COVID-19 Treatment Algorithm

Adapted from NIH Covid Guidelines, Upstate Institutional Guideline

1. Complete diagnostic work-up
2. Ensure code status and HCP
3. Assess prognostic factors (see page 2)
4. Determine severity of illness (see below)

Non-hospitalized patients (outpatient)

- Outpatient IV remdesivir
  - Given for 3 days to outpatients with at least one risk factor for severe COVID who are within 7 days of symptom onset and have not contraindications for remdesivir
- Anti-SARS-CoV-2 mAb
  - Single dose of appropriate mAb (NIH recommended) with at least one risk factor for severe COVID who are within 10 days of symptom onset
- Paxlovid (nirmatrelvir/ritonavir) OR molnupiravir 5-day oral courses for high-risk outpatients within 5 days of symptom onset; locations to access prescriptions can be found at https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/
- Full list of risks for severe COVID can be referenced here: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
- At this time, a limited spectrum of patients are being accepted for IV infusions, according to patient risk level and availability. Patients or providers can call the Upstate COVID hotline at 315-464-3979 to determine eligibility.

Patient hospitalized for some other indication (Gen Med floor)
Asymptomatic/ mild symptoms
SpO2 > 94% on RA

- Monitor for worsening clinical status and hypoxia
- Ensure prophylactic anticoagulation is ordered unless contraindicated.
- Patients who are hospitalized for reasons other than COVID and who are found to have COVID on an admission test, or have a positive test while in the hospital after a negative admission test are candidates for a 3-day course of Remdesivir therapy (approved by Upstate Institutional Guidelines)
  - Course is three days- 200 mg IV on day 1 followed by 100 mg IV daily for 2 days
  - Priority is for patients with at least 1 risk factor for progression to severe disease (as above), unvaccinated patients, or unboosted patients
  - No need to keep in the hospital to complete 3 days if clinically stable for outpatient care
- Inpatient use of Anti-SARS-CoV-2 mAb with activity against Omicron, sotrovimab, is limited by severe shortage. ID approval is required. Excellent candidates include pregnant patients, transplant patients NOT on oxygen, w/in 10 days of illness

UPSTATE MEDICAL UNIVERSITY

Moderate to severe disease (Gen Med floor)
SpO2 < 92% on RA, RR>30, PaO2/FiO2 < 300

- Maintain oxygenation: SpO2 92-96%, COPD patients: 88-92%, Pregnant patients: >95%. Maintain stable breathing: RR < 24, normal effort
- Ensure prophylactic anticoagulation is ordered unless contraindicated. Per latest NIH guidelines, therapeutic anticoagulation is now recommended for covid patients who are requiring supplemental oxygen AND have elevated D-dimer AND there is no contraindication (high bleeding risk); in pregnancy prophylactic anticoagulation should be used unless VTE is documented
- Consider antibiotics if there is concern for superimposed bacterial pneumonia
- **Specific COVID-19 therapy**: Remdesivir, Dexamethasone, proning per protocol, therapeutic anticoagulation
  - Remdesivir for 5 days: 200 mg IV on day 1, followed by 100 mg IV daily. If patient can come off supplemental oxygen, therapy can be discontinued before 5 days
  - Dexamethasone for up to 10 days: 6mg IV or PO daily
  - JAK inhibitor (baricitinib) or IL-6 inhibitors (sarilumab or tocilizumab (N/A at Upstate at this time)) should be used in patients with rapidly worsening hypoxia
- If worsening hypoxia >4-6L NC and increased work of breathing, consider MICU consult.

Formatted: Normal, Space After: 8 pt

Critical disease (ICU)
SpO2 <92% on > 6L, PaO2/FiO2 <200, rapidly increasing oxygen requirements

- MICU consult and evaluation for ICU admission
- Worsening hypoxia (>6L) and work of breathing (RR>30), hemodynamic instability (SBP <90, HR > 120s), lactate >2 after fluids, acidosis (ABG pH < 7.30), multi-organ failure
- **Specific COVID-19 therapy**: Dexamethasone, tocilizumab/sarilumab, baricitinib, and proning per protocol
- Patients who require ICU-level care and who were receiving therapeutic anticoagulation with no evidence of VTE should be transitioned back to prophylactic anticoagulation

Poor Prognostic Factors:

- **Epidemiology:** Age ≥65 years; having cardiovascular disease, chronic lung disease, sickle cell disease, diabetes, cancer, obesity, or chronic kidney disease; being pregnant; being a cigarette smoker; being a transplant recipient; and receiving immunosuppressive therapy
- **Vitals:** HR > 125, RR > 24, SpO2 < 94% on RA, PaO2/FiO2 < 300

1A Risk Group based on the NYS DOH guidelines for Prioritization of Anti-SARS-CoV-2 Monoclonal Antibodies During Times of Resource Limitations

- Unvaccinated patients over 65yo with at least 1 comorbidity
- Any age with moderate to severe immunocompromise regardless of vaccine status
  - Organ transplant
  - Currently getting chemotherapy
  - Received a stem cell transplant
  - Have an immunodeficiency disorder and/or you are taking meds that suppress the immune system such as Humira
  - Have HIV (if yes, CD4<200, OR off HIV meds for more than 1 month OR have never taken HIV meds)

UPSTATE MEDICAL UNIVERSITY

ADMISSION AND ISOLATION

- COVID-positive patients should be admitted to **INPATIENT** status.
- 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 must also be placed on Enhanced airborne precautions.

- For updated hospital policy regarding discontinuation of transmission precautions, please refer to COV D-04.

- Saliva PCR testing is also available now, approval may be required from COVID team (details in EPIC order). Criteria for saliva testing – nasal precautions, anatomic defect, medical contraindication, combative or uncooperative patient, patient refusal.

Admission criteria for COVID positive patients (any two):

- Respiratory Rate > 24 breaths/min
- Heart Rate > 125 beats/min
- SpO2 ≤ 92% 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 risk factors - 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.

DIAGNOSTIC WORKUP

Labs

On admission:
CBC with diff, BMP, LFTs, D-dimer are routinely done in the ED
ESR, CRP, Ferritin are not usually needed for clinical management, however, might have prognostic utility
Women of childbearing age: B-HCG
Consider blood cultures if suspecting bacteremia

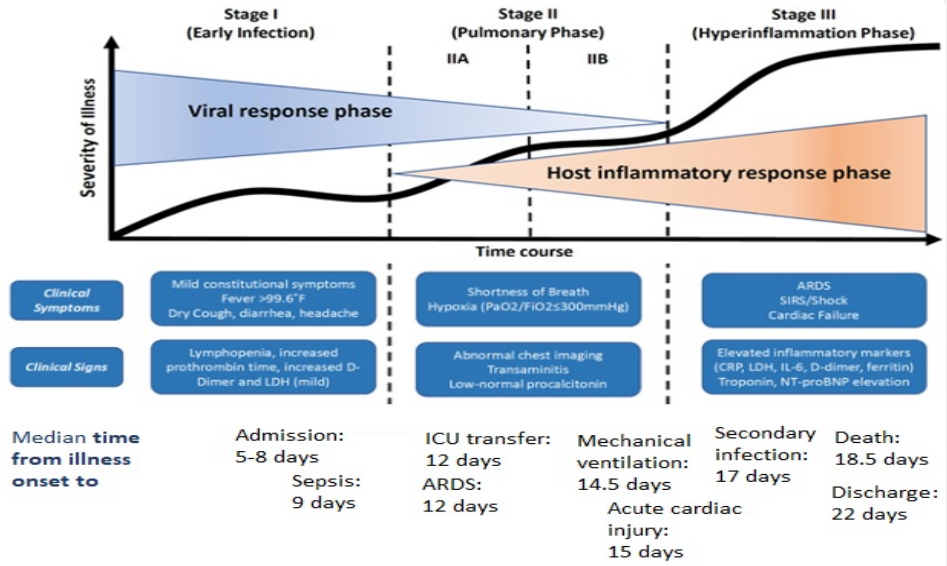
Follow up labs:
No indication for "routine labs". Order labs based on need for clinical decision making

Imaging

Portable chest X-Ray on admission or if any change in clinical status
CT chest without contrast is not routinely recommended unless otherwise indicated
Consider CTA Thorax if PE suspected
Evaluate for any thrombotic disease if clinical suspicion present

Trans-thoracic echocardiography:
No indication for TTE in every covid patient. Use clinical judgement in ordering TTE.

CLINICAL COURSE



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

DOCUMENTATION

COVID-19 specific smartphrases have been created on EPIC for appropriate documentation
To look up these smartphrases go to: 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

COVID-19 specific discharge instructions are also available for lookup on
Discharge instructions > Insert smart-text tab > Search COVID

GENERAL MANAGEMENT AND SUPPORTIVE THERAPY

Applicable for all patients admitted for COVID-19 regardless of disease severity.

- Maintain oxygenation SpO2 92-96% (88-92% for COPD). >95% for pregnant patients.
- Ensure continuous pulse oximetry is ordered with appropriate parameters.
- Analgesic and anti-pyretic – acetaminophen first line, NSAIDs second line.
- Continue home statin, ACE/ARBs, inhalers.
- Conservative fluid management.
- Avoid empiric antibiotics unless there is a specific concern for superimposed bacterial pneumonia
- Ensure all patients receive pharmacologic DVT prophylaxis unless contraindicated.

- Monitor for complications: Respiratory failure, ARDS, thromboembolic phenomena, AKI, DIC, secondary infections, acute cardiac injury, heart failure, encephalopathy.

- Ensure code status and HCP is established on admission, update families with changes in status.
- Do not initiate specific COVID-19 therapies unless the patient meets criteria for administration.
- If concern for rapid deterioration or for guidance on interventions, consider MICU and/or ID consult.

Anticoagulation

- Due to the increased risk of thrombotic events with COVID-19, all patients should receive pharmacologic DVT prophylaxis unless contraindicated. Enoxaparin (preferred, unless contraindicated, due to less frequent dosing) or heparin can be used
- Per latest NIH guidelines, therapeutic anticoagulation is now recommended for covid patients who are requiring supplemental oxygen AND have elevated D-dimer AND there is no contraindication (see guidelines for specific contraindications)

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

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 (PaCO2 <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

- 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 mmHg)
- 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~~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.

Dexamethasone
Dexamethasone is shown to reduce mortality among hospitalized patients with severe disease.

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.
NIH does not recommend use of steroids in patients not on supplemental oxygen, however they can be considered if a patient has significant symptoms and chronic supplemental 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)

Remdesivir is a nucleotide prodrug of an adenosine analog. It binds to the viral RNA-dependent RNA polymerase and inhibits viral replication by terminating RNA transcription prematurely

Eligible Patients

Hospitalized patients requiring supplemental oxygen
Onset of symptoms < 7-10 days

Dose

200 mg IV on day 1, followed by 100 mg IV daily for 4 days
In order to conserve Remdesivir it is recommended to prescribe a 3 day course unless the patient requires ICU care or is severely immune compromised; if patient is still requiring oxygen after 3 days then 2 additional days can be prescribed. Full course of 5 days need not be completed if patient has improved and is stable for discharge.

Adverse effects:

Gastrointestinal symptoms (e.g., nausea), elevated transaminase levels, an increase in prothrombin time without a change in the international normalized ratio, and hypersensitivity reactions

Liver function tests and prothrombin time tests should be performed for all patients before they receive remdesivir, and these tests should be repeated during treatment as clinically indicated. Remdesivir may need to be discontinued if a patient's alanine transaminase (ALT) level increases to >10 times the upper limit of normal, and it should be discontinued if an increase in ALT level and signs or symptoms of liver inflammation are observed

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

Baricitinib

Immunosuppression induced by JAK inhibitors potentially reduce the inflammation and associated immunopathologies observed in patients with COVID-19. Additionally, baricitinib has theoretical direct antiviral activity through interference with viral endocytosis potentially preventing it from entering and infecting susceptible cells

Eligible Patients

To be used in combination with remdesivir in patients with COVID-19 who require supplemental oxygen, ventilatory support, or ECMO and/ or for rapidly increasing oxygen requirement and systemic inflammation.

Dose

4 mg oral once daily in combination with remdesivir. Duration of baricitinib is 14 days or until hospital discharge, whichever is first

Anti-SARS-CoV-2 Monoclonal Antibodies

Currently, 3 anti-SARS-CoV-2 mAb products have received Emergency Use Authorizations (EUAs) from the Food and Drug Administration (FDA) for the treatment of mild to moderate COVID-19 in non-hospitalized patients with laboratory-confirmed SARS-CoV-2 infection who are at high risk for progressing to severe disease and/or hospitalization

Treatment should be started as soon as possible after the patient receives a positive result on a SARS-CoV-2 antigen test or nucleic acid amplification test (NAAT) and within 10 days of symptom onset.

The use of anti-SARS-CoV-2 mAbs should be considered for patients with mild to moderate COVID-19 who are hospitalized for a reason other than Covid-19

- Sotrovimab: This mAb was originally identified in 2003 from a SARS-CoV survivor. It targets an epitope in the RBD of the spike protein that is conserved from SARS-CoV. **Active against Omicron but is severe short supply. ID consult needed for inpatient use.**
    - Sotrovimab 500 mg administered as an IV infusion

- Bamlanivimab plus etesevimab: These are neutralizing mAbs that bind to different, but overlapping, epitopes in the spike protein RBD of SARS-CoV-2. **Not active against Omicron**
    - Bamlanivimab 700 mg plus etesevimab 1,400 mg administered as an intravenous (IV) infusion

- Casirivimab plus imdevimab (Regeneron): These are recombinant human mAbs that bind to nonoverlapping epitopes of the spike protein RBD of SARS-CoV-2. **Not active against Omicron**
    - Casirivimab 600 mg plus imdevimab 600 mg administered as an IV infusion or as subcutaneous (SQ) injections

There is evidence AGAINST the following therapy in routine clinical settings:

Chloroquine/ hydroxychloroquine

Azithromycin

Interferon Alpha, Beta, or Lambda

Ivermectin

Lopinavir/ritonavir and other HIV protease inhibitors

COVID-19 Convalescent Plasma

DISCHARGE

Discharge of Covid positive patients can be considered when patients are no longer requiring any further specific or supportive therapy that requires inpatient stay.

For patients admitted with principal diagnosis of Covid, if there is no other indication to keep them inpatient, consider discharging after remdesivir course (typically 5 days) is completed or once they have been weaned off supplemental oxygen, whichever is earlier. If such patients have persistent need for supplemental oxygen which is stable, <4-6L/min O2, they can be discharged with home oxygen therapy.

If patients continue to require inpatient stay for other indications, discontinuation of enhanced airborne precaution and transfer to non-covid unit will be considered based on institutional guidelines. Refer to policy COV D-04 for most up-to-date information.

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 enhanced airborne precautions have been discontinued, please refer to policy COV D-04.

Formatted: Heading 4, Indent: Left: 0", Line spacing: single

CM, infection control, DOH, and SW are helping provide information on discharge.
COVID discharge kits are available for patients on discharge, please contact CM for the same.
Please refer to discharge procedure policy COV D-02 for detailed guidance.

Appendix

APNIC PROTOCOL FOR AWAKE PRONING