Clinical Presentation

a. Symptoms: Fever, cough, dyspnea, myalgias, and diarrhea. Some patients develop hypoxic respiratory failure with no significant preceding dyspnea. Functional hypoxemia develops, sats<93% may indicate more severe clinical outcome.
b. Time to evolution of disease: Dyspnea 6 days, Admission 8 days, ARDS and ICU admission about 10 days after exposure
c. Labs: WBC normal to low with lymphopenia, c-reactive protein (CRP) elevated, serum creatinine increases upon deterioration, elevated D-dimer, elevated AST, ALT in more severe disease
d. Imaging Guidance for patients with suspected COVID-19
   i. Bilateral infiltrates on chest X-ray. The typical finding is patchy opacities, which tend to be predominantly peripheral and basal. The number of involved lung segments increases with more severe disease. Over time, patchy opacities may coalesce into more dense consolidation.
   ii. Findings which are not commonly seen, and might argue for an alternative or superimposed diagnosis:
      1. Pleural effusion is uncommon
      2. No mass, cavitation, or lymphadenopathy
   iii. In the majority of cases, a CT scan will probably add little to chest X-ray results. CT scans should be conserved for equivocal cases when it will change management. Overutilization of CT scan (especially in mild disease) can cause significant throughput issues and may place healthcare personnel at increased exposure risk.
   iv. Consider CT in undifferentiated respiratory illness when the patient is moderately to severely ill, and COVID-19 is high on the differential but CXR is not pathognomonic. Typical findings on CT are bilateral ground glass opacities and “crazy paving” consolidation.

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Clinical Management

No specific treatment for COVID-19 is currently available.\(^1\) Clinical management includes:

1. Prompt implementation of recommended infection prevention and control measures. For any suspected case, please contact Infection Prevention as soon as possible and refer to the 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*\(^2\) and *Interim Considerations for Infection Prevention and Control of Coronavirus Disease 2019 (COVID-19) in Inpatient Obstetric Healthcare Settings*.\(^3\)

2. Supportive management of complications. Infectious Diseases consultation is highly recommended.
   a. **Respiratory Care** (refer to the Ascension COVID-19 Respiratory Care Guidelines for additional guidance)
      * Consider early intubation in rapidly evolving hypoxemic respiratory failure, since early intubation may reduce transmission and may improve survival.
      * Noninvasive ventilation (NIV) likely causes increased risk of viral spread due to aerosol generation with unclear benefit in morbidity and mortality to the patient, and should therefore be discouraged until further data is available.
      * Patients on respiratory isolation are not recommended to utilize nebulizers for medication administration. A metered dose inhaler (MDI) should be utilized in this patient population.
      * Refer to the World Health Organization recommendations for the *Clinical Management of Severe Acute Respiratory Infection (SARI) When Novel COVID-19 Disease Is Suspected*\(^4\) for additional guidance.
   b. **Fluid Management**
      * Use a conservative fluid management strategy for acute respiratory distress syndrome (ARDS) patients without tissue hypoperfusion.\(^27\)
   c. **Systemic corticosteroid therapy**
      * **Steroids should not generally be used** as they may be associated with increased viral replication due to immunosuppression as well as several adverse side effects, including increased risk of nosocomial infections.\(^2,5\)

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Given lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason; for example, chronic obstructive pulmonary disease exacerbation or septic shock.\textsuperscript{1,4}

d. **Antimicrobial therapy**
   - Alone, COVID-19 is not an indication for antibiotics.
   - Initially, there may be concerns regarding the possibility of a superimposed bacterial pneumonia.
     - If that is a concern, consider obtaining bacterial cultures prior to initiation of empiric antibiotic therapy. Based on culture results and clinical evaluation, de-escalation and discontinuation may be considered if there is no evidence of a bacterial infection (similar to management of influenza pneumonia).

e. **Antiviral therapy**
   - While there are currently no antiviral drugs licensed by the U.S. Food and Drug Administration (FDA) to treat patients with COVID-19, the use of certain off-label and investigational therapeutic agents may be considered as outlined in the table below (\textit{Table. COVID-19 Treatment Options}).
   - Refer to the World Health Organization recommendations for the \textit{Clinical Management of Severe Acute Respiratory Infection (SARI) When Novel COVID-19 Disease Is Suspected}\textsuperscript{4} for additional guidance.
<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Treatment options</th>
<th>Suggested dosing* and duration</th>
<th>Adverse Events</th>
<th>Pregnancy Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUI/confirmed infection with NO fever or respiratory compromise</td>
<td>Do not treat with empiric antiviral therapy.</td>
<td>Supportive care only</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>PUI/confirmed infection with fever and NO respiratory compromise</td>
<td></td>
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</tr>
</tbody>
</table>

- For adults with more severe disease, may consider the use of agents with potential therapeutic activity against SARS-CoV-2.
- Due to the described benign course of COVID-19 in pediatrics, risks and benefits of these investigational therapies should be carefully considered prior to initiation. There is no approved pediatric dosing for any of the investigational therapies below for COVID-19. All pediatric dosing in this guideline is extrapolated from other indications.

<table>
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</thead>
<tbody>
<tr>
<td>Initiation of either of the below therapies should be considered in patients with comorbidities, symptomatic disease and abnormal chest X-ray without other cause.</td>
<td>Hydroxychloroquine * OR Chloroquine** OR Alternate Therapy Lopinavir/ritonavir (LPV/r)**</td>
<td>Adult Dosage:  • Hydroxychloroquine: 400 mg PO bid x 2 doses, followed by 400 mg PO daily x 4 days.  • Chloroquine: 500 mg PO bid x 10 days.  Pediatric Dosage:  • Chloroquine: 8.3 mg/kg chloroquine phosphate salt (5 mg/kg chloroquine base; maximum dose: 500 mg chloroquine phosphate = 300 mg base) PO bid x 10 days.  • Hydroxychloroquine: 6.5 mg/kg (max 400 mg/dose) PO q12h x 1 day, followed by 6.5 mg/kg (max 400 mg/dose) PO daily x 4 days</td>
<td>Hydroxychloroquine/chloroquine: Most toxicities are associated with long-term use.  • Dizziness, headache, loss of appetite, nausea, vomiting  • LFT abnormalities  • QTc prolonging effects  • G6PD testing only recommended for patients of Asian, African and Mediterranean descent</td>
<td>Pregnant and Nursing Mothers: Hydroxychloroquine has been associated with fetal ocular toxicity in animal studies. Additionally, hydroxychloroquine is excreted into breast milk. Thorough evaluation of the risk:benefit should be discussed with the patient prior to starting therapy.  Alternate Therapy: Lopinavir/ritonavir (LPV/r)**</td>
</tr>
<tr>
<td>Age ≤ 1 year: 16 mg/kg/dose PO bid (80 mg/20 mg oral solution preferred) Age &gt; 1 year weight-based dosing:  &lt; 15 kg: Lopinavir 12 mg/kg/dose PO bid 15 to 40 kg: Lopinavir 10 mg/kg/dose PO bid &gt; 40 kg: Lopinavir 400 mg PO bid</td>
<td>Adult Dosage: LPV/r: 400 mg/100 mg PO bid x 7 days; may consider treatment for up to 14 days based on clinical response.  Pediatric Dosage: LPV/r: Dose PO bid x 7 days; may consider treatment for up to 14 days based on clinical response. Age ≤ 1 year: 16 mg/kg/dose PO bid (80 mg/20 mg oral solution preferred) Age &gt; 1 year weight-based dosing:  &lt; 15 kg: Lopinavir 12 mg/kg/dose PO bid 15 to 40 kg: Lopinavir 10 mg/kg/dose PO bid &gt; 40 kg: Lopinavir 400 mg PO bid</td>
<td>Adults:  • Nausea Vomiting  • Transaminitis  • Significant drug interactions (e.g., azoles, anticoagulants, anti-epileptics), review medication list with pharmacy</td>
<td>Safe in pregnancy</td>
<td></td>
</tr>
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</table>

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### Remdesivir

**Adult Dosage:**
- 200 mg IV load, then 100 mg IV q24h

**Pediatric Dosage:**
- <40 kg: 5 mg/kg IV load, then 2.5 mg/kg IV q24h
- ≥40 kg: 200 mg IV load, then 100 mg IV q24h

**Key Inclusion Criteria:**
- Confirmed SARS-CoV-2 by PCR
- Hospitalization
- Mechanical ventilation

**Key Exclusion Criteria:**
- Evidence of multi-organ failure
- Pressor requirement to maintain blood pressure
- ALT levels > 5 x ULN
- Cr Clearance < 30 mL/min or dialysis of continuous veno-venous hemofiltration

### Tocilizumab

**Adult Dosage:**
- 400 mg IV x1

**Pediatric Dosage:**
- <6 kg: 12 mg/kg (actual body weight)
- 6-9.9 kg: 80 mg
- 10-14.9 kg: 160 mg
- 15-17.9 kg: 200 mg
- 18-21 kg: 240 mg
- 22-24.9 kg: 280 mg
- 25-27.9 kg: 320 mg
- 28-49.9 kg: 360 mg
- ≥50 kg: refer to adult dosing

**Key Inclusion Criteria:**
- ≥3 SIMIT testing criteria or ARDS
- H-score > 169 (requires results of a CBC, CMP, ferritin, fibrinogen and triglycerides - bone marrow aspirate is not recommended or necessary).

**Exclusion Criteria:**
- AST / ALT > 5 x ULN
- Neutrophils < 500 cells/mm3
- Platelets < 50,000 cells/mm3
- Documented sepsis from other pathogens that are not COVID-19
- Complicated diverticulitis or intestinal perforation
- Anti-rejection immunosuppressive therapy

**PLEASE NOTE:** Refer to the Gilead website (https://rdvcu.gilead.com), as it states that these criteria are subject to change without notice and may be subject to additional considerations and limitations. It is requested that if your patient does not meet these minimal criteria, please do not submit a request at this time.

- Continued therapy with lopinavir/ritonavir OR hydroxychloroquine should be used until remdesivir is acquired via compassionate use program unless program provides other guidance (refer to supplementary SBAR for additional information).
- Not FDA approved for any use, currently in clinical trials.
- Available for compassionate use on patient-specific basis by taking the following steps:
  1. Contact Gilead (manufacturer) to request use at https://rdvcu.gilead.com/

**For additional information on tocilizumab refer to Tocilizumab for the Treatment of COVID-19 SBAR.**

**Tocilizumab**

**Remdesivir**

**Dosage and Administration**

- Elevating transaminases
- Reversible kidney injury
- Hypotension during infusion
- AVOID acetaminophen use through day 15

**No information**

**Tocilizumab**

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- Complicated diverticulitis or intestinal perforation
- Anti-rejection immunosuppressive therapy

**LFT abnormalities**
- Local injection site reactions
- Increased risk of serious infections, including tuberculosis and invasive fungal infections as well as other opportunistic pathogens.
- Providers should consider testing for tuberculosis (interferon gamma release assay) and ordering hepatitis B serologies prior to prescribing of tocilizumab although results are not required prior to administration.

**Avoid in pregnancy**
- Tocilizumab may be harmful to newborns, and mothers should stop breastfeeding if receiving tocilizumab.

**PUI: person under investigation**

*Stepper recommendations provided for patients with normal renal function.

**Ribavirin may be considered as an adjunct to (LPV/r) OR hydroxychloroquine on a case by case basis in consultation with Infection Diseases.** Ribavirin is associated with several toxicities, including hemolytic anemia (dose-related), bradycardia, transaminitis and teratogenicity. Weigh risks versus benefits when considering initiation of...
Optimal dose has not been established. Adult dosage: 2000 mg PO loading dose, then 1,200 mg PO q8h (day 1-4), then 600mg PO q8h (day 5-10); may consider treatment for up to 14 days based on clinical response. Pediatric dosage: 15-20 mg/kg/day divided into TID administration for 7-10 days. Ribavirin oral solution was discontinued in June 2019. Ribavirin is a hazardous agent and compounding of the oral suspension must be done in the chemo hood.

Hydroxychloroquine higher dose may be considered in adults with more severe disease on a case by case basis. Adult higher dosage: 600mg PO bid x 2 doses load, then 200mg PO tid. Pediatric dosage expressed as hydroxychloroquine sulfate. Hydroxychloroquine sulfate 200 mg is equivalent to 155 mg hydroxychloroquine base. Administer with food or milk. Do not crush or divide film-coated tablets. A 25 mg/mL hydroxychloroquine sulfate oral suspension may be made with tablets. With a towel moistened with alcohol, remove the coating from fifteen 200 mg hydroxychloroquine sulfate tablets. Crush tablets in a mortar and reduce to a fine powder. Add 15 mL of Ora-Plus and mix to a uniform paste; add an additional 45 mL of vehicle and mix until uniform. Mix while adding sterile water for irrigation in incremental proportions to almost 120 mL; transfer to a calibrated bottle, rinse mortar with sterile water; and add sufficient quantity of sterile water to make 120 mL. Label "shake well." A 30-day expiration date is recommended, although stability testing has not been performed.

Chloroquine can be used for mild, moderate and severe cases. Chloroquine has been associated with improved patient outcomes and shortened hospital length-of-stay for patients with COVID-19. Chloroquine pediatric dosage expressed as chloroquine phosphate. Chloroquine phosphate 16.6 mg is equivalent to 10 mg chloroquine base. Administer with meals to decrease GI upset; chloroquine phosphate tablets have also been mixed with chocolate syrup or enclosed in gelatin capsules to mask the bitter taste.

LPV/r adult optimal dose has not been established. Further information on this is available in a recent review. LPV/r pediatric optimal dose has not been established. Use of tablets in patients < 15 kg or < 0.6 m² is not recommended; oral solution preferable. Oral solution bioavailability increased with food and is not recommended for use with polyurethane feeding tubes (potential incompatibility); silicone and polyvinyl chloride feeding tubes may be used. Further information on this is available in a recent review.

References:

1. CDC. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19).
2. CDC. Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings.


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