION GOAL: PaO₂ 55-80 mmHg or SpO₂ 88-95%</th>
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<tbody>
<tr>
<td>Use a minimum PEEP of 5 cm H₂O. Consider use of incremental FiO₂/PEEP combinations such as shown below (not required) to achieve goal.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Lower PEEP/higher FiO₂</th>
<th>FiO₂</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
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<tr>
<th>Higher PEEP/lower FiO₂</th>
<th>FiO₂</th>
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<table>
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<th>FiO₂</th>
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<th>0.9</th>
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</thead>
<tbody>
<tr>
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<td>22</td>
<td>22</td>
<td>22</td>
<td>22</td>
<td>24</td>
</tr>
</tbody>
</table>
**Airway Pressure Release Ventilation**

- The respiratory cycle usually spends 1 second in inhalation and up to 3 seconds in exhalation in a 1:3 ratio.
- APRV utilizes CPAP at a high and low pressure for different periods of time to promote alveolar recruitment.
- These settings are reflected as Time at high and low levels ($T_{high}$, $T_{low}$) in seconds and pressure at high and low levels ($P_{high}$ and $P_{low}$) in cm H2O.
- FiO2 is titrated as needed
- Adjusting these settings to maintain a high pressure (usually 25-30cmH2O) for about 3 to 4.5 seconds and then a low pressure (usually 0cmH2O) for about 0.3 to 0.8 seconds allows for recruitment of alveoli in ARDS to maintain oxygenation and a short release to allow ventilation without collapse of those same alveoli.
- This is often used as a “rescue” mode of ventilation in ARDS but is being studied as a primary mode of ventilation due to its ability to limit shear stress to alveoli from recruitment and derecruitment.96,97
- Like the other modes of ventilation, the role of APRV is currently unclear in COVID-19.

**Sedation/Analgesia/Paralysis**

- **Goal**: To achieve ventilator synchrony and maintain comfort.
- Try non-pharmacological methods first to prevent and manage delirium and agitation.
- Non-benzodiazepines are preferred over benzodiazepines
- Monitor with Richmond Agitation-Sedation Scale (RASS).98 Target RAAS of 0 to -2 to maintain sedation/comfort
- Bispectral Index (BIS) monitoring can be used for titration during deep sedation and paralysis.
- Perform daily sedation interruption99

**Propofol**

- 5-50mcg/kg/min, titrate in increments of 5-10mcg/kg/min every 5-10 min
- Safe in hepatic and renal impairment
- Monitor for hypotension and bradycardia
- Get lipid panel every 7 days to monitor for triglycerides if persistently on propofol

**Dexmedetomidine**
- 0.2 to 1.4 mcg/kg/hr
- Provides light sedation and can be continued following extubation if needed
- It can be used in combination of propofol
- Needs dose adjustment in hepatic or renal impairment
- Monitor for hypotension and bradycardia
- Abrupt discontinuation can cause rebound tachycardia

**Midazolam**
- Second line
- 0.01-0.05 mg/kg loading dose with 0.02-0.1 mg/kg/hr infusion.
- Use as a short-term anxiolytic and for acute agitation
- Needs dose adjustment in hepatic or renal impairment.
- Use PRN over drip if possible

**Pain**
- Monitoring scales are Critical care Pain Observation Tool (CPOT)\(^\text{100}\) and Behavioral Pain Scale (BPS)\(^\text{101,102}\)
- Vital signs can be used as cues to further assess pain but not to be used alone.
- Treat pain prior to initiating sedation
- Consider preprocedural analgesia when applicable
- Agents -
  - Preferred opioid agents: IV fentanyl or morphine
  - Non opioids: IV acetaminophen, gabapentin for neuropathic pain

**Delirium**
- Tools to monitor are: \(^\text{102}\)
  - Confusion Assessment Method for the ICU (CAM-ICU)\(^\text{103}\)
  - Intensive care Delirium Screening checklist (ICDSC)
- Review and reduce medications
- Etiology:
  THINK mnemonic
  Toxic situations (CHF, liver failure, kidney failure, dehydration, meds)
  Hypoxemia
  Infections/sepsis (nosocomial), Immobilization
  Nonpharmacological interventions
  K+ (for electrolyte problems)

- Medicate if necessary
  - Consider atypical antipsychotics such as seroquel or haloperidol for mild delirium or agitation not due to pain or benzodiazepine withdrawal.
  - If patient has prolonged QTc > 500ms, consider risperidone, olanzapine, or valproic acid

Tracheostomy
- There are no clear studies regarding timing for tracheostomy in patients with COVID-19. For patients with prolonged intubation with COVID-19, tracheostomy can be considered.
- The threshold/timing, however, may be increased to 3 weeks (based on studies on SARS-CoV1) instead of the usual 7-15 days.
- If the intubation is approaching 21 days, tracheostomy can be considered after discussion with ENT or surgery.
- It is a significant risk of exposure to the proceduralists/healthcare workers, as it is also an aerosol generating procedure.\textsuperscript{104}
Weaning, Extubation and Liberation from Mechanical Ventilation

Weaning
- Allowing patients to ↑ their ventilation while ↓ support given by the ventilator.
- It is done via spontaneous breathing trial (SBT) or a gradual reduction in the pressure or volume support provided by the ventilator over hours or days.\textsuperscript{105}

Extubation
- Extubation\textsuperscript{105} is considered if
  - The patient’s primary reason for intubation has been addressed (e.g. acute encephalopathy, pneumonia, pulmonary edema, angioedema, etc.)
  - The patient demonstrates an ability to breathe without ventilator support
  - The airway is patent (minimal respiratory secretions)

COVID-19 specific guidance
- COVID-19 patients may require additional specific precautions and a higher degree of readiness given the risk for aerosolization with extubation, re-intubation and the duration of intubation in these patients.
- Most ICUs have a 10-20% reintubation rate which can be a dangerous risk for exposure to healthcare staff during a COVID-19 pandemic.\textsuperscript{106}
- Use closed systems instead of the T-piece trial for SBTs.
- The patient may have to be able to tolerate a longer duration of SBT (2-4 hours over 45 minutes to 1 hour). Anecdotal experience has shown increased airway secretions in COVID-19 patients.
- Cuff leak testing should be performed in a negative pressure room and some institutions are administering methylprednisolone 20mg IV every 4 hours for 4 doses before performing this test to reduce airway edema.
Upstate Extubation Protocol

Checklist for extubation:

- Disease Resolution:
  - Respiratory failure and/or the disease that prompted initiation of mechanical ventilation has resolved / improved

- Ventilation Criteria:
  - FiO₂ < 0.4, PEEP < 8 - 10 mmH₂O, Pressure Support Ventilation (PSV) < 10
  - Comfortable respiration | Minimal sputum load | Presence of cuff leak

- Hemodynamic Criteria:
  - Low dose vasopressor (e.g. < 5 mcg/min norepinephrine)
  - SBP >90mmHg or MAP >60mmHg
  - Stable cardiac rhythm | No significant tachycardia

- Neurological Criteria:
  - Awake | Follows commands | Effective Cough
  - Not aggressive or agitated
  - No significant neuromuscular weakness | Pain controlled

- Diagnostic Investigations:
  - CXR stable or improving | paO₂ > 60 mmHg on FiO₂ < 0.4 | pH > 7.3
  - Normal K + | Normal PO₄-

- Other Considerations:
  - Staffing availability: avoid extubation later in the day or at night.

- If all of the above criteria are met, proceed to Spontaneous Breathing Trial (SBT):
  - Place the patient on SPONT mode with PEEP 5, Pressure support 0-5 and FiO₂<40% for at least 30 minutes.

- Following signs indicate failure of SBT:
  1) RR>35/min for 5 minutes or more.
  2) Rapid Shallow Breathing Index (RSBI) >105 cycles/min/L.
  3) SaO₂<90% for > 5 minutes or PaO₂/FiO₂ ratio <150 on 40% FiO₂.
  4) HR >120/min or sustained increase 20% greater than baseline.
  5) SBP<90mmHg or >180mmHg for >5 minutes.
  6) Emergence of chest pain or ECG changes.
  7) Dyspnea, anxiety and diaphoresis.
Prepare and perform extubation
- Consider extubation under a tent, poncho or plastic cover to limit aerosol spread.
- Place the ventilator in standby mode, immediately prior to extubation.
- Drugs
  - Consider using low dose dexmedetomidine 0.4mcg/kg/hr to decrease agitation.
  - Consider 2% lidocaine 1 mg/kg instilled down the ETT tube 5 minutes before extubation to suppress cough.\(^{108}\)

Post-Extubation
- Obtain SLP consult
- Avoid excessive suctioning
- Patient may require re-intubation if there is:
  o Stridor
  o Obstructed breathing pattern or RR > 30 bpm
  o Increased oxygen flow rate or delivery by >50% to achieve SpO\(_2\) > 92%.
  o Agitation
Refractory Hypoxemia
- Defined by PaO$_2$ < 75, PaO$_2$/FiO$_2$<150, despite PEEP optimization, on FiO$_2$ >0.6
- Optimize volume status and diuresis if needed. Pulmonary edema is common in ARDS.
- Look for other complications including PE, VAP, or pneumothorax.

Specific strategies

Prone Ventilation
- Use Upstate ICU proning order set
- Improves recruitment and perfusion to bases of the lungs that are usually compressed by non-pulmonary intrathoracic structures. Limited and anecdotal studies noted that patients with COVID-19-related ARDS respond well to this.$^{109}$
- Initiate early when P/F ratio is <150, < 12 hours of worsening hypoxia (FiO$_2$>60%), < 36 hours of ARDS onset. Prone ventilation duration should be between 12 to 16 hours.
- Complications include pressure sores, line and ET tube displacement, facial edema, hemodynamic instability, corneal abrasions, brachial plexus injury, and hemodialysis flow issues.
- Absolute contraindications for prone ventilation: shock, acute bleeding, trauma or fractures, pregnancy, spinal instability, chest wall surgery, spinal instability, tracheal surgery.$^{110}$

High PEEP
- Increase PEEP as tolerated
- In severe or refractory ARDS, driving pressure best predicted survival in patients with ARDS.
- Driving pressure = Pplat - applied PEEP (or) $V_t$/respiratory system compliance.$^{111}$

Pulmonary Vasodilators
- Per SCCM, a trial of inhaled pulmonary vasodilator as a rescue therapy can be used in ventilated adults with COVID-19, severe ARDS, and refractory hypoxemia (weak recommendation).
- If no rapid improvement in oxygenation is observed, treatment should be tapered off.
- **Inhaled Nitric Oxide (iNO)**
  - A rapid-acting vasodilator which dilates vessels associated with well-ventilated alveoli and reduces pulmonary artery pressure and pulmonary vascular resistance → improves gas exchange.
  - Using iNO can result in short-term improvement in oxygenation, but studies have yet to show an impact on mortality.
  - Hence iNO is not commonly used but used mostly as a rescue therapy.
  - Monitor methemoglobin due to risk of methemoglobinemia
  - Limited supply of iNO, so use judiciously

- **Inhaled Epoprostenol (iEPO)**
  - Synthetic analog of prostacyclin which causes relaxation of smooth muscle cells and in aerosolized form, causes selective pulmonary vasodilation.
  - Currently not used at Upstate

- A retrospective study done on 105 mechanically ventilated patients revealed no difference in efficacy and safety outcomes when comparing iNO and iEPO in hypoxic, critically ill patients. Inhaled epoprostenol was associated with less drug expenditure than iNO.\textsuperscript{112}
Extracorporeal Membrane Oxygenation (ECMO)

- Consider ECMO consultation for refractory hypoxemia.
- Consult the ECMO team early to help determine candidacy.

Relative contraindications to ECMO\textsuperscript{113}

- Age > 65 years
- Obesity BMI > 40
- Immunocompromised status
- No legal medical decision maker available
- Advanced chronic underlying systolic heart failure
- High dose vasopressor requirements (and not under consideration for V-A or V-VA ECMO)

Absolute contraindications for ECMO\textsuperscript{113}

- Advanced age
- Clinical Frailty Scale Category > 3
- Mechanical ventilation > 10 days
- Significant underlying comorbidities:
  - CKD > 3
  - Cirrhosis
  - Dementia
  - Baseline neurological disease without rehab potential
  - Disseminated malignancy
  - Advanced lung disease
  - Uncontrolled diabetes with chronic end-organ dysfunction
  - Severe deconditioning and protein energy malnutrition
  - Severe peripheral vascular disease
  - Life limiting medical conditions and poor functional status
- Severe multi-organ failure
- Severe acute neurological injury
- Uncontrolled bleeding
- Contraindications to anticoagulation
- Ongoing CPR
- Inability to accept blood products
Ventilator-Induced Lung Injury (VILI)

- VILI is an acute lung injury that occurs as a result of mechanical ventilation. VILI occurs after initiation of mechanical ventilation however it can be difficult to differentiate from progressive ARDS because the symptoms are similar including pulmonary edema, worsening hypoxemia or P/F ratio, new bilateral chest infiltrates on imaging, and new organ failure.

- The proposed mechanisms of VILI are:
  - Volutrauma/Barotrauma (alveolar overdistension)
  - Atelectrauma (repeated opening and collapse of alveoli)
  - Biotrauma (inflammation due to triggered release of cytokines)

- If all other etiologies are eliminated and lung injury is attributed to mechanical ventilation, then it is appropriate to diagnose VILI.

- Some studies have suggested that those with ARDS or ALI are at higher risk of developing VILI, therefore prevention of VILI is essential.114,115

- Lung protective ventilation strategies include116:
  - Low tidal volumes while maintaining a low plateau pressure, to limit volutrauma
  - Applying PEEP to keep alveoli open and limit risk of atelectrauma.
  - Maintaining a low plateau pressure (<30mmHg) and driving pressure (plateau pressure - PEEP) <15cmH2O, to limit barotrauma.

Ventilator Associated Pneumonia (VAP)

- VAP is defined as a pneumonia occurring > 48 hours after the patient has been intubated and received mechanical ventilation.

- Prolonged intubation has been associated with the onset of ventilator associated pneumonia (VAP) with a median time of 8 days in a retrospective study in 191 patients in Wuhan. 117,118,119

Diagnosis

- Blood cultures and sputum cultures (endotracheal aspiration or sputum expectoration) should be obtained.

- Non-invasive methods are preferred over invasive bronchoalveolar lavage, protected specimen brush (PSB) and blind bronchial sampling

- CRP and procalcitonin are not reliable and hence not necessary for diagnosing VAP
Empiric therapy

- **Suspected pathogens:** staphylococcus aureus, gram-negative organisms including pseudomonas aeruginosa

- Antibiotic coverage
  - MRSA coverage with vancomycin or linezolid
  - Add dual pseudomonas antibiotic coverage for those with risk factors for antimicrobial resistance including:
    - Prior IV antibiotics within 90 days
    - Septic shock at time of VAP
    - ARDS preceding VAP
    - >5 days of hospitalization prior to occurrence of VAP
    - Acute renal replacement therapy prior to VAP
**Shock**

**Definition**

- Sustained hypotension (MAP <65 or SBP <90) with signs of hypoperfusion requiring IVF or vasopressors
- Signs of end organ damage: low urine output, altered mental status, lactic acidosis, AKI, coagulopathy, acute liver injury, respiratory failure

**Types of Shock**

<table>
<thead>
<tr>
<th>Type of Shock</th>
<th>Examples</th>
<th>Pre-load (PCWP, JVD)</th>
<th>Pump function (CO)</th>
<th>Afterload (SVR)</th>
<th>Perfusion (MvO2, O2 sat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distributive</td>
<td>Sepsis, cytokine, anaphylaxis, adrenal crisis</td>
<td>↓/-</td>
<td>↑</td>
<td>↓</td>
<td>↑/-</td>
</tr>
<tr>
<td>Cardiogenic</td>
<td>Arrhythmia, valve failure, MI, cardiomyopathy, pericarditis, PE</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Hypovolemic</td>
<td>Fluid loss, hemorrhage</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
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<tr>
<td>Obstructive</td>
<td>Tamponade, PE, pneumothorax</td>
<td>↑</td>
<td>↓</td>
<td>↑/-</td>
<td>↓/-</td>
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</tbody>
</table>
Septic Shock

Workup
- CBC with differential, CMP, Cortisol level
- Chest x-ray, urinalysis
- Blood cultures (2), urine legionella antigen, urine culture, sputum culture
- Perform a detailed skin exam

Management
- **Antibiotics:**
  - Although bacterial infection rates remain low (10-20%), empiric antibiotics should be initiated within 1 hour of presenting with septic shock.
  - Use ID antibiotic order set to assist with choosing antibiotics as this should follow usual practice.
  - Assess for de-escalation daily and re-evaluate the duration of therapy and spectrum of coverage based on culture results and clinical status.

- **Fluids:**
  - Clinical reports indicate a conservative fluid strategy is protective in the setting of ARDS and COVID-related shock.
  - Instead of maintenance IVF, consider giving boluses and reassessing frequently.
  - There is no specific consensus on the limit of fluids to be administered but a positive fluid balance should be avoided.
  - Use crystalloids over colloids, and avoid hypotonic fluids, starches, gelatins, or dextrans.

- **Vaspressors:**
  - Goal MAP of 60-65.
  - If unable to maintain goal MAP after fluid resuscitation, initiate norepinephrine as first line vasoactive therapy. If unavailable, use epinephrine or vasopressin.
  - Add vasopressin as a second-line agent, over titrating norepinephrine dose, if MAP cannot be achieved by norepinephrine alone.

- **Steroids:**
  - Consider stress dose hydrocortisone (200 mg/day) if refractory shock on > 2 pressors.\textsuperscript{122}
Cardiogenic Shock

Etiology
- Direct viral toxicity into cardiac myocytes, ACS, demand ischemia, or stress/inflammatory cardiomyopathy

Onset
- Generally late in the course of illness (troponin elevation about 14 days from onset of illness)\textsuperscript{95}

Workup
- Assess for JVD, edema, and cold extremities on exam
- Obtain:
  - ProBNP
  - Troponins to peak
  - EKG
  - Lactate Q6h
  - LFTs daily to monitor for congestive hepatopathy
  - Central venous oxygen saturation
- Consider bedside ultrasound or TTE to assess ventricular function

Management
- Consult Cardiology
- Place on norepinephrine for goal MAP 65-75. If persistent hypoperfusion, add inotropic support with dobutamine drip over increasing norepinephrine dose (weak recommendation)\textsuperscript{122}
- Initiate diuretic therapy
Cytokine Activation Syndrome/Cytokine Release Syndrome (CRS)

Pathophysiology
- Small subset of patients may have cytokine activation syndrome causing rapid progression to ARDS, shock, and multiorgan failure with fever, hyper-ferritinemia, and cytopenias
- Likely due to neutrophil activation and proinflammatory cytokine production
- Autopsy results in COVID-19 patients showed interstitial mononuclear inflammatory infiltrates in both lungs dominated by lymphocytes and flow cytometry showed overactivation of T cells

Workup
- Suspect if clinical deterioration with shock and multiorgan failure
  - Obtain:
    - CBC with differential
    - PT/INR, PTT, fibrinogen, D-dimer
    - Ferritin, CRP, ESR
    - IL-6, IL-2 (markers for prognosis)
    - Hepatic function panel
    - Triglycerides
  - Consider using HScore on Mdcalc to assess probability of HLH syndrome

Management
- Discuss IVIG, steroids, and tocilizumab use with Infectious Disease
  - Tocilizumab: Recombinant monoclonal antibody specific for IL-6 receptor which is felt to potentially combat CRS
  - Limited retrospective study showed treatment with tocilizumab led to decrease in fever and lung opacities with recovery in percentage of lymphocytes in blood
  - In China, it is recommended for use in severe or critically ill patient with extensive bilateral lung lesions and confirmed elevated IL-6 level
  - Per NIH COVID-19 Treatment Guidelines Panel, there is insufficient data to recommend either for or against use at this time
  - Adverse effects include anaphylaxis, elevated LFTs, and increased risk of opportunistic infections
DISCHARGE GUIDELINES

- Formal guidelines are currently in progress, but consider discharge if patients have:
  - Resolution of fever > 48 hours without antipyretics
  - Improvement in signs and symptoms (cough, oxygen requirement).

COVID Transition Team

- There is a COVID Transition Team (Juliann Axton, MS, RN and Dr. Amit Dhamoon) that will follow COVID discharges for clinical stability and facilitate triage. Find under “COVID-19 Transitions Clinic” on Amion.

Discontinuation of transmission-based precautions

- Guidelines for discontinuation of transmission-based precautions and disposition of patients with COVID-19 per Upstate Policy COV D-04 (Appendix 6) as per CDC’s recommendations (Appendix 10)

Discharge pending test results

- Patients with a pending test who are clinically stable may be discharged provided patient is given the Mandatory Self Quarantine Order from the County. The DOH does NOT need to be notified. If the subsequent test result is positive, the DOH is notified by the lab and will contact the patient. If the result is negative, our mammography staff are notifying them that they can come off quarantine.

AMA Discharges:

- If a patient has the capacity in determining medical decisions and the discharge plan is not a threat to the public (i.e., they can and will quarantine), we cannot hold them against their will and they likely have the right to leave AMA. Infection Control and DOH notified by team or case manager.
- If the patient is not willing/able to quarantine, our policy will be to raise all such cases to Dr. Housam Hegazy (HegazyH@upstate.edu); he will do legal and ethical analysis mainly assessing the public health risk and guiding safe discharge planning. If there is a public health concern or other legal concerns, then he will raise it to legal and possible ethical departments for further action.
Skilled Nursing Facilities:
- There is a requirement of a negative COVID-19 test for all patients prior to discharge to SNF. Please anticipate this need and order the non-priority COVID-19 rest the day before discharge for any patients going to a SNF. For any patients that were COVID+, please see above Policy COV D-04/Appendix 6

Discharge Instructions:
- Call our ‘COVID discharge team’ if anticipating discharge, their info can be found on Amion.

- Patients with a positive COVID-19 test may be discharged following
  1. DOH notified/approval (this is done by the case manager in conjunction with infection control).
  2. Patient is given the Mandatory Self Quarantine Order from the County Executive (dot phrase: COVIDSELFQUARNOTICE). Required only for patients being discharged to home.

- COVID discharge team is working to help explain discharge instructions to patients on discharge and to enable follow up with the COVID transition clinic.
- Oximetry bands are available for patients going home without home care for continued oxygen monitoring. Patient’s qualification for this is up to the discretion of team attending upon discussion with COVID discharge team.
- Please give COVID-confirmed patients information regarding the convalescent plasma clinical trial, as they will be eligible to donate, and this may provide real benefit to future patients (dot phrase: COVIDPLASMAPROJECT).
COVID-19 Research and Clinical trials at Upstate

Hydroxychloroquine (HCQ) Inpatient Treatment Trial: An open-label randomized trial in a 2:1 ratio to a 5-day course of HCQ or supportive care alone. Primary outcome is improvement in the WHO Ordinal scale used in multiple other COVID related studies. This study is currently stalled due to the lack of overall benefit seen in literature to date in hospitalized patients.

Convalescent Plasma Trial: Therapeutic administration of convalescent plasma from recovered COVID-19 patients in COVID-19 patients with severe disease in a non-randomized manner. The study aims to collect data pertaining to outcomes and complications.

Post-Exposure Prophylaxis Study: This is a randomized (1:1 ratio) blinded, placebo controlled post-exposure prophylaxis study comparing standard dose HCQ given once daily versus placebo (low dose vitamin C) for a period of 14 days. Healthcare workers or household contacts of known exposure can be enrolled in this trial. Primary outcome is evidence of infection via PCR from self-collected swabs. Secondary and exploratory end points include assessing safety/tolerability, incidence of shedding of virus in index patients (if enrolled), viral genotyping, adherence assessment, and pharmacokinetics.

Outpatient early treatment study: This is a randomized (1:1:1 ratio), blinded, placebo controlled early treatment study focusing of initiating therapy early in the disease course after diagnosis (within 72 hours of positive test). Patients are randomized to receive placebo (Vit C+ folic acid) vs. hydroxychloroquine + folic acid(placebo) vs. Hydroxychloroquine + azithromycin for 10 days. Outcomes will be to test the efficacy to include clearance of nasal shedding.

Inpatient study looking at using an ELI Lilly monoclonal: Randomized, placebo-controlled study looking at infusions on day 1 and day 15 (if still inpatient) with a monoclonal Ang2 inhibitor. This study is IRB approved, but still awaiting start up approval to include the drug.

Outpatient COVID vaccine trial in June
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APPENDIX – 1 : Donning / Doffing PPE

**Donning PPE**

1. Place new chux on PPE cart(s)
2. Pull back long hair to ensure a tight seal
3. Perform Hand Hygiene
4. Remove ear loop mask and place in bag #1
5. Perform Hand Hygiene
6. Don gown
7. Perform Hand Hygiene
8. Don N95
9. Perform Hand Hygiene
10. Don Face Shield
11. Perform Hand Hygiene
12. Don Gloves

**Doffing PPE**

1. While still in the patient's room remove gown & gloves
2. Perform hand hygiene. Open door, exit room, perform hand hygiene
3. Remove face shield place on chux pad
4. Perform Hand Hygiene
5. Remove respirator by rubber straps, careful not to touch the front or inside of the respirator.
6. Place in Bag #2
7. Perform Hand Hygiene
8. Don ear loop mask from Bag #1
9. Don Gloves
10. Disinfect face shield with PDI wipes - Hang shield on bag, discard chux, & remove gloves
11. Perform Hand Hygiene
**Donning PAPR**

1. Place new chux on PPE cart
2. Pull back long hair to ensure a tight seal
3. Perform Hand Hygiene
4. Remove ear loop mask and place in bag #1
5. Perform Hand Hygiene
6. Don PAPR
7. Perform Hand Hygiene
8. Don gown
9. Ensure that PAPR is not covered by the gown
10. Perform Hand Hygiene
11. Don Gloves

**Doffing PAPR**

1. While still in the patients room remove gown & gloves
2. Perform hand hygiene. Open door, exit room
3. Perform hand hygiene
4. Unclip belt
5. Place PAPR on cart in front of self
6. Remove Hood
7. Turn off PAPR
8. Perform Hand Hygiene
9. Don ear loop mask from Bag #1
10. Proceed to disinfection process
11. Perform Hand Hygiene
APPENDIX – 2 : PPE Table for COVID exposure scenario

<table>
<thead>
<tr>
<th>Personal Protection Equipment (PPE) Table for COVID-19 Exposure Scenario</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Policy Number:</strong> COV P-01</td>
</tr>
<tr>
<td><strong>Issue Date:</strong> 03/18/2020</td>
</tr>
<tr>
<td><strong>Value(s):</strong> Innovation, Respect, Integrity, Community</td>
</tr>
</tbody>
</table>

**Review Date:** 04/30/2020  
**Change Description:**  
Revision to table; added last 2 rows pertaining to patient and staff positives

**Revised Date:** 04/30/2020

** Applies to:**  
All staff

**Policy:**

<table>
<thead>
<tr>
<th>Exposure Scenario</th>
<th>Patient’s PPE</th>
<th>Staff PPE</th>
<th>Staff Action after Contact / Potential Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Known Exposure</td>
<td>None Recommended</td>
<td>None Recommended</td>
<td>No action</td>
</tr>
<tr>
<td>COVID Ruleout Patient</td>
<td>Appropriate PPE* for Patient</td>
<td>Appropriate PPE for Staff**</td>
<td>No action</td>
</tr>
<tr>
<td></td>
<td>Patient without PPE</td>
<td>Appropriate PPE for staff</td>
<td>No action</td>
</tr>
<tr>
<td></td>
<td>Patient without PPE</td>
<td>Inappropriate PPE for staff</td>
<td>***Continue to work, wear a mask, monitor symptoms and temperature for 14 days or until symptoms develop. For symptoms, seek medical care</td>
</tr>
<tr>
<td>COVID Positive Patient</td>
<td>Appropriate PPE* for Patient</td>
<td>Appropriate PPE **</td>
<td>No action</td>
</tr>
<tr>
<td></td>
<td>Patient without PPE</td>
<td>Appropriate PPE for staff</td>
<td>No action</td>
</tr>
<tr>
<td></td>
<td>Patient without PPE</td>
<td>Inappropriate PPE for staff</td>
<td>***Continue to work, wear a mask, monitor symptoms and temperature for 14 days or until symptoms develop. For symptoms, seek medical care</td>
</tr>
<tr>
<td>COVID Positive Patient having a High Risk Procedure.</td>
<td>N/A</td>
<td>Appropriate PPE **</td>
<td>No action</td>
</tr>
<tr>
<td>(e.g., FOB/BAL, NP swab collection, intubation, surgical procedures which could aerosolize)</td>
<td>N/A</td>
<td>Inappropriate PPE for staff</td>
<td>***Continue to work, wear a surgical mask, monitor symptoms and temperature, continue monitoring for 14 days or until symptoms develop. For symptoms, seek medical care</td>
</tr>
<tr>
<td>Staff member positive for COVID</td>
<td></td>
<td></td>
<td>Should not work for at least 7 consecutive days. Contact Infection Control and Employee Health. Must contact Employee Health again prior to returning to work.</td>
</tr>
<tr>
<td>Staff member awaiting COVID result</td>
<td></td>
<td></td>
<td>Self-quarantine at home until results are available. For symptoms seek medical care</td>
</tr>
<tr>
<td>Staff member returning from domestic travel with unknown COVID+ contact</td>
<td></td>
<td></td>
<td>***Continue to work, monitor symptoms and temperature, continue monitoring for 14 days or until symptoms develop. For symptoms, seek medical care</td>
</tr>
<tr>
<td>Exposure Scenario</td>
<td>Patient’s PPE</td>
<td>Staff PPE</td>
<td>Staff Action after Contact / Potential Exposure</td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
<td>--------------------------</td>
<td>----------------------</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Patient reports that they are positive for COVID after being seen at one of our ambulatory sites</td>
<td>None at time of exposure</td>
<td>None at time of exposure</td>
<td>Identify employees in direct contact with patient during the time of encounter and identify Infection Control for appropriate tracking and guidance.</td>
</tr>
<tr>
<td>Staff positive for COVID-19</td>
<td>None at time of exposure</td>
<td>None at time of exposure</td>
<td><strong>COVID positive staff</strong> should not work for at least 7 consecutive days. Contact Infection Control and Employee Health. Must contact Employee Health again prior to returning to work. <strong>Staff (w/o ear loop mask) exposed to the positive staff member</strong> for more than 10 minutes and less than 6 feet apart and patients exposed to positive staff member within 2 days from onset of symptoms: wear mask and monitor symptoms for 14 days. <strong>If symptomatic visit employee testing site.</strong> <strong>Inpatients exposed to staff:</strong> moved to a private room with mask if tolerated and monitor symptoms for 14 days. <strong>Outpatients exposed to staff:</strong> will be contacted by Infection Control, self-quarantine at home with a mask for 14 days and monitor symptoms. Do not share living spaces, bathrooms or bedrooms with family. If symptoms develop call the triage line 464-2592 for instructions on how to get tested.</td>
</tr>
<tr>
<td>None at time of exposure</td>
<td>Surgical ear loop mask</td>
<td>No exposure to staff or patient</td>
<td><strong>Surgical ear loop mask</strong> exposed to the positive staff member for more than 10 minutes and less than 6 feet apart: wear mask and monitor symptoms for 14 days. <strong>If symptomatic, visit employee testing site. Patient exposed to staff:</strong> no exposure.</td>
</tr>
<tr>
<td>Surgical ear loop mask</td>
<td>None at time of exposure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTES:**
* Appropriate patient PPE = surgical mask

** Appropriate provider PPE = N95 mask or PAPR for clinician OR both patient & provider wearing surgical mask; goggles or shield; gloves; gown

*** Incubation period from time of exposure to time of symptoms ~5 days; Earliest time from exposure to time of potential infectiousness estimated at 2.5 days; Current time from sample collection to COVID test results < 48 hours
Airway Procedures During COVID-19

1. Enhanced Precaution for Airway Procedures During COVID-19 Pandemic

   Applies to all patients undergoing AGPs until further notice during COVID-19 Pandemic.

   A. Aerosol Generating Procedures (AGPs)
      AGPs include procedures that are believed to generate aerosols and droplets.

   B. Enhanced PPE (EPPE) will be worn for all the following AGPs:
      1. Noninvasive positive pressure ventilation (BiPAP, and CPAP) including home machines.
         • A pulmonary consult is required to initiate this treatment.
      2. High flow oxygen ONLY if patient is unable to wear ear loop mask
      3. Endotracheal intubation
      4. Endotracheal extubation
      5. Bronchoscopy
      6. Open airway suction
      7. High frequency oscillatory ventilation
      8. Placement or changing of tracheostomy tube
      9. Trach care
     10. Chest physiotherapy
     11. Nebulizer treatment
     12. Sputum induction
     13. Obtaining Nasopharyngeal specimens
     14. Nasogastric and orogastric placement
     15. Chest Tube placement/removal/ dressing change/manipulation of suction

   These patients must be in a private room until they no longer require aerosol generating procedures.

   C. Enhanced PPE (EPPE)
      1. N95 and face shield or PAPR
      2. Gloves
      3. Gown
Bouffants are approved for use. Please note this is not PPE but can be used by individuals to decrease touch contamination to the hair.

The N95 will be discarded when the staff exits the room after the above procedure has been completed.

After an AGP is completed all high touch surfaces are required to be wiped down with bleach or approved cleaning product.

High touch surfaces include, i.e.:
- Doorknob/Handle
- Bedside table
- Bed rails
- Patient remote
- Alaris Pump
- Surface of the ventilator screen if applicable

II. Intubation and Extubation – COVID Positive, COVID R/O

A. Intubate as early as clinically appropriate: Controlled/Non-Emergent Ideal.

B. Intubation Does Not require patient being in Negative Pressure Room.

C. Clinical judgement by Airway Provider and Primary Team will be used if patient severely decompensating and an AGP may be necessary.

D. If the patient requires manual ventilation w/o ETT
   - Place viral/bacterial filter on mask before giving a breath
   - Use SMALL Tidal Volumes with a tight seal.

E. The most experienced Provider will perform intubation.

F. Airway Provider and Assistant will wear Enhanced PPE:
   - Gown
   - PAPR or N95 and face shield
   - Gloves
   - Bouffant- This is not PPE but can be used by individuals to decrease touch contamination to the hair

G. Limit number of staff in room to three (3) when possible
   - Airway Provider
   - Airway Assistant
   - Medication Nurse

H. In absence of contraindications, favor Rapid Sequence Induction (RSI): Ensure paralysis to avoid cough.
   - If available use Virtual RSI Kits: currently on 6I, 6H, and 6K.

I. Airway Provider consider using a Glide scope for ease of visualization. If patient is a known to be an “easy” airway may consider intubated with a Disposable Laryngoscope (discard after).
J. In event of failed attempt/difficult intubation, consider LMA versus BVM for stabilization before subsequent attempts.

K. POST INTUBATION:
   - If tube becomes disconnected and open to air, clamp ETT VERY briefly to avoid aerosolization - if the patient is not paralyzed this will become uncomfortable.
   - Immediately secure ETT
   - Connect Viral/Bacterial Filter to Circuit and Manual Ventilator
   - Positive Pressure Ventilation only AFTER Cuff inflated
   - Lowest gas flows needed to maintain Oxygenation should be used
   - Use a CLOSED suctioning system and AVOID disconnecting the circuit
   - All staff involved will doff and discard all PPE per PPE guidelines- keep and disinfect face shield/goggles
   - Staff will immediately wash hands or use an alcohol-based Sanitizer following event.
   - All used Airway Equipment will be placed in biohazard bags and disposed of or sterilized per policy.
   - All PPE will be disposed of or cleaned per COVID-19 PPE cleaning guidelines and returned to original location.

L. EXTUBATION:
   - Consider extubation under tent shield.
   - Floor or O.R. patients extubated: an ear loop surgical mask is to be placed immediately to reduce droplet transmission during recovery phase.
   - For Known/Suspected COVID patients extubated in O.R.: patients will be recovered in O.R. (will not go to PACU) once recovered they will be a direct admit to appropriate Floor/ICU.

**IMPORTANT** Other than EPPE, the patients should continue to be treated clinically using standard protocols (ex. BVM, preoxygenation, NIPPV, etc.).

Corresponding Clinical Procedure(s):
None

Education/Related Resources:
- Respiratory Procedures During Prevalence of COVID-19, COV R-01

Form Names(s) and Number(s):
None

Originating Department: Nursing
Contributing Department(s): Infection Prevention, ICU Governance, Respiratory
APPENDIX – 4: Respiratory Procedures during prevalence of COVID-19

Respiratory Procedures During Prevalence of COVID-19

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Change Description</th>
</tr>
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<tbody>
<tr>
<td>04/27/2020</td>
<td>Specified that MDI therapy is non-aerosolizing and doesn’t require enhanced PPE or private room. Added that pediatric patients requiring a neonatal circuit (&lt;10kg) should be bagged with an infant HME. Pediatric definitions revised. Added that Door should be closed. Added applies to any direct care staff. Combined process for both ped and adult populations. Removed pediatric definitions.</td>
</tr>
</tbody>
</table>

Standard:
Guidelines below will be followed to ensure procedures ordered during prevalence of COVID-19 will be given appropriate clinical consideration.

Applies to:
Any direct care staff for adult and pediatric populations.

Policy:
See below for guidelines for procedures being performed by a Respiratory Therapist during prevalence of COVID-19.

Therapist administering the below therapies and healthcare providers caring for patients receiving these therapies (regardless of whether they are COVID-19, R/O COVID-19 or non-COVID-19) are required to wear enhanced PPE (N-95 mask with face shield or PAPR, and gown and gloves). Patients should be placed in private rooms, with closed door, when these therapies are being administered. A sign (F95383) indicating that an aerosolizing procedure is being performed should place on the door. This sign should be removed once procedure has ended and contaminated surfaces should be wiped clean. At the completion of any of these procedures the PPE should be discarded. Hand Hygiene should be performed before and after. MDI therapy is non-aerosolizing and doesn’t require enhanced PPE or a private room.

A. Aerosol Therapy
Aerosol therapy should be avoided on COVID-19 positive and R/O COVID-19 patients. MDI Therapy is the preferred method of bronchodilator administration.

1. Metered dose inhalers are in short supply. If they are ordered, a one-time aerosol treatment should be given using a filtered nebulizer to test therapeutic effectiveness. If the patient responds to the aerosol, MDI should be ordered. In situations where no response is noted, a recommendation to discontinue bronchodilator therapy should be made.

2. MDIs will be left in the room for all COVID-19 positive and R/O COVID-19 patients.
B. High-Flow

High-flow systems can be used on COVID-19 rule out or positive patients. ear-loop is in place enhanced PPE is not required. If the patient is wearing an ear-loop mask, enhanced PPE is not required. If the patient's ear-loop mask is removed, enhanced PPE should be worn (in pediatric populations, when wearing an ear-loop mask is not possible, full enhanced PPE will be worn).

Precautions should be taken when using this device:
1. Flows will be kept below 60 lpm.
2. Patients will need to wear an ear-loop mask while on high flow and masks should be changed when moistened (the addition of an ear-loop mask decreases risk to the equivalent of a patient on a nasal cannula at a flow of <6lnc). Ear-loop masks should be assessed for moisture Q2h and prn. These masks do not serve as filters but decrease aerosol velocity when expelled. The ear-loop mask should fit over patients face and cover the nose, nasal cannula prongs, and mouth.
3. These patients require a private room, but do not require negative pressure rooms.
4. As a precaution when possible the flow should be turned off before removal of mask.

C. Cpap/Bipap

Cpap and Bipap should be avoided on COVID-19 positive patients and R/O COVID-19 patients. Any orders for either of these need to be cleared through pulmonary attending (via a Pulmonary Consult).

D. Ventilation

1. All ventilators on patients require an inspiratory filter as well as one expiratory filter. Filters on expiration should be changed every 8 hours and prn for moisture collection or changes in Peak inspiratory pressures.
2. Once a patient is extubated all disposables should be thrown out in the room and ventilator should be wiped down with appropriate dwell time (3 min) before leaving the room.
3. During CPR, if possible, leave COVID-19 positive patients and R/O COVID-19 patients on the ventilator. Pressure limits may need to be increased maintaining a rate of 10 if possible. If synchrony with compressions is difficult, changing the patient to Cpap and manually ventilating the patient using the manual inspiration button is an option.
4. When ventilator supply decreases, choose ventilator based on patient ventilation requirements and needs.
5. V60 units used as ventilators (in the event that they are needed) require filtered expiration. Due to the concern that moisture may impede exhalation these filters should be changed (q8h and prn).
E. BVM/ETT-Bag Ventilation
   1. While using BVM/ETT bag ventilation, an HME or Bacteria/Viral filter will be placed between the face mask and Ambu bag (patients bagged who are <10Kg and require a neonatal circuit should be bagged with infant HMEs). This applies to all inpatient settings and patients.
      a. The RT carrying the Code Blue/RRT pager will carry a filter when responding, and will also be placed on all Difficult Airway carts and Code Carts.
   2. ALL transport bagging requires an HME or Bacteria/Viral filters.

F. Tracheal/Laryngectomy Patients
   1. Patient will wear ear-loop mask over trach collar, and assessed/changed for excessive moisture Q2h/prn (in Pediatric populations when wearing an ear-loop mask is not possible enhanced-PPE will be worn). If the patient is wearing the ear-loop mask, enhanced PPE only needs to be worn during mask changes, succioning procedures, and bagging.
   2. These patients rely on humidification, so Oxytrach will be used for transport and not long term.

Corresponding Clinical Procedure(s):
   None

Education/Related Resources:
   Guideline: Adult Airway Procedures Including Intubation/Extubation During COVID-19, COV A-02

Form Name(s) and Number(s):
   AGP’s In Progress, F95383

Originating Department: Respiratory Therapy
Contributing Department(s): Chief of Pulmonary, Medical Director for Respiratory Therapy, Medical Director for Respiratory Therapy, Pediatrics, Nursing

References:
   None cited
APPENDIX – 5 : CODE BLUE Room layout

Code Blue Guidelines (Excludes ED) During COVID-19 (cont.)  COV R-02

Addendum B

CODE ROLES:

- CPR Compressor
- CPR Compressor
- Med Nurse
- Team Leader
- Zoll Nurse (SWAT)
- Anesthesia
- RT
- Primary Team (Mobile)*
- Scribe Nurse
- 2ND SWAT
- Cart Nurse (pharmacist)
- Utilize In Room As Needed
- MEDS
- Bedside Table

OUTSIDE ROOM

- Utilize In Room As Needed
- Primary Team (Mobile)*
- Scribe Nurse
- 2ND SWAT
- Cart Nurse (pharmacist)
APPENDIX – 6: Discontinuation of transmission-based precautions and disposition of patients with COVID-19

COVID-19 POLICY MANUAL

Policy Number: COV D-04
Approved by: Hospital Officers Leadership Team
Issue Date: 04/24/2020
Value(s): Innovation, Respect, Integrity, Community
Applies to: Upstate University Hospital
Page(s): 1 of 3

Discontinuation of Transmission Based Precautions and Disposition of Patients with COVID-19

Review Date: Change Description:
05/28/2020

Revised Date: Change Description:
05/28/2020 Added portion on admitting patients to rehab, psych and TCU. Clarified managing homeless population for admission to psych. Added new process for SNF patients to be removed from precautions

Applies to:
Medical Providers, RNs, Infection Prevention staff, Administrative Supervisors

Policy:
Defining the process for discontinuing transmission-based precautions and placement of patients with resolving COVID-19 infections. This process is for movement of internal patients. For discharges, refer to COV D-02, In-Patient Discharge Procedure for COVID-19 Patients, including Patients Unable or Unwilling to Comply with the Quarantine Order.

A. Removal of precautions and movement of patients with resolving COVID-19 infection.
   1. The following guidelines will be utilized to make decisions on removal of isolation precautions and movement of patients to non COVID units when able. If there are additional questions please contact Infection Prevention at 315-464-5258 M-F; for off hours please check AMION.

Discharging of all inpatients to long-term care and assisted living center (including patients that were never tested):
   All patients being discharged to a Nursing Home or Adult Care Facility require 1 negative COVID-19 PCR.
   If patient tests positive wait at least 72 hours prior to retesting for COVID
   The 1 negative test is only for discharge if looking to remove precautions follow the removing of isolation precautions below.

Patients that are NOT High Risk* going to the following locations 2N, 4E, TCU, 4B, 5W require 1 negative COVID-19 PCR. COVID positive patients should not be admitted to these locations until isolation precautions have been removed. See below on process for removing isolation precautions.

*High Risk Patients:
- Patients who are immunocompromised (on immunosuppressive therapy)
- Patients who are over the age of 65
- Patients who have chronic lung disease
- Patients who have diabetes
- Patients who have cancer
- Patients who have other serious lung conditions
- Patients who have heart disease
- Patients who have kidney disease
- Patients who have liver disease
- Patients who have other serious conditions

Version 1.2, Last Updated – June 7, 2020
Removing isolation precautions from COVID-19 positive patients:

**Test-based strategy:**
- Resolution of fever without the use of fever-reducing medications and
- Improvement in respiratory symptoms (e.g., cough, shortness of breath), and
- Negative results of an authorized COVID-19 SARS-CoV-2 RNA from at least two consecutive respiratory specimens collected > 24 hours apart. (total of two negative specimens)

**Symptoms-based strategy**
- At least 3 days have passed since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g. cough, shortness of breath; and
- At least 14 passed since symptoms first appeared

Removing isolation precautions from High-Risk* patients (internal patients only):
- No COVID symptoms (fever, cough shortness of breath) or alternate diagnosis for symptoms and
- 1 negative test on day 7 or greater

Optional protocol to remove isolation from Nursing Home patients during admission
1. In the Emergency Department or upon admission to an isolation unit collect both an antibody test IgG for COVID and a nares PCR for COVID (do not order a rapid PCR).
2. If the COVID IgG Antibody test is positive and the nares COVID PCR is negative, the Enhanced Airborne precautions may be removed.

***Removing isolation precautions from Homeless patients being admitted to Inpatient Psychiatric***
This is for homeless patients including homeless patients living in shelters.
- No COVID symptoms (fever, cough shortness of breath) or alternate diagnosis for symptoms and
- 1 negative test on day 3 or greater

*Includes patients from: nursing homes, assisted living, memory care units, correctional facilities, group homes, group homes for adults with disabilities, rehab facilities, homeless patients, and homeless patients living in shelters

Corresponding Clinical Procedure(s):
None

Education/Related Resources:
In-Patient Discharge Procedure for COVID-19 Patients, including Patients Unable or Unwilling to Comply with the Quarantine Order, COV D-02
APPENDIX - 7 : APNIC PROTOCOL

AWAKE PRONING IN NON-INTUBATED COVID-19 PATIENTS (APNIC) PROTOCOL

BASICS:
- This involves non-intubated patients receiving oxygen via nasal cannula who can prone themselves by lying on their belly.
- It can be combined with simultaneous use of any other non-invasive support device, e.g.: low-flow nasal cannula, high-flow nasal cannula (HFNC)
- Requires cooperative patients with intact mentation.

HOW DOES IT WORK?
- Improves secretion clearance
- Recruitment of posterior lung regions which often become atelectatic
- Improved ventilation/perfusion matching

WHO ARE THE CANDIDATES?
- Isolated hypoxemic respiratory failure without substantial dyspnea (the “paradoxically well appearing” hypoxemic patient)

A reasonable candidate should meet the following criteria:
1. Patient should be able to move independently
2. Not have multi-organ failure
3. Patient expected to have a reversible lung injury and might avoid intubation
4. No hypercapnia (Pac02 <50) or substantial dyspnea (Respiratory rate <35, not using accessory muscles)
5. Normal mental status, able to communicate distress
6. No anticipation of difficult airway

- Patients who don’t wish to be intubated (DNI):

VERSION 1.2, Last Updated – June 7, 2020
The main risk of awake proning is that it could cause excessive delay in intubation.

In a DNI patient, who is failing other modes of ventilation, there is little to be lost by trial of prone positioning.

- Stop-gap measure for a hypoxemic patient when intubation is not immediately available (Desaturation during transportation). Many awake patients are capable of proning themselves. So, this could be achievable without utilizing additional manpower.

CONTRAINDICATIONS:
- Signs of respiratory failure (RR >35, PacO2 >50 or pH <7.3)
- Unstable hemodynamics (HR >120, SBP <90 mm hg)
- Spinal instability
- Facial or pelvic fractures
- Open chest or unstable chest wall
- Relative contraindications include delirium, confusion, immediately after meals, inability to change position independently, recent nausea/vomiting, advanced pregnancy

EQUIPMENT:
- Pillow, supplemental oxygen as needed, foam dressings to protect pressure points (if indicated), continuous oxygen monitoring.

PATIENT MONITORING

1. EKG leads should remain on the anterior chest wall for continuous monitoring (if clinically indicated)
2. spO2 probe (continuous) should be placed on the patient if not already in use.
3. Patient’s spO2, oxygen device (i.e. NC, simple face mask) L/min of oxygen, respiratory rate and dyspnea should be assessed just prior to proning and two hours after proning with appropriate documentation.
PRONING PROTOCOL

- House staff will place an order in EPIC to start awake proning
- Following this, nursing staff will instruct patient to lie on their belly if the patient is able to change position in bed independently.
- The patient should lie on the stomach, supported by the arms and a pillow in such a manner that oxygen supply tubing is unobstructed.
- Place pillows under the hips or under the legs for comfort and to avoid pressure
- Consider comfort strategies such as: using the bathroom beforehand, having the call bell within reach, having their phone or other devices within view and utilizing music or television as a distraction to minimize interruptions during prone position.
Covid-19 positive or rule out patients requiring oxygen support

SpO2 >92% on ≥2-6L of oxygen or P/F ratio ≤ 300 with bilateral infiltrates on CXR

Consider eligibility for awake proning if
- No signs of respiratory fatigue RR≥35 or Paco2 >50 or pH<7.3
- No hemodynamic instability
- Patient able to change position in bed independently
- Please refer to other exclusion criteria

Initiate Proning for 2 hours
Avoid proning immediately after meals; wait for at least 2 hrs.
Stop and return to supine if patient has worsening hypoxia, complains of dyspnea, chest pain or discomfort and inform the team

If SpO2 increases >2.4% or P/F ratio >300, patient will benefit with continued proning

Encourage 2 hours on and 2 hours off during the day, and as tolerated at night, for a total of 8-10 hours/day.
Continue awake proning until SpO2 >96 on ≤ 2L of O2

SpO2 <92% on ≥ 6L of oxygen or P/F ratio ≤ 200 or rapidly increasing oxygen requirements with bilateral infiltrates on CXR

Consult MICU

If patient transferred to MICU, consider arterial line placement
If no signs of respiratory fatigue RR≥35 or Paco2 >50 or pH<7.3
Start HFNC with a protective face mask

Prone for 2 hours
Physician to measure ROX index (SpO2/Fio2/RR) at 2h
If SpO2<90%, ROX index <3.85 or PF ratio<200 indicates awake prone failure

If good response to proning, encourage 2 hours on and 2 hours off during the day, and as tolerated at night, for a total of 8-10 hours/day until SpO2>96 on ≤ 2L of O2
## APPENDIX – 8 : Anticoagulation in COVID-19 patients

<table>
<thead>
<tr>
<th>Criteria</th>
<th>GROUP 1</th>
<th>GROUP 2</th>
<th>GROUP 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td>D-Dimer &lt; 3 mcg/mL</td>
<td>D-Dimer &gt;= 3 mcg/mL</td>
<td>Confirmed VTE OR Unexplained worsening hypoxemia and suspected VTE with D-Dimer &gt;= 3 mcg/mL</td>
</tr>
<tr>
<td><strong>Stable Renal Function eCrCl&gt;30 mL/min</strong></td>
<td>Enoxaparin 40mg sq daily (BMI &lt;40)</td>
<td>Enoxaparin 0.5mg/kg sq q12 hrs</td>
<td>Enoxaparin 1mg/kg subQ q12hrs</td>
</tr>
<tr>
<td></td>
<td>40mg sq q12hr (BMI 40-49.9)</td>
<td>Stable Renal Function eCrCl&gt;30 mL/min</td>
<td>Stable Renal Function eCrCl&gt;30 mL/min</td>
</tr>
<tr>
<td></td>
<td>50mg sq q12 hr (BMI &gt;=50)</td>
<td>Enoxaparin 0.5mg/kg subQ daily</td>
<td>Enoxaparin 1mg/kg subQ daily</td>
</tr>
<tr>
<td><strong>Stable Renal Function eCrCl&lt;30 mL/min</strong></td>
<td>Enoxaparin 30mg sq daily (BMI &lt;40)</td>
<td>Or</td>
<td>Or</td>
</tr>
<tr>
<td></td>
<td>BMI &gt;= 40 use heparin, see below</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Any GFR or Acute Kidney Injury</strong></td>
<td>Adult heparin infusion low dose protocol (anti-Xa target range 0.3-0.5)</td>
<td>Any GFR or Acute Kidney Injury</td>
<td>Any GFR or Acute Kidney Injury</td>
</tr>
<tr>
<td><strong>Heparin</strong></td>
<td>If anticipated procedures and/or high risk bleeding utilize heparin infusion</td>
<td>Adult heparin infusion high dose protocol (anti-Xa target range 0.3-0.7)</td>
<td>If anticipated procedures and/or high risk bleeding utilize heparin infusion</td>
</tr>
<tr>
<td></td>
<td>5000 U sq q8 hours (BMI &lt;40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7500 U sq q8 hours (BMI &gt;=40)</td>
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</tr>
</tbody>
</table>

### Monitoring
- Check daily CBC with diff, D-Dimer and Fibrinogen, PTT, PT/INR. Can consider Hematology consult.

### Precautions
- **Active bleeding**
  - Platelet count < 50 000
  - Decreased renal function (GFR<30) and/or BUN > 80
- **Active bleeding**
  - Platelet count < 50 000
  - Decreased renal function (GFR<30) and/or BUN > 80
- If clinician assesses bleeding risk is too high (age, multiple organ failure, significant co-morbidities, previous bleeding, recent surgery), can move to Group 1

### Discharge
- If D-Dimer > 0.5mcg/mL and/or patient has decreased mobility:
  - Apixaban 2.5mg BID x 14 days OR Rivaroxaban 10mg daily x 14 days
- Apixaban 2.5mg BID OR Rivaroxaban 10mg daily x 4 total weeks of anticoagulation
- Apixiban 5mg BID x 3 total months of anticoagulation OR Rivaroxaban 15mg BID for 21 days then 20mg daily for total 3 months of anticoagulation

### Notes
- Physician should assess for bleeding daily and can stop anticoagulation if suspected. Physician should complete necessary work up for suspected DVT or pulmonary embolism if clinically appropriate and deemed safe for patient.
APPENDIX – 9: Convalescent Plasma as a Therapeutic for the Treatment of Severe Respiratory Illness from COVID-19

Background:
New York State is becoming the new epicenter for COVID-19 transmission and severe illness. Central NY and Onondaga County specifically currently has 60 confirmed cases as of March 25, 2020 and is at the beginning of the epidemic curve for new cases. Currently there are no licensed therapeutics, antivirals or vaccines to treat or prevent COVID-19 infections. The use of convalescent sera from patients who recovered from an acute COVID-19 infection has been proposed as a potential therapeutic to diminish the severity of severe COVID-19 infection. The use of convalescent plasma as passive antibody therapy has been historically been useful in the treatment of a number of infectious diseases both prophylactically and therapeutically. Concentrated antibody as hyperimmune globulin has been used as prophylaxis for rabies, hepatitis A and B, and varicella-zoster infection. Historically it has been shown to have beneficial effects in severe streptococcal disease. Thus, the concept that convalescent plasma from recovered COVID-19 patients may contain high enough titer of COVID-19 specific antibody to neutralize virus and diminish disease severity is based on a sound premise (The convalescent sera option for containing COVID-19 Arturo Casadevall, Liise-anne Pirofski J Clin Invest. 2020. https://www.jci.org/articles/view/138003).

The potential benefits of using convalescent plasma as a therapeutic for severe disease are the following:
1. Rapid decline and clearance of virus
2. Decrease in the cytokine storm seen in acute respiratory distress syndrome associated with severe COVID-19 infection
3. Improved morbidity and mortality
4. Decrease of time on ventilator with improved oxygenation
5. Decrease in total hospitalization days

The potential risks of giving convalescent plasma includes:
1. allergic reaction
2. volume overload
3. potential antibody enhancement of virus.

The Food and Drug Administration (FDA or Agency) created the ability to use convalescent plasma for the treatment of severe COVID-19 on a compassionate use emergency IND (eIND).
Protocol per FDA Guidance:

1. This protocol and informed consent will be SUNY IRB reviewed and approved.

2. This protocol will be done in collaboration with the American Red Cross who will process, test and prepare the convalescent plasma for therapeutic use.

3. Patients identified as COVID-19 PCR positive either in the hospital or as outpatients will be identified and informed consent obtained. COVID-19 convalescent plasma must only be collected from recovered individuals if they are eligible to donate blood (21 CFR 630.10, 21 CFR 630.15). Required testing must be performed (21 CFR 610.40) and the donation must be found suitable (21 CFR 630.30).

4. Donor eligibility will be addressed, as follows:
   - Prior diagnosis of COVID-19 documented by a laboratory test
   - Complete resolution of symptoms at least 14 days prior to donation
   - Female donors negative for HLA antibodies or male donors
   - Negative results for COVID-19 either from one or more nasopharyngeal swab specimens or by a molecular diagnostic test from blood. A partial list of available tests can be accessed at https://www.fda.gov/medical-devices/emergency-situations-medicaldevices/emergency-use-authorizations.
   - Defined SARS-CoV-2 neutralizing antibody titers, if testing can be conducted (e.g., optimally greater than 1:320)

5. The container label of COVID-19 convalescent plasma units must include the following statement, “Caution: New Drug--Limited by Federal (or United States) law to investigational use." (21 CFR 312.6 (a))

6. Eligible patients for use under expanded access provisions:
   - Must have laboratory confirmed COVID-19
   - Must have severe or immediately life-threatening COVID-19, for example:
     - Severe disease is defined as:
       - Dyspnea,
       - respiratory frequency ≥ 30/min,
       - blood oxygen saturation ≤ 93%,
       - partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, and/or
       - lung infiltrates > 50% within 24 to 48 hours
     - Life-threatening disease is defined as:
       - respiratory failure,
       - septic shock, and/or
       - multiple organ dysfunction or failure
   - Must provide informed consent
7. Treatment Protocol: Patients meeting the eligibility criteria will be treated with 1 unit of convalescent plasma per the hospital care team. This may be repeated once per day for a maximum of 3 doses. Data will be collected prospectively on each patient including the following:

- Demographics
- Vital signs and pulse oximetry daily
- Daily laboratory values
- Time on ventilator
- Hospital days
- Daily radiographic reports
- Complications including infectious complications.
- Outcome

8. FDA Communication and Regulatory Compliance:

For request that are not highly time sensitive (response from FDA provided within 4 to 8 hours), the requesting physician may contact FDA by completing form 3926 (https://www.fda.gov/media/98616/download) and submitting the form by email to CBER_eIND_Covid-19@FDA.HHS.gov.

- The completed form should include a brief clinical history of the patient, including: diagnosis, current therapy, and rationale for requesting the proposed investigational treatment in order to meet the expanded access use requirements of 21 CFR 312.305 and 312.310.
- The form should include information regarding where the COVID-19 convalescent plasma will be obtained.
- Providers should complete the form to the extent possible, and FDA will work with the provider if additional information is required.
- FDA will review the request, and upon approval, FDA will send the requesting physician a confirmatory email that includes the emergency IND number.

- In the event of an emergency that is highly time sensitive (response required in less than 4 hours) or where the provider is unable to complete and submit form 3926 due to extenuating circumstances, the provider may contact FDA’s Office of Emergency Operations at 1-866-300-4374 to seek verbal authorization.
  - If verbal authorization is given, the requestor must agree to submit an expanded access application (e.g., form 3926) within 15 working days of FDA’s authorization of the use.

9. Statistical Analysis: The effects of the treatment will be assessed by determining the effects of therapy on vital signs and pulse oximetry daily, improvement of laboratory values, time on ventilator, hospital days, time to radiographic improvement, complication rate including infectious complications, and outcome. Comparison to historical controls will be made.
10. Process (Treatment IND Team will process all eINDs to the FDA)

<table>
<thead>
<tr>
<th>Donor Donation Procedures</th>
<th>Treatment Procedures</th>
<th>Database</th>
<th>Research Sampling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential Donors identified: hospital PCR positive, community PCR positive, advertisements.</td>
<td>Treatment team gets a call requesting plasma treatment. Information taken by phone, criteria checklist taken.</td>
<td>FDA approves, physician notified, Red Cross informed and plasma delivered.</td>
<td>Donor blood draw at each donation: 1 red top, 2 CPT tubes.</td>
</tr>
<tr>
<td>Phone interview: Qualifies by criteria and checklist. Appointment made to CRU.</td>
<td>Informed consent faxed to HCP and faxed back signed. Information into FDA form and eIND submitted.</td>
<td>Donor information entered into donor database.</td>
<td>Patient blood draw: 1 red top. Times: 1. Before plasma 2. 24 hours after each dose. 3. Every 7 days for 28 days. 4. 3 months post-treatment. 5. 6 months post-treatment.</td>
</tr>
<tr>
<td>At CRU, donor informed consent signed, specimen for PCR. If negative, appointment made to Red Cross for plasma.</td>
<td>Patient information acquired daily and entered into database and samples taken for research.</td>
<td>Patient information entered into patient database.</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX – 10 : CDC - Disposition of patients

Discontinuation of transmission-based precautions for patients with COVID-19:

The decision to discontinue Transmission-Based Precautions should be made using a test-based strategy or a non-test-based strategy (i.e., time-since-illness-onset and time-since-recovery strategy). Meeting criteria for discontinuation of Transmission-Based Precautions is not a prerequisite for discharge.

1. Test-based strategy.
   - Resolution of fever without the use of fever-reducing medications and
   - Improvement in respiratory symptoms (e.g., cough, shortness of breath), and
   - Negative results of an FDA Emergency Use Authorized COVID-19 molecular assay for detection of SARS-CoV-2 RNA from at least two consecutive nasopharyngeal swab specimens collected ≥24 hours apart (total of two negative specimens).

2. Non-test-based strategy.
   - At least 3 days (72 hours) have passed since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath); and,
   - At least 7 days have passed since symptoms first appeared

When a Testing-Based Strategy is Preferred

Hospitalized patients may have longer periods of SARS-CoV-2 RNA detection compared to patients with mild or moderate disease. Severely immunocompromised patients (e.g., medical treatment with immunosuppressive drugs, bone marrow or solid organ transplant recipients, inherited immunodeficiency, poorly controlled HIV) may also have longer periods of SARS-CoV-2 RNA detection and prolonged shedding of infectious recovery. These groups may be contagious for longer than others. In addition, placing a patient in a setting where they will have close contact with individuals at risk for severe disease warrants a conservative approach.

Hence, a test-based strategy is preferred for discontinuation of transmission-based precautions for patients who are

- Hospitalized or
- Severely immunocompromised or
- Being transferred to a long-term care or assisted living facility

If testing is not readily available, facilities should use the non-test-based strategy for discontinuation of Transmission-Based Precautions or extend the period of isolation beyond the
non-test-based-strategy duration, on a case by case basis in consultation with local and state public health authorities.

**Discontinuation of empiric transmission-based precautions for patients suspected of having COVID-19:**

The decision to discontinue empiric Transmission-Based Precautions by excluding the diagnosis of COVID-19 for a suspected COVID-19 patient can be made based upon having negative results from at least one FDA Emergency Use Authorized COVID-19 molecular assay for detection of SARS-CoV-2.

- If a higher level of clinical suspicion for COVID-19 exists, consider maintaining Transmission-Based Precautions and performing a second test for SARS-CoV-2.
- If a patient suspected of having COVID-19 is never tested, the decision to discontinue Transmission-Based Precautions can be made based upon using the *non-test-based strategy* described above.

Ultimately, clinical judgement and suspicion of SARS-CoV-2 infection determines whether to continue or discontinue empiric Transmission-Based Precautions.

**Disposition of Patients with COVID-19:**

Patients can be discharged from the healthcare facility whenever clinically indicated.

If discharged to home:

- Isolation should be maintained at home if the patient returns home before discontinuation of Transmission-Based Precautions. The decision to send the patient home should be made in consultation with the patient’s clinical care team and local or state public health departments. It should include considerations of the home’s suitability for and patient’s ability to adhere to home isolation recommendations.

If discharged to a long-term care or assisted living facility, AND

- Transmission-Based Precautions *are still required*, they should go to a facility with an ability to adhere to infection prevention and control recommendations for the care of COVID-19 patients. Preferably, the patient would be placed in a location designated to care for COVID-19 residents.
- Transmission-Based Precautions *have been discontinued*, but the patient has persistent symptoms from COVID-19 (e.g., persistent cough), they should be placed in a single room, be restricted to their room, and wear a facemask during care activities until all symptoms are completely resolved or until 14 days after illness onset, whichever is longer.
- Transmission-Based Precautions *have been discontinued* and the patient’s symptoms have resolved, they do not require further restrictions, based upon their history of COVID-19.
For everyone's health and safety

Call your primary care provider and describe your symptoms:

- cough
- shortness of breath
- sore throat
- fever
- flu-like symptoms
- loss of smell

Or, use the online assessment tool at www.upstate.edu/COVID
For everyone’s health and safety

Cover Your Cough

Cover your mouth and nose with a tissue when you cough or sneeze.

Or, cough or sneeze into your upper sleeve, not your hands.

You may be asked to put on a surgical mask to protect others.

Put your used tissue in the waste basket.

Wash your hands with soap and water.

Or, clean your hands with an alcohol-based hand cleaner.
For everyone’s health and safety

Please keep your social distance

Social distancing means 6 feet apart from others