

UPSTATE MEDICAL UNIVERSITY
DEPARTMENT OF MEDICINE
BOOK OF COVID-19 : INPATIENT GUIDELINES

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UPSTATE
MEDICAL UNIVERSITY

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 March 1, 2021, more than 114 million people have been infected, with over 2.5 million 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.

AUTHORS

Primary Authors

Sanchit Panda, MD; Geetanjali Johri, MD
ICU Supplement – Pardeep Masuta, MD

Resident Authors

Nimisha Srivastava, MD, Prateek Harne, MBBS, Jasmine Sandhu, MD

Contributors

Department of Medicine

Division of Hospital Medicine

Kathryn Anderson, MD/PhD
Emily L Albert, MD, MPH
Pratistha Gupta, MD
Anupa Mandava, MD
Omar Hadzipasic, MD
Catherine White, MD
Ian Dargon, MD
Jessica Wagenblatt, FNP-C

Division of Pulmonary, Critical Care and Sleep Medicine

Dragos N Manta, MD
Birendra P Sah, MD
Sumendra Joshi, MD
Amish Shah, MD

Division of Infectious Disease

Elizabeth Asiago Reddy, MD, MS
Kristopher M. Paolino, MD
Mitchell Brodey, MD

Residents and Fellows

Hanish Jain, MD
Vrinda Vyas, MD
Akhila Sunkara, MD
Ghansham Das, MD
Komal Akhtar, MD
Basel Abuzuaiter, MD

Department of Radiology

Sahir Quraeshi, MD
Abtin Jafroodifar, MD
Peter Wei, MD

Reviewers

Division of Hospital Medicine

- **Associate Division Chief** - Zac Shepherd, MD, FACP
- **Division Chief** - Housam Hegazy, MD, MLS, SFHM, FACP, CHCQM

Division of Pulmonary, Critical care and Sleep medicine

- **Division Chief** - Dana Savici, MD

Division of Infectious Disease

- **Division Chief** - Stephen Thomas, MD

Department of Medicine

- **Chair** - Sriram Narsipur, MD, FASN, FACP

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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, Department of Radiology 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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Medical student contributors:

Robertha Barnes, Nick Bender, Kate Bunch, Audrey Butler, Danielle Cannon, Anumita Chakraborty, Fanny Chen, Joan Chou, Tom Comerford, Katherine Cuan, Gregory Despotidis, Mauro Dispagna, Ben Fuller, Gretchen Goble, Christian Kasianko, Erik Klein, Ji Young Lee, Dan Lichtenstein, Joshua Long, Sam Mackoff, Jada McMahon, Ashley Miller, Craig Pille, Madison Pomerantz, Malika Rajamani, , Sudie Ann Robinson, Alyssa Scher, Rosalie Siciliano, Prabhdeep Singh, Ashis Sinha, Katie Skolnick, Jared Sweeney, Dylan Taylor, Joseph Toth, Zach Visco, Cait Ward, Samuel Weeks, Zoe Weiss, Vincent Xiao, and Hannah Yoo.

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Table of Contents

PREFACE	2
AUTHORS	3
ACKNOWLEDGEMENTS	4
EPIDEMIOLOGY	11
Virology	11
<i>Global Data:</i>	11
<i>New York State Data:</i>	11
<i>Onondaga County Data:</i>	11
TIMELINE OF THE PANDEMIC	12
TRANSMISSION:	13
<i>Source:</i>	13
<i>Modes of transmission</i>	13
<i>Infectivity:</i>	13
<i>Incubation period</i>	14
<i>Serology:</i>	14
PATHOPHYSIOLOGY	15
LIFE CYCLE INSIDE HOST CELL	15
ACTIVATION OF IMMUNE SYSTEM	15
INFECTION CONTROL	17
INFECTION CONTROL PRECAUTIONS FOR ROUTINE CARE:	17
○ <i>COVID 19 positive and rule out patients:</i>	17
○ <i>High risk patients:</i>	17
○ <i>Low Risk patients:</i>	17
○ <i>Behavioral Health High Risk inpatients requiring transfer to inpatient psychiatric units:</i>	17
INFECTION CONTROL PRECAUTIONS FOR HIGH RISK CARE:	17
<i>Aerosol generating procedures:</i>	18
PAPR TRAINING/INFECTION CONTROL	18
CRITICAL STRATEGIES TO PRESERVE PPE:	19
<i>Extended use PPE:</i>	19
<i>Tele-Health visits:</i>	19
<i>Consultants:</i>	19
CODE BLUE GUIDELINES	19
DISCONTINUATION OF PRECAUTIONS FOR COVID-19 INFECTION:	20

TESTING PROCEDURES	21
APPROACH TO TESTING:	21
REVERSE TRANSCRIPTASE PCR TESTING	21
<i>Wadsworth PCR assay:</i>	22
<i>Cepheid Rapid test:</i>	22
<i>Saliva testing</i>	23
RESPIRATORY VIRAL PANEL (RVP) AND COVID TESTING:	23
ANTIBODY TESTING (SARS-COV-2 IgG Assay):	23
<i>Abbott Architect SARS-CoV-2 IgG assay</i>	24
DOCUMENTATION AND EPIC	25
ADMISSION GUIDELINES	26
PATIENT GROUPS BASED ON COVID TEST RESULTS	26
<i>Confirmed COVID-19</i>	26
COVID RULE-OUT	26
WHEN TO SUSPECT COVID-19	27
<i>Most common symptoms:</i>	27
<i>Less common symptoms:</i>	27
<i>Serious symptoms:</i>	27
ADMISSION CRITERIA FOR COVID POSITIVE PATIENTS (ANY TWO):	27
ORDER SETS AND LAB PANELS:	28
CODE STATUS/ ADVANCED DIRECTIVES/ MOLST/ HEALTH CARE PROXY:	28
TRIAGE FROM OUTSIDE HOSPITALS:	28
COVID-19 INPATIENT TREATMENT ALGORITHM	29
DIAGNOSTIC WORKUP	30
LABORATORY TESTING:	30
IMAGING:	31
<i>Chest X-Ray:</i>	31
<i>Contrast enhanced or Non-contrast chest CT:</i>	32
<i>Transthoracic echocardiogram:</i>	33
ROLE OF IMAGING IN GUIDING DECISIONS TO DISCONTINUE ISOLATION:	35
BRONCHOSCOPY:	35
CLINICAL COURSE	36
TIMELINE	36
SPECTRUM OF SEVERITY OF DISEASE	36
MANIFESTATIONS	37

<i>PULMONARY MANIFESTATIONS</i>	37
<i>CARDIAC MANIFESTATIONS</i>	39
<i>GASTROINTESTINAL MANIFESTATIONS</i>	41
<i>NEUROLOGIC MANIFESTATIONS</i>	43
<i>NEPHROLOGIC MANIFESTATIONS</i>	47
<i>HEMATOLOGIC MANIFESTATIONS</i>	49
<i>SECONDARY INFECTIONS AND HIV</i>	54
<i>DERMATOLOGIC MANIFESTATIONS</i>	55
<i>MULTI-SYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)</i>	57
PROGNOSTIC FACTORS	59
EPIDEMIOLOGY:.....	59
VITALS:	59
LABS:	59
GENERAL MANAGEMENT	60
EARLY ADVANCED CARE PLANNING:	60
OXYGENATION:	60
<i>Goals</i>	60
<i>Consult MICU if patient has</i>	61
FLUID RESUSCITATION:	61
ANTIBIOTICS:	61
DVT PHARMACOLOGIC PROPHYLAXIS:	62
<i>LMWH and Heparin</i>	62
ANALGESIC AND ANTIPYRETICS.....	62
ACE INHIBITOR/ARB, STATINS.....	62
SPECIFIC THERAPY	63
NON-PHARMACOLOGICAL THERAPY	63
<i>Awake Proning</i>	63
PHARMACOLOGICAL THERAPY	65
THERAPIES FOR INPATIENT USE	66
<i>Anticoagulation</i>	66
<i>Dexamethasone and other glucocorticoids</i>	66
<i>Remdesivir (RDV)</i>	66
<i>Baricitinib</i>	67
<i>Convalescent plasma</i>	68
THERAPIES FOR OUTPATIENT USE.....	70

<i>Monoclonal Antibodies</i>	70
<i>Casirivimab and Imdevimab (REGN-COV2)</i>	70
<i>Bamlanivimab</i>	71
<i>Bamlanivimab and Etesevimab</i>	71
THERAPIES WITHOUT CLEAR EVIDENCE OF BENEFIT	72
<i>IL-6 pathway inhibitors</i>	72
<i>Kinase inhibitors</i>	72
<i>Chloroquine or hydroxychloroquine with or without azithromycin</i>	72
<i>Lopinavir-Ritonavir</i>	73
<i>Ivermectin</i>	73
<i>Interferons</i>	73
SPECIAL POPULATIONS	74
PREGNANCY:	74
<i>Background:</i>	74
<i>Presentation:</i>	74
<i>General Management:</i>	75
TRANSPLANT RECIPIENTS	78
ICU CARE SUPPLEMENT	80
WHEN TO CONSULT MICU	80
ACUTE LUNG INJURY (ALI) AND ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)	80
<i>Berlin Definition of ARDS</i>	80
<i>Severity of ARDS and mortality</i>	81
H AND L PHENOTYPE THEORY IN COVID-19 PNEUMONIA	81
<i>Phenotype L (Early Stage, Atypical ARDS)</i>	81
<i>Phenotype H (Late Stage, Typical ARDS)</i>	81
<i>Systemic Corticosteroids</i>	82
<i>Bronchodilator Therapy</i>	82
<i>Awake prone positioning</i>	82
<i>Supplemental Oxygen</i>	82
INTUBATION	84
<i>Indications</i>	84
<i>Preparation</i>	84
<i>Preoxygenation</i>	84
<i>Sedation</i>	84
<i>Placement (Intubation)</i>	85

<i>Post-intubation management</i>	85
MECHANICAL VENTILATION	86
<i>Basics</i>	86
<i>Initial Ventilator Settings</i>	86
<i>Subsequent Tidal Volume adjustment</i>	86
<i>Additional ventilator adjustment</i>	87
<i>Airway Pressure Release Ventilation</i>	88
<i>Sedation/Analgesia/Paralysis</i>	88
<i>Pain</i>	89
<i>Delirium</i>	89
<i>Tracheostomy</i>	90
<i>Weaning, Extubation and Liberation from Mechanical Ventilation</i>	91
<i>Refractory Hypoxemia</i>	94
<i>Extracorporeal Membrane Oxygenation (ECMO)</i>	96
<i>Ventilator-Induced Lung Injury (VILI)</i>	97
<i>Ventilator Associated Pneumonia (VAP)</i>	97
SHOCK	99
<i>Septic Shock</i>	100
<i>Cardiogenic Shock</i>	101
<i>Cytokine Activation Syndrome/Cytokine Release Syndrome (CRS)</i>	102
DISCHARGE GUIDELINES	103
DISCONTINUATION OF TRANSMISSION PRECAUTIONS	103
<i>Symptom-based strategy (Must meet all criteria)</i>	103
<i>Test-based strategy (Must meet all criteria)</i>	103
DISCHARGE WORKFLOW	104
RESIDUAL EFFECTS OF COVID-19 INFECTION	106
COVID-19 VACCINES	107
THE PFIZER-BIONTECH COVID-19 VACCINE (BNT162B2 VACCINE).....	107
MODERNA COVID-19 VACCINE (MRNA-1273 VACCINE).....	107
JANSSEN COVID-19 VACCINE (Ad26.COV2-S).....	107
ABBREVIATIONS	108
REFERENCES	112
APPENDIX – 1 : DONNING / DOFFING PPE	122
APPENDIX – 2 : PPE TABLE FOR COVID EXPOSURE SCENARIO	124
APPENDIX – 3 : AIRWAY PROCEDURES DURING COVID-19	126

APPENDIX – 4 : RESPIRATORY PROCEDURES DURING PREVALENCE OF COVID-19	131
APPENDIX – 5 : CODE BLUE ROOM LAYOUT	134
APPENDIX – 6 : DISCONTINUATION OF TRANSMISSION-BASED PRECAUTIONS AND DISPOSITION OF PATIENTS WITH COVID-19	135
APPENDIX - 7 : APNIC PROTOCOL.....	139
APPENDIX – 8 : ANTICOAGULATION IN COVID-19 PATIENTS	143
APPENDIX – 9: CONVALESCENT PLASMA AS A THERAPEUTIC FOR THE TREATMENT OF SEVERE RESPIRATORY ILLNESS FROM COVID-19	144
APPENDIX – 10 : CDC - DISPOSITION OF PATIENTS	148
APPENDIX – 11 : BEHAVIORAL HEALTH HIGH RISK INPATIENTS REQUIRING TRANSFER TO INPATIENT PSYCHIATRIC UNITS 4B, 5W, AND 7W	150

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.

Global Data:

- Global number of reported cases: 114 million
- Updated information can be found at <https://coronavirus.jhu.edu/map.html>

New York State Data:

- First reported case: March 1, 2020⁵
- Updated information can be found at <https://covid19tracker.health.ny.gov/views/NYS-COVID19-Tracker/NYSDOHCOVID-19Tracker-Map?%3Aembed=yes&%3Atoolbar=no&%3Atabs=n>

Onondaga County Data:

- First reported case: March 16, 2020⁶
- Local updated data can be found at <https://covid19.ongov.net/data/#dashboards>

TIMELINE OF THE PANDEMIC

- **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:** US declares a national emergency
- **March 20, 2020:** FDA grants EUA to Hydroxychloroquine and chloroquine
- **May 1, 2020:** FDA grants EUA to Remdesivir for Certain Hospitalized COVID-19 Patients
- **May 28, 2020:** US COVID-19 death toll crosses the 100,000 mark
- **June 15, 2020:** FDA revokes EUA to use hydroxychloroquine and chloroquine
- **August 23, 2020:** FDA grants EUA to COVID-19 convalescent plasma
- **September 3, 2020:** Steroids shown to reduce mortality in severe cases
- **September 28, 2020:** Global COVID-19 deaths cross 1 million
- **October 8, 2020:** South Africa identifies a new variant B.1.351
- **October 22, 2020:** FDA approves Remdesivir as the first drug for COVID-19
- **November 9, 2020:** FDA grants EUA to Bamlanivimab
- **November 19, 2020:** FDA grants EUA to Baricitinib (Olmiant) in Combination with Remdesivir (Veklury)
- **November 21, 2020:** FDA grants EUA to REGEN-COV (Casirivimab and Imdevimab)
- **December 8, 2020:** UK announces a new variant B.1.1.7 that appears to be more contagious
- **December 11, 2020:** FDA grants EUA to Pfizer-BioNTech COVID-19 Vaccine
- **December 18, 2020:** FDA grants EUA to Moderna COVID-19 vaccine
- **December 29, 2020:** First US case of B.1.1.7 variant
- **January 28, 2021:** First US case of B.1.351 variant
- **February 9, 2021:** FDA grants EUA to Bamlanivimab and Etesevimab
- **February 22, 2021:** US COVID-19 death toll crosses 500,000 mark
- **February 27, 2021:** FDA grants EUA to Janssen COVID-19 vaccine

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 transmission primarily occurs via respiratory secretions which can be transmitted through droplets within a close range (6 Feet).
- This has prompted worldwide social distancing measures and universal mask usage to reduce transmission.
- 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.⁷⁻⁹
- Airborne transmission via aerosolized particles has not been clearly established. However the transmissibility of SARS-CoV-2 in experimentally generated aerosols has been shown.¹⁰
- Airborne precautions are hence universally recommended when any aerosol-generating procedures are performed.

Infectivity

- It is unknown how long an infected individual may remain infectious.
- The risk of transmission starts prior to symptom presentation and is highest in the early stages of the disease. Viral RNA levels from upper respiratory specimens correspond with this, however they have been detected before and after a clinical illness, if present.¹¹⁻¹⁴
- Risk of transmission depends on type and duration of exposure, use of preventive measures and individual factors.¹⁵
- Transmission from individuals without symptoms (asymptomatic) and before development (pre-symptomatic) has been clearly observed and is likely responsible for continued widespread community transmission.^{16,17(p24)}
- 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.¹⁸
- The use of disinfectants has been shown to inactivate other coronaviruses.¹⁹

- This makes environmental decontamination and infection control especially important in a home and health-care setup.

Incubation period

- Incubation period for COVID-19 is believed to be up to 14 days. Most cases occur 4-5 days after exposure.²⁰

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.²¹
- 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.^{22,23}
- 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.²⁴
- 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 steps²³
 - 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.²⁵ The expression of this receptor has been categorically seen to be high in the lung, heart, ileum, kidney and bladder.²⁶
- Using ACE2 receptors which are highly expressed on the lung epithelial cells^{27–29}, 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.³⁰
 - Adaptive Immunity - Innate immune cells fight against the virus till an adaptive immunity is involved.²⁷
- 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.²⁷

- 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.^{27,31,32}
- IL-6 levels seem to correspond to the severity of the disease.^{27,23}
- 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.³³
- This promotes a cascade of increased inflammation induced injury to the host tissue in the setting of continued viral replication.

INFECTION CONTROL

Infection Control precautions for Routine care:

- **COVID 19 positive and rule out patients:**
 - Enhanced airborne precautions
 - 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](#).
- **High risk patients:**
 - High risk patient groups are patients from nursing homes, group homes, assisted living facilities, rehab facilities, memory care unit, correctional facilities, homeless or homeless patients living in shelters.
- **Low Risk patients:**
 - Patients who are asymptomatic and being tested prior to discharge to a facility.
 - Surgical mask with standard precautions
 - To determine appropriate PPE for staff and patients, refer to [Appendix 2](#).
- **Behavioral Health High Risk inpatients requiring transfer to inpatient psychiatric units:**
 - Please refer to [Appendix 11](#) for detailed guidance.

Please refer to hospital policy [COV D-04 - Discontinuation of Transmission Based Precautions of Patients with COVID-19](#) for the latest policies.

Infection Control precautions for High risk care:

- It is important to minimize procedures that carry a risk of nebulization ³⁴:

- Positive airway devices for chronic nocturnal ventilation support
- 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. Please refer to [face shield disinfection process](#).
- 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.
- Please refer to policy [COV P-08](#) for current PPE requirements.

Tele-Health visits:

- iPads are available for use with approved HIPAA compliant applications for communicating with patients.
- Please contact the charge nurse/nursing supervisor to arrange for an iPad if not already available.

Consultants:

- Consultants who can complete their assessment via a virtual visit are encouraged to use the same.
- 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](#)

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 - Discontinuation of Transmission Based Precautions of Patients with COVID-19](#) for the latest.

TESTING PROCEDURES

Approach to testing:

- 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.

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.³⁵

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.³⁶⁻³⁹
- 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.^{40,41}

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, Pediatric ED and Community Hospital ED who require admission
2. Patients transferred to UUH who have been assigned a bed on a specialty, nonCOVID-19 unit, subsequently found to be symptomatic on arrival, need to be tested, and the result may change their bed assignment
3. Inpatients who become symptomatic and would be moved to a COVID-19 unit if positive result.
4. Symptomatic actively laboring patients at Community Hospital in Labor and Delivery.
5. Transplant patients who require testing.
6. Symptomatic homeless patients

Saliva testing

- Saliva testing is now available
- Look for saliva COVID test order, if patient location is not in an approved department (pediatrics, Fairgrounds, Suite 1K, etc.), approval will be needed from a member of the COVID team (Can be found in the order).
 - A saliva COVID test can be ordered if:
 - Nasal precautions
 - Anatomic defect
 - Medical contraindication to nasal instrumentation
 - Combative or uncooperative patient
 - Patient refusal

Respiratory Viral Panel (RVP) and COVID Testing:

- RVP and COVID test are linked
- Given the risk of co-infection, symptomatic patients should be for all respiratory pathogens via the RVP.

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.⁴²
- The test's performance in clinical setting is currently unknown.
- 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.^{43,44}

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.⁴⁵
- 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. ⁴⁵

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.

DOCUMENTATION AND EPIC

- COVID-19 specific smartphrases have been created on EPIC for appropriate documentation.
- To look up these smartphrases go to
 - o Personalize > Smartphrase manager > User phrases > User: PANDA, SANCHIT [00119762] > Sharing > + Add me

COVID-19 Smartphrases

- .COVID19HPI - H&P template
- .COVID19PROGRESS - Progress note template
- .COVID19VIRTUALVISIT - Virtual visit note for telehealth services
- .COVID19ATTESTATION - Attending attestation for patient
- .COVID19DCATTEST - Attending attestation for discharge summary
- .APNICPROTOCOL – Document relevant details as per APNIC protocol prior to and then 2 hours after initiating proning protocol.

Discharge instructions

.COVIDSELFQUARNOTICE – Notice for self-quarantine
.COVIDPLASMAPROJECT – Plasma donations after discharge

- COVID-19 specific discharge instructions are also available for lookup on Discharge instructions > Insert smart-text tab > Search COVID
- For COVID specific order sets
- In EPIC hyperspace, manage orders:
 - o For inpatient admissions, utilize the **Adult COVID Admission IP (UMU)** order set
 - o For ordering routine and non-routine labs use **Labs for COVID Inpatient** order panel

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.
- COVID-positive patients (and rule-outs) should be admitted to **INPATIENT** status.

Patient groups based on COVID test results

Confirmed COVID-19 -

- All patients with confirmed COVID-19 infection should be placed on Enhanced airborne precautions.

COVID Rule-out –

- Patients with high suspicion of COVID based on clinical presentation but testing negative.
- Rule out patients should be placed on Enhanced airborne precautions for 10 days since onset of symptoms.

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

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.

As per WHO⁴⁶

Admission criteria for COVID positive patients (any two):

- Respiratory Rate > 24 breaths/min
 - Heart Rate > 125 beats/min
 - SpO2 \leq 94% on ambient air
 - Dyspnea (Clinically defined as the inability to speak in full sentences)
 - Sepsis
 - Suspicion of ARDS (Consider MICU Evaluation)
 - Suspicion of Acute coronary event, Stroke, or thrombotic phenomenon
 - Historical RF - Age > 65, Active cancer (especially hematologic, lung cancer and metastatic disease), History of transplant or other immunosuppression, use of biologic agents, uncontrolled HIV
- COVID-19 patients with mild symptoms should not be admitted solely based on abnormal investigational findings.

Order sets and lab panels:

In EPIC hyperspace, manage orders:

- For inpatient admissions, utilize the **Adult COVID Admission IP (UMU)** order set
- For ordering routine and non-routine labs use **Labs for COVID Inpatient** order panel

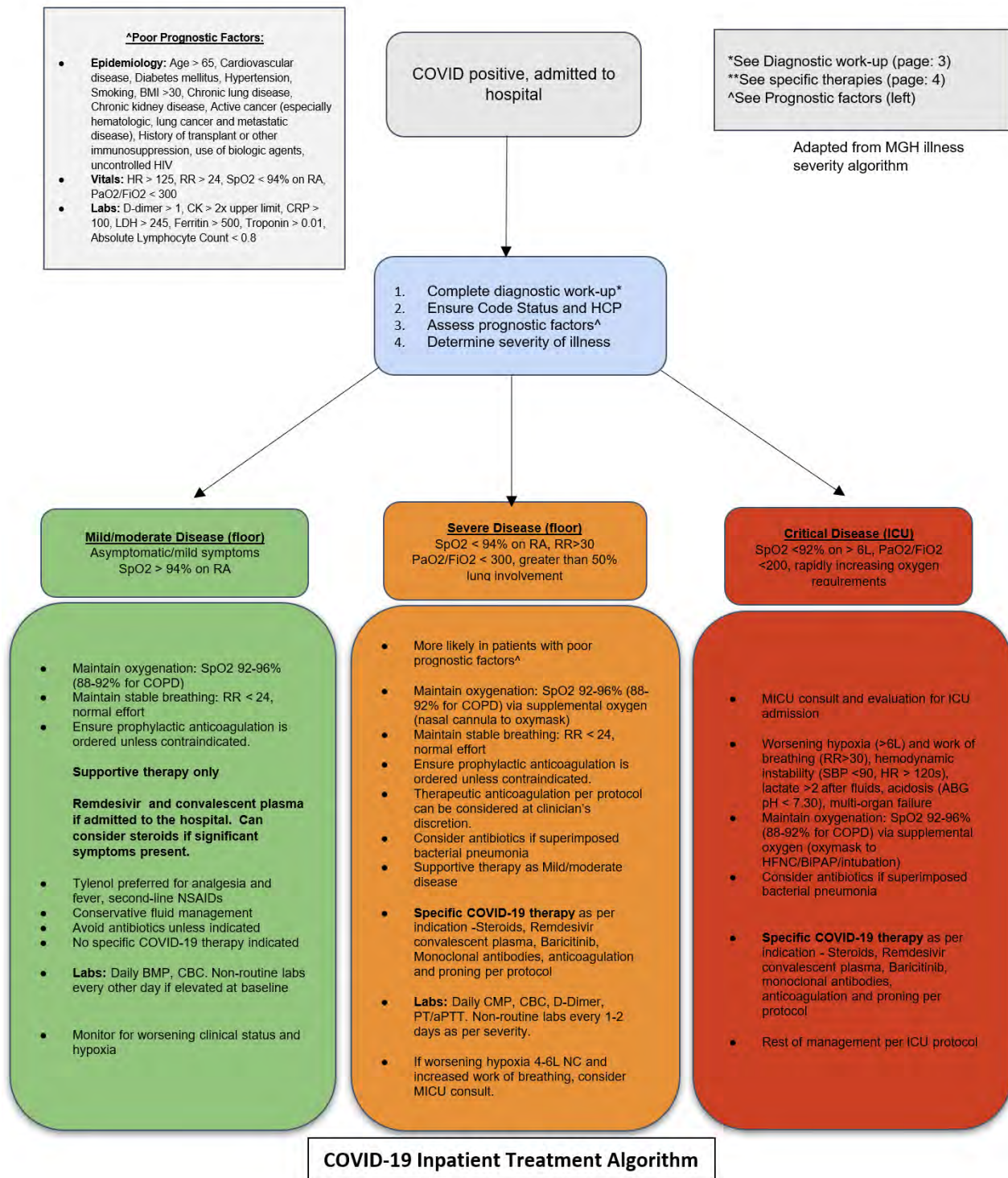
Code status/ Advanced directives/ MOLST/ Health care proxy:

- 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 based on 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).
- See policy COV D-04 (**Appendix 6**) for discontinuation of Isolation precautions for COVID

COVID-19 Inpatient Treatment Algorithm



DIAGNOSTIC WORKUP

- Diagnostic workups include evaluation for signs of a multi organ failure.⁴⁷
- Although the full relevance of every test is not known now, abnormal values might work as a heralding sign for systemic damage.

LABORATORY TESTING:

On admission (Routine): ^{48,49}

CBC with diff, BMP, Mg, Phos, LFTs, D-Dimer, LDH, CRP, PT/PTT, Fibrinogen, Ferritin, Troponin, CPK, proBNP, Procalcitonin, EKG

If LFTs elevated: Acute hepatitis panel, HCV antibody, and HIV Ab/Ag

If AKI present: UA and urine protein: Cr ratio

Women of childbearing age: B-HCG

Consider blood cultures if suspecting bacteremia

Follow up labs:

Routine

CBC with diff, BMP, Mg, Phos (D-Dimer, PT/PTT if severe disease)

Non-Routine :

Consider every 1-2 days if elevated at baseline or depending on clinical severity

LFTs, D-Dimer, LDH, CRP, PT/PTT, Fibrinogen, Ferritin, Troponin, CPK, Procalcitonin

If clinically worsening:

Fibrinogen, LDH, Troponin, EKG, ABG

CRP, Ferritin, D-dimer if rising LFTs and hypotension with concern for cytokine storm

For ordering labs utilize [Labs for COVID Inpatient order panel](#) in Manage orders.

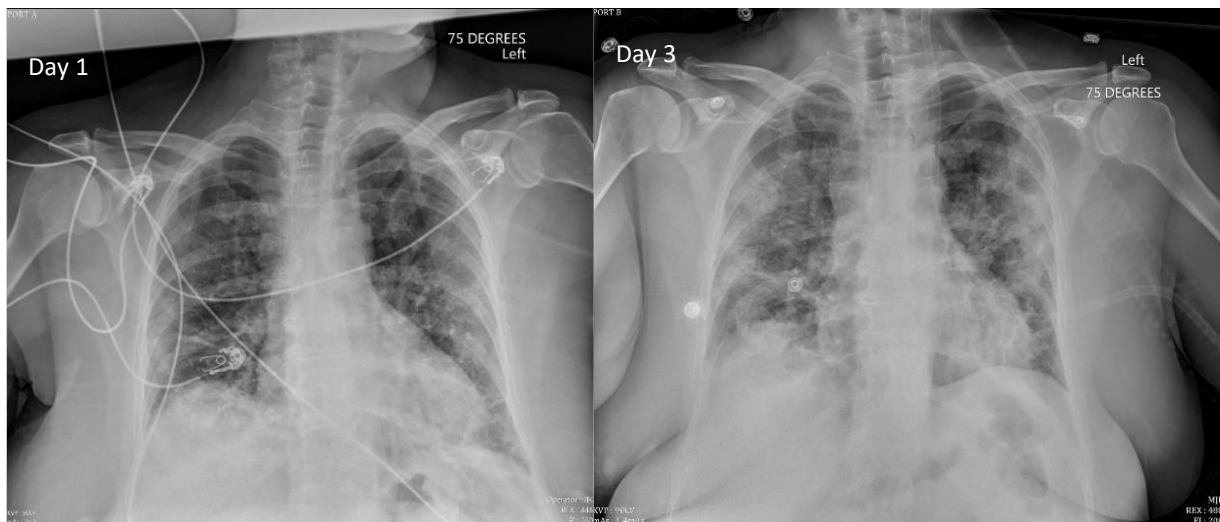
IMAGING:

The Center for Disease Control (CDC) and American College of Radiology (ACR) do NOT recommend radiography or CT to diagnose COVID-19.⁵⁰

Chest X-Ray:

- Initial workup should include a chest radiograph. It is imperative for clinicians to remember that a negative chest radiograph does not preclude the presence of COVID-19, as it is relatively insensitive during the early phases of the disease.
- Portable CXR is the preferred modality for tracking disease process (including evolution of ARDS) in confirmed COVID-19.
- Findings: 20% normal, expect consolidation or bilateral ground glass opacities in lower lung fields⁵¹
- The power of radiography arises from its portability and the rapid evolution of findings over a short period of time, as illustrated by the following case:

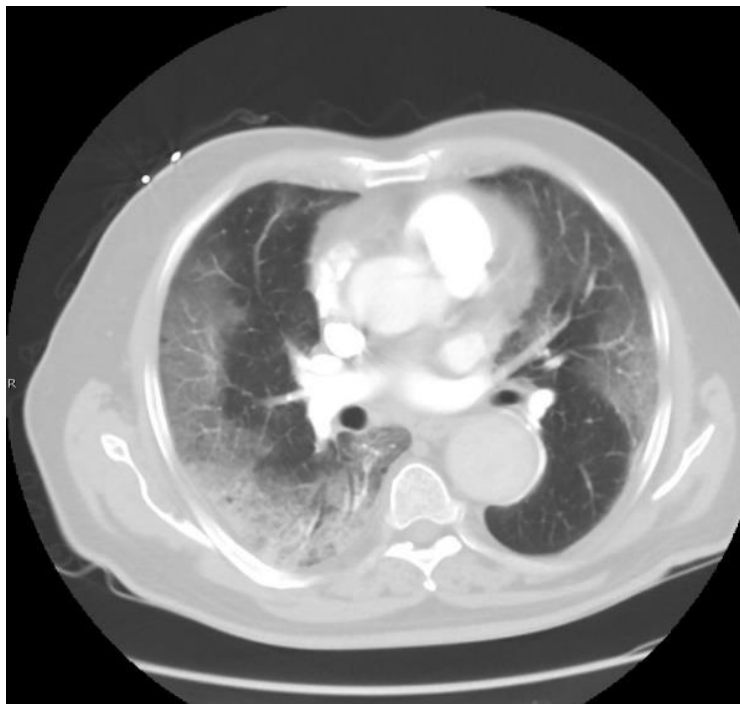
Imaging Case 1: A 63-year-old female presented with shortness of breath and cough. She tested positive for COVID-19 1 week prior to admission. Side by side comparison using similar portable AP semi-erect view shows worsening of predominantly peripheral bilateral patchy and hazy opacities. There are no pleural effusions. Image on Left is Day 1 of admission, Image on right is Day 3 of admission.



Contrast enhanced or Non-contrast chest CT:

- Clinicians should consider CT imaging of the thorax for evaluation of COVID patients; however, it should NOT be the first study ordered, and it should not be used for screening nor the basis of diagnosis.⁵⁰
- Majority of cases involving infections of the lower respiratory tract, such as COVID-19 or Influenza, should be evaluated with a CT Thorax WITHOUT Contrast.
- According to the ACR Appropriateness Criteria, intravenous contrast administration should only be considered if a clinician is evaluating a patient with known COVID-19 for a pulmonary embolism, evolving pneumonia, a parapneumonic effusion or collection/abscess, or patients who suffer from asthma or COPD.⁵²
- The most common findings on CT, as demonstrated by Salehi et. Al⁵³, include:
 - Ground glass opacities (88%)
 - Bilateral involvement (88%)
 - Posterior distribution (80%)
 - Peripheral distribution (76%)
 - “Consolidation” (32%)

Imaging Case 2: 74-year-old male presented with 39.2C fever, fatigue, tachypnea, and increased oxygen requirement. CTA Thorax demonstrates bilateral peripheral ground glass opacities, with a more confluent opacity in the right lung base.



Progression of Pulmonary findings on CT⁵⁴

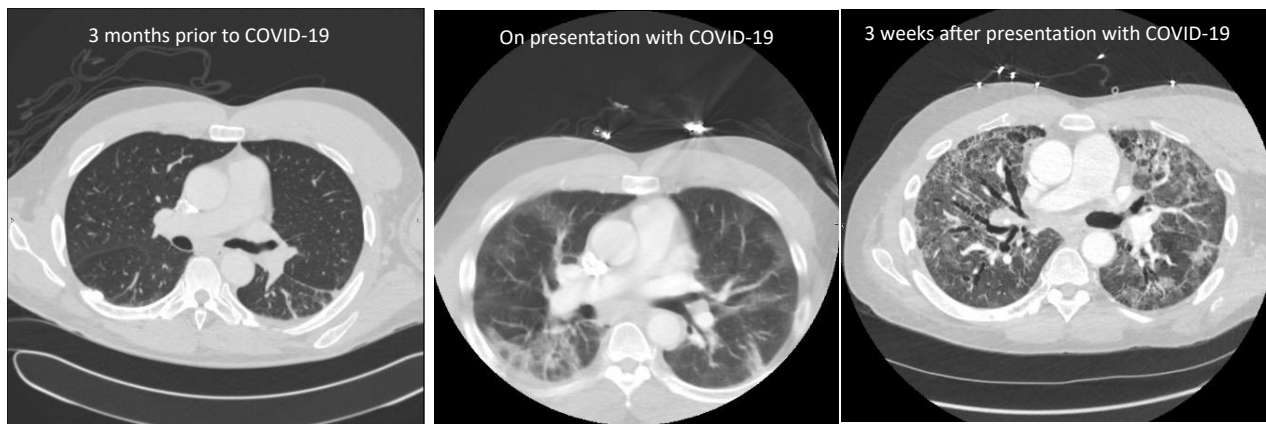
Early Phase (0-4 days): ground glass opacities

Progressive Phase (5-8 days): increased ground glass opacities, dilated vessels

Peak stage (10-13 days): Consolidation, crazy paving pattern, traction bronchiectasis

Absorption stage (>14 days): gradual resolution

Imaging Case 3: 57-year-old male presented for cough, shortness of breath and fever. On presentation, he was tachypneic (RR 26-29) and hypoxic (O2 sat 83-86 on room air). CT imaging shows radiographic changes before, at and after presentation. Traction bronchiectasis and crazy paving pattern are present 3 weeks after presentation. These findings raise concern for permanent chronic fibrosis secondary to COVID infection.



Transthoracic echocardiogram:

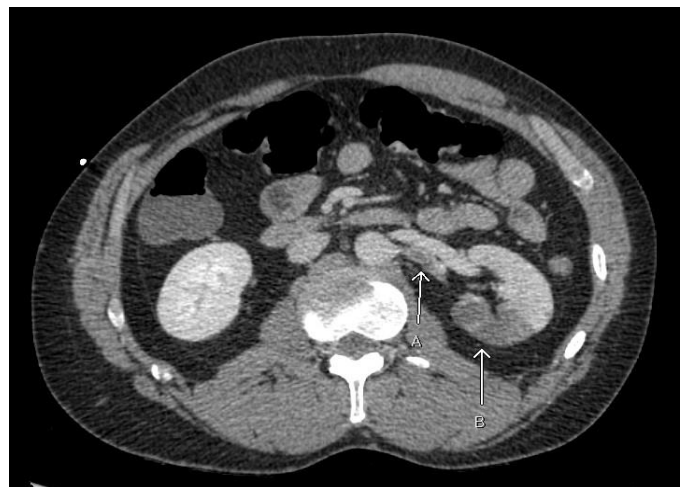
- Obtain if markedly elevated troponin (>5x ULN), shock, new heart failure, or arrhythmia. Avoid routine TTE.

Extrapulmonary Manifestations of COVID-19

Although COVID-19 is principally a respiratory illness, the infection is not limited to the respiratory system. Renal dysfunction, gastrointestinal complications, liver dysfunction, cardiac manifestations, mediastinal findings, neurological abnormalities, and hematological manifestations are among the reported extrapulmonary features.⁵⁵

Imaging Case 4: (Left) 41-year-old male with no known significant past medical history was under ICU care for hypoxic respiratory failure with ARDS secondary to COVID-19. CT head without contrast demonstrates a right PCA territory infarct, scattered embolic hemorrhages at the grey-white matter junction, a large left frontal hemorrhage, and diffuse cerebral edema.

Imaging Case 5: (Right) 29-year-old male COVID-19 positive patient presented for left lower quadrant pain. CT Abdomen with IV contrast demonstrates a filling defect in the left renal artery (label A), and segmental hypoattenuation of the left lower pole (label B) representing a renal infarct.



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.

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).

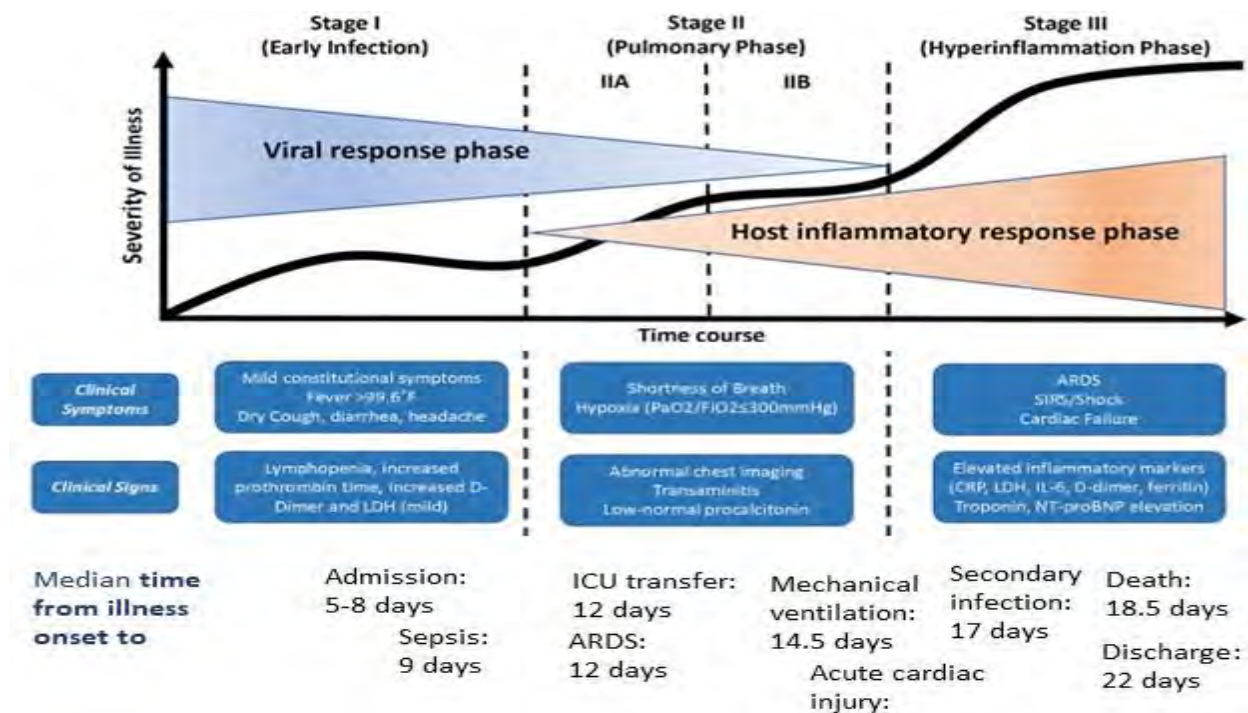
CLINICAL COURSE

TIMELINE

- Time from exposure to first symptoms (**incubation**): 4-14 days⁵⁷⁻⁵⁹
- Median **time from illness onset to**:⁶⁰
 - 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)
 - 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%



- Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: A clinical–therapeutic staging proposal. *The Journal of Heart and Lung Transplantation*. 2020;39(5):405-407. doi:[10.1016/j.healun.2020.03.012](https://doi.org/10.1016/j.healun.2020.03.012)⁵⁷

MANIFESTATIONS

- COVID-19 is primarily a respiratory illness, however patients with COVID-19 infection often have signs and symptoms of systemic involvement at varying rates.
- For a systematic discussion, the manifestations are elaborated further depending on the organ systems involved.

PULMONARY MANIFESTATIONS

- 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.
- 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
- Histologically, bilateral diffuse alveolar damage with cellular fibromyxoid exudates, desquamating pneumocytes, pulmonary edema, and hyaline membrane formation may be seen.⁴⁹
- 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.
- Detailed evaluation and management of pulmonary conditions can be found in the ICU supplement.

Pulmonary fibrosis

- Pulmonary fibrosis is a permanent lung condition that develops after lung tissue sustains significant damage and scarring.

- Survivors of COVID-19 have shown evidence of pulmonary fibrosis, several mechanisms have been proposed for the same although the degree and frequency of long-term sequelae are still unknown. ⁶³
- A retrospective study done at Zhongnan Hospital of Wuhan University that involved 32 patients who were admitted with COVID-19 pneumonitis between January to February 2020 and underwent CT chest on admission and after discharge. Fourteen patients developed pulmonary fibrosis. Fibrosis was more likely to develop in patients with severe clinical conditions, especially in patients with elevated inflammatory markers like CRP and IL-6. ⁶⁴
- Adverse risk factors that place patients at high risk of development of pulmonary fibrosis include advanced age, illness severity, length of ICU stay and mechanical ventilation, smoking, and chronic alcoholism. ⁶⁵
- There are no proven effective therapies for pulmonary fibrosis, and it has a potential to be a continuing chronic health problem in the future.
- To minimize risk of pulmonary fibrosis in survivors, clinicians must attempt to limit illness severity and protect the lung from other incidental injuries. ⁶⁵

CARDIAC MANIFESTATIONS

- Acute myocardial injury, acute coronary syndromes, heart failure, cardiogenic shock, and cardiac arrhythmias including sudden cardiac arrest have been recognized as cardiac manifestations of COVID-19 infection.
- "Myocardial injury" encompasses all conditions causing cardiomyocyte death and is identified by the presence of at least one cardiac troponin value above the 99th percentile upper reference limit^{60,66}
- Incidence of acute cardiac injury is variable among hospitalized patients with COVID-19, with reported frequencies of 7 to 22 percent.^{66,67} It is associated with higher rates of ICU admission and mortality.⁶⁰

Evaluation

- A baseline EKG is generally performed in all patients
- For elevated troponin levels (>2 times ULN), obtain repeat troponin in 24 hours. Echo is not required unless otherwise indicated for unexplained hypotension.
- For marked elevation in troponin (>5 times ULN), rising troponins, hemodynamic compromise, new arrhythmia, EKG changes, or new onset CHF, obtain a TTE.
- Consult Cardiology for ACS, myocarditis, cardiogenic shock, new reduction in LVEF, new onset CHF, or unstable arrhythmia.

Management

- The optimal management for myocardial injury associated with COVID-19 has not been determined. Management currently involves supportive care, diuretics for heart failure, therapy for arrhythmias, and avoidance of cardiotoxins.

Pericarditis and Myocarditis

- Multiple case reports have identified myocarditis and pericarditis as a source of acute cardiac injury in COVID -19 infection.^{68–70}
- Clinical presentation varies from mild symptoms (fatigue, dyspnea) to chest pain. Patients may even develop acute-onset heart failure with cardiogenic shock.^{68,70}
- ECG may show diffuse ST elevations and PR depression, a new bundle branch block, QT prolongation, premature ventricular complexes, or advanced AV nodal block.
- Evaluation for myocarditis in patients with COVID-19 by endomyocardial biopsy (with or without prior cardiac MRI) may be appropriate only in a few cases.⁷¹
- Supportive treatment and antiviral treatment are the mainstay of therapy.

Acute Coronary Syndrome

- There is no current available data on the incidence of ACS in COVID.
- If the clinical presentation is suggestive of ACS, timely evaluation is required to determine if urgent intervention is indicated.
- In patients with known or suspected COVID-19, the diagnosis and management of ACS is similar to those without COVID -19, including aspirin, clopidogrel, heparin, statin, nitrates (if hypertensive), and opioids (if persistent pain). Beta blockers should be used with caution in those with myocarditis/ decompensated heart failure.⁷²
- Cardiology should be consulted to determine if PCI is required.

GASTROINTESTINAL MANIFESTATIONS

- Up to 61% of patients hospitalized with COVID-19 reported having at least one GI symptom.⁷³
- The most commonly reported symptoms were loss of appetite and diarrhea, followed by nausea, vomiting, and abdominal pain.^{74,75}
- Other COVID-19 related symptoms are also present, but in some patients, GI symptoms may precede the development of other symptoms.⁷⁶
- Isolated GI symptoms as the only manifestation of COVID-19 is uncommon.
- The diarrheal symptoms are mild and self-limiting. (>3 loose stools per day, lasting 1-9 days in duration).⁷⁷

Evaluation

- Test for COVID-19 in the following patients:
 - o Hospitalized patients with new onset of GI symptoms.
 - o Patients with established GI disease (e.g. Crohn's) with symptoms suggestive of a disease flare (e.g. diarrhea, vomiting).⁷⁸
- In patients with diarrhea, stool testing to exclude *C. diff* should be obtained.⁷⁷
- For patients with known or suspicion for IBD who are also at risk for COVID-19, additional evaluation should include fecal calprotectin and lactoferrin.⁷⁹
- Depending on the severity of symptoms, further laboratory and imaging studies may be indicated in case of complications such as bowel ischemia.

Management

- GI manifestations in COVID-19 are generally mild and self-limited.⁷⁷
- Supportive treatment with anti-diarrheals, anti-emetics, and hydration.

Bowel Ischemia

- Bowel ischemia in COVID-19 is rare but has emerged in critically ill patients.
- In a study of 184 patients with ARDS at a single academic hospital, nearly half of patients with COVID-related ARDS developed ileus (48% vs. 22% in patients with non-COVID ARDS).
- 4 patients had ileus that progressed to bowel ischemia, and 3 of them required emergent surgical intervention.⁸⁰

- Intraoperative findings of these patients suggest microvascular thrombi and contain distinct necrotic features. Further studies are warranted to examine the pathophysiology of these findings.⁸¹
- Metabolic disturbances, higher opioid requirements, and/or COVID-induced coagulopathy may also explain the higher rates of ileus and bowel ischemia.^{7,8}
- Clinicians should keep a high index of suspicion for GI symptoms warranting surgical consultation in critically ill patients with COVID-19 ARDS.

Hepatic Injury

- Elevated serum liver biochemistries have been reported in 14 to 83 percent of hospitalized patients with COVID-19.⁸²⁻⁸⁷
 - o Abnormal LFTs may be associated with more severe infection.
 - o AST and ALT are elevated 1-2 times the upper limit of normal (ULN), may be greater in more severe disease (but still <5 times ULN), a pattern of AST > ALT is associated with greater mortality.
 - o Bilirubin or ALP may or may not be elevated
 - o Severe liver injury appears to be rare
 - o Hypoalbuminemia is associated with severe COVID-19 infection
- Liver histology is nonspecific, ranging from moderate microvesicular steatosis to focal necrosis.
- Injury may be virally mediated or due to secondary effects of COVID-19 (SIRS, cytokine storm, ischemic hepatitis/shock, sepsis, drug hepatotoxicity)⁸⁷

Management

- Liver injury is most often mild and self-resolving. No specific therapy is typically needed.
- Abnormal levels of serum liver biochemistries are not a contraindication for COVID-19 drug treatments (Remdesivir, Tocilizumab, statins), unless values are greater than 5 times the upper limit of normal.⁸⁸
- Consider non-COVID etiologies, such as hepatitis A, B, C, and drug-induced liver injury.⁸⁹
- If liver function worsens, evaluate other causes such as myositis, ischemia, cytokine storm.
- Imaging is generally not necessary unless there is concern for biliary obstruction, cholangitis, or venous thrombosis.
- Consult hepatology for LFTs >5 times the ULN.⁸⁸

NEUROLOGIC MANIFESTATIONS

Approximately $\frac{1}{3}$ of hospitalized patients with COVID-19 have at least one neurologic complication, most common of which are myalgias, headache, and encephalopathy.^{90,91}

Pathophysiology

Hypothesized mechanisms include:

Neurologic injury from systemic dysfunction:

- Hypoxemia due to COVID-19 could lead to acute hypoxic ischemic damage. Neuroimaging findings of leukoencephalopathy and cerebral microbleeds were found in some patients with severe COVID infections. These imaging findings are associated with increased mortality and worse functional outcomes.^{92,93}

Immune dysfunction:

- Proinflammatory state with COVID-19 can cause a cytokine release-like presentation with fever, elevated inflammatory markers (D-dimer, ferritin) and cytokines (e.g. TNF-alpha, IL-6). Confusion and altered consciousness can be caused by high levels of circulating proinflammatory cytokines. A proinflammatory state in severe COVID-19 and complement activation leading to thrombotic microvascular injury can increase risk of stroke and other thrombosis.⁹⁴

Renin-angiotensin system dysfunction: ACE2 converts angiotensin II to angiotensin-(1-7), a protein with vasodilatory, antiproliferative, and antifibrotic properties.^{95,96}

Anosmia

- Altered taste and smell are frequently reported in COVID-19 infections and often precede the diagnosis, occurring in more than 80% of patients in one series of 417 patients with mild-to-moderate COVID-19 infection.⁹⁷
- It spontaneously improved without further intervention within days to weeks of recovery from illness.
- Median time to recover is between 7 days and 3 weeks.

Encephalitis and myelitis

- Typically seen in critically ill COVID-19 patients, occurring in approx. $\frac{2}{3}$ of a sample of 58 patients with COVID-19 related ARDS.⁹⁸
- Encephalopathy is a risk factor for poor outcomes.⁹⁶

- Presentation: Delirium and agitation, or somnolence and decreased level of consciousness. Hyperreflexia and extensor plantar responses (corticospinal tract signs) are common. Seizures can also occur.
- Changes on MRI are noted in 37%-62% of COVID-19 patients.⁹⁶
- Direct CNS involvement could be evidenced by SARS-CoV-2 in CSF by RT-PCR, but is often negative.⁹⁹
- Management: Consult neurology, follow the general approach to encephalitis
- If focal/lateralizing neurologic signs, evaluate with neuroimaging
- Glucocorticoids currently do not have an established role in the management of COVID-19 related encephalopathy.
- Case reports suggest autoimmune meningoencephalitis shows improvement with plasmapheresis.

Stroke

- It is recommended to test all patients with acute stroke or intracranial hemorrhage for COVID-19 infection.
- Covid-19 patients have an increased risk of prothrombotic disorders including stroke likely due to ACE2 depletion leading to endothelial damage, systemic inflammatory effects and a hypercoagulable state (as evidenced by significantly elevated D-dimer), along with the usual risk factors (e.g. old age, vascular risk factors).⁹⁶
- The incidence of stroke is typically 1-3 weeks after onset of COVID-19 symptoms.⁹⁶
- Presentation: Ischemic stroke may present with non-focal deficits (e.g. encephalopathy) and involve multiple vascular territories.⁹⁶
- Workup and management: CT chest, CTA head and neck should be ordered.
- If tPA (alteplase) is required, D-dimer levels will be elevated for 24 hours and should not be used for prognostication purposes.¹⁰⁰
- Providers can consider therapeutic anticoagulation as with any other stroke patient
- Ischemic stroke patients should be evaluated for mechanical thrombectomy.
- COVID-19 infection is not a contraindication to ACEI/ARB treatment continuation as adverse effects of these medications have not been seen in observational studies.⁹⁶

Headache

- Headaches in COVID-19 patients are associated with its systemic infection or are related to a previous history of headaches

- Once other causes are ruled out such as subarachnoid hemorrhage, and encephalitis, patients can be treated with acetaminophen or NSAIDs, antidopaminergics or antihistamines can be used if needed
- If the patient appears dehydrated, fluids can be used with caution as COVID-19 patients with lung injury are often sensitive to excessive fluid volume.

Altered Mental Status (AMS)

- Altered mental status in COVID-19 patients is commonly associated with systemic infection, metabolic derangements, medication side effects causing psychosis, or stroke
- Metabolic derangements associated with encephalopathy
- hypoxemia or hypercarbia due to respiratory distress
- renal and hepatic involvement
- nutritional deficiencies due to poor oral intake
- Other commonly associated hospital acquired infections should be considered.
- Imaging to be considered: MRI brain to diagnose structural abnormalities, lumbar puncture in patients with signs of worsening headache and meningeal involvement.
- Routine EEG can be deferred if possible until COVID-19 precautions are removed

Neuromuscular disorders

Guillain- Barre syndrome (GBS)

- GBS is an autoimmune disorder of the peripheral nervous system. Consider GBS in patients with progressive ascending muscle weakness or if chest imaging findings do not correlate with respiratory insufficiency.
- It is relatively uncommon; incidence was 0.4% in one study of 1200 patients admitted with COVID-19 in three Italian hospitals.¹⁰¹
- Onset is usually between 3-10 days of initial symptoms of COVID-19.
- Presentation: Progressive ascending muscular weakness developing over 1-4 days, with decreased deep tendon reflexes, paresthesias, dysautonomia, and cranial nerve involvement.
- Respiratory insufficiency due to GBS will manifest as hypercarbia initially prior to hypoxemia
- Diagnose with lumbar puncture and sending CSF for covid-19 PCR, although Covid-19 PCR can be false-negative.⁹⁶

- Management: Plasmapheresis or IVIG, but use IVIG with caution due to a hypercoagulable state in severe COVID-19 infection and increased risk of thrombosis.⁹⁶
- Respiratory failure in GBS is a clinical emergency and can occur quickly, high degree of vigilance is required in any patient suspected of having GBS.

Myasthenia gravis (MG)

- MG patients on lymphocyte or B-cell depleting immunosuppressive medications (rituximab, cladribine, alemtuzumab, ocrelizumab) are thought to be at a higher risk of contracting severe COVID-19 infection, and consider holding these medications in the setting of COVID-19.¹⁰²
- Avoid investigative therapies that could cause an MG flare such as chloroquine, hydroxychloroquine and azithromycin.¹⁰³
- Adjust steroid dosages, can consider increasing in MG flare.
- Can hold IVIG therapy during active COVID-19 infection given a hypercoagulable state and risk of thrombotic complications.¹⁰⁴

Other neuromuscular manifestations

- ICU acquired weakness is seen in 25-46% of ICU patients.
- Prone ventilation is associated with brachial plexopathy and intubation is associated with hypoglossal and vagal nerve injuries (Tapia syndrome).¹⁰⁵
- Mild CK elevation is seen in COVID-19 patients, with up to 10% of patients developing rhabdomyolysis and acute kidney failure.
- If renal function is normal, CK usually trends down in 3-5 days.
- Rhabdomyolysis: It carries a risk of AKI. Correct electrolyte disturbances. Remove any offending medication contributing to it. (Statins, Lopinavir)

NEPHROLOGIC MANIFESTATIONS

- Renal manifestations of COVID-19 present usually with an AKI, proteinuria or hematuria.¹⁰⁶
- It has not been clearly established if the renal disturbances are secondary to hemodynamic changes, cytokine release or due to direct toxicity from the virus.

Acute Kidney Injury

- Studies of patients with COVID-19 have shown that presence of AKI is associated with increased morbidity and mortality.^{32,61}
- In a post-mortem analysis of patients with COVID-19, acute kidney injury was present in 94% of patients. Among those, 62% had acute tubular necrosis as predominant finding.¹⁰⁷
- Possible mechanisms causing renal disturbance by COVID 19 include volume depletion caused by fever or decreased oral intake. Other etiologies include sepsis caused by COVID-19 and hypoxia, causing injury to the kidneys.¹⁰⁸
- Other possible etiologies to consider include volume depletion, contrast-associated nephropathy, interstitial nephritis, and obstruction.

Evaluation

- Monitor BMP and electrolytes daily
- Order urine electrolytes (sodium, creatinine, and urea) and urinalysis with sediment
- Obtain renal ultrasound

Management

- Optimize volume status to avoid hypervolemia.
- Avoid nephrotoxic medications and iodinated contrast with CT imaging as much as possible.
- Indications for RRT for AKI remain the same regardless of COVID-19 status.
- Consider Nephrology consult if:
 - o CrCl < 30 ml/min
 - o Oliguria: UOP < 500 cc/day or 0.5 cc/kg/hour
 - o Volume overload despite diuresis
 - o Hyperkalemia >5.5
- COVID-19 patients should be dialyzed in isolation rooms.¹⁰⁹ CRRT machines, if available, are preferred over hemodialysis as hemodialysis requires 1:1 nursing support and it is essential to limit contact with COVID-19 positive patients.¹¹⁰

- When available hemodialysis or CRRT machines are in short supply, clinicians may need to consider peritoneal dialysis as an emergent treatment for AKI.

Collapsing glomerulopathy

- Collapsing glomerulopathy (CG) is defined by glomerular capillary collapse with hypertrophy and hyperplasia of the overlying epithelial cells has been increasingly identified in patients with COVID-19.¹¹¹
- CG can present with severe acute kidney injury, proteinuria, and hypoalbuminemia. There are some cases in which the kidney insult was clinically apparent up to 1 week after recovery from the respiratory symptoms. It appears that kidney and lung involvement are two separate, nonrelated insults.¹¹²
- CG appears to be, in most cases, progressive and nonreversible¹¹³. Its pathogenesis is unknown, current theories suggest a multifactorial etiology involving genetic predisposition, direct action of the virus, and the cytokine storm.¹¹²
- Of special importance is the APOL1 genotype, seen in up to 10%-15% of African Americans.^{114,115} It has been hypothesized that COVID-19 infection acts as a second hit by up regulating its expression leading to CG.^{112,113} However more studies are required to determine the association between African American ethnicity, APOL1 gene, and the risk for CG development secondary to COVID-19.
- We do not know the specific prognosis for COVID-19 induced CG. Studies from the pre-COVID era on GC have reported that most patients develop end stage renal disease for an average of 13 months after the kidney biopsy.¹¹⁶

Hyponatremia and COVID-19

- Multiple underlying pathophysiologic mechanisms are likely for hyponatremia associated with COVID-19.
- These include syndrome of inappropriate antidiuretic hormone secretion (SIADH), gastrointestinal loss, reduced sodium intake or diuretic therapy.¹¹⁷
- COVID-19 related SIADH has been reported with and without the presence of respiratory symptoms.^{118,119}
- Serum osmolality, Urine osmolality and Urine sodium should be obtained for further evaluation.

HEMATOLOGIC MANIFESTATIONS

Thromboembolic complications

- The thrombotic complications in COVID-19 disease have been hypothesized to be multifactorial, with factors working in sync, very similar to the Virchow's triad.

Direct Endothelial Injury

- In addition to direct endothelial injury by SARS-Cov-2 virus, microvascular inflammation, endothelial exocytosis, and endothelitis play a role in the pathogenesis of acute respiratory distress syndrome and organ failure in patients with severe COVID-19.
- It has also been postulated that neutrophil extracellular traps (NETs), a form of decondensed chromatin released by dead or dying neutrophils, play a role in the prothrombotic state seen very commonly in COVID patients.
- An in-vitro study found that SARS-CoV-2 spike protein can activate the alternative complement pathway.¹²⁰

Stasis

- Stasis is a contributory factor in all sick patients, most patients with severe COVID-19 infection have decreased mobility and hospitalization itself increases risk of thrombosis.

Hypercoagulable state

- Several prothrombotic factors have been found in high numbers in patients with COVID infection including factor VIII, fibrinogen, and NETs.
- Some studies performing thromboelastography on ICU patients revealed a complete absence of clot lysis, "fibrinolysis shutdown" which was found to be associated with renal failure and high rate of thromboembolic events.
- Patients infected with SARS-CoV-2 have been found to have a transient antiphospholipid antibody (aPL) positivity due to high levels of Lupus anticoagulant (LA) leading to aPTT elevation.
- Prolonged aPTT due to lupus anticoagulant phenomenon doesn't reflect decreased risk for thrombosis and is not a contraindication for anticoagulation.

Comparison with DIC:

- The hypercoagulable state in COVID has been compared to DIC like illness by some experts as patients meet criteria for probable DIC. Similarities include elevated D-Dimer, mild thrombocytopenia and discrepancies include elevated fibrinogen and factor VIII

(which suggest that coagulation factors are not being actively consumed). Also, major clinical presentation in patients is thrombosis rather than bleeding.

- In acute decompensated DIC, bleeding occurs and in chronic compensated DIC, thrombosis is seen. Hence, hypercoagulability seen in COVID is comparable to chronic compensated DIC.

Clinical features

- There is an increased risk of DVT and PE in patients with COVID, especially in ICU patients despite prophylactic anticoagulation therapy. The risk of arterial thrombosis such as stroke, myocardial ischemia, abdominal and thoracic aortic thrombosis, and limb ischemia is also high. Few case reports have reported mesenteric ischemia.
- In a study involving 3000 individuals, risk of VTE were higher in older, male, Hispanic ethnicity, CAD, prior MI and D-Dimer >500ng/mL on presentation.¹²¹
- The risk of VTE in non-ICU patients is also increased but not as much as in ICU patients.
- Data on thromboembolic events in outpatients is limited, however, the incidence seems to be very low despite inconsistent anticoagulation use.

Evaluation:

- Patient work up and response to abnormal labs is challenging as many of them are acute phase reactants which are usually elevated in acutely ill patients

Inpatients:

- CBC, PT, aPTT, fibrinogen, D-Dimer
- Repeat testing can be performed as per acuity of illness, initial labs, and trend.
- Routine screening for DVT in patients is not currently indicated, irrespective of coagulation markers.

Outpatients:

- There is no data to support the measurement of coagulation markers (e.g., D-dimers, prothrombin time, platelet count, fibrinogen) outpatient. These coagulation markers at higher levels have been associated with worse outcomes in Covid patients but there is not sufficient evidence that these markers can predict the risk of VTE in those who are asymptomatic or have a mild infection.

Diagnosis of Venous thromboembolism

- Routine use of ultrasound screening and/or biomarkers (i.e., D-dimer) should not be used for detection of asymptomatic DVT.
- For suspected VTE, doppler ultrasound or computed tomography angiogram should be performed.

MANAGEMENT:

Indications for inpatient VTE prophylaxis:

- All patients admitted to the hospital must receive thromboprophylaxis unless contraindicated.
- A retrospective study showed reduced mortality in patients who received prophylactic anticoagulation, particularly if the patient had a sepsis-induced coagulopathy score ≥ 4 .¹²²

Indications for full dose anticoagulation:

- For known or suspected VTE
- For patients on therapeutic anticoagulation prior to admission where agents with a shorter half-life are warranted due to clinical status, (i.e., renal dysfunction, potential procedures, etc.)

Indications for tPA:

- Appropriate for usual indications other than Limb threatening DVT, massive PE, acute stroke/MI.
- tPA should also not be used for non-specific findings such as hypoxia or laboratory evidence of hypercoagulability.

Outpatient thromboprophylaxis:

- Use of VTE prophylaxis after discharge is not suggested
- For patients requiring therapeutic anticoagulation, a DOAC (apixaban, dabigatran, rivaroxaban or edoxaban) should be utilized for 3 months
 - o Initial parenteral anticoagulation is needed before dabigatran and edoxaban

- For patients who are not able to be treated with a DOAC, warfarin should be utilized
- Parenteral anticoagulation needs to be overlapped with vitamin K antagonists
- For patients who required therapeutic anticoagulation prior to admission, the therapeutic agent that was utilized prior to admission should be restarted if not done so during admission unless a change therapy was instituted.
- Other points to note:
 - LMWH is preferred over unfractionated heparin.
 - In case of bleeding, management is similar to non-COVID patients
 - Role of antiplatelet agents is under review. Continued if patient has been on it for other indications.
 - Antifibrinolytic agents, similar to in DIC are not indicated as it may lead to a procoagulant state

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

- COVID-19 infection has been reported to cause hyperinflammatory response in some patients but signs of HLH are not seen commonly.
- Pathogenesis that leads to conversion of these hyper-inflammatory response to HLH is currently unknown but is hypothesized to be multifactorial.
- In vitro studies have suggested that SARS-CoV-2 could activate NLRP3 inflammasomes that are potent activators of macrophages, with a marked release of IL-1 β , which contributes to IL-6 release.¹²³
- Studies have reported molecular docking analysis predicting spontaneous interaction between the spike glycoprotein of SARS-CoV-2 and Toll-like receptors 5 (TLR5) expressed on monocytes and contributing to IL-6 release thorough activation of nuclear factor- κ B activation.¹²⁴
- An early and significant rise in IL-6 levels during Covid infection has been linked with a poor outcome.
- Screening with ferritin and CRP in cases of severe COVID-19 with findings of hyperinflammation can be considered, because CRP is known to be an indirect marker of IL-6 .

- If significant elevation is seen, the diagnosis can be supported by IL-6 levels. There have been case reports documenting good response of patients with severe COVID infection and elevated CRP with Tocilizumab with remarkable reduction in CRP levels.¹²⁵
- Studies are underway analyzing the beneficial effects of Tocilizumab in severe COVID-19 infection.

SECONDARY INFECTIONS AND HIV

- Empiric antibiotic and antifungal treatment should **not** be the standard of care.^{60,126–128}
- For empiric coverage for a presumed pulmonary source of infection:
 - In patients **without** risk factors for MRSA or *Pseudomonas* (*i.e.*, living in community, no prior MDROs), initiate Ceftriaxone and Azithromycin
 - In patients **with** risk factors for MRSA or *Pseudomonas* (*i.e.*, chronic hospitalization, prior MDR infections), obtain a respiratory culture and a MRSA nares screen and initiate Cefepime and Vancomycin. Ciprofloxacin may be considered if there is a high concern for *Pseudomonas aeruginosa*
- Give oral antibiotics when possible to reduce volume load unless there are concerns for poor oral absorption.
- Unnecessary antibiotics should be discontinued as soon as possible (ideally, within 48 hours) upon culture maturation. It is suggested to discontinue empiric antibiotics when the following criteria are met:
 - Clinical status is not deteriorating
 - Cultures do not reveal pathogens at 48 hours and/or procalcitonin and WBC are relatively stable from 0 to 48 hours

COVID-19 and HIV

- Recommendations for the triage, management, and treatment of COVID-19 in patients with HIV are the same as those for the general population.
- In patients with HIV and suspected or documented COVID-19, HIV-associated opportunistic infections (OI) should also be considered in the differential diagnosis of febrile illness.
- When initiating treatment for COVID-19 in a patient with HIV, attention should be given to potential drug-drug interactions and overlapping toxicities among COVID-19 treatments, antiretroviral (ARV) medications, antimicrobial therapies, and other medications.
- HIV patients developing COVID-19, including those requiring hospitalization, should continue their antiretroviral therapy (ART) and OI prophylaxis.
- An ART regimen should not be switched or adjusted to prevent or treat SARS-CoV-2 infection.
- Infectious Diseases should be consulted before adjusting or switching ARV medications while treating COVID-19 in people with HIV

DERMATOLOGIC MANIFESTATIONS

- Incidence ranges from 0.2% to 20.4% of cases¹²⁹
- Average latency of onset from respiratory illness symptoms to cutaneous findings¹³⁰
 - o 1.5 days in children
 - o 7.9 days in adults
- Most common manifestations^{129,130}
 - o Chilblains/pernio-like lesion (18 - 51.5%)
 - o Erythematous maculopapular rashes (13.3%)
 - o Viral exanthem (7.7 - 22%)
 - o Urticaria (16%)
 - o Vesicular eruption (11%)

Perniosis, Pseudo-Chilblains, COVID Toes¹³¹

- Erythematous-violaceous papules over acral surfaces
- Typically, in younger patients and associated with less severe disease
- Proposed mechanism involves strong IFN-1 response, possible virus induced vascular injury
- Treatment includes conservative measures including avoiding cold exposure, wearing socks, smoking cessation.
- It is self-limited and usually resolves in 2-4 weeks. High potency topical steroids can be considered.

Erythematous maculopapular rash¹³⁰⁻¹³²

- Lasts for 2-9 days, associated with more severe disease
- Seen on legs, thighs, forearms, arms, trunk, shoulders
- Histological examination shows superficial lymphocytic infiltrate in combination with dilated vessels in upper and mid dermis
- Consider topical corticosteroid for symptomatic treatment of pruritis

Viral Exanthem (Morbilliform Rash)^{130,132}

- Latency between 2-12 days and symptoms last 4-15 days
- Mostly scattered vesicular lesions on the trunk and on extremities
- Secondary to immune response to viral antigens
- Treat with topical corticosteroids

Urticaria^{131,132}

- Can present before onset of other COVID symptoms

- Hives or wheals, swollen, edematous, erythematous papules or plaques
- Type I hypersensitivity mediated reaction
- Treatment includes oral antihistamines

Vesicular (Varicella Like) Eruptions^{131,132}

- Small monomorphic fluid filled vesicles <1cm on trunk
- Seen in middle age patients
- Self-limited with resolution in 7 days

Livedo Reticularis/Racemosa-like Lesion^{131,132}

- Mottling, net like cyanotic pattern
- Reticularis is symmetric and continuous
- Racemosa is asymmetric and discontinuous
- Due to thrombotic vasculopathy
- Transient symptoms which do not require treatment
- Consider therapeutic anticoagulation for possible ischemia/necrosis

MULTI-SYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

- It is an abnormal immune system reaction to the initial COVID-19 infection that occurs 2-3 days after first being infected with the virus.
- It is a rare complication of COVID-19 seen in young adults and children, Black and Hispanic adolescents have a higher incidence of developing MIS-C.¹³³
- The incidence of MIS-C is 2 in 100,000 cases of patients < age 21 with COVID-19 infection.¹³³
- The exact underlying pathophysiology leading to its development is unknown, presentation can be diverse.

Clinical Presentation ^{134,135}

Fever (4-6 days in 100% of cases)

With

- Respiratory symptoms (tachypnea, sore throat in 21-65% of cases with cough being uncommon)
- Neurologic symptoms (headache, lethargy, confusion in 29-58% of cases with possibly more severe development of seizures, coma, muscle weakness, or brainstem and/or cerebellar signs)
- GI symptoms mimicking appendicitis (abdominal pain, nausea, vomiting, non-bloody diarrhea in 60-100% of cases)

With or without

- Rash (45-76% of cases)
 - Edema involving the soles or palms (9-16% of cases)
 - Lymphadenopathy (9-16% of cases)
 - Mucositis (27-76% of cases)
 - Myalgias (8-17% of cases)
 - Conjunctivitis (30-81% of cases)
 - Shock (32-76% of cases)
 - Arrhythmia (12% of cases)
 - Serositis seen in (24-57% of cases)
- GI symptoms can occur 1-2 weeks prior to the presentation of MIS-C and may be linked to the underlying effects of acute COVID-19 infection
 - Inflammatory markers are elevated even in the presence of mild disease.

- Features are similar to Kawasaki disease; patients remain at a risk of developing coronary artery aneurysms with subsequent cardiac related malfunction.¹³⁵

Laboratory findings

- Generally, negative COVID-19 PCR test & positive serologies, however PCR positive and negative serology can be seen as well
 - Neutrophilia, thrombocytopenia, anemia, lymphopenia seen on complete blood picture
 - Elevated CRP, ESR, Ferritin, D-Dimer, procalcitonin, triglycerides, LFTs
 - ProBNP, Troponin T can be elevated with cardiac involvement
-
- Imaging can reveal presence of bowel involvement with colitis, ileitis, mesenteric adenopathy, ECHO with decreased LV function, pericardial effusion, valvulopathy like mitral valve regurgitation.
 - Major differentiating factor for Kawasaki disease vs MIS-C is based on COVID-19 exposure history along with serology and PCR evaluation
 - Consider hospitalization for patients with unstable hemodynamics or signs of end organ damage
 - In hospitalized patients or severe disease, treat this syndrome such as IVIG, corticosteroids, or high-dose anakinra (IL-1 blockers)¹³⁶

PROGNOSTIC FACTORS

- Studies have shown the association of certain risk factors and a worse outcome with COVID-19. ^{137,138}
- Patients with severe disease and following risk factors are at higher risk of development of ARDS: (Adapted from MGH COVID-19 guidelines)
- Progressive decline in the lymphocyte count and rise in the D-dimer over time were observed in non-survivors compared with more stable levels in survivors. ⁶²

Epidemiology:

Age > 65, Cardiovascular disease, Diabetes mellitus, Hypertension, Smoking, BMI >30, Chronic lung disease, Chronic kidney disease, Active cancer¹³⁹ (especially hematologic, lung cancer and metastatic disease), History of transplant or other immunosuppression, use of biologic agents, uncontrolled HIV

Vitals:

HR > 125, RR > 24, SpO₂ < 94% on RA, PaO₂/FiO₂ < 300

Labs:

D-dimer > 1, CK > 2x upper limit, CRP > 100, LDH > 245, Ferritin > 500, Troponin > 0.01, 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.
- Applicable for all patients admitted for COVID-19 regardless of disease severity.

Early advanced care planning:

- Obtain HCP and discuss code status on admission. Educate the patient and family on disease course and prognosis.
- Do not initiate specific COVID-19 therapies unless the patient meets criteria for administration

Oxygenation:

Goals

- Maintain adequate oxygenation
 - Target SpO₂ 92-96%
 - Target 88-92% 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.
- 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.¹⁴⁰
- Avoid empiric antibiotics unless there is a specific concern for superimposed bacterial pneumonia or 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.¹²⁸

DVT pharmacologic prophylaxis:

- COVID-19 infection places patients at increased risk for thromboembolism.
- Should be prescribed for all hospitalized patients unless contraindicated.
- If there is a concern for increased risk of thrombosis, therapeutic anticoagulation can be considered as per [protocol](#).

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.^{141,142}
- Significantly elevated D-dimers were shown to be associated with the development of ARDS and increased mortality^{143,144}
- Anticoagulant treatment using chemical VTE prophylaxis was found to decrease 28 day mortality in patients with D-dimer > 6x upper limit of normal.¹⁴⁵
- 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.^{94,146,147}
- There is also evidence for preference of LMWH as the primary choice of anticoagulation due to its anti-inflammatory effects.¹⁴⁸

Analgesic and antipyretics

- Acetaminophen first line medication, second line NSAIDs.
- Can be used unless otherwise contraindicated

ACE inhibitor/ARB, Statins

- There is no convincing data supporting discontinuing them, please continue them on admission unless otherwise contraindicated.

SPECIFIC THERAPY

NON-PHARMACOLOGICAL THERAPY

Awake Proning

Awake proning is an effective non-pharmacologic intervention to improve oxygenation/hypoxia in cooperative patients.

It can be combined with simultaneous use of any other non-invasive oxygen supplementation (NC/HFNC/Oxymask)

Ideal candidate – Patient with isolated hypoxemic respiratory failure without substantial dyspnea (the “paradoxically well appearing” hypoxemic patient)

The main risk of awake proning is that it could cause excessive delay in intubation

Criteria for patient selection

- Patient should be able to move independently
- Not have multi-organ failure
- Patient expected to have a reversible lung injury and might avoid intubation
- No hypercapnia (PacO₂ <50) or substantial dyspnea (Respiratory rate <35, not using accessory muscles)
- Normal mental status, able to communicate distress
- No anticipation of difficult airway

Can consider proning patients whose code status reflects DNI (Do Not Intubate).

Can be used as a Stop-gap measure for a hypoxemic patient when intubation is not immediately available (Desaturation during transportation).

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

Patient Monitoring

- EKG leads should remain on the anterior chest wall for continuous monitoring (if clinically indicated)
- SpO2 probe (continuous) should be placed on the patient if not already in use.
- 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. (.APNICPROTOCOL)

Proning protocol can be ordered from EPIC order sets.

For further details refer to [APNIC protocol](#).

PHARMACOLOGICAL THERAPY

- Decision on specific therapy depends on disease severity, risk factors and presence of significant symptoms.

Monoclonal Antibodies

Disease Severity	Bamlaniv imab	Casirivi mab and Imdevim ab	Bamlaniv imab and Etesivim ab ***	Awake proning	Remdesivir	Convalescent Plasma	Dexamethasone or other glucocorticoids	DVT prophylaxis	Therapeutic Anticoagulation	Baricitinib
Outpatient Mild or Moderate	Yes	Yes	Yes	Yes	No	No	No	No	No	No
Inpatient Mild or Moderate	Yes	Currently being evaluated in a Clinical trial	Yes	Yes	Yes (Priority < 6 days of illness and O2 requirement at baseline)	Yes (Likely most effective early)*	Consider (for patients with significant symptoms and baseline O2 requirement)^	Yes	Consider only if High risk	No
Severe	No	No	No	Yes	Yes (most effective early)	Yes (Likely most effective early)*	Yes	Yes	Consider only if High risk	Consider**
Critical	No	No	No	Yes, if feasible	Yes (most effective early)	Yes (Likely most effective early)*	Yes	Yes	Strongly Consider	Consider**

*RCT did not show benefit, but patients were late in course of illness by the time they entered the trial (Li et al JAMA. 3 June 2020)

** Baricitinib combined with Remdesivir was shown to improve outcomes vs Remdesivir alone, particularly for pts on non-invasive mechanical ventilation and those later in the course of illness.

***Not currently available at Upstate, expect availability in the future

^Based on clinical judgement

SPECIFIC THERAPY IN COVID-19

THERAPIES FOR INPATIENT USE

Anticoagulation

- Due to the increased risk of thrombotic events with COVID-19, all patients should receive pharmacologic DVT prophylaxis unless contraindicated.
- Please refer to updated anticoagulation [protocol](#) for reference.
- With clinical trials currently underway (REMAP-CAP, ACTIV-4, ATTACC) new evidence and guidance is expected in the future.

Dexamethasone and other glucocorticoids

Eligible patients

- Has been found to improve survival in hospitalized patients requiring supplemental oxygen, mechanical ventilation, or ECMO. Therefore, the use of dexamethasone is strongly recommended in this setting. ^{149–152}
- NIH does not recommend use of steroids in patients not on supplemental oxygen¹⁵³, however they can be considered if a patient has significant symptoms and baseline oxygen requirement.

Dose

6 mg daily for 10 days or until discharge, whichever is shorter

If Dexamethasone is unavailable, can use other glucocorticoids at equivalent dose
Monitor closely for adverse effects while on steroids

Remdesivir (RDV)

Background

- It is an RNA dependent RNA polymerase inhibitor that inhibits viral replication. RDV should be used as early as possible and best within 7-10 days of onset of symptoms
- 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%. ¹⁵⁴

- 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* ¹⁵⁵ (SpO2 of 94% or lower on room air requiring supplemental oxygen, mechanical ventilation, or ECMO)

Eligible Patients

It can be used in all symptomatic patients requiring supplemental oxygen with COVID-19, however there is insufficient data to recommend for or against it. NIH recommends it may be appropriate to use in patients at high risk of progression to severe disease. ¹⁵³

Dose

200 mg IV on day 1, followed by 100 mg IV for 4 days

Full course of 5 days need not be completed if patient has improved and is stable for discharge.

Adverse effects:

Diarrhea, transaminitis, rash, renal impairment¹⁵⁶

Contraindications: Hypersensitivity to RDV or ALT \geq 10x upper limit of normal

Baricitinib

Background

- It is a JAK-1&2 inhibitor with potential direct antiviral activity through interference with viral endocytosis, potentially preventing entry into and infection of susceptible cells.
- For the treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in certain hospitalized patients requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO), Baricitinib in combination with Remdesivir has received Emergency Use Authorization (EUA) from the FDA on November 19, 2020. ¹⁵⁷
- ACTT-2 trial compared Baricitinib and RDV with RDV and placebo and found improvement in the median time to recovery (7 days to 8 days), proportion of patients who died or progressed to noninvasive ventilation/high-flow oxygen or invasive

mechanical ventilation by Day 29 23% vs 28% and proportion of patients who died by Day 29 was 4.7% vs. 7.1%.¹⁵⁸

- Consider Baricitinib for patients who cannot tolerate steroids but receiving Remdesivir or who were already previously taking the equivalent of a standard steroid dose for COVID when they acquired COVID-19 infection.

Dose

- 4 mg once daily in combination with Remdesivir. Duration of Baricitinib is 14 days or until hospital discharge, whichever is first

Indication

- To be used in combination with Remdesivir in patients with COVID-19 who require oxygen, ventilatory support, or ECMO

Convalescent plasma

- There are insufficient to recommend either for or against the use of COVID-19 convalescent plasma for the treatment of COVID-19 as per NIH.¹⁵³
- Currently not indicated in hospitalized patients outside of clinical trials.

The potential benefits

- Rapid decline and clearance of virus
- Decrease in the cytokine storm seen in acute respiratory distress syndrome associated with severe COVID-19 infection
- Improved morbidity and mortality
- Decrease of time on ventilator with improved oxygenation
- Decrease in total hospitalization days

The potential risks

- Allergic reaction
- Volume overload
- Potential antibody enhancement of the virus

Eligible patients

Can be used in all symptomatic patients with COVID-19 admitted to the hospital

Dose

Treat with 1 unit of convalescent plasma.

Dose can be repeated up to 3 times especially in High risk patients who are symptomatic and <10 days in their illness

High risk patients - Age \geq 65 with any one of the following risk factors or Age <65 with more than one risk factors

Risk Factors - Cardiovascular disease, Diabetes mellitus, Hypertension, Smoking, BMI >30, Chronic lung disease, Chronic kidney disease, Active cancer (especially hematologic, lung cancer and metastatic disease), History of transplant or other immunosuppression, use of biologic agents, uncontrolled HIV

Refer to [APPENDIX – 9](#) for further details. ^{21,159}

THERAPIES FOR OUTPATIENT USE

Monoclonal Antibodies

- Eligible patient should have
 - Mild or moderate symptoms
 - Must be within 10 days of their onset of symptoms or diagnosis, whichever was first
 - Have any of the following risk factors for progression to severe disease¹⁶⁰
 - Body mass index (BMI) ≥ 35 kg/m²
 - Chronic kidney disease
 - Diabetes mellitus
 - Immunosuppression (immunosuppressive disease or treatment)
 - ≥ 65 years of age
 - ≥ 55 years of age and who have cardiovascular disease, and/or hypertension, and/or chronic obstructive pulmonary disease (or other chronic respiratory disease)
- All of the following antibody therapies have received emergency use authorization from the FDA for outpatient use in these patient groups.¹⁶¹
- Mildly symptomatic COVID-19 patients being admitted or currently inpatient should be evaluated for monoclonal antibody therapy if they meet the above criteria.

Casirivimab and Imdevimab (REGN-COV2)

- An antibody cocktail administered together for the treatment of COVID-19 in adults developed to neutralize SARS-CoV-2 by targeting the SARS-CoV-2 spike protein and preventing viral cell entry.

Recommendation

- Available for use in an outpatient setting.
- Not to be used inpatient except in a clinical trial, (Primary investigator – Kristopher Paolino, MD). Please contact ID if a patient is interested in the antibody cocktail to see if they would be eligible candidates.
- Patients receiving convalescent plasma are excluded from the trial.

Bamlanivimab

- A monoclonal antibody to the spike protein of SARS-COV-2 used in the ED for patients early in course and with mild disease.
- Shown in clinical trials to reduce COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo.

Recommendation

- Available for use in an outpatient setting.
- Can be used in inpatients with mild/moderate disease if they meet eligibility criteria.

Bamlanivimab and Etesevimab

- An antibody cocktail administered together for treatment of COVID-19 in adults.
- Being evaluated in BLAZE-1, a randomized, controlled trial including 577 outpatients with mild to moderate illness, comparing different doses of Bamlanivimab monotherapy with combination bamlanivimab-etesevimab therapy with placebo.
- Results of phase 2 trial at one month showed, treatment with bamlanivimab and etesevimab compared with placebo was associated with a statistically significant reduction in SARS-CoV-2 viral load at day 11 (IRR 4.9%, 95% CI -8.9 to -0.8).¹⁶²

Recommendation

- Not currently available for use at Upstate, expected to be available in the future.

THERAPIES WITHOUT CLEAR EVIDENCE OF BENEFIT

IL-6 pathway inhibitors

- Interleukin (IL)-6 is a proinflammatory cytokine. COVID-19-associated systemic inflammation and hypoxic respiratory failure can be associated with heightened cytokine release, as indicated by elevated blood levels of IL-6, and other inflammatory markers and acute phase reactants. It is hypothesized that modulating the levels of IL-6 or its effects may alter the course of the disease.

Recommendation

- Not to use either IL-6 receptor blockers tocilizumab and sarilumab and the direct IL-6 inhibitor siltuximab for the treatment of COVID-19, except in a clinical trial.¹⁶³

Kinase inhibitors

- These have broad immunosuppressive effects. They can prevent phosphorylation of critical proteins involved in the signal transduction that leads to immune activation and inflammation (e.g., the cellular response to proinflammatory cytokines such as interleukin [IL]-6). This immunosuppression could potentially reduce the inflammation and associated immunopathologies that have been observed in patients with COVID-19.

Recommendation

- Not to use except in a clinical trial.

Chloroquine or hydroxychloroquine with or without azithromycin

- Both chloroquine and hydroxychloroquine increase the endosomal pH, inhibiting the fusion of SARS-CoV-2 and the host cell membranes, implicated in blocking the transport of SARS-CoV-2 from early endosomes to endolysosomes, possibly preventing the release of the viral genome, and have immunomodulatory effects. Chloroquine inhibits glycosylation of the cellular angiotensin-converting enzyme 2 receptors, which may interfere with the binding of SARS-CoV to the cell receptor. It has been hypothesized that these effects are other potential mechanisms of action for the treatment of COVID-19.

Recommendation

- Not to use either based on the results of randomized clinical trials.¹⁶⁴

Lopinavir-Ritonavir

- The replication of SARS-CoV-2 depends on the cleavage of polyproteins into an RNA-dependent RNA polymerase and a helicase. Two proteases are responsible for this cleavage: 3-chymotrypsin-like protease (3CLpro) and papain-like protease (PLpro). Lopinavir/ritonavir is an inhibitor of SARS-CoV 3CLpro in vitro, and this protease appears to be highly conserved in SARS-CoV-2

Recommendations:

- Not to use either based on the results of randomized clinical trials.¹⁶⁵

Ivermectin

- Ivermectin has been shown to inhibit the replication of SARS-CoV-2 in cell cultures. It acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host antiviral response.

Recommendations:

- Not to use except as part of clinical trials.

Interferons

- These are a family of cytokines with antiviral properties suggested as a potential treatment for COVID-19 because of their in vitro and in vivo antiviral properties.

Recommendations:

- Not to use except as part of clinical trials.
- Therapeutic options currently being evaluated as potential treatments however with insufficient clinical data supporting current use : Vitamin C, Vitamin D¹⁶⁶, Fluvoxamine, Famotidine, Colchicine, NAC¹⁶⁷, Favipiravir, and Zinc¹⁶⁸.

SPECIAL POPULATIONS

Pregnancy:

Background:

- Based on data and findings thus far, pregnancy does not appear to increase the risk for acquiring COVID-19 infection but does appear to have a higher risk for more severe illness and worse clinical course compared to non-pregnant individuals of the same sex and age.
- Pregnant and non-pregnant individuals from racial and ethnic minority groups have higher rates of COVID-19, associated hospitalizations, and severe in-hospital outcomes. However, most (> 90% infected pregnant patients) recover without undergoing hospitalization or delivery.
- Hospitalization and severe disease in pregnant patients tend to be present in greater proportion in pregnant patients with pre-existing risk factors such as obesity, hypertension, diabetes, etc., similar to non-pregnant patients.^{169–171}
- For updated recommendations in this population, please reference ACOG.org and SMFM.org

Presentation:

- In general, pregnant patients tend to present with similar symptoms to that of the general population, with the most common presenting symptoms: cough, headache, myalgias, fever, sore throat, dyspnea, and anosmia/ageusia.
- Other common symptoms include nausea, vomiting, fatigue, diarrhea, rhinorrhea.
- Pregnant patients may also present asymptotically.

- Laboratory findings on presentation are also similar to non-pregnant populations with common findings that include lymphopenia, leukocytosis, elevated procalcitonin level, abnormal liver chemistries, and thrombocytopenia.

- In general, laboratory and imaging findings are similar to those in non-pregnant persons. However, important considerations must be made when interpreting abnormal laboratory findings as leukocytosis can be normal in pregnancy and other laboratory findings overlap with those caused by pregnancy-related disorders such as pre-eclampsia and HELLP syndrome.

- In addition, avoiding radiographic studies which would not otherwise change clinical management is recommended to reduce fetal radiation dosing.

General Management:

- Decision to hospitalize pregnant patients who test positive for COVID-19 should be based on clinical assessment and risk stratification. The following categories of patients are recommended for hospitalization: ¹⁷²
 - Mild symptoms plus a comorbid condition.
 - Fever >39°C despite use of Acetaminophen
 - Moderate or severe signs and symptoms (oxygen requirements, tachypnea)
 - Critical disease
- General considerations:
 - COVID-19 is a novel viral disease with limited therapeutic trials completed to date. The pregnant population is not only generally limited in these trials, but is often excluded, limiting the external validity of results to this population.
 - As multiple considerations regarding regular maternal care must also be considered on top of these novel therapeutics, OB/GYN consultation is advised when managing a patient with moderate/severe disease given need for fetal monitoring, preterm labor, general obstetric care, and consideration for fetal toxicity and maternal health associated with these therapeutic interventions given evolving clinical data.
- Oxygenation:
 - Maternal peripheral oxygen saturation (SpO₂) should be maintained at ≥95 percent.
 - Maternal PaO₂ greater than 70 mmHg is desirable to maintain a favorable oxygen diffusion gradient from the maternal to the fetal side of the placenta.¹⁷³
- Prone positioning:
 - Prone positioning may be considered in patients with severe ICU level care illness.

- Most data thus far have been based on prone positioning for ARDS in pregnant patients prior to COVID-19.
- If prone positioning is to be considered, an OB/GYN consult is recommended for clinical management and to determine candidacy due to the multiple relative and absolute contraindications to prone positioning and special positioning considerations.¹⁷⁴
- DVT prophylaxis:
 - Prophylactic anticoagulation is recommended for pregnant patients hospitalized for severe COVID-19, if there are no contraindications to its use.
 - For pregnant patients who are unlikely to be delivered within a few days, prophylactic LMWH (enoxaparin) is reasonable (e.g., enoxaparin 40 mg subcutaneously daily).
 - Unfractionated heparin is generally preferred for pregnant patients who might be proximate to delivery because it is more readily reversed than low molecular weight heparin (LMWH).
 - Intermittent pneumatic compression is suggested when pharmacologic prophylaxis is contraindicated.
- Antipyretics:
 - Acetaminophen is recommended as the preferred antipyretic and analgesic agent. Clinical or population-based data on the risk of NSAIDs remain limited.
 - However, ACOG, WHO, and the European Medicines Agency (EMA) recommend not avoiding nonsteroidal anti-inflammatory drugs (NSAIDs) in COVID-19 patients when clinically indicated, using the lowest effective dose, ideally for less than 48 hours and guided by gestational age-related potential fetal toxicity.^{173,175}
- Dexamethasone:
 - Dexamethasone can be used in pregnant patients who meet criteria for use of glucocorticoids for maternal treatment of COVID-19 (SpO₂ < 94%), however the regimen depends on whether the patient also meets criteria for use of antenatal corticosteroids to induce fetal maturity.¹⁷⁶
 - For gestational periods 24 weeks 0/7 days to 33 weeks 6/7 days, antenatal corticosteroids to induce fetal maturity is considered given the fetus is at risk of preterm delivery. The recommended regimen is:

Dexamethasone 6mg IV q12h x4 doses, followed by Dexamethasone 6mg IV/PO daily to complete 10-day course.

- For all other pregnant patients, the following regimen is recommended: Dexamethasone 6mg IV/PO daily. Others have suggested using glucocorticoids such as methylprednisolone or hydrocortisone to complete the course of maternal treatment because they result in less fetal steroid exposure, however, the efficacy of such steroids for reducing maternal mortality due to COVID-19 is less clear. Pregnant patients were included in the landmark Dexamethasone RECOVERY trial.

- Remdesivir:

- For pregnant patients who would otherwise qualify for Remdesivir, it is recommended for use. Pregnant patients were not included in the landmark Remdesivir ACTT-1 trial.¹⁷⁷

- Convalescent plasma:

- Convalescent plasma has been used successfully in a few pregnant women. There are no concrete clinical recommendations as of yet, but there are two ongoing governmental clinical trials: (ClinicalTrials.gov Identifier: NCT04397757, NCT04388527).

- Bamlanivimab and Casirivimab/Imdevimab (REGN-COV2)

- Although clinical data is limited, after a discussion of the potential benefits and theoretic risks, these therapies should not be withheld from pregnant patients who are deemed to be at high risk for progression to severe disease if they would otherwise qualify for its use.

Transplant recipients

Background:

- It is unclear if solid organ transplant recipients have a higher risk of severe disease compared with nontransplant patients. Limited data suggest that solid organ transplant recipients with SARS-CoV-2 infection may have severe disease similar to that described in non-solid organ transplant patients with serious underlying comorbidities.^{178–180}
- The impact of immunosuppression in the solid organ transplant population on COVID-19 disease severity remains unclear. At this point, additional studies are required to determine the impact of specific immunosuppressive agents on the course of COVID-19.¹⁸¹

Presentation:

- In general, clinical features of COVID-19 among solid organ transplant recipients are variable and similar to those in immunocompetent patients. However, fever appears to be less common, possibly related to immunosuppression, and lymphopenia is also common and may be more profound than in non-transplant patients.¹⁷⁸

General Management:

- The approach to the management of acute COVID-19 in solid organ transplant recipients is similar to that for non-transplant patients.
- Transplant recipients represent a population with likely poor prognostic factors owing to their immunosuppressive therapy and immunocompromised state, as well as the relative elevated incidence of co-morbidities in this population.
- Immunosuppressive therapy management: Adjustments to the immunosuppressive regimen are necessarily individualized, based upon disease severity, the specific regimen used, type of organ transplanted, time post-transplant, and the risk of acute allograft rejection. In general, it is recommended to reduce immunosuppression in patients with moderate to severe COVID-19.

- It is recommended to generally reduce or hold the antimetabolite (e.g. mycophenolate mofetil/sodium), particularly for patients with lymphopenia (e.g. absolute lymphocyte count <700 cells/mL).
- It is also recommended to generally continue the calcineurin inhibitor (CNI). Trough levels should be checked as soon as possible. Other medications used can cause interactions and affect drug levels, daily levels should be carefully monitored.
- The need for glucocorticoids should be evaluated on a case-by-case basis. In all cases the decision to reduce immunosuppression must be carefully weighed against the risk for acute rejection, particularly in transplant recipients who generally require high levels of maintenance immunosuppression (e.g. lung or heart recipients).^{179–184}
- Transplant patients should be evaluated for monoclonal antibody treatments as soon as possible after positive diagnosis and within 10 days from symptom onset.

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.^{185,186}

When to Consult MICU

1. Respiratory failure
 - a. If the patient needs $O_2 \geq 6$ LPM to maintain $SpO_2 > 92\%$ or $PaO_2 > 65$.
 - b. Rapid escalation of oxygen requirements
 - c. Significant work of breathing
2. Hemodynamic instability after initial conservative fluid resuscitation
 - a. SBP < 90, Mean arterial pressure < 65, or Heart rate > 120.
3. Acidosis
 - a. ABG with pH < 7.3 or $PCO_2 > 50$ (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
- PF ratio <300mmHg with a minimum of 5cm H₂O PEEP (or CPAP)
- Must not be fully explained by cardiac failure or fluid overload

Severity of ARDS and mortality

Severity	PaO ₂ /FiO ₂ (on PEEP/CPAP >5)	All-cause mortality
Mild	200-300	27 %
Moderate	100-200	32 %
Severe	<100	45 %

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

- Has been found to improve survival in hospitalized patients requiring supplemental oxygen, mechanical ventilation, or ECMO. Therefore, the use of dexamethasone is strongly recommended in this setting. ^{149–152}
- If associated with shock, can consider using hydrocortisone.

If Dexamethasone is unavailable, can use other glucocorticoids at an equivalent dose

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)¹⁸⁷

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 6L NC/oxymask.
- Due to larger diameter of tubing and humidification → up to 100% FiO₂ 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 FiO₂ to keep SpO₂>92%.
 - When possible, turn off flow before removal of the mask.

Non-Invasive Ventilation

- CPAP and BIPAP are used in an Airborne Infection Isolation Room when available.
- For infection control precautions for aerosol generating procedures, please refer to [Appendix 3.](#)

Intubation

Indications

- Respiratory distress (accessory muscle use, paradoxical abdominal breathing)
- Rapid progression of disease
- SpO₂ <90% despite maximal supplemental oxygen
- Arterial pH <7.3 with PaCO₂ >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 another 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% O₂ 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 (SpO₂ <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

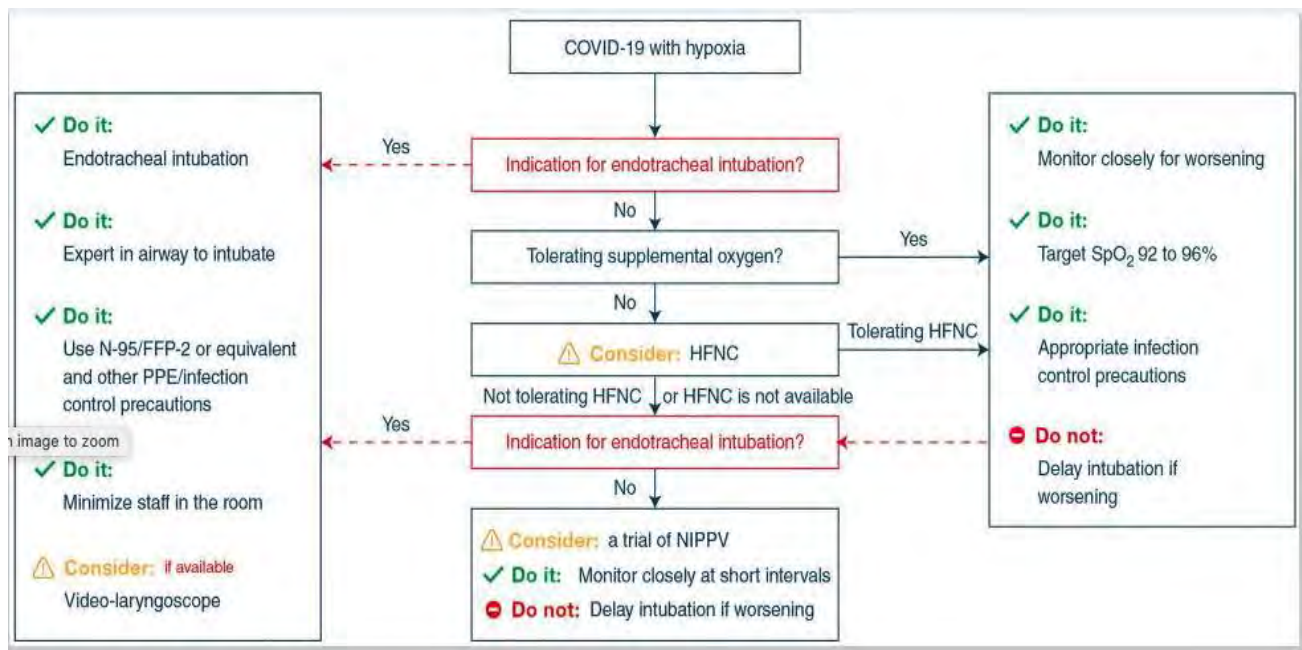
- Sedation and paralysis with Neuro muscular blocking agents (NMBA) to prevent cough.

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.



Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med.* 2020;46(5):854-887. doi:10.1007/s00134-020-06022-5

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/1QgvczLYZaTLpqGF_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^{188,189}
 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 H₂O to start.
 4. FiO₂: Start with FiO₂ 100% and titrate oxygen to target PaO₂ 55 to 80 or SpO₂ 90 to 96
 5. Plateau pressure (Pplat) <30 cm H₂O.
 6. Goal pH >7.20

Subsequent Tidal Volume adjustment

- **GOAL - Pplat ≤30 cm H₂O**
- 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 H₂O, decrease tidal volume in 1 mL/kg IBW decrements to 5 or 4 mL/kg IBW.
 - If Pplat <25 cm H₂O and tidal volume <6 mL/kg, increase tidal volume by 1 mL/kg IBW until Pplat >25 cm H₂O 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 H₂O.¹⁸⁹

Additional ventilator adjustment

Minute Ventilation = Respiratory Rate (RR) x Tidal Volume (TV)¹³⁴

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 FiO₂¹⁸⁹
- **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%

OXYGENATION GOAL: PaO₂ 55-80 mmHg or SpO₂ 88-95%

Use a minimum PEEP of 5 cm H₂O. Consider use of incremental FiO₂/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher FiO₂

FiO₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO₂	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO₂

FiO₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO₂	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

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.^{190,191}
- 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).¹⁹² 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 interruption¹⁹³

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)¹⁹⁴ and [Behavioral Pain Scale](#) (BPS)^{195,196}
- 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: ¹⁹⁶
 - [Confusion Assessment Method for the ICU](#) (CAM-ICU)¹⁹⁷
 - 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.¹⁹⁸

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.¹⁹⁹

Extubation

- Extubation¹⁹⁹ 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.²⁰⁰
- 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 Protocol²⁰¹

Checklist for extubation:

- ☐ Disease Resolution:
 - ☐ Respiratory failure and/or the disease that prompted initiation of mechanical ventilation has resolved / improved
 - ☐ Ventilation Criteria:
 - ☐ $\text{FiO}_2 < 0.4$, $\text{PEEP} < 8 - 10 \text{ mmH}_2\text{O}$, Pressure Support Ventilation (PSV) < 10
 - ☐ Comfortable respiration | Minimal sputum load | Presence of cuff leak
 - ☐ Hemodynamic Criteria:
 - ☐ Low dose vasopressor (e.g. $< 5 \text{ mcg/min}$ norepinephrine)
 - ☐ $\text{SBP} > 90 \text{ mmHg}$ or $\text{MAP} > 60 \text{ mmHg}$
 - ☐ 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 | $\text{paO}_2 > 60 \text{ mmHg}$ on $\text{FiO}_2 < 0.4$ | $\text{pH} > 7.3$
 - ☐ Normal K^+ | Normal PO_4^-
 - ☐ 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 $\text{FIO}_2 < 40\%$ for at least 30 minutes.
- Following signs indicate failure of SBT:
- 1) $\text{RR} > 35/\text{min}$ for 5 minutes or more.
 - 2) Rapid Shallow Breathing Index (RSBI) $> 105 \text{ cycles/min/L}$.
 - 3) $\text{SaO}_2 < 90\%$ for > 5 minutes or $\text{PaO}_2/\text{FiO}_2$ ratio < 150 on $40\% \text{ FiO}_2$.
 - 4) $\text{HR} > 120/\text{min}$ or sustained increase 20% greater than baseline.
 - 5) $\text{SBP} < 90 \text{ mmHg}$ or $> 180 \text{ mmHg}$ 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.²⁰²

Post-Extubation

- Obtain SLP consult
- Avoid excessive suctioning
- Patient may require re-intubation if there is:
 - Stridor
 - Obstructed breathing pattern or RR > 30 bpm
 - Increased oxygen flow rate or delivery by >50% to achieve SpO₂>92%.
 - Agitation

Refractory Hypoxemia

- Defined by $\text{PaO}_2 < 75$, $\text{PaO}_2/\text{FiO}_2 < 150$, despite PEEP optimization, on $\text{FiO}_2 > 0.6$
- 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.²⁰³
- Initiate early when P/F ratio is < 150 , < 12 hours of worsening hypoxia ($\text{FiO}_2 > 60\%$), < 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 surgery²⁰⁴

High PEEP

- Increase PEEP as tolerated
- In severe or refractory ARDS, driving pressure best predicted survival in patients with ARDS.
- Driving pressure = $\text{P}_{\text{plat}} - \text{applied PEEP}$ (or) $\text{V}_\text{T}/\text{respiratory system compliance}$ ²⁰⁵

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.²⁰⁶

Extracorporeal Membrane Oxygenation (ECMO)

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

Relative contraindications to ECMO²⁰⁷

- 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 ECMO²⁰⁷

- 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.^{208,209}
- Lung protective ventilation strategies include²¹⁰:
 - 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.^{211,212,213}

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

Definition²¹⁴

- 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^{214,215}

Type of Shock	Examples	Pre-load (PCWP, JVD)	Pump function (CO)	Afterload (SVR)	Perfusion (MvO ₂ , O ₂ sat)
Distributive	Sepsis, cytokine, anaphylaxis, adrenal crisis	↓/-	↑	↓	↑/-
Cardiogenic	Arrhythmia, valve failure, MI, cardiomyopathy, pericarditis, PE	↑	↓	↑	↓
Hypovolemic	Fluid loss, hemorrhage	↓	↓	↑	↓
Obstructive	Tamponade, PE, pneumothorax	↑	↓	↑/-	↓/-

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.
- **Vasopressors:**
 - 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.²¹⁶

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)¹³⁴

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).²¹⁶
- 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 cells²¹⁷

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)²¹⁸
 - Hepatic function panel
 - Triglycerides
- Consider using [HScore](#) on Mdcalc to assess probability of HLH syndrome²¹⁹

Management

- Discuss IVIG, steroids, and tocilizumab use with Infectious Disease
- Tocilizumab²²⁰
 - 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

Discharge of COVID positive patients can be considered when patients have resolution of symptoms and do not require any further specific or supportive therapy.

Discontinuation of transmission precautions

Following strategies can be followed, refer to policy [COV D-04](#).

Symptom-based strategy (Must meet all criteria)

- Resolution of fever > 24 hours without antipyretics
- Improvement in signs and symptoms (cough, dyspnea, oxygen requirement)
- > 10 days since the onset of COVID (1st day of symptoms or 1st positive test)

Test-based strategy (Must meet all criteria)

- Resolution of fever without antipyretics, improvement in symptoms
- 2 negative RT-PCR from at least 2 consecutive respiratory specimens collected > 24 hours apart
- > 10 days since the onset of COVID (1st day of symptoms or 1st positive test)

Medications

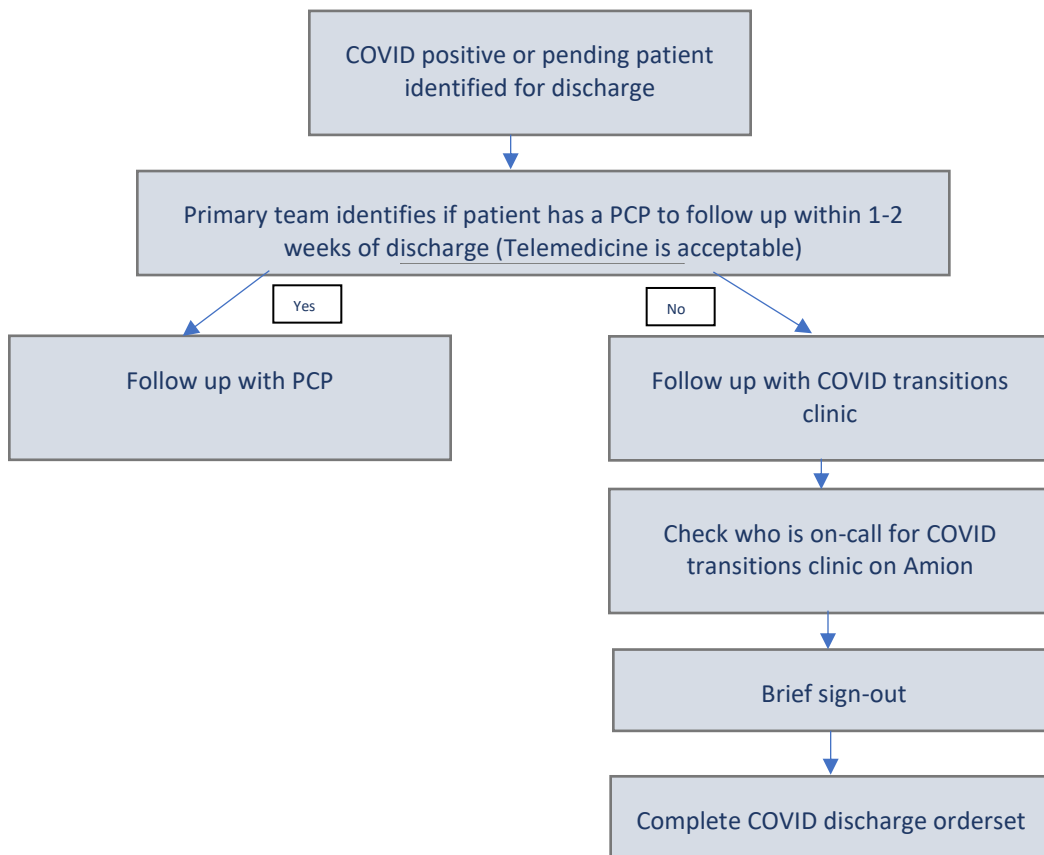
If the patient has decreased mobility or D-Dimer >0.5 on day of discharge can consider anticoagulation for DVT prophylaxis at discharge for 14 days. (Group 1).

If therapeutic anticoagulation was used during hospital admission, discharge with anticoagulation as per [protocol](#). (Group 2/3)

COVID Transitions Team

Will follow COVID discharges for clinical stability and facilitate triage. Find under "COVID-19 Transitions Clinic" on Amion.

Discharge workflow



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. They can follow up in My Chart or with PCP for negative results.

AMA Discharges

- If a patient has the capacity to make his or her own health care decisions and the discharge plan determines that the patient is not a threat to the public (i.e., the patient

can and will agree to quarantine), the patient may be discharged AMA. Infection Control and DOH notified by team or case manager.

- If the patient is not willing/able to quarantine, Dr. Housam Hegazy [C: (315) 491-9588] must be contacted; he will do a 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 as per policy [COV D-02](#).

Skilled Nursing Facilities

- COVID positive patients can be discharged to SNF after transmission precautions have been discontinued, please refer to policy [COV D-04](#).

Patients with a positive COVID-19 test may be discharged following

- DOH notified/approval (this is done by the case manager in conjunction with infection control).
- Patient is given the mandatory self-quarantine order from the County Executive (dot phrase: COVIDSELFQUARNOTICE). Required only for patients being discharged to home.
- Case Management, Infection control, Department of Health and Social work are helping provide information on discharge.
- CM can help arrange follow up with the COVID transition clinic (also see AMION).
- COVID discharge kits are available for patients on discharge, please contact CM for the same.
- Please give COVID-confirmed patients information regarding the convalescent plasma donations.
- Patients that receive convalescent plasma or antibody treatments will not be candidates for plasma donation for 6 months.

Residual effects of COVID-19 infection

- Several patients who have recovered from COVID-19 have described a post-infectious syndrome with different symptoms and presentations.
- These symptoms/patients are often referred as “Long COVID”, “Post-COVID”, “Long haulers”.
- As per CDC ²²¹
 - The most commonly reported long-term symptoms include:
 - Fatigue
 - Shortness of breath
 - Cough
 - Joint pain
 - Chest pain
 - Other reported long-term symptoms include:
 - Difficulty with thinking and concentration (sometimes referred to as “brain fog”)
 - Depression
 - Muscle pain
 - Headache
 - Intermittent fever
 - Palpitations
- They can persist for weeks to months and the severity of symptoms can range from mild to debilitating.
- Huang et al followed up 1733 patients (52 % men, 48 % women) after recovery from COVID-19 infection (6 months after the illness. They reported 76 % of the patients had at least one persistent symptom. Fatigue was reported in 63% of the patients, residual chest imaging abnormalities was reported in more than 50% of the patients. Disease severity during the acute phase was independently associated with the extent of lung diffusion impairment at follow-up (odds ratio 4.60, 95% CI 1.85–11.48), with 56% (48 of 86) of patients requiring high-flow nasal cannula, non-invasive ventilation, and invasive mechanical ventilation during their hospital stay having impaired pulmonary diffusion capacity. ²²²
- Current data on pathophysiology is limited, future research is being initiated by NIH to further study and evaluate this condition. ²²³

COVID-19 Vaccines

As of March 1, 2021; 3 vaccines are authorized and recommended by the CDC to prevent COVID-19, Pfizer-BioNTech COVID-19 vaccine, Moderna COVID-19 vaccine and Janssen COVID-19 vaccine.²²⁴

The Pfizer-BioNTech COVID-19 vaccine (BNT162b2 vaccine)

- This vaccine is a lipid nanoparticle–formulated, nucleoside-modified RNA that encodes the viral spike protein.
- It was tested in a multinational, placebo-controlled trial and was observer- blinded. Individuals aged 16 and older were assigned in a 1:1 ratio with a total of 43,548 participants. Individuals received 2 doses of the vaccine 21 days apart.
- Pfizer-BioNTech COVID-19 vaccine was 95% effective in preventing COVID-19 infection 7 days after receiving the second dose. (95% CI, 90.3 to 97.6).²²⁵
- Some authorities report an efficacy of 52.4% 2 weeks after the first dose alone, but true efficacy is uncertain if only one dose of the vaccine is given.²²⁶

Moderna COVID-19 vaccine (mRNA-1273 vaccine).

- This vaccine is a lipid nanoparticle-encapsulated mRNA-based vaccine that encodes the spike protein of the virus.
- The vaccine was tested at 99 centers in the United State of America. Individuals were randomly assigned in a 1:1 ratio and 2 doses of mRNA-1273 (100 mcg) 28 days apart were given to the group who received the vaccine4.
- Moderna COVID-19 vaccine achieved 94.1 % efficacy (95% CI, 89.3 to 96.8%; P<0.001) in preventing COVID-19 infection.²²⁷

Janssen COVID-19 vaccine (Ad26.COV2-S)

- This is a single dose vaccine, that uses an adenovirus vector which has been genetically modified to prevent replication in humans but induces a protective immune response.
- On February 27, 2021 FDA granted EUA to Janssen COVID-19 vaccine and CDC’s Advisory Committee on Immunization Practices’ (ACIP) recommendation endorsed the safety and effectiveness of Janssen (Johnson & Johnson)’s COVID-19 vaccine and its use in people age 18 and older.²²⁸
- This decision was based on data from the Phase 3 ENSEMBLE study that demonstrated the vaccine was 85 percent effective in preventing severe disease across all regions studied and showed protection against COVID-19 related hospitalization and death, beginning 28 days after vaccination.²²⁹

Abbreviations

ABG	Arterial Blood Gas
ACE	Angiotensin Converting Enzyme
ACEI	Angiotensin Converting Enzyme Inhibitor
ACOG	American College of Obstetricians and Gynecologists
ACR	American College of Radiology
ACS	Acute Coronary Syndrome
ACTIV	Accelerating COVID-19 Therapeutic Interventions and Vaccines
ACTT	Adaptive COVID-19 Treatment Trial
AKI	Acute Kidney Injury
ALI	Acute Lung Injury
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AMA	Against Medical Advice
AMS	Altered Mental Status
APNIC	Awake Prone in Non-Intubated COVID-19 Patients
APRV	Airway Pressure Release Ventilation
ARB	Angiotensin II Receptor Blockers
ARDS	Acute Respiratory Distress Syndrome
ART	Anti-Retroviral Therapy
AST	Aspartate Aminotransferase
ATTACC	Antithrombotic Therapy to Ameliorate Complications of COVID-19
BIPAP	Bilevel Positive Airway Pressure
BMI	Body mass index
BMP	Basic Metabolic Panel
BNP	Brain Natriuretic Peptide
BPS	Behavioral Pain Scale
CAD	Coronary Artery Disease
CAP	Community Acquired Pneumonia
CBC	Complete Blood Count
CDC	Centers for Disease Control and Prevention
CG	Collapsing Glomerulopathy
CHF	Congestive Heart Failure
CI	Confidence Interval
CK	Creatine Kinase
CKD	Chronic Kidney Disease
CM	Case Manager
CMP	Complete Metabolic Panel
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease

CPAP	Continuous Positive Airway Pressure
CPK	Creatine Phosphokinase
CPOT	Critical Care Pain Observation Tool
CPR	Cardiopulmonary Resuscitation
CRP	C-reactive protein
CRRT	Continuous Renal Replacement Therapy
CSF	Cerebrospinal Fluid
CT	Computerized Tomography
CTA	Computerized Tomography Angiography
CXR	Chest X-Ray
DIC	Disseminated intravascular coagulation
DNI	Do Not Intubate
DNR	Do Not Resuscitate
DOAC	Direct Oral Anticoagulant
DOH	Department of Health
DVT	Deep Vein Thrombosis
ECG/EKG	Electrocardiogram
ECHO	Echocardiogram
ECMO	Extracorporeal Membrane Oxygenation
ED	Emergency Department
EMA	European Medicines Agency
ESR	Erythrocyte Sedimentation Rate
ETT	Endotracheal Tube
EUA	Emergency Use Authorization
FDA	United States Food and Drug Administration
FIO ₂	Fraction of Inspired Oxygen
GBS	Guillain-Barré syndrome
GI	Gastrointestinal
GYN	Gynecology
HCG	Human chorionic gonadotropin
HCP	Health Care Proxy
HCV	Hepatitis C Virus
HFNC	High Flow Nasal Cannula
HIPAA	The Health Insurance Portability and Accountability Act of 1996
HIV	Human Immunodeficiency Virus
HLH	Hemophagocytic Lymphohistiocytosis
HR	Heart Rate
ICU	Intensive Care Unit
ID	Infectious Diseases
iNO	Inhaled Nitric Oxide

IL	Interleukin
INR	International Normalized Ratio
IVF	Intravenous fluids
IVIG	Intravenous Immunoglobulin
JAMA	Journal of the American Medical Association
JVD	Jugular Venous Distension
LA	Lupus Anticoagulant
LDH	Lactate Dehydrogenase
LFT	Liver Function Tests
LMWH	Low Molecular Weight Heparin
LPM	Liters per minute
LV	Left Ventricle
LVEF	Left Ventricular Ejection Fraction
MAP	Mean Arterial Pressure
MDI	Metered Dose Inhaler
MDR	Multi-drug resistance
MDRO	Multi-drug resistant organisms
MERS	Middle East Respiratory Syndrome
MG	Myasthenia Gravis
MI	Myocardial Infarction
MICU	Medical Intensive Care Unit
MOLST	Medical Orders for Life-Sustaining Treatment
MRI	Magnetic Resonance Imaging
MRSA	Methicillin-resistant Staphylococcus aureus
MS	Multiple Sclerosis
NC	Nasal Cannula
NIH	National Institutes of Health
NIPPV	Noninvasive Positive-Pressure Ventilation
NMBA	Neuromuscular Blocking Agents
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
NY	New York
NYS	New York State
OB	Obstetrics
OT	Occupational Therapy
PAP	Positive Airway Pressure
PAPR	Powered Air Purifying Respirator
PCI	Percutaneous Coronary Intervention
PCP	Primary Care Physician
PCR	Polymerase Chain Reaction
PE	Pulmonary Embolism
PEEP	Positive end-expiratory pressure

PPE	Personal Protective Equipment
PPV	Positive Predictive Value
PR	Pulse Rate
PRN	As needed
PSV	Pressure Support Ventilation
PT	Prothrombin Time
PTT	Partial Thromboplastin Time
RAAS	Renin-Angiotensin-Aldosterone System
RASS	Richmond Agitation and Sedation Scale
RCT	Randomized Clinical Trial
RDV	Remdesivir
RR	Respiratory Rate
RRT	Rapid Response Team
RSBI	Rapid Shallow Breathing Index
RT	Respiratory Therapy
RVP	Respiratory Viral Panel
SARS	Severe Acute Respiratory Syndrome
SBP	Systolic Blood Pressure
SCCM	Society of Critical Care Medicine
SIADH	Syndrome of inappropriate antidiuretic hormone ADH release
SIRS	Systemic inflammatory response syndrome
SLP	Speech and Language Pathology
SMFM	Society for Maternal-Fetal Medicine
SUNY	State University of New York
TNF	Tumor Necrosis Factor
TTE	Transthoracic Echocardiogram
TV	Tidal Volume
UA	Urinalysis
UC	Urine Culture
ULN	Upper Limit of Normal
UOP	Urine Output
US	Ultrasonography
UUH	Upstate University Hospital
VAP	Ventilator Associated Pneumonia
VILI	Ventilator-Induced Lung Injury
VTE	Venous Thromboembolism
WHO	World Health Organization

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APPENDIX – 1 : Donning / Doffing PPE

Donning PPE



Place new chux on PPE cart(s)



Pull back long hair to ensure a tight seal



Perform Hand Hygiene



Remove ear loop mask and place in bag #1



Perform Hand Hygiene



Don gown



Perform Hand Hygiene



Don N95



Perform Hand Hygiene



Don Face Shield



Perform Hand Hygiene



Don Gloves

Doffing PPE

While still in the patients room remove gown & gloves



Perform hand hygiene. Open door, exit room Perform hand hygiene



Remove face shield place on chux pad-



Perform Hand Hygiene



Remove respirator by rubber straps careful not to touch the front or inside of the respirator Place in Bag #2



Perform Hand Hygiene



Don ear loop mask from Bag #1

Don Gloves



Disinfect face shield with PDI wipes- Hang shield on bag, discard chux, & Remove gloves

Perform Hand Hygiene



PSCBH Review 4/2020

Donning PAPR



Place new chux
on PPE cart



Pull back long
hair to ensure a
tight seal



Perform Hand
Hygiene



Remove ear loop
mask and place
in bag #1



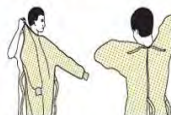
Perform Hand
Hygiene



Don PAPR



Perform Hand
Hygiene



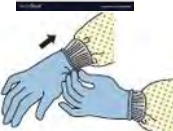
Don gown



Ensure that PAPR is not
covered by the gown



Perform Hand
Hygiene



Don Gloves

F95386 Reviewed 5/2020

Doffing PAPR

While still in the patients
room remove gown &
gloves



Perform hand hygiene.
Open door, exit room
Perform hand hygiene



Unclip belt



Place PAPR on cart in front of self



Remove Hood

Turn off PAPR

Perform Hand
Hygiene



Don ear loop mask
from Bag #1



Proceed to disinfection process

Perform Hand
Hygiene



APPENDIX – 2 : PPE Table for COVID exposure scenario



COVID-19 POLICY MANUAL

Policy Number: COV P-01

Approved by: Hospital Officers Leadership Team

Issue Date: 03/18/2020

Applies to: Upstate University Hospital

Value(s): Innovation, Respect, Integrity, Community

Page(s): 1 of 3

Personal Protection Equipment (PPE) Table for COVID-19 Exposure Scenario

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

Applies to:

All staff

Policy:

Exposure Scenario	Patient's PPE	Staff PPE	Staff Action after Contact / Potential Exposure
No Known Exposure	None Recommended	None Recommended	No action
COVID Ruleout Patient	Appropriate PPE* for Patient	Appropriate PPE for Staff**	No action
	Patient without PPE	Appropriate PPE for staff	No action
	Patient without PPE	Inappropriate PPE for staff	***Continue to work, wear a mask, monitor symptoms and temperature for 14 days or until symptoms develop. For symptoms, seek medical care
COVID Positive Patient	Appropriate PPE* for Patient	Appropriate PPE **	No action
	Patient without PPE	Appropriate PPE for staff	No action
	Patient without PPE	Inappropriate PPE for staff	***Continue to work, wear a mask, monitor symptoms and temperature for 14 days or until symptoms develop. For symptoms, seek medical care
COVID Positive Patient having a High Risk Procedure. (e.g., FOB/BAL, NP swab collection, Intubation, Surgical procedures which could aerosolize)	N/A	Appropriate PPE **	No action
	N/A	inappropriate PPE for staff	***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
Staff member positive for COVID			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.
Staff member awaiting COVID result			Self-quarantine at home until results are available. For symptoms seek medical care
Staff member returning from domestic travel without known COVID+ contact			***Continue to work, monitor symptoms and temperature, continue monitoring for 14 days or until symptoms develop. For symptoms, seek medical care

Page: 14

Revision: 3.0

Printed On: 05/12/2020

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PPE Table for COVID-19-Exposure Scenario (continued)

COV P-01

Page 2 of 3

Exposure Scenario	Patient's PPE	Staff PPE	Staff Action after Contact / Potential Exposure
Patient reports that they are positive for COVID after being seen at one of our ambulatory sites	None at time of exposure	None at time of exposure	Identify employees in direct contact with patient during the time of encounter and identify Infection Control for appropriate tracking and guidance.
Staff positive for COVID-19	None at time of exposure	None at time of exposure	<p>COVID positive staff 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.</p> <p>Staff (w/o ear loop mask) exposed to the positive staff member 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. If symptomatic visit employee testing site.</p> <p>Inpatients exposed to staff: moved to a private room with mask if tolerated and monitor symptoms for 14 days.</p> <p>Outpatients exposed to staff: 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-EZPZ for instructions on how to get tested.</p>
	None at time of exposure	Surgical ear loop mask	No exposure to staff or patient
	Surgical ear loop mask	None at time of exposure	<p>Staff (w/o ear loop mask) 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. If symptomatic, visit employee testing site.</p> <p>Patient exposed to staff: no exposure.</p>

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

APPENDIX – 3 : Airway procedures during COVID-19



COVID-19 POLICY MANUAL

Policy Number: COV A-02

Approved by: Hospital Officers Leadership Team

Issue Date: 03/30/2020

Applies to: Upstate University

Value(s): *Innovation, Respect, Integrity, Community*

Page(s): 1 of 5

Infection Control for Aerosol Generating Procedures During COVID-19

Review Date:	Change Description:
11/03/2020	
Revised Date:	Change Description:
11/03/2020	Added the requirement of a HEPA filter when performing AGPs. Added AGP's can only be performed if there is no solid enclosed room available.

Applies to:

All Staff

Policy:

This policy describes current recommendations during the COVID-19 pandemic for patients undergoing aerosol generating procedures (AGP). This policy will provide guidance on how to prioritize the use of an air filtration or and Airborne Infection Isolation Room (AIIR, “negative pressure” rooms) versus standard rooms.

This policy excludes Bronchoscopies. Please see policy COV B-02, Bronchoscopy Procedures During the Prevalence of COVID-19.

Definitions:

Aerosol Generating Procedures (AGPs):

- AGPs include procedures that are believed to generate aerosols and droplets.

Enhanced PPE (EPPE)

- N95 and face shield or PAPR, N95 discarded after procedure
- Gloves
- Gown

Room Disposition for COVID-19 and COVID-19 Rule Out

- Two positive COVID-19 patients may share a semi-private room
- COVID-19 + and COVID Rule-Out patients may NOT share a semi-private room
- Two COVID Rule-Out patients may NOT share a semi-private room
- Two patients undergoing high risk AGPs may NOT share a semi-private room

COVID Testing Time Frame

- A COVID test must be obtained within 5 days from the initiation of the AGP.
- The result from and outside testing facility is acceptable and will need to be documented in the Electronic Medical Record (EMR) or in the physical chart.
- Word of mouth testing results are not acceptable for proof of testing.

A. Outpatients

1. Outpatients in whom AGPs are planned should be tested for COVID-19 within 5 days prior to the procedure to establish their COVID-19 status. Providers are encouraged to schedule testing as close the day of admission/procedure as can be reasonably accommodated by Upstate University Hospital testing systems.
 - a. This excludes diagnostic testing departments
 - b. Patients who test negative for COVID-19 will be on standard precautions
 - c. If the COVID-19 test was not performed or results are still pending at the time of the AGP, the procedure will be done under Enhanced Airborne Precautions (EAP). Once the AGP is complete the EAP may be discontinued in asymptomatic patients. (see Procedure for AGP section below)

B. Inpatients

1. Patients have a negative COVID-19 test will be on Standard Precautions during their admission, including for AGPs during their admission.
2. If a COVID-19 test was not performed or the results are still pending at the time of the AGP, the AGP will be performed using EAP.
 - a. Once the AGP is complete the room will remain under EAP for 1-hour post AGP and precautions may be removed at the 1-hour mark.
3. Inpatients who have completed their evaluation and holding for COVID-19 and their COVID-19 status has been removed from the Electronic Medical Record (EMR) do not required EAP.
4. Inpatients who have recovered from COVID-19 and their infection status has been removed from the EMR do not require EPPE for AGPs.
5. Individuals involved in a CODE BLUE will wear EPPE regardless of COVID-19 status.

Enhanced Airborne Precautions for AGPs during COVID-19 Pandemic

- The list of AGPs will be assessed on a regular basis of inclusion

	AGP
Qualifying Procedures	<ol style="list-style-type: none"> 1. Airway Surgeries/procedures (e.g. ENT, thoracic, transsphenoidal surgeries) 2. Intubation 3. Extubation 4. Chest Compressions 5. Nebulization 6. High flow oxygen, including nasal canula, at >15L without an ear loop mask. 7. Non-invasive positive pressure ventilation (e.g. CPAP, BIPAP) 8. Oscillatory ventilation 9. Sputum induction 10. Open suctioning of tracheostomy or endotracheal tube (ETT)

	AGP
Qualifying Procedures (continued)	11. Tracheostomy change 12. Manual ventilation (e.g. manual bag-mask ventilation before intubation) Disconnecting patient from ventilator 13. Upper endoscopy (including transesophageal echocardiogram) 14. Lower endoscopy 15. Ventilator circuit manipulation 16. Dental procedures 17. Fiberoptic laryngoscopy and anterior nasal endoscopy with biopsy or manipulation
PPE Required	N95 and face shield or PAPR <u>***N95 discarded after procedure***</u> Gloves Gown
AGP sign	Yes
Recovery	OR and Procedural areas will recover patient in the procedure room
Time frame to enter room without PPE after procedure	1 hour from completion of the AGP.
Cleaning Requirements (performed by staff providing treatment or caring for patient)	Upon completion of the AGP, high touch surfaces are required to be wiped down with hospital approved disinfectant product. High touch surfaces include, i.e.: <ul style="list-style-type: none"> • Doorknob/handle • Bedside table • Bed rails • Patient remote • Alaris Pump • Surface of the ventilator screen if applicable
EVS	Does not require immediate clean from EVS. EVS will continue to clean the room per their regular cleaning schedule per protocol.

Procedures not considered aerosol-generating
1. Non-rebreather, face mask, or face tent up to 15L 2. Humidified trach mask up to 20L with in-line suctioning 3. Routine trach care (e.g., replacing trach mask, changing trach dressing) 4. In-line suctioning of and endotracheal tube 5. Coughing, sneezing, vomiting or breathing heavily 6. Suctioning of oropharynx 7. Nasopharyngeal swab 8. Nasogastric tube placement

Proning is not inherently aerosol-generating but aerosols are possible if the ETT becomes disconnected during the proning process.

AGP priority for assignment of an AIIR (Airborne Infectious Isolation Room)

1 st priority COVID 19 confirmed	2 nd priority COVID-19 Rule-out	3 rd priority High Risk COVID-19 population (see COV D-04)	4 th priority Other Respiratory Viral Infection
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Tuberculosis, varicella, and measles patients require an AIIR and are not included in this guidance. Consult with Infection Prevention regarding patient placement for these infections.

Note: It is not always possible to anticipate the need for an AGP; lifesaving care (e.g. intubation, chest compressions) should not be delayed in order to transfer a patient to an AIIR.

I. Use of a Standard Patient Room for AGPs for Patients on EPPE

- A. If an AIIR is not available, AGPs may be performed in a standard patient room or exam room with the door closed, a HEPA filter must be to filter the room air, see policy IC F-14 for reference.
- B. AGPs can only be performed in a curtain enclosed area if all solid enclosed rooms are unavailable. A HEPA filter must still be placed at the head of the bed.
- C. If a patient is in a positive pressure room and has not been tested for COVID-19 or if their test is pending, AGPs should be avoided except in emergency situations.

II. Procedure for AGPs For Patients on EPPE (Standard and AIIR rooms)

- A. Conduct in a private room only. Semi-private rooms are permitted if it is occupied by only one patient or if both patients in the room have confirmed COVID-19.
 1. Not all AGPs can be planned. If a patient needs an urgent or emergent AGP and cannot be placed in a private room or in a semi-private without a roommate, ensure that the other patient (roommate) is either moved out of the room for the AGP and for the period of airing afterwards (see below) or, if this is not possible, ensure that the roommate is masked with a surgical mask during the time period.
- B. Limit staff in the room.
- C. All staff in the room must wear EPPE.
- D. Door must remain closed per EPPE.
- E. After procedure:
 1. Wipe down all high touch surfaces with a hospital-approved disinfectant.
 2. An N95 or PAPR is required for respiratory protection for up to 1 hour after the procedure.
 3. Gowns, gloves, and eye protection must be worn per EPPE by staff remaining in the room.

- F. If an AGP is performed and patient is moved from the room; staff that clean the room within the airing time after patient leaves must wear EPPE while cleaning room. Room can be opened to general use after cleaning is completed and airing time has passed.

Corresponding Clinical Procedure(s):

None

Education/Related Resources:

Bronchoscopy Procedures During the Prevalence of COVID-19, COV B-02
 Respiratory Procedures During Prevalence of COVID-19, COV R-01
 Discontinuation of Transmission Based Precautions of Patients with COVID-19, COV D-04
 Microcon Air Disinfecting Machine, IC F-14

Form Names(s) and Number(s):

None

Originating Department: Infection Prevention

Contributing Department(s): ICU Governance, Nursing, Respiratory

References/Evidence-Based Reference(s):

Centers for Disease Control and Prevention (CDC). Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings. Updated March 10, 2020. Accessed March 22, 2020.

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FDA Press Release: Coronavirus (COVID-19) Update: FDA and CDC take action to increase access to respirators, including N95s, for health care personnel. Updated March 2, 2020. Accessed March 22, 2020

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WHO. Rational Use of Personal Protective Equipment for Coronavirus Disease (COVID-19) and considerations during severe shortages), accessed June 2020

APPENDIX – 4 : Respiratory Procedures during prevalence of COVID-19



COVID-19 POLICY MANUAL

Policy Number: **COV R-01**

Approved by: Hospital Officers Leadership Team

Issue Date: 04/01/2020

Applies to: Upstate University Hospital

Value(s): *Innovation, Respect, Integrity, Community*

Page(s): 1 of 4

Respiratory Procedures During Prevalence of COVID-19

Review Date:	Change Description:
04/27/2020	
Revised Date:	Change Description:
04/27/2020	Specified that MDI therapy is non-aerosolizing and doesn't require enhanced PPE or private room. Added that pediatric patients requiring a neonatal circuit (<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.

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.

Page: 1/4

Revision: 6.0

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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 <6lmc). 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.**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/EET-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. Trached/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, suctioning 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 Names(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:

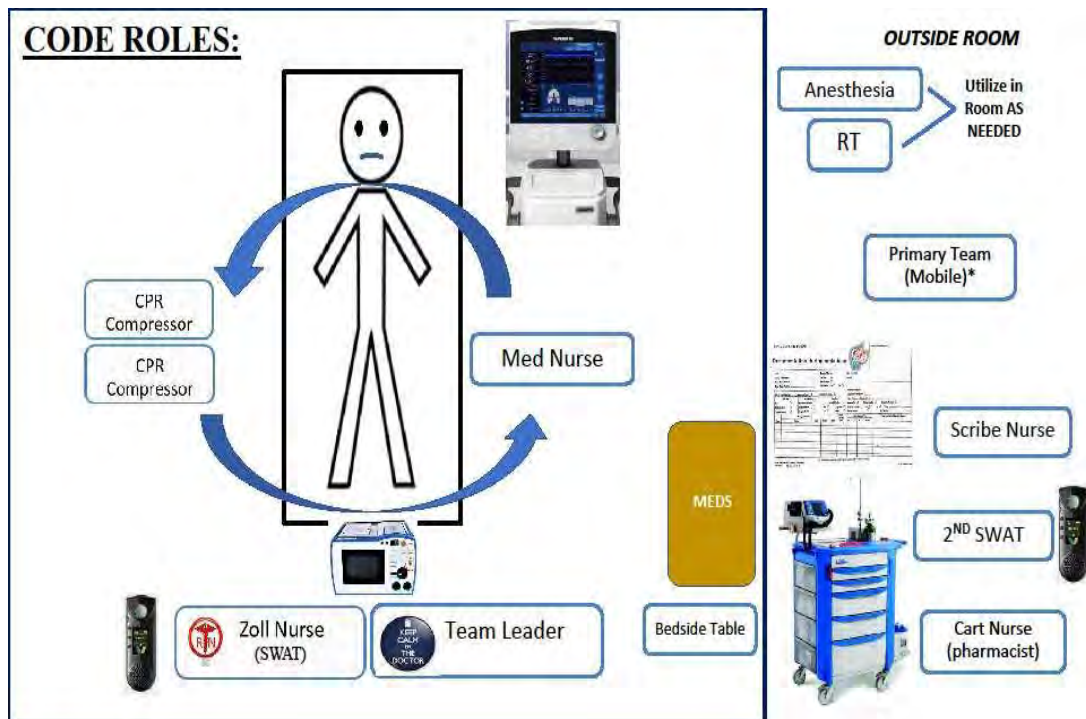
None cited

APPENDIX – 5 : CODE BLUE Room layout

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

Page 5 of 6

Addendum B



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

Applies to: Upstate University Hospital

Value(s): *Innovation, Respect, Integrity, Community*

Page(s): 1 of 5

Discontinuation of Transmission Based Precautions of Patients with COVID-19

Review Date:	Change Description:
11/23/2020	
Revised Date:	Change Description:
11/23/2020	Removed high risk group of homeless patients and homeless patients living in shelters.

Applies to:

Medical Providers, RNs, Infection Prevention staff, Administrative Supervisors

Policy:

Discontinuing transmission-based precautions and placement of patients with resolving COVID-19 infections

1. This process is for movement of internal patients.
2. 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.

Removal of precautions and movement of patients with resolving COVID-19 infection

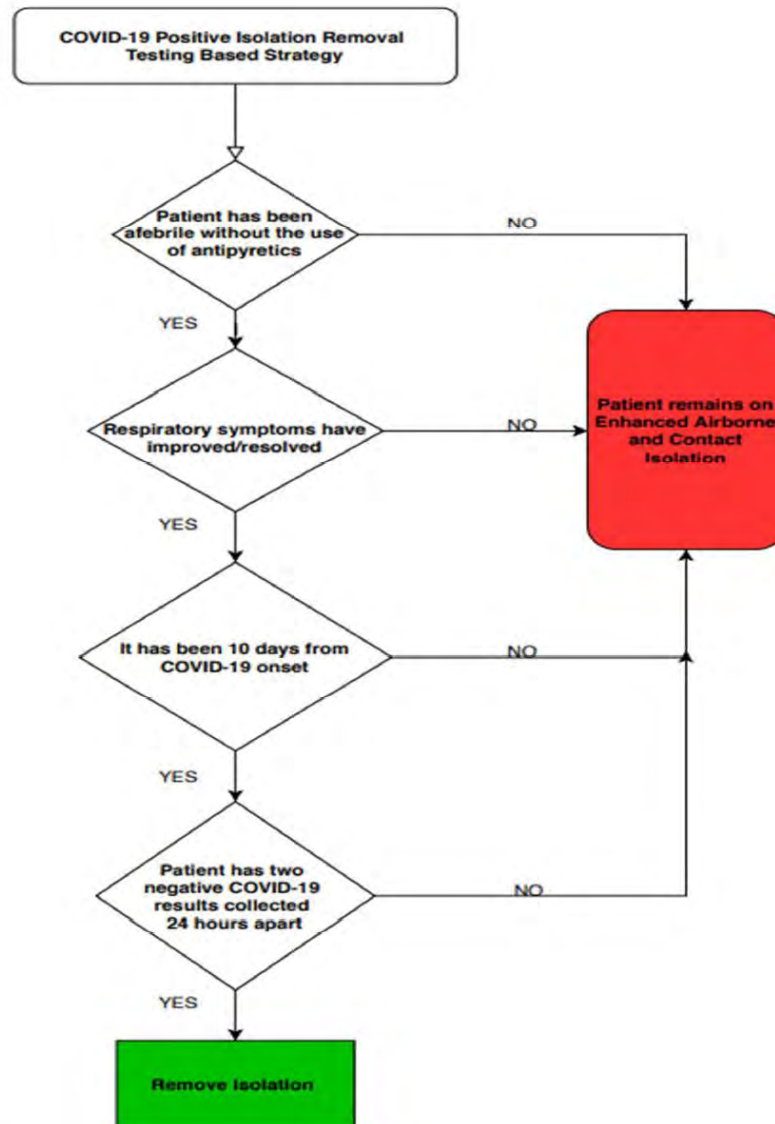
1. The following guidelines will be utilized to make decisions on removal of isolation precautions and movement of patients to non COVID units when able.
2. Any person traveling will be managed as a high risk patient; Excludes travel within New York State or to/from contiguous states (Connecticut, Massachusetts, New Jersey, Pennsylvania, and Vermont).
3. For additional questions please contact Infection Prevention Monday through Friday:
 - a. Downtown Hospital at 315-464-5258
 - b. Community Hospital 315-492-5907
 - c. For Infection Prevention on-call refer to [AMION](#).

Removing isolation precautions from COVID-19 positive patients

Test-based strategy: Must meet all criteria before removal

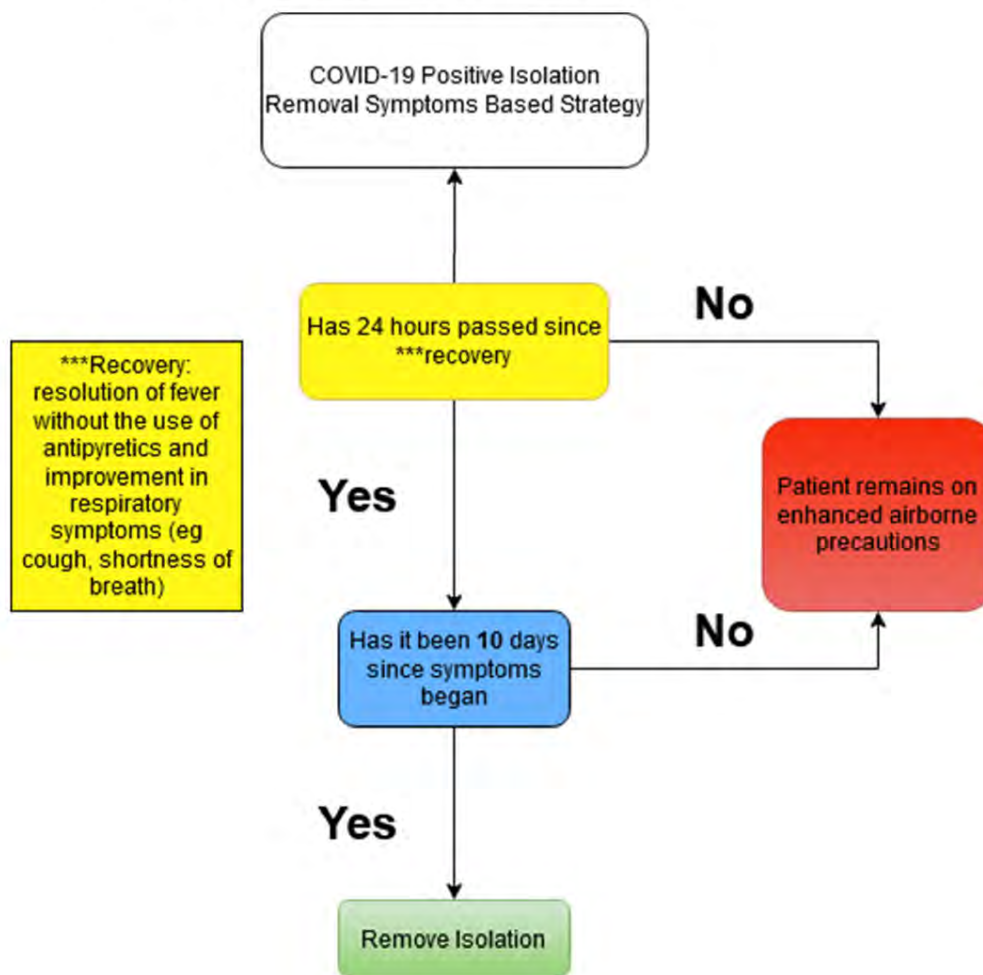
COVID-19 onset is defined as the first day of COVID-19 symptoms or date of first positive test

- 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, and
- It has been 10 days from the onset of COVID-19



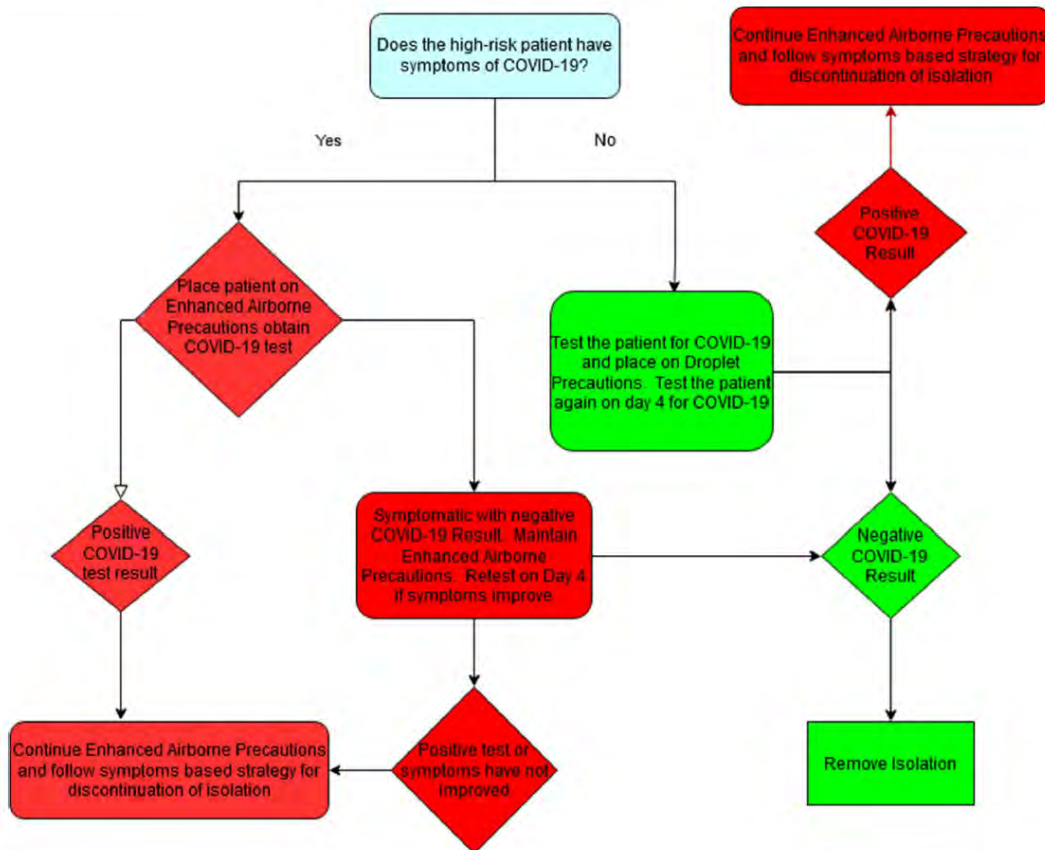
Symptoms-based strategyMust meet all criteria before removal

- At least 24 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 10 days passed since symptoms first appeared



NON COVID-19 High Risk* Patients

*High Risk Patients	
Patients from nursing homes	Patients from group homes
Patients from assisted living	Patients from rehab facilities
Patients from memory care unit	Patient with travel history
Patients from correctional facilities	

**Optional protocol to remove isolation from Nursing Home patients during admission**

- 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).
- If the COVID IgG Antibody test is positive and the nares COVID PCR is negative, the Enhanced Airborne precautions may be removed.

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 ($P_{aCO_2} < 50$) 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):**
 - 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

Anticoagulation Management in Critically Ill and Non-Critically Ill COVID-19 Positive Adult Patients

VTE Diagnosis

- Routine use of ultrasound screening and/or biomarkers (i.e., D-dimer) should not be used for detection of asymptomatic DVT.
- For suspected VTE, doppler ultrasound or computed tomography angiogram should be performed.
- The utilization of enoxaparin for thromboprophylaxis is preferred over heparin to limit staff exposure to COVID positive patients.

VTE Prophylaxis

	CrCl \geq 30 mL/min	CrCl < 30 mL/min
Standard	Enoxaparin 40 mg sq daily	Heparin 5,000 units sq q8h
Weight \geq 120 kg OR BMI \geq 40	Enoxaparin 40 mg sq twice daily	Heparin 7,500 units sq q8h
Weight < 50 kg	Enoxaparin 30 mg sq daily	Heparin 5,000 units sq q12h
<ul style="list-style-type: none"> • <i>Intermediate dosing of enoxaparin is not recommended for VTE prophylaxis</i> 		

Therapeutic Dosing

- For known or suspected VTE
- For patients on therapeutic anticoagulation prior to admission where agents with a shorter half-life are warranted due to clinical status, (i.e., renal dysfunction, potential procedures, etc.)

	CrCl \geq 30 mL/min	CrCl < 30 mL/min
Standard	Enoxaparin 1 mg/kg sq q12h	Heparin Infusion – High Dose
<ul style="list-style-type: none"> • <i>For critically ill patients on enoxaparin and requiring vasopressors the use Anti-factor Xa peaks should be considered to guide dosing</i> • <i>For patients on enoxaparin who are \geq 140 kg, BMI $>$ 40, or $<$ 50 kg, use of Anti-factor Xa peak should be considered to guide dosing due to risk of over anticoagulation</i> • <i>Dose adjustments to be made in accordance with policy CM A-29</i> 		

Heparin Allergy, History of Diagnosis or Suspicion of Heparin Induced Thrombocytopenia

	Prophylaxis with CrCl \geq 30 mL/min	Treatment with CrCl \geq 30 mL/min
< 50 kg	Fondaparinux is contraindicated	Fondaparinux 5 mg sq daily
50 – 100 kg	Fondaparinux 2.5 mg sq daily	Fondaparinux 7.5 mg sq daily
> 100 kg	Fondaparinux 2.5 mg sq daily	Fondaparinux 10 mg sq daily
<ul style="list-style-type: none"> • <i>Use of fondaparinux is contraindicated in patients with a CrCl < 30 mL/min</i> • <i>If therapeutic anticoagulation is required the use of argatroban should be considered.</i> 		

Discharge VTE Prophylaxis and Treatment

- Use of VTE prophylaxis after discharge is not suggested
- For patients requiring therapeutic anticoagulation, apixaban, dabigatran, rivaroxaban or edoxaban should be utilized for 3 months
 - Initial parenteral anticoagulation is needed before dabigatran and edoxaban
- For patients who are not able to be treated with a DOAC, warfarin should be utilized
 - Parenteral anticoagulation needs to be overlapped with vitamin K antagonists
- For patients who required therapeutic anticoagulation prior to admission, the therapeutic agent that was utilized prior to admission should be restarted if not done so during admission unless a change therapy was instituted.

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 $\geq 30/\text{min}$,
 - blood oxygen saturation $\leq 93\%$,
 - 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

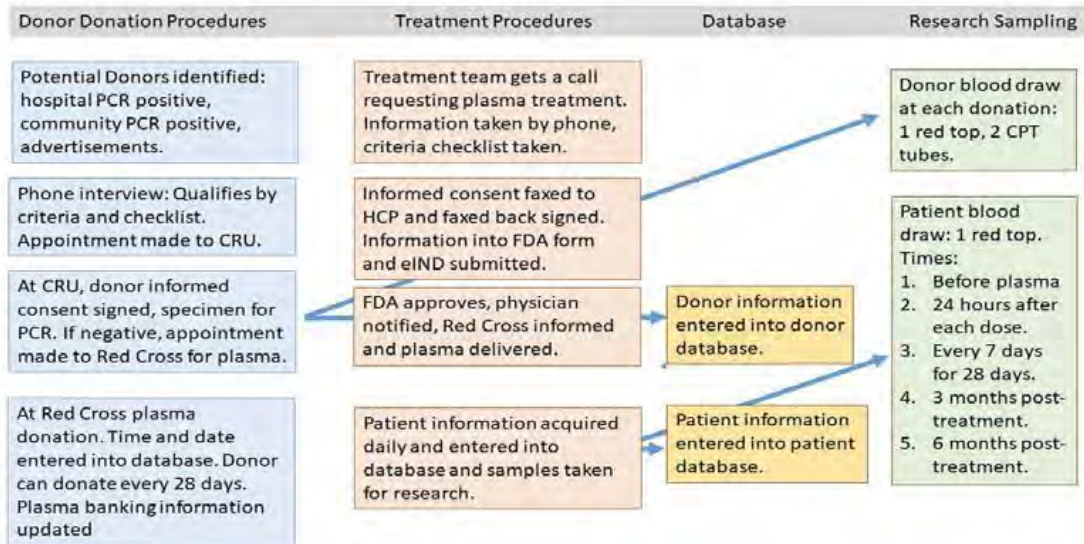
8. FDA Communication and Regulatory Compliance:

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)



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.

APPENDIX – 11 : Behavioral Health High Risk inpatients requiring transfer to inpatient psychiatric units 4B, 5W, and 7W

Patient preadmission disposition	Quarantine on Unit	Requirements for admission to psychiatric unit
Asymptomatic Homeless	4 days	Must have negative test ON day 4
<u>Asymptomatic High-Risk Group</u> <ol style="list-style-type: none"> 1. Nursing Home 2. Group Home Facilities 3. Rehabilitation Facilities 4. Assisted Living or Memory Care 5. Correctional Facilities 6. On quarantine from travel 7. Recent exposure to someone positive for COVID (within last 14 days) 	4 days	Must have negative test ON day 4
NON-Homeless Asymptomatic Adult	0 days	<ul style="list-style-type: none"> • Patients will be evaluated, upon decision to admit, the patient will receive Rapid COVID-19 test in ED without isolation and resulted before admission. • If test is negative nothing changes. • If test is positive the patient is quarantined and diverted to Medicine for treatment as per policies and procedures.

UPSTATE

UNIVERSITY HOSPITAL

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**

Page: 1/2

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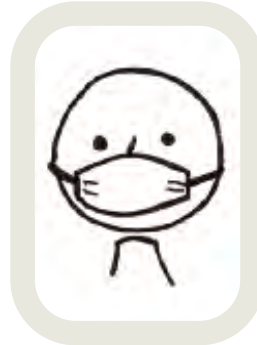
Cover Your Cough



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.

Page: 1/2

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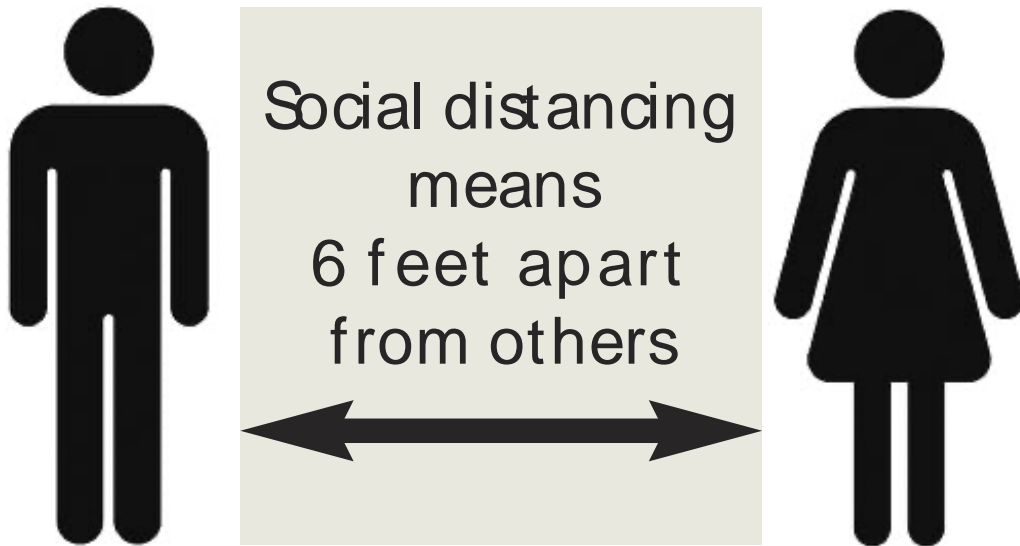
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Please keep
your social distance



Page: 1/2

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