Internal Medicine COVID-19 Survival Guide

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Table of Contents

A. Introduction

Welcome to the Internal Medicine COVID-19 Team. First, we want to thank you for your service in caring for these sick patients during these unprecedented and uncertain times. Additionally, we want to thank you for the sacrifice you made by being on the front lines during this pandemic. Although, we hope the public health initiatives will curtail the spread of this disease to avoid overwhelming levels, we understand the paramount importance of preparation for mass casualty and disaster events. In this light, we have provided a survival guide with important information on COVID-19 as well as the evaluation, admission, management, and discharge of COVID-19 patients as it pertains to Naval Medical Center Portsmouth. Again, thank you for continuing to make Naval Medical Center Portsmouth the "First and Finest".

Disclaimer: Please note that information regarding the appropriate diagnosis, management, and disposition of COVID-19 Persons Under Investigation (PUI) or positive patients is changing rapidly. This document is meant to serve as a guideline but may inevitably change as new research or command decisions come to light. Lastly, this guide was designed to be an adjunct to assist with patient management but is in no way a substitute for individual clinical judgment and medical decision making.

B. Basic Science/Epidemiology

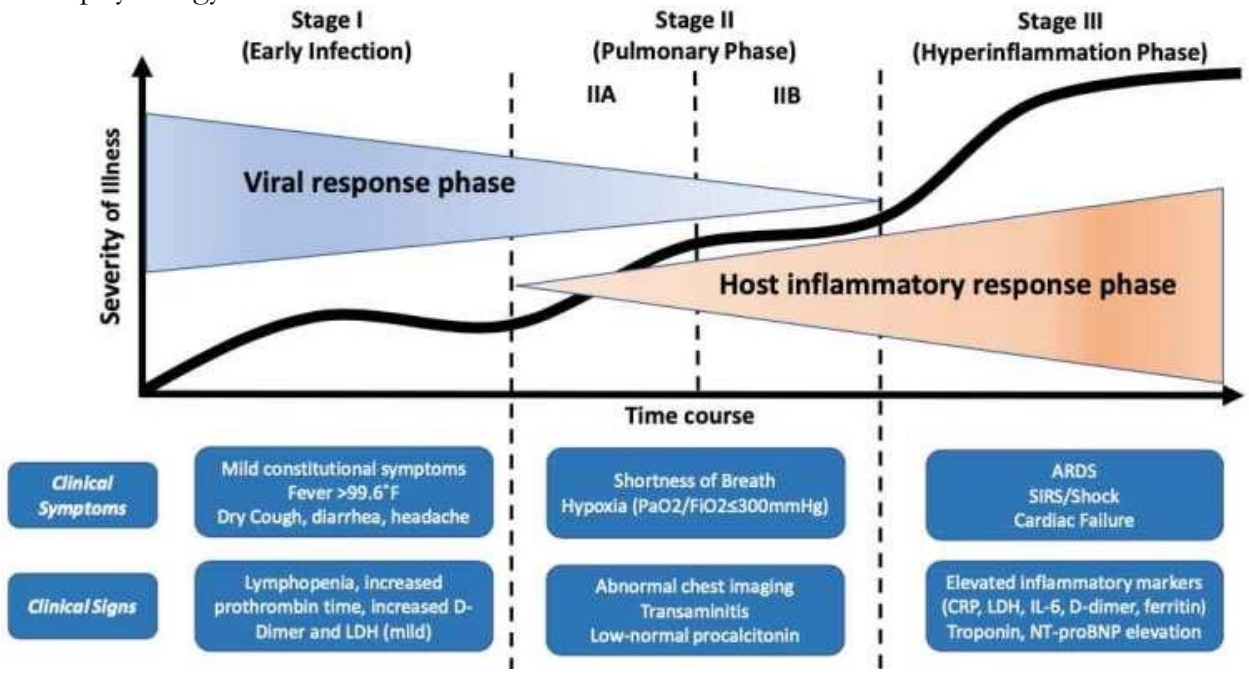
1. Biology

Novel coronavirus, or SARS-CoV-2, is a **non-segmented, positive sense RNA virus** that belongs to the larger coronavirus family, of which there are now **seven known members.** Four of these viruses are responsible for mild respiratory illness including the common cold [**229E, NL63, OC43, HKU1**] while **MERS-CoV** and **SARS-CoV-1** cause MERS and SARS respectively.

SARS-CoV-2, which causes novel coronavirus 2019 or **COVID-19**, is most closely associated with SARS-CoV-1, the virus responsible for the SARS epidemic in 2003. A significant relation between the two viruses is the mechanism by which they enter host cells: the **ACE2 receptor**, a receptor that has been shown to be present on **type II pneumocytes, intestinal epithelia, and nasal mucosa** in addition to many other locations.

Variant strains have become increasingly important with three varients currently circulating in the US that were originally identified in Brazil, South Africa, and the UK. These variants may be less susceptible to vaccines or treatments and may increase risk of re-infection in those previously infected with the wild-type virus.

2. Pathophysiology



1. Hypoxemic respiratory failure
    a. Pneumocytes have been shown undergo **cytopathic effect**, indicating **direct viral damage** rather than damage secondary to inflammation.
    b. COVID-19 has also been shown to **reduce surfactant levels**, leading to alveolar collapse, **atelectasis**, and de-recruitment.
    c. Likely mechanism of lung injury is "diffuse alveolar damage" or **Acute Respiratory Distress Syndrome (ARDS**), which has led to the adoption of many principles of ARDS management for COVID-19 patients.

2. Cytokine Storm
    a. Around **day 7-10** of illness patients can acutely worsen which can manifest as recalcitrant **fever, cytopenias**, elevated liver associated enzymes, multi-organ system failure, **elevated ferritin levels**, and **disseminated intravascular coagulation**.
    b. This has been shown to likely be related to **immunological hyperactivation** triggered by the virus or its associated immune response, similar to hemophagocytic lymphohistiocytosis (HLH) or CAR-T cell cytokine release syndrome but appears to be distinct from these conditions.

3. Disseminated Intravascular Coagulation
    a. Later in the disease course, patients can present with signs of disseminated intravascular coagulation (DIC) with rising d-dimer correlated to poorer prognosis.
    b. Etiology could be secondary **to HLH-like immunologic activation** and associated **up-regulation of fibrinogen** versus direct binding of the virus to ACE2 receptors on **endothelial cells**.
4. Pro-thrombotic and inflammatory pathophysiology and consequences
    a. Venous thromboembolism (VTE), including extensive deep vein thrombosis (DVT) and pulmonary embolism (PE), is very common in acutely ill patients with COVID-

19, **seen in up to one-third of patients in the intensive care unit (ICU), even when prophylactic anticoagulation is used.**

b. This state has been termed **thromboinflammation or COVID-19-associated coagulopathy (CAC)** by some experts. It appears to be distinct from disseminated intravascular coagulation (DIC), though DIC has been reported in severely affected patients (as discussed above).
c. There are also reports of **arterial thrombosis**, including in the central nervous system (CNS). The largest study, which included 3334 individuals (829 ICU and 2505 non-ICU) reported stroke in 1.6 percent and myocardial infarction in 8.9 percent.

3. Transmission

COVID-19 has been shown to have **various modes of transmission** that impact how we appropriately care for these patients as well as the healthcare staff to ensure safety and limit spread of infection. The incubation period from inoculation to symptoms is most commonly 5.6-6.7 days in 60 year old individuals although longer periods up to 14 days have been described with the mean duration of incubation increasing by a day for every 10 years of age increase.

1. Large **Droplet** Transmission
    a. A primary mode of transmission was found in large droplet transmission, which is typical for respiratory viruses such as influenza. Most societies recommend that risk is **greatest within 6 feet of an actively infected patient**.
    b. Risk is mitigated to an acceptable degree by the patient and provider wearing a **standard surgical mask**.
2. **Airborne** Transmission
    a. There is increasing evidence that COVID-19 can also be transmitted via an **airborne** route, thus implying the need for a provider to wear a **fitted N95 mask**.
    b. There have been recent studies to suggest that COVID-19 can persist in aerosols for hours.
    c. Most transmission is still believed to occur by droplet rather than aerosol transmission, though certain medical procedures may increase the risk of aerosolization.
    d. **Negative pressure isolation is ideal**; however, **availability and initial risk assessment** will determine which patients are placed in isolation
3. **Contact** Transmission
    a. How long the virus can survive on surfaces and how important fomites are to transmission remains unestablished.
    b. When a patient coughs, droplets deposit on fomites creating a thin film. A second, uninfected person can come in contact with the fomite, touch mucosal membranes and become inoculated.
    c. This can be mitigated with regular **deep cleaning of rooms** during turnover, **thorough and frequent hand washing**, and avoidance of **facial touching**.

The Basic Reproduction Number, Rø, is an epidemiologic term that can be thought of as the **expected number of cases directly generated by one case** in a population where all individuals are susceptible to infection. If Rø is < 1, the disease will eventually burn out. If Rø is > 1, the

disease will increasingly infect hosts in an exponential fashion. Current Rø estimates for COVID-19 are approximately **2.5-2.9**.

C. Personal Protective Equipment

Protecting yourself, as a healthcare worker (HCW), before entering the room of a patient suspected of having COVID-19 with the proper equipment is paramount **to limiting the spread of infection** to yourself and other coworkers. This could have significant **consequences regarding staff shortages** for our hospital as well as putting the **community at risk.** Even more important is learning the correct protocol for donning and doffing this equipment.

Important for preventing transmission of SARS-CoV-2 in the healthcare settings is having at least two layers of protection for all contacts (non-COVID-19 patient to HCW, HCW to HCW, etc.). One layer is your own mask. The second can be a mask on the patient or eye protection on you (or both). The following are the PPE expectations for the Military Health System as published in the DoD clinical practice guideline.

Clinical Management of COVID-19, v7

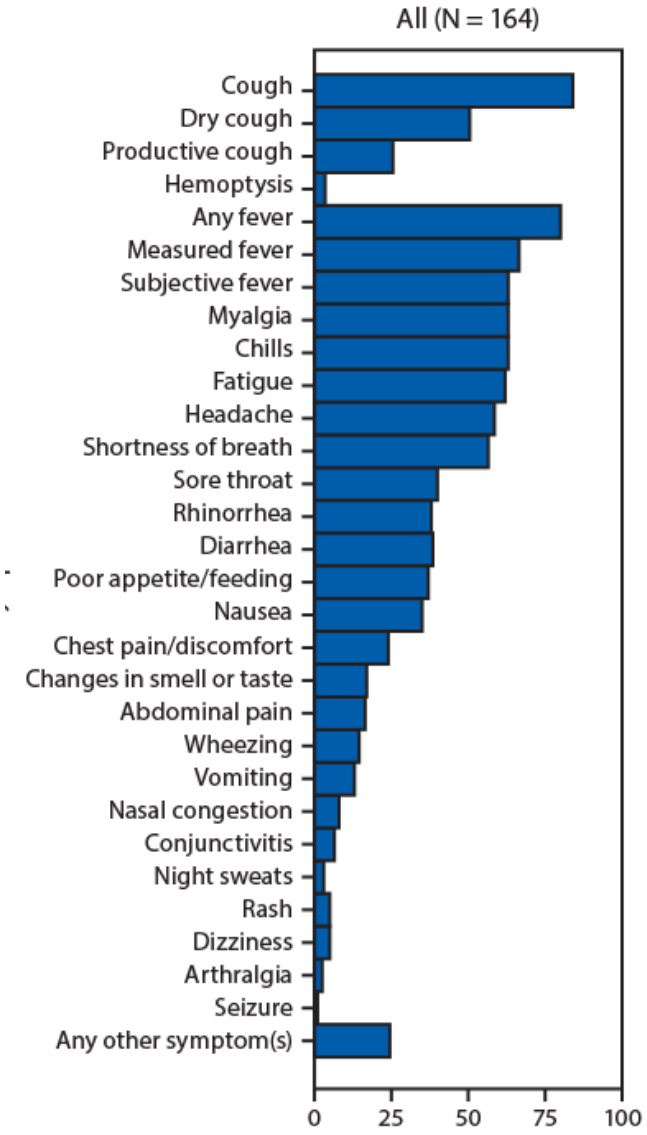
CATEGORY	DEFINITION	REQUIRED ISOLATION/PPE
0	Patient not suspected of having COVID-19	**STAFF:** • Surgical mask • PPE according to task. See Standard Precautions. **PATIENTS:** Masking (e.g., cloth without valves, surgical mask)
1	Asymptomatic patient with known exposure or high-risk for exposure to COVID-19 within the last 14 days	**STAFF:** • Surgical mask • PPE according to task. See Standard Precautions. **PATIENTS:** MUST wear surgical mask if traveling outside room for medically essential purposes
2	Patient under investigation (PUI) or positive COVID-19	**STAFF:** • Contact Precautions (gown and gloves) • Droplet Precautions (N95 Respirator preferred; Surgical mask if insufficient supply of N95 if no aerosol-generating procedures performed in room) • Eye protection (face shield or goggles) **PATIENTS:** MUST wear surgical mask if traveling outside room for medically essential purposes
3	Positive COVID-19 requiring aerosol- generating procedures (i.e., BiPAP, CPAP, endotracheal intubation, high- flow nasal cannula, nebulizers, tracheal suctioning)	**STAFF:** • Contact Precautions (gown and gloves) • Consider head and foot covers • Airborne Precautions (N95 Respirator or PAPR) • Eye protection (face shield or goggles) • Negative pressure room **PATIENTS:** MUST wear surgical mask if traveling outside room for medically essential purposes

This video from the DoD CPG Guideline reviews procedures:
https://www.youtube.com/watch?v=bG6zISnenPg

1. Donning
    a. The correct order for donning personal protective equipment (PPE) prior to entering the room of a patient suspected of having COVID-19 is **GOWN, MASK, GOGGLES/FACE SHIELD, THEN GLOVES**.
2. Doffing
    a. Doffing PPE is often considered the **more challenging** step as well as the **most important** to ensure mitigation of potential spread.
    b. Prior to beginning the doffing process, **first apply hand sanitizer from inside the room to your gloves.**
    c. Carefully remove gown by **pulling the chest area forward**, ensuring to keep the gown forward and have the waste bin open.
    d. **Carefully roll the gown inside out over the gloves** while simultaneous removing the gloves.
    e. **Discard bundle of rolled gown and gloves** into waste bin.
    f. Clean your hands with soap and water and re-don gloves. Carefully remove your eyewear touching only the rear-most part of the ear pieces and wipe them down thoroughly with approved sanitizer wipes .
    g. Only **once a-f is complete**, can you leave the room into **the ante room**.
    h. Once in the ante room, follow standard procedure for **washing hands**
    i. While **leaning over the waste bin** the ante room, carefully remove the straps from the **N95 mask and let the mask fall into the waste bin**.
    j. **NOTE**: If conserving goggles and/or N95 mask please follow ward instructions for proper conservation.

D. Clinical Features at Presentation

The clinical illness script for COVID-19 is constantly changing as more cases are discovered. However, many patients present with **lower respiratory symptoms** such as cough or dyspnea, **fever**, **upper respiratory symptoms**, and/or **gastrointestinal** symptoms. Incubation period is a median of **4 days** with a range of **14 days**. Common presenting symptoms (with percent displaying this symptom at presentation include:



1. Fever
    a. Data has shown that **fever is present in about 50% of patients at the time of hospital admission**, signifying that absence of **fever does not exclude COVID-19**.
2. Gastrointestinal Symptoms
    a. **10% of patients** may present with nausea or diarrhea which ***precede*** the onset of respiratory symptoms.
3. "Silent hypoxemia"
    a. There is a subset of patients that present with nonspecific symptoms and are found to be **hypoxemic without dyspnea**.
4. Taste/Smell: About 25% of patients will have disturbance in taste or smell.

E. Additional Resources

Additional resources for more detail (and that are updated routinely) include:

1. The Internet Book of Critical Care (IBCC): A continuously peer reviewed and updated summary of the literature is available from the IBCC at: https://emcrit.org/ibcc/covid19/

2. DoD Clinical Practice Guideline (CPG): The DoD has a published practice guideline for COVID-19 available in the same drive as this document.

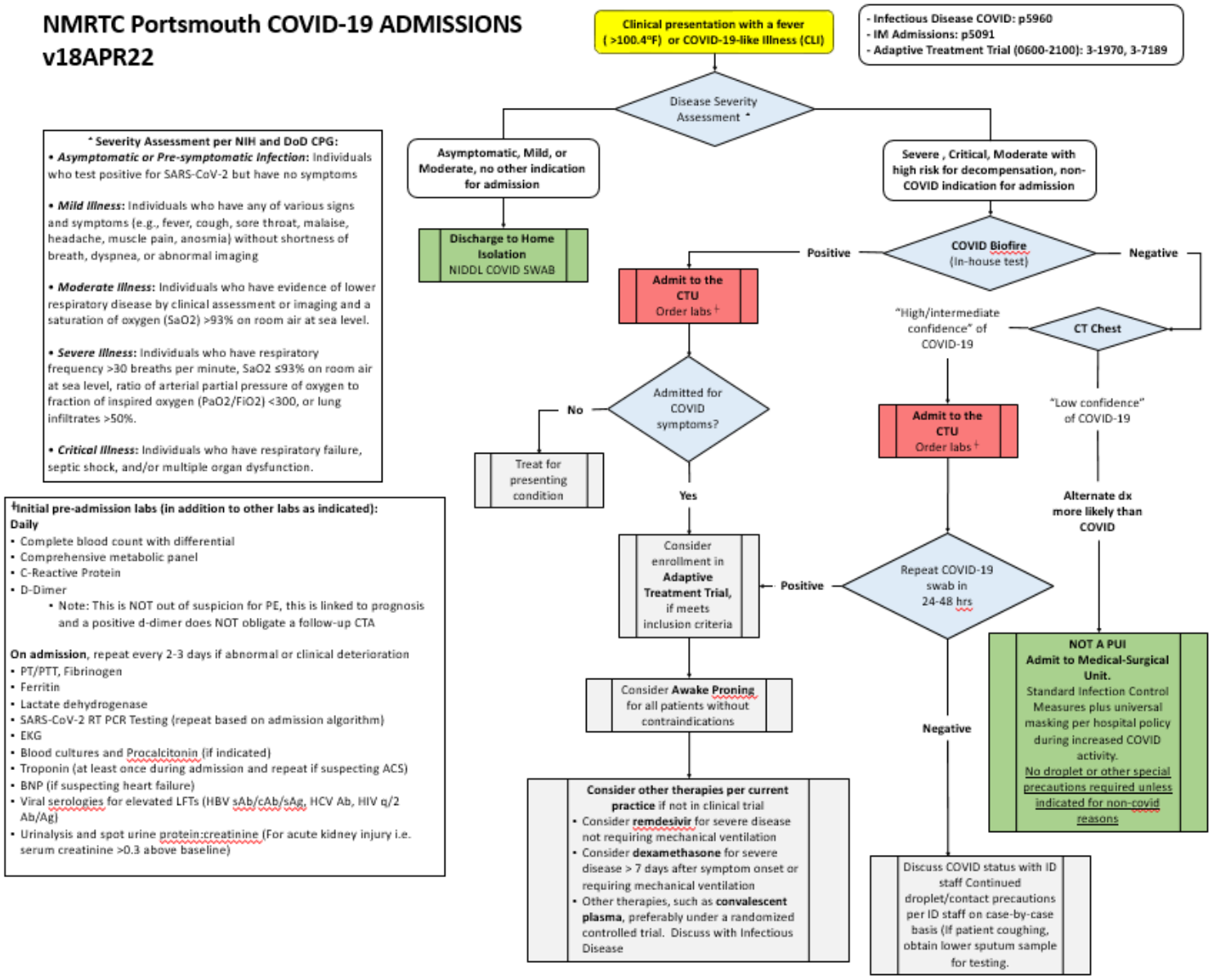
3. American College of Physicians Course on COVID-19: The ACP (internal medicine professional society) has a more in-depth course on COVID that is also updated regularly that walks through the basics of coronaviruses up through current treatments and approaches to COVID-19 and provides a large assortment of resources for further information.

4. Infectious Disease Society of America Guidelines

5. National Institute of Health Guidelines

6. Surviving Sepsis COVID-19 Guidelines

F. Triage Algorithm



G. Laboratory Evaluation

1. Basic Laboratory Evaluation

Initial testing should include labs that will either **1. aid in risk stratification or 2. add prognostic information**. The following are important laboratory tests that add may add to the above information:

1. Complete blood count
    a. WBC counts are typically normal, although **lymphopenia** commonly is present in COVID-19 patients. Lymphopenia on admission has been associated with later need for ICU level care and with mortality (ALC of 800 cells/μL and 1100 cells/μL have both been used as cutoffs in analyses)
    b. **Elevated Neutrophil to Lymphocyte ratios (NLR)** has also been identified as a risk factor for poor outcomes (≥9) .
    c. **Lower platelet counts (<100) are associated with poorer prognosis**.
2. Coagulation studies
    a. Laboratory values consistent with **DIC** can be seen and elevated prothrombin time is associated with poor outcome.
    b. **D-dimer > 1.00** is an indicator for poor prognosis but not necessarily indicative of active clotting in these patients, though pulmonary thromboembolism is a common complication.
3. Inflammatory markers
    a. COVID-19 increases **C-reactive protein**, which can be **marker of disease severity** as well as prognosis.
4. Procalcitonin
    a. **Markedly elevated procalcitonin** may **suggest bacterial superinfection** and have some negative predictive value in COVID-19.
    b. In those that have **known COVID-19**, **elevated procalcitonin may have negative prognostic value.**
5. Respiratory Viral Panel
    a. NOTE: A positive RVP for a different respiratory pathogen does not rule out COVID-19. **Co-infection has been documented in approximately 5% of patients**.

Our department has collaborated on an **Internal Medicine COVID-19 Order Set** that can be found in Essentris. The following labs are included in the Order Set and should be ordered **if not ordered AND collected in the Emergency Department**:

Recommended Per DoD CPG:

Daily

1. Complete blood count with differential
2. Comprehensive metabolic panel
3. C-Reactive Protein
4. D-Dimer

a. Note: This is NOT necessarily out of suspicion for PE, this is linked to prognosis and a positive d-dimer does NOT obligate you to get a CTA of the chest but may influence decisions regarding degree of anticoagulation

On admission, repeat every 2-3 days if abnormal or clinical deterioration

1. PT/PTT, Ferritin
2. Lactate dehydrogenase
3. SARS-CoV-2 RT PCR Testing (repeat based on admission algorithm above)
4. EKG

If Clinically Indicated

1. Blood cultures (if starting antibiotics for bacterial infection)
2. Procalcitonin
3. Troponin (if suspecting ACS)
4. BNP (if suspecting heart failure)
5. Viral serologies for elevated LFTs (HBV sAb/cAb/sAg, HCV Ab, HIV q/2 Ab/Ag)
6. Urinalysis and spot urine protein:creatinine (For acute kidney injury i.e. serum creatinine >0.3 above baseline)

Bear in mind, just because the Emergency Department ordered the test does not mean it was collected and sent to the lab. You should verify specimens have been drawn and received by the lab.

2. COVID-19 RT-PCR (How to Order COVID-19 swab test)

The following is the process for ordering nasopharyngeal swab for RT-PCR COVID-19 to be sent to **National Infectious Disease Diagnostic Lab (NIDDL**), which has a **1-3 day turnaround**, or **NMCP Lab** test, which uses one of our biofire machines and **takes approximately 45 minutes to run but may be delayed if the machines are already in use** as they can only run one test at a time. Labcorp has greatest capacity for tests, but turnaround time varies. In general admitted patients should get rapid in house test with biofire and outpatients should get NIDDL, unless high risk conditions warrant biofire testing.

1. Go into CHCS order section and find your patient
2. New -> Lab -> COVID -> COVID-19 (NIDDL) or "Rapid" (In House test)
3. For NIDDL only, select 5. NASOPHARYNGEAL SWAB (For in-house just answer the questions that will pop up)
4. For in-house/rapid select diagnosis if admitting for potential SARS-CoV-2 infection
5.

```
Select LABORATORY TEST: covid
      1    COVID -EPI LAB   SARS-CoV-2 PCR
      2    COVID -LABCORP   SARS-COV-2, NAA
      3    COVID -NMCP   SARS-CoV-2 RAPID
      4    COVID-NIDDL   SARS-CoV-2 PCR (REF)
Choose 1-4:
```

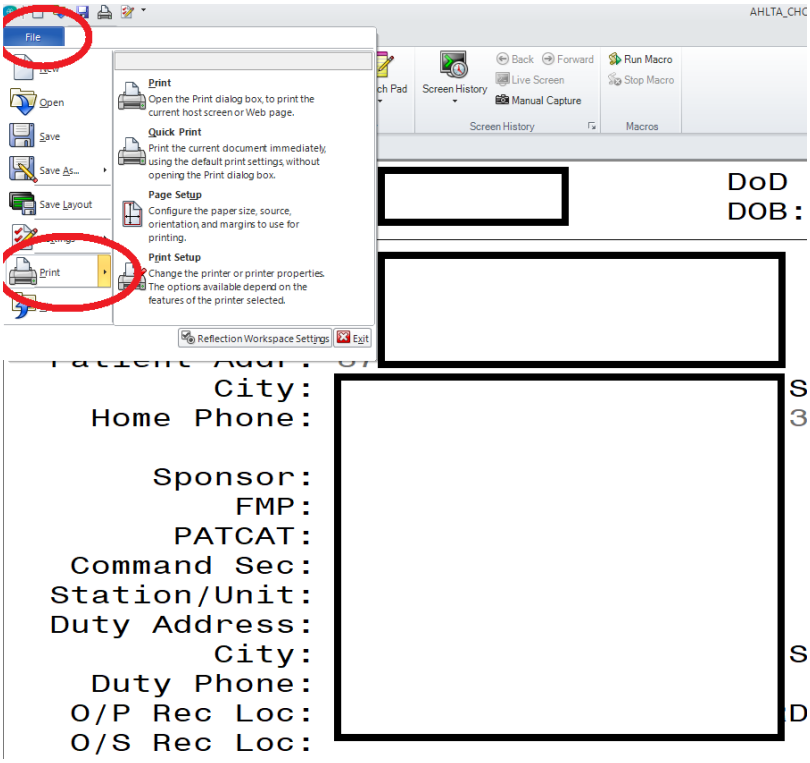
```
Order Required Data:
  Please indicate the testing category.

  Use the arrow keys to edit responses or press Return to continue
```

```
+ group movements and/or engagement. Surveillance-identify incidence in a
  specified population or geo-location.

  Select one of the following:
  DIAGNOSIS       DIAGNOSIS
  SCREENING       SCREENING
  SURVEIL         SURVEILLANCE
```

6. Quit back out and print the order to your local printer ("slave" will print to your computer's default printer)
7. Exit back to the main CHCS menu
8. Type ^MRG
9. Type a space and hit enter to select the same patient you just ordered the swab on
10. Select file > Print



11. ENSURE BOTH PRINTOUTS WITH YOU AND TRANSPORT TO THE LAB WITH THESE FORMS IN THE BAG WITH THE MINI-REGISTRATION FACING OUT.

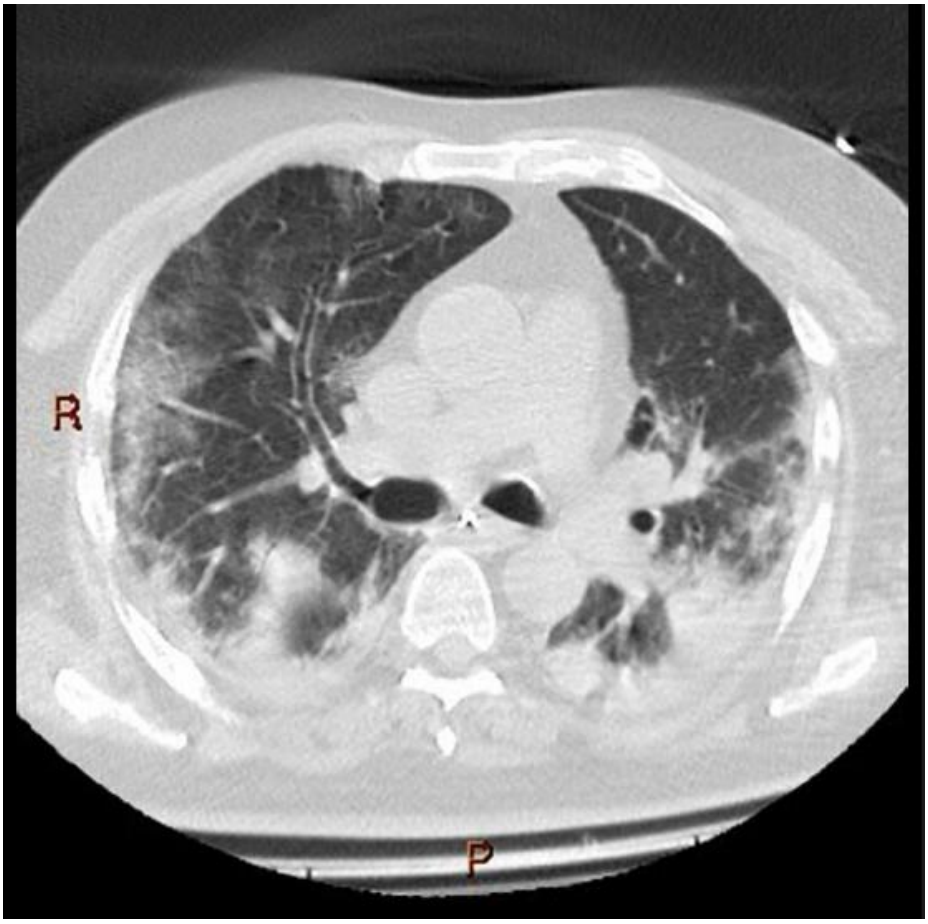
NOTE: **Nasopharyngeal swabs should only be performed by personnel trained to appropriately swab patients.** If you are unsure about whether or not you've been trained, you should not be doing swabs.

H. Imaging Evaluation

Typical imaging findings include **bilateral patchy ground glass opacities**, which are concentrated in the **periphery and basal segments**. Findings that **suggest an alternative diagnosis include pleural effusions, masses, cavitation, or lymphadenopathy**.

The radiology department at NMCP risk stratifies cases features on Chest CT **scans** in patients with potential COVID-19 on a scale of "confidence." At NMCP, patients **with high and intermediate confidence features are determined "radiologically positive"** and treated as such,

even if initial PCR testing is negative. The algorithm they use for this is available in the same folder as this guide.



1. Example of a CT consistent with "high to intermediate confidence" for COVID-19.

I. Nasopharyngeal Swab Procedure

An adequate specimen retrieved via a nasopharyngeal swab is paramount to successful risk stratification, diagnosis, and management of patients with suspected COVID-19. There is a high likelihood for false negative swabs if not performed correctly, which not only could result in morbidity and a delay in appropriate care for the patient but poses a public health and infection control risk.

DO NOT DO THIS UNLESS YOU HAVE COMPLETED THE COMMAND TRAINING. You may think you know how but time and time again people who have been very confident have been found out to not know what they're doing leading to false negatives and patient harm. If you are unsure if you've completed the training, then you haven't. This section is a reminder for those who have completed the training, not an alternative to completing the command training.

1. Specimen Handling

A. Preparation

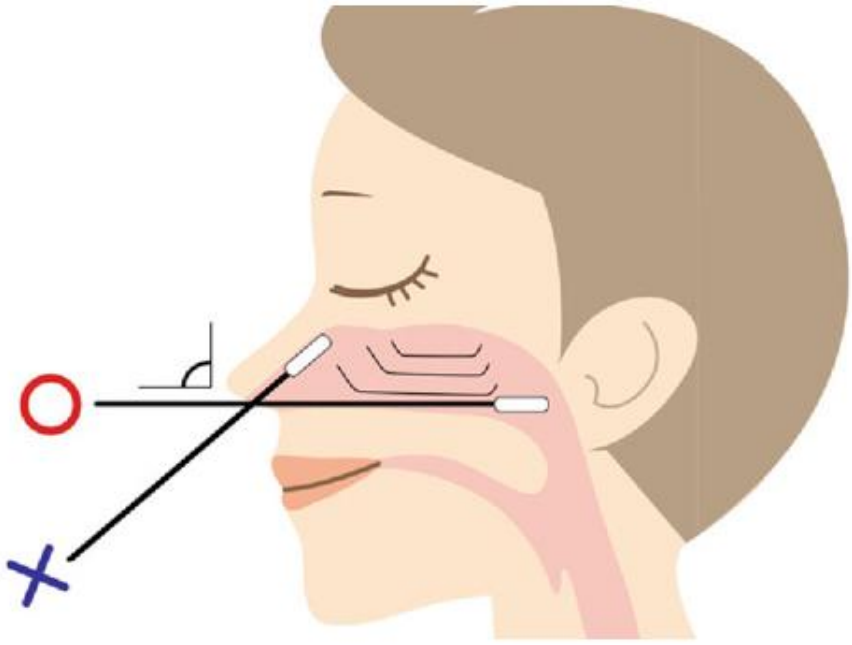
1. Prepare appropriate tubes/containers, labels, plastic specimen transport bags, a clean Chux (do not use one already in the room) and 2 clean emesis basins. Label one basin "Clean" and the second basin "Dirty".
2. Place all items in the "dirty" emesis basin. This will be used to transport these items into the patient room and this basin will remain in the room after specimen collection.
3. Disinfect hands and don personal protective equipment (PPE), putting on a second pair of clean gloves.

B. Procedure

1. Place a Chux Pad in the "clean" emesis basin and leave in the Anteroom. Bring "dirty" emesis basin containing supplies and unused specimen transport bags into the patient's room, do not place on patient bed.
2. Follow standard procedures for patient identification and specimen collection.
3. Place specimen containers/tubes in the dirty basin in the patient room.
4. Label all specimens at patient bedside.
5. Remove 1st pair of gloves and discard.
6. With clean gloves, place labeled specimens into the unused specimen transport bag and seal the bag.
7. Wipe outside of bag with hospital-approved disinfectant wipes. At this time, the bag is considered "clean"
8. Place "clean" bagged specimens in the "clean" emesis basin (previously placed next to the door in the Anteroom).
9. Bagged specimens should be hand-delivered directly to the lab. Staff should use a one hand gloving technique, by donning gloves on one hand to carry specimen and keeping the other hand clean (to open doors or operate elevators). Remove gloves after drop-off and perform hand hygiene after removal of gloves. Please refer to the COVID-19 Laboratory SOP on the COVID-19 SharePoint Site."

2. Specimen Collection

1. Stand to one side of the patient with their head in the neutral position facing forward, NOT in a sniffing position
2. Be aware that the patient may sneeze or cough, stay out of the line of fire!
3. Insert swab into nasal cavity parallel and along the nasal floor **LOW AND SLOW**
4. The nasopharynx is about 9-10cm from the naris opening, this 2/3 of your 15cm swab
5. At the nasopharynx you will feel some increased resistance. STOP HERE. If you feel like you are hitting a "wall," DON'T PUSH THROUGH IT
6. Position Twirl in place gently for 3-5 seconds
7. Slowly withdraw the swab with a rotating motion
8. Repeat with the other naris
9. Place the swab into the transfer medium/vial and remove from the room according to the applicable SOP (such as the one above)



- O – correct technique
- X – incorrect technique

J. Admissions

1. Severity Assessment

The current disease severity assessment published by the NIH and DoD is as follows:

• ***Asymptomatic or Pre-symptomatic Infection*:** Individuals who test positive for SARS-CoV-2 but have no symptoms

• ***Mild Illness*:** Individuals who have any of various signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal imaging

• ***Moderate Illness*:** Individuals who have evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SaO2) >93% on room air at sea level.

• ***Severe Illness*:** Individuals who have respiratory frequency >30 breaths per minute, SaO2 ≤93% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300, or lung infiltrates >50%.

• ***Critical Illness*:** Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Other currently identified risk factors for poor outcomes include:

1. The **laboratory assessments** as in the previous section
2. Demographics
    a. Age > 55
    b. History of **pulmonary disease**
    c. History of cardiac disease including **hypertension**
    d. History of **chronic kidney disease**
    e. **Immunosuppression**
    f. **Obesity**
3. Vital signs
    a. Respiratory rate >24
    b. Heart rate > 125
    c. >2 liter oxygen requirement to keep SpO2 >90%

2. Patient Placement

Patient placement will guidelines will be fluid as patient volume changes but in general, risk of intubation should be the guiding metric when deciding if an ICU/CTU consult is indicated. Communicate early and often with ICU staff and nursing staff to determine appropriate placement based on patient condition and resource availability.

3. Admission Order Set Checklist

Our NMCP COVID-19 Working Group has devised a **COVID-19 Standard Order Set** that can be used for all COVID-19 admissions. The following should be checked on **every suspected COVID-19 admission before arriving to the floor**.

Admission Orders

- Team assignment (COVID Team 1, COVID Team 2, Ward Team 1, Ward Team 2, etc.). The patient will not populate on the rounding list without this order.
- Provider contact information (in admission orders and on discharge tracking screen)
- Code status order
- COVID risk stratification order (note "confirmed" if positive by PCR or CT)

Activity

- **Restricted** to room for everyone
- Order for negative pressure room if required. **Not every patient requires negative pressure** and we don't have bed space to accommodate everyone in negative pressure**.**

Labs

- COVID **admission labs** as above in "workup"
- Repeat labs as warranted for other conditions (**THERE IS NO SUCH THING AS ROUTINE LABS WITH THESE PATIENTS.** Each lab should be to answer a specific question that could change management and will require staff exposure to collect)

Diet

Ensure is ordered with an **isolation tray** (completely disposable)

Medications

- **Home medications** as indicated
- Insulin as indicated
- **Community acquired pneumonia treatment** if indicated
- **Investigational Drug or other therapy**
- **DVT prophylaxis** ordered if not contraindicated

Treatments

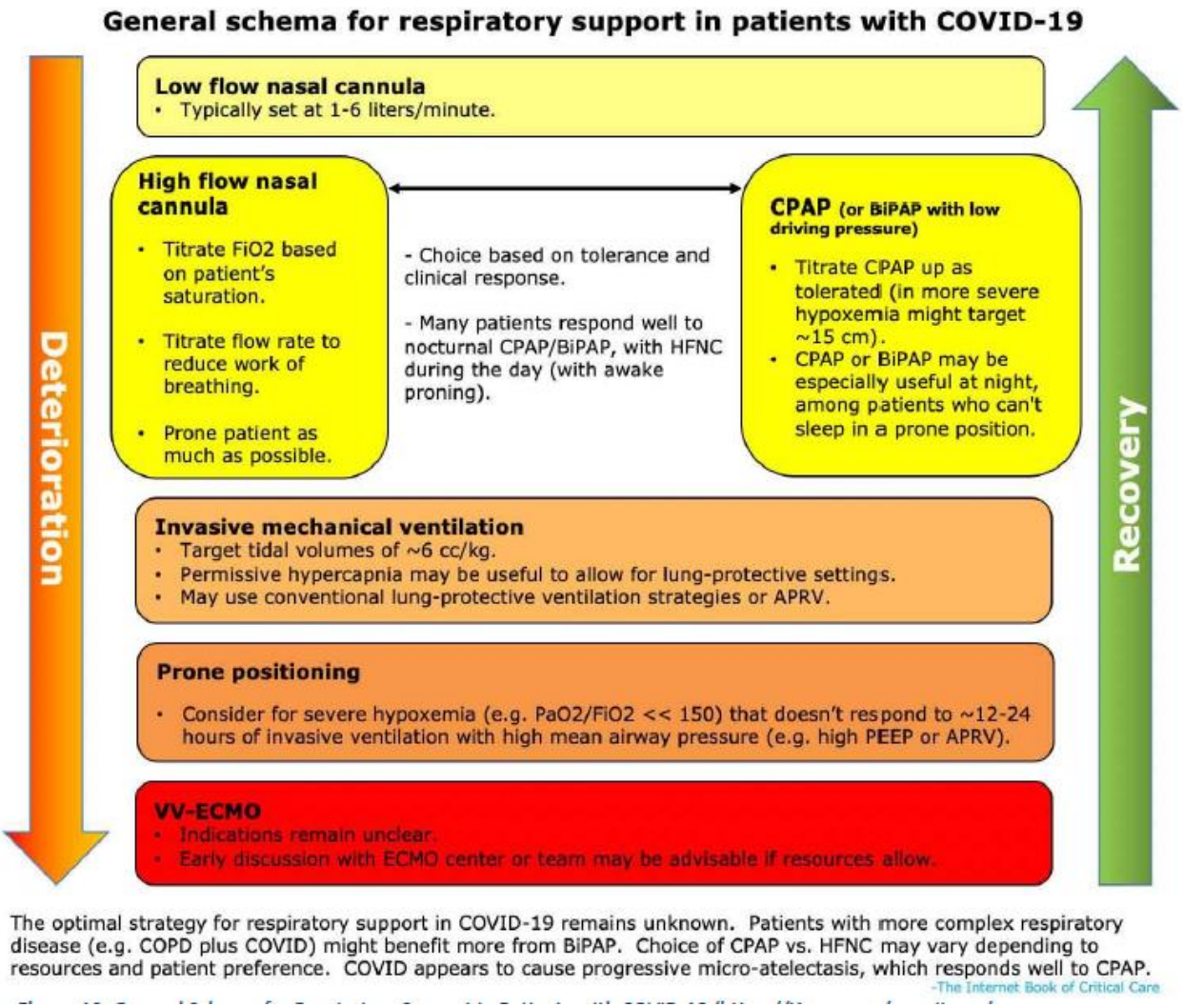
- Oxygen orders with goal **92-96%**
- Orders to **alert provider for increasing O2 requirements which may be heralding a need for high flow oxygen, non invasive ventilation or intubation**
- Telemetry orders (order "no telemetry" if it is not desired)
- Order for **telemedicine monitor** to be appropriately aligned and activated at all times
- **Awake proning per protocol** (see appendix B)
- **Exercise per protocol**

Vital signs orders

Select frequency keeping in mind limiting staff exposure as much as is safe for the patient

4. Respiratory Support

In general, start with nasal cannula (1-6L/min) and progress to HFNC if not able to maintain O2 saturations >88%. Concomitant proning or side positioning can be used as well (see "tummy time" protocol). Non-invasive ventilation (BiPAP) can be considered to help with atelectasis if requiring >80% FiO2 however this will be at the discretion of the attending intensivist.



5. Adaptive COVID-19 Treatment Trial 3 (ACTT3)

ACTT 2 is currently closed. ACTT3 is pending. See Appendix B for the ACTT-3 information when it becomes available.

6. Remdesivir

The antiviral Remdesivir has been approved by the FDA (in large part due to ACTT-1) for patients age 12 or older, weighing at least 40kg, and requiring hospitalization for COVID-19. The IDSA recommends this only for those with oxygen saturation <95% on room air. The medication is contraindicated in patients with known hypersensitivity to any ingredient in remdesivir. It must be discontinued for ALT > 10x the upper limit of normal, ALT elevation accompanied by signs of liver inflammation, or for eGFR <30ml/min.

The recommended adult dosing for non-mechanically-ventilated patients is: 200mg IV x1 on day one followed by 100mg IV daily on days four through five. If the patient does not have clinical improvement the daily dose can be extended for up to 5 more days for a total of 10 days.

This medication is discontinued when the patient is well enough to be discharged.

Monitoring includes daily

- Hepatic panel
- BMP (for eGFR)
- Prothrombin time

7. Dexamethasone

Like remdesivir, dexamethasone (6mg PO daily for 10 days) can be considered in patients with SpO2 ≤ 94% on room air. The order is also present in the COVID-19 Standard Admission order set. Benefit was seen for patients with symptoms > 7 days and was most pronounced for those requiring mechanical ventilation. This medication is discontinued when the patient is well enough to be discharged.

8. Anticoagulation

COVID-19 is known to elicit a **pro-thrombotic state** in patients, leading to venous increased risk of thromboembolism **even on prophylactic dosing of anticoagulation**. This seems to be due to a combination of increased levels of clotting factors, acquisition of antiphospholipid antibodies, decreased endogenous anticoagulant proteins and excessive platelet and neutrophil activation with viral mediated endothelial inflammation. **AT MINIMUM, DVT prophylaxis is of paramount importance**, and patients may even need higher doses than typical prophylaxis as heparin resistance has been seen in some patient with the disease.

In summary, please ensure that **chemical DVT prophylaxis is on all suspected COVID-19 patients** and can be adjusted as necessary by the primary team. Consideration should be given to increasing anticoagulation dose if deemed appropriate. Additionally, there should be **a high index of suspicion for venous/arterial thromboembolism** in patients presenting with **acute worsening of hypoxia or symptoms consistent peripheral emboli**. The below are the current guidelines for anticoagulation published in JAMA in November, 2020:

Table. Current Guideline Recommendations for Venous Thromboembolism Prevention in Hospitalized Patients With Coronavirus Disease 2019

Patient/setting	Recommendation	
	American College of Chest Physicians	International Society on Thrombosis and Hemostasis
Critically ill	Prophylactic-dose LMWH	Prophylactic-dose LMWH; half-therapeutic-dose LMWH can be considered if patient is high risk
Non-critically ill	Prophylactic-dose LMWH or fondaparinux	Prophylactic-dose LMWH
After discharge	Extended prophylaxis not recommended	LMWH/DOAC for up to 30 d can be considered if high thrombosis risk and low bleeding risk
Nonhospitalized	Routine prophylaxis not recommended	Routine prophylaxis not recommended

Abbreviations: DOAC, direct oral anticoagulant; LMWH, low-molecular-weight heparin.

K. Rounding

1. Daily Rounding Routine

Typically, the **rounding schedule is determined by the attending running the COVID-19 Team**. Based on that schedule, you should consider the following daily events to be documented and checked prior to rounds:

1. 24 Hour events
2. Talk to the patient via phone or VTC (**physical exam is NOT required unless to address a specific question**)
3. Review vitals with attention to **O2 requirements and fever** (as well as antipyretic use)
4. Review **labs**
    a. **Replete potassium** to level of 4 as indicated

SERUM K+ (mmol/L)	K+ REPLETION (mEq)
3.3-3.5	40 IV or PO
3.0-3.2	50 IV and/or PO
2.6-2.9	60 IV and/or PO
<2.6	80 IV and/or PO

- It is best to give mag first if possible
- Separate doses of >40mEq PO by 4 hours, for very low can give both IV and PO simultaneously. K-Dur is delayed release.
- Peripheral infusion rate is limited to 10mEq/hr; 20mEq/hr by central line
- If creatinine > 2 reduce the above recommendations by 20mEq

b. **Replete magnesium** to a level of 2 as indicated

SERUM Mg++ (mg/dL)	**Mg++ REPLETION**
1.6-1.9	1gm IV x1 **or** 400mg PO q8h x3
1.4-1.5	2gm IV
0.8-1.4	2-4gm IV, check K+
<0.8	4-6gm IV, check K+

- The slower the infusion, the less gets eliminated in the urine.
- Recommend 1gm/hour if asymptomatic
- Consider reducing dose by 50% if renal dysfunction

5. **Review imaging** if not already done

2. Rounding List

The COVID-19 Working Group ™ has created a **Rounding List** similar to rounding list used by traditional inpatient medicine teams. It is located by accessing the inpatient medicine rounding list and selecting your COVID team number. Please see the Supplementary Appendix if you are unable to locate these lists or have difficulty with acquiring them.

3. Daily COVID-19 Rounding Checklist

In the event that the **patient load becomes significant** for each COVID-19 Internal Medicine Team, our group wanted to provide an **efficient, memorable method for rounding** that ensures that **key decision points, disposition criteria, and other important factors of care** are not overlooked. The following **mnemonic will also be printed on placards** to be passed out to rounding teams:

COF AND SPIT

COVID status: (Confirmed, Under Investigation, Ruled out), symptom day #
Oxygen requirement: How much. When it was last required?
Fever: Time of last fever, antipyretic use.

Antibiotics: Agents used, day __ of __ (if applicable)
Novel Medications
- Agent day __ of __ (if applicable)

De-escalation
- Current vital signs frequency. Can it be reduced?
- Current lab orders. Can they be discontinued or frequency reduced?
- Current telemetry orders. Can it be discontinued?

Status: Code status
Prophylaxis: Are they on chemical DVT prophylaxis? If not, why not?

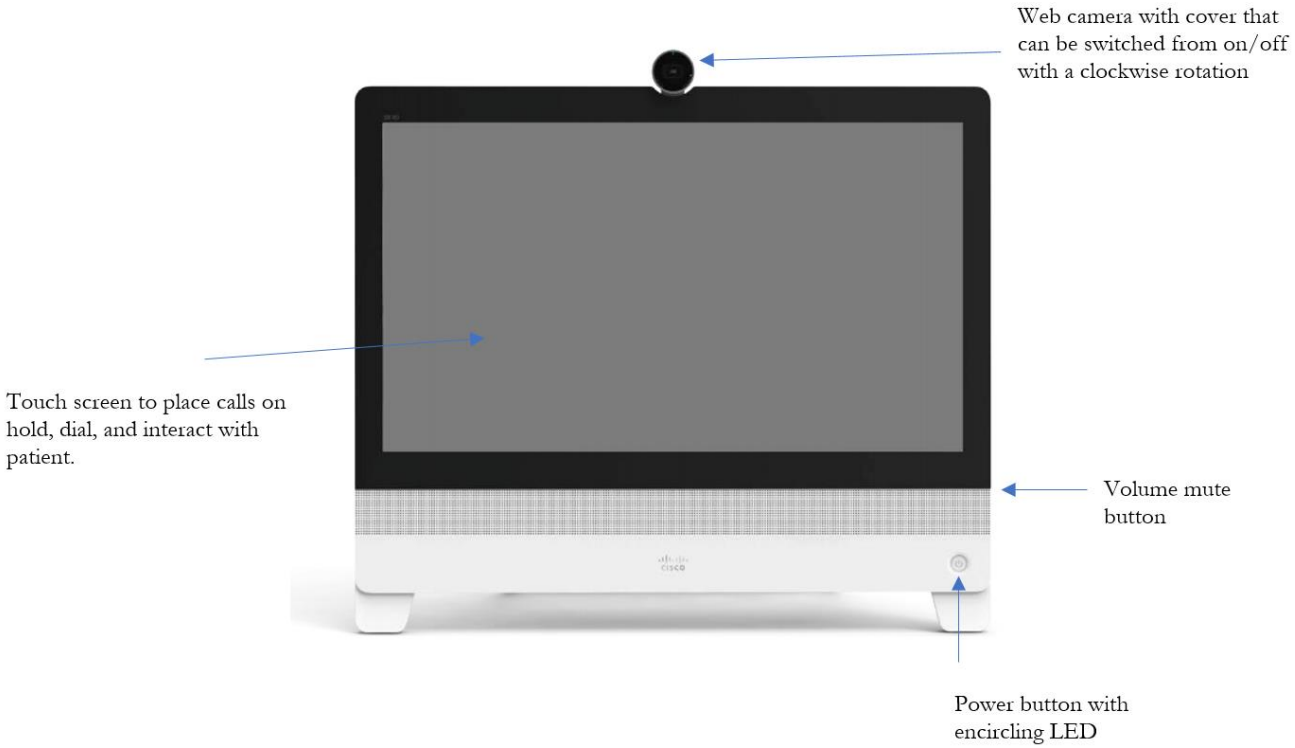
Indication for admission: What is keeping them from de-escalating level of care or going home?
Transition: What barriers to safe discharge exist? (e.g. is there a good plan for where they will go after the hospital)

4. Telemedicine

In an effort to reduce unnecessary patient exposures and conserve PPE, NMCP has installed telemedicine monitors to be placed in as many patient rooms as possible and at the main nursing station located in the COVID-19 Treatment Unit (CTU). Through the course of a patient's stay, the majority of markers for improvement [and discharge] such as respiratory rate, supplemental O2 requirement, and fever, can be assessed through telemetry and remote video teleconferencing rather than direct contact.

NOTE: **Each patient should have an initial admission physical examination** upon admission for suspected COVID-19. Telemedicine should be used as an adjunct for daily monitoring and should not be used in lieu of proper examination and clinical judgment.

Anatomy of a Cisco Webex DX80



Remember: Mute and close the microphone when done and **DO NOT END THE CALL**. **INSTEAD, PLACE THE CALL ON HOLD SO THE CONNECTION IS NOT SEVERED**. If you end the call then someone will have to go back into the room to answer a new call next time you want to talk to that patient. Placing the call on hold (instead of ending it) allows the call to remain connected but inactive, ready to be taken off hold for subsequent use.

L. Discharge

1. Discharge Considerations

Starting the day of admission begin planning for where the patient will go after discharge and what barriers may unnecessarily extend their hospital stay and thus their risk of iatrogenic complication.

Ensure they are able to effectively self-isolate at home if needed.

If they are going to a facility on discharge, they will likely need one more negative COVID tests before transfer. Plan for this early so that the required testing can be complete by the day of discharge.

2. Home Isolation Categories

When a **patient meets discharge criteria**, the provider must then determine a **home isolation instruction plan** to provide to the patient which **corresponds the categories listed below**. These categories can be selected on your **daily progress notes**. You will work with **family liaison and discharge planning** to ensure the patient has a **good home isolation plan** in place if needed. These are important to make clear **even if the patient is transferring to another service** and not going home immediately.

- COVID Positive by PCR or CT scan: Self isolation until both of the following are true
    - Outpatients: 10 days from onset of symptoms or from day of positive test if asymptomatic
    - Inpatients: Most will require 20 days from onset of symptoms
        1. This is because most admissions meet criteria of "severe COVID" i.e. O2 sat <94%. The exception would be an admission with COVID for another indication, where they may not have the respiratory features to categorize as "severe COVID." In this case, 10 days from symptom onset (or 10 days from date of test) is appropriate.
    - Both outpatient and inpatient: 1 days without fever, cough, or dyspnea (off of antipyretics)
- COVID Negative, Influenza-Like-Illness (ILI) present: Self isolation until both of the following are true
    - 7 days from the day of discharge
    - 3 days without fever, cough, or dyspnea (off of antipyretics)
- COVID Negative, no respiratory illness: No self-isolation required.

3. Self-Isolation versus Self Quarantine

- Self-Isolation: The patient is **completely isolated from the public AS WELL AS members of his/her household**. They stay in their **own room**

with their own bathroom. Food is left at the door. They **do not have any face-to-face interactions** with a human except through video calls and closed windows until isolation ends. **This is for patients with COVID or CLI**

- Self-Quarantine: Those **with possible exposure to COVID** remain in their house for the duration of quarantine. **Household members may interact with each other** but must remain **separated from public life** including visits with/from friends and trips outside the home if possible. Exposed persons may transmit virus before symptoms or if symptoms never manifest, so social distancing, masks, etc. minimize risk of transmission from persons in quarantine without symptoms.

4. Discharge Instruction Templates

When discharging a patient with suspected or known COVID-19 home from the hospital, it is imperative to **provide complete and accurate discharge instructions** in order to keep **both the patient and the public safe**. The following are **templates to be used for COVID-19 discharges**. It is important to include **these instructions into discharge summaries**, **even if the patient is being transferred off the service to another non-COVID-19 unit** in the hospital. These instructions are to be **pasted into the Non-Template section** of the discharge summary following the typical **Hospital Course Summary** format.

***** HOSPITAL COURSE SUMMARY *****

On the day of discharge, the patient was tolerating a PO diet, ambulating without difficulty, and hemodynamically stable. The patient had an opportunity to ask questions and all questions were answered.

The patient desired to go home and felt comfortable doing so.

Please go to the nearest Emergency Department if experiencing severe headache, dizziness, vision loss, chest pain, palpitations, shortness of breath, coughing up blood, vomiting up blood, abdominal pain, diarrhea, passing bloody stools, passing bloody urine, or any other concerning symptoms that you cannot manage at home, or that cannot wait for a scheduled appointment.

###################### IMPORTANT ############################

COVID-19 POSITIVE

You have tested positive for COVID-19. We strongly recommend you self-isolate at home until both of the following statements are true:

It has been 20 days since your symptoms started, or since the day of your first positive test if you did not have COVID-19 symptoms

AND

For the day prior to stopping isolation you have not had a fever (defined as temperature over 100.4 F) and your symptoms are much better or resolved.

This means NO face-to-face interaction or physical contact with others, including members of your household. Maintain at least 6 feet of distance between members of your household.

Your family members and anyone living in your home should remain on self-quarantine (they should not leave the house or interact with people outside the house) for 14 days from the date they most recently had close contact with you.

FAMILY QUARANTINE UNTIL: 14 days from time of last contact with you.

YOU SHOULD SELF ISOLATE UNTIL AT LEAST: XXXX AND YOU HAVE NO SYMPTOMS FOR 1 DAY

IF YOU OR ANY OF YOUR FAMILY MEMBERS DEVELOP NEW OR WORSENING SYMPTOMS CALL THE COVID CALL CENTER AT 757-953-6200

RETURN TO FULL DUTY CRITERIA, PROVIDE THIS TO YOUR PRIMARY CARE DOCTOR FOR CLEARANCE TO RETURN TO UNRESTRICTED DUTY STATUS:

NO HEART INJURY OR LIMDU

1. **Patient meets return to work criteria plus 2 weeks of exercise limitations (no more than brisk walking) after symptom resolution.**
2. **Focused clinical exam by primary care provider without clinically significant findings and normal vital signs.**
3. **Privileged provider reviewed inpatient discharge summary to assess for end organ involvement or other significant COVID-19 sequelae. Specific focus should be placed on the assessment of myocardial and pulmonary injury. ECG and cardiac biomarkers should be obtained if not completed during hospitalization. Pulmonary studies should be thoroughly reviewed for evidence of injury or decreased function. If myocardial or pulmonary injury is present, consider expert consultation.**
4. **After (1), (2), and (3) above, gradual return to physical activity over two to four weeks. Repeat medical evaluation is only necessary if symptoms develop. If no symptoms, may return to duty**

HEART INJURY, STROKE, VENOUS THROMBOEMBOLISM, RESPIRATORY FAILURE, CARDIAC FAILURE, RENAL FAILURE, END-ORGAN FAILURE

1. **Return to duty based on expert consultation and case-by-case consideration for retention vs. referral to DES for Active Component (AC) or Line of Duty (LOD) or Medical Retention Review (MRR) for Reserve Component (RC). Pulmonary consultation is recommended 2-4 weeks after discharge for advanced pulmonary support to include high-flow nasal cannula, non-invasive positive pressure ventilation (NIPPV), invasive mechanical ventilation, or extracorporeal life support.**

################### IMPORTANT ##############################

NON-COVID-19 INFLUENZA LIKE ILLNESS

You have tested negative for COVID-19 but have symptoms of a flu-like illness. We strongly recommend you self-isolate at home until both of the following statements are true:

It has been 7 days since your symptoms started, or since the day of your first positive test if you did not have COVID-19 symptoms

AND

You have 3 consecutive days with no fevers (defined as temperature over 100.4 F), cough, or trouble breathing.

This means NO face-to-face interaction or physical contact with others, including members of your household. Maintain at least 6 feet of distance between members of your household.

Your family members and anyone living in your home may discontinue self-quarantine but should still practice careful hand washing and avoid being in close proximity with others as well as minimizing leaving the home as much as is possible.

YOU SHOULD STAY AT HOME AND SELF ISOLATE UNTIL AT LEAST: XXXX AND YOU HAVE NO SYMPTOMS FOR 3 DAYS

IF YOU OR ANY OF YOUR FAMILY MEMBERS DEVELOP NEW OR WORSENING SYMPTOMS CALL THE COVID CALL CENTER AT 757-953-6200

********** MEDICATIONS**
****
SEE BELOW FOR MORE DETAIL

START TAKING:

STOP TAKING:

********** APPOINTMENTS AND FOLLOW UP**
****

Labs/Tests that will need follow up **

Please bring or send all paperwork and medication lists with you to your primary care manager so they can be aware of the care you received during this admission.

You need to schedule a follow-up with your primary care manager (PCM). If your doctor is a military physician, call 1-866-MIL-HLTH.

You already have a scheduled follow-up appointment see below for details. To cancel/reschedule your appointment call 1-866-MIL-HLTH.

M. Notes

Appendix A: Non-intubated Awake Proning Protocol ™ ("NAPP TIME")

Non-Intubated Awake Pronation Protocol (™) "NAP TIME"

AKA "Tummy Time"

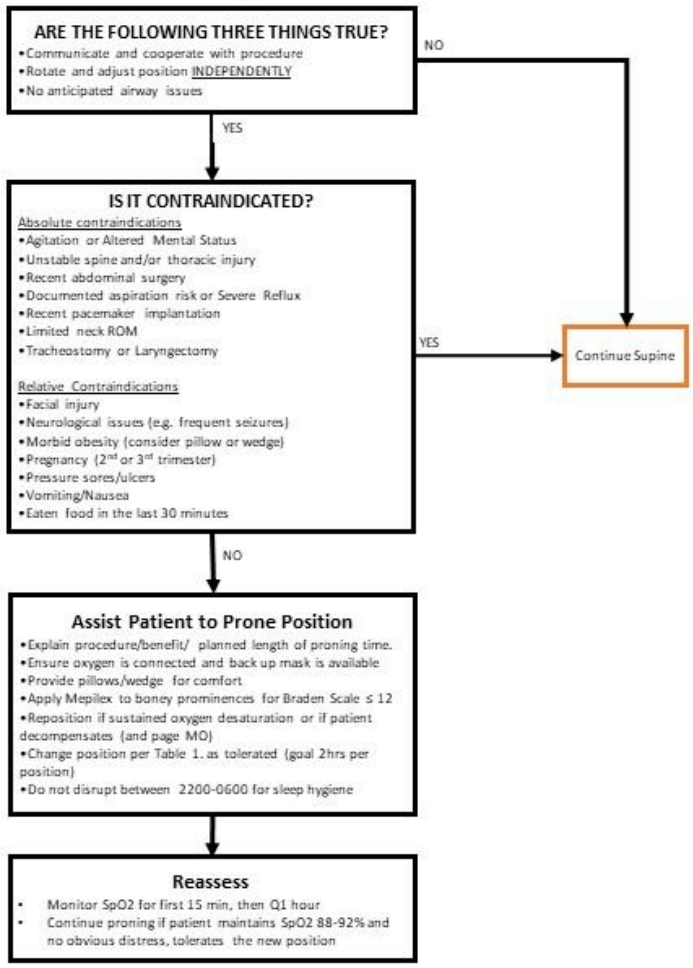


Table 1: Timed Position Changes:

1. 30min-2hrs lying fully prone (bed flat)
2. 30min-2hrs lying right lateral decubitus (bed flat)
3. 30min-2hrs sitting up (30-60 degrees head of bed) or out of bed in chair
4. 30min-2hrs lying fully prone (bed flat)
5. 30min-2hrs lying left lateral decubitus (bed flat)

- Repeat steps 1-5 except between 2200-0600 for sleep hygiene. Encourage patient to sleep prone/ with bed flat
- Goal is 2hrs per position

Appendix B: Adaptive COVID-19 Treatment Trial (ACTT 2) Information (ACTT 3 Pending)

Lead Nurse Coordinators: Janet McNiff (Ph: 757 953 1970; 240 534 9079)
Susan Banks (Ph: 757 953 7189; 240 534 9029)
Physician Investigator: Tahaniyat Lalani (Ph: 304 356 6603)

Description of Study. ACTT-2 will evaluate the safety and efficacy of remdesivir and baricitinib in hospitalized adult patients diagnosed with COVID-19. Half of patients will be randomized to receive remdesivir plus oral placebo, and the other half will receive remdesivir plus baricitinib. The study is double-blinded; that is, subject and study staff will not know whether baricitinib or oral placebo is given. The coating for the oral placebo is identical to the active baricitinib. All subjects will receive:

Remdesivir as a 200 mg IV infusion loading dose on Day 1, followed by a 100 mg once daily IV infusion while hospitalized up to a 10-day course

AND

Either Baricitinib **OR** oral placebo given as two tablets po or crushed for NG tube, daily while hospitalized up to a 14-day total course.

No Remdesivir or oral study product will be given after discharge.

NOTE: VTE prophylaxis is recommended for all subjects unless there is a contraindication such as active bleeding events or history of heparin-induced thrombosis.

Drug Characteristics and Safety

Remdesivir, an investigational IV medication, inhibits an enzyme needed for viral replication.
• **GI symptoms:** constipation, heartburn, loss of appetite, nausea, vomiting, loose stool, upset stomach
• **Other symptoms**: headache, itching, unusual feelings in the ear, dizziness, and shaking of the leg/arm.
• **Elevations of the liver enzymes** ALT and AST and increase in prothrombin time (PT) without any clinically significant change in INR.

Baricitinib, an orally administered, immune modulator (selective inhibitor of Janus kinase (JAK) 1 and 2), and is FDA-approved for treatment of rheumatoid arthritis.
• **Serious infections**: new and/or reactivation of infections, such as TB
• **Blood clots:** increased risk including deep venous thrombosis and pulmonary embolism
• **Laboratory changes:** increase in ALT and AST, decrease in WBCs, ANC and ALC, and hemoglobin
• Baricitinib should not be given with live or live-attenuated vaccines.
• **Drug-drug interaction** with probenecid. No DDI between remdesivir and baricitinib anticipated.

Prohibited Medications while on study

• Any biologic therapy outside of local written standards of care is prohibited: TNF inhibitors; IL-1, IL-6, or T-cell or B-cell targeted therapies; JAK inhibitor(s) other than baricitinib; interferon, convalescent plasma, or IV IgG therapies for COVID-19
• High dose corticosteroids, that is, at doses >10 mg per day (prednisone equivalent)

• Strong inhibitors of organic anion transporter 3 (OAT3) such as probenecid (DDI as above)

Recruiting and Consenting

- Call the research team if you have a potential patient, to review the enrollment criteria
- The primary team will approach the patient to see if they are interested in participating.
- If interested, the research team will conduct a verbal (phone) consent process with the patient
- Once enrolled, the study team will review labs and randomize subject and contact team to enter orders (see COVID-19 Adaptive Treatment Trial Order Set)

Study procedures:
Daily labs: CRP, D-dimer, CBC with auto-diff, CMP, PT,
Every other day: Research Labs (1 OP swab, 3 SST, 2 EDTA)
Medications as listed previously

CHECKLIST VERIFICATION BEFORE EACH DOSE: Study Team and Pharmacy will Review Safety Labs for Dose Modification and Discontinuation (below)

- ALT and /or AST,
- eGFR (actual calculated value)
- CBC with differential ALC, ANC, WBC
- Assess if suspected drug induced liver injury (DILI)

Hold remdesivir if either or both of the following occurs:

• If eGFR < 25mL/min, remdesivir infusion should **not** be given on that day. The infusion may be resumed when the eGFR returns to ≥ 30 mL/min.
• If ALT or AST > 5 times upper limits of normal (ULN), remdesivir should be held and not be restarted until ALT and AST ≤ 5 times ULN

Discontinue remdesivir if any of the following occurs:

• ALT or AST > 5 times ULN and ALT and AST do NOT return to ≤ 5 times ULN
• eGFR < 25mL/min, and does NOT return to eGFR ≥ 30 mL/min
• Renal function worsens to the point that subject requires hemodialysis or hemofiltration

Oral study product dosing considerations

Subjects with eGFR <60 mL/min will receive dose of only 1 tablet (2-mg or placebo) once daily. The tablets can be orally administered OR crushed and administered via soft food (like pudding) OR dissolved as a slurry in 10 mL room temperature water and administered via any gastric tube (GT)

Hold oral study product if any of the following and resume defined below:

• Total white blood cells (WBC) <1000 cells/μL; resume when WBC ≥ 1000
• Absolute neutrophil count (ANC) <500 cells/μL; resume when ANC ≥ 500
• Absolute lymphocyte count (ALC) <200 cells/μL; resume when ALC ≥ 200
• ALT or AST >5 times ULN; resume if, and when ALT and AST ≤ 5 times ULN
• Infection that, in the opinion of the investigator, merits study drug being withheld
• eGFR < 30 mL/min, resume when eGFR returns to ≥ 30 mL/min

Discontinue oral study product if any of the following occurs:

- Decrease in renal function so that subject requires hemodialysis or hemofiltration
- Active tuberculosis (TB) infection or evidence of latent TB (see protocol for more details)
- Subjects has a DVT or PE diagnosed
- Suspected drug-induced liver injury (DILI) with the appearance of fatigue, nausea, vomiting, right upper-quadrant pain or tenderness, fever, rash, and/or eosinophilia (>5%)
- New malignancy diagnosed
- ALT or AST >8 times ULN