Henry Ford Hospital Division of Infectious Diseases
Management and Treatment of Confirmed COVID-19 Cases (3.23.2020 version)

All confirmed COVID-19 inpatients **require Infectious Diseases consultation** for management. For testing recommendations, please refer to **SARS-CoV-2 (COVID-19) Testing Criteria** from HFHS infection prevention and control. https://onehenry.hfhs.org/departments/infectionpreventionandcontrol/Documents%20%20Testing%20and%20Specimens/SARS-CoV-2%20COVID-19%20Testing%20criteria.pdf

Preemptively starting COVID medications prior to return of test results is not recommended due to limited medication supply unless there is high suspicion based upon clinical judgement per below criteria:

- **influenza negative, hypoxia requiring oxygen, presence of bilateral infiltrates, leukopenia, critical illness**

Currently, there are no FDA approved therapies to treat COVID-19. The Division of Infectious Diseases is coordinating investigational remdesivir. The below treatments should be started immediately once COVID test is positive (when indicated), pending remdesivir availability. These guidelines are interim recommendations and may change according to drug availability and new data published. Supportive care and infection control measures are indicated for all hospitalized patients. **For patients who are stable for hospital discharge, no outpatient continuation of COVID-19 treatment is recommended.**

Initial labs for all hospital inpatients (see below for ongoing treatment **monitoring)**:

- Suspected or confirmed patients: CBC with differential, BMP, LFTs, procalcitonin, ferritin, CRP, LDH, d-dimer, cpk, high sensitivity troponin, Influenza A & B PCR
- Draw upon admission to **ICU**: Triglyceride, IL-6, DIC panel (in addition to labs listed above if not previously ordered)
- Baseline EKG

Treatment for Positive Patients			
	Mild symptoms, outpatient	**Moderate symptoms, hospitalized**	**Severe, hospitalized**
Characteristics	Cough, fever, myalgias On Room air / baseline SAO2 94% or above May have vague to minimal radiographic evidence of pulmonary infiltrates	**supplemental oxygen use or Sao2 less than 94%**, fever of ≥ 36.6°C armpit, ≥ 37.2 °C oral, or ≥ 37.8°C rectal, radiographic evidence of pulmonary infiltrates	Respiratory failure requiring **mechanical ventilation** Cough, fever, myalgias
Recommended treatment	Social distancing recommended Consider OTC Symptom relief Cough: -vaporizer or humidifier -dextromethorphan (dry cough) -guaifenesin (productive cough) Fever: Acetaminophen	**Hydroxychloroquine** 400 mg PO BID x 2 doses, then 200 mg PO BID x 4 days OR **Remdesivir**: Requires patient informed consent for clinical trial. Not an FDA approved therapy	**Remdesivir**: Compassionate use/ expanded access. Requires patient informed consent. Not an FDA approved therapy OR ***Hydroxychloroquine** 400mg PO BID x 2 doses, then 200 mg PO BID x 4 days
Adjunctive Therapy		Room Air - steroids are **not** recommended	Mechanical ventilation with ARDS (PaO2/FiO2 < 200) - If positive influenza, steroids are **not** recommended

		<u>New or Worse supplemental oxygen with early ARDS</u> (PaO2/FiO2 < 200) - If positive influenza, steroids are not recommended - If negative influenza recommend **low dose methylprednisolone** with a short course (e.g. 0.5-1 mg/kg/day based on actual body weight divided in 2 doses for 3 days)	- If negative influenza, recommend **low dose methylprednisolone** with a short course (e.g. 0.5-1 mg/kg/day based on actual body weight divided in 2 doses for 3 days; can extend to 7 days if patient is improving) - Additional immunomodulator usage will be determined on a case-by-case basis with the ICU and ID COVID team (see appendix 1 below for Tocilizumab dosing) - Prone ventilation (inclusion criteria: severe ARDS (defined as a PaO2:FiO2 ratio of <150 mm Hg, with an FiO2 of ≥0.6, a PEEP of ≥5 cm of water, and a tidal volume of about 6 ml per kilogram of predicted body weight) o If proning used, must use the low PEEP, high FiO2 table (APPENDIX 2)

***Monotherapy hydroxychloroquine preferred for most patients.**

Consider combination with azithromycin 500 mg PO x 1 dose, then 250 mg PO x 4 days in carefully selected patients after discussion with ID**.** COVID-19 infection has been associated with cardiovascular complications including acute myocardial injury, myocarditis, and arrhythmias. Hydroxychloroquine and azithromycin have cardiovascular side effects that may exacerbate these complications. Combination therapy is NOT recommended for patients with a history of cardiac comorbidities, baseline QTc > 450 for men or >470 for women, other concomitant QT prolonging medications, or uncorrected electrolyte abnormalities. Use caution in patients with severe liver disease. QTc > 500 should be considered an absolute contraindication to hydroxychloroquine and azithromycin.

NOTE: Multiple dose hydroxychloroquine has a terminal half-life of up to 50 days, azithromycin has a half-life of 68 hours. Therefore, the patient will be "on treatment" for an extended time after drug discontinuation.

Monitoring Parameters:

- Hydroxychloroquine: Cardiotoxicity, Torsade de Pointes, depression, psychosis. Perform daily ECG if used in combination with azithromycin. Discontinue if QTc increases by 60 msec or is > 500. Maintain potassium at least 4 mEq/L, and magnesium at least 2 mEq/L.
- Remdesivir: Phlebitis, Constipation, Nausea, Headache, Bruising, Liver Function test abnormalities. Obtain daily BMP and LFTs.

Laboratory Monitoring			
		Moderate symptoms, hospitalized	**Severe, hospitalized (ICU)**
Once			IL-6, DIC panel
Daily		BMP, Magnesium, CBC with differential, ferritin, CRP, LDH, CPK, LFTs	BMP, Magnesium, CBC with differential, ferritin, CRP, LDH, CPK, LFTs
Every 48 hours		High sensitivity troponin, d-dimer	High sensitivity troponin, d-dimer, triglycerides

Other Treatment Modalities	
Fluids	Conservative fluid management
Anticoagulation	Recommend against the use of heparin for DIC
ACEi/ARB	Continue home ACEi/ARB for conditions with known mortality benefit (e.g. heart failure, ischemic heart disease, or hypertension with diabetes). If therapy for no compelling indication, consider alternate therapy
Statin	Continue home statin and monitor for side effects (e.g. LFTs, CPK) and hold if deemed clinically necessary. Do not initiate statin therapy if no medical indication exists.

Appendix 1: Tocilizumab dosing

Tocilizumab

- One-time non-formulary request form required for usage
- Consult pharmacy for dosing and drug availability
- Infectious Disease consult is required for usage

Dosing:

- < 64.9 kg: 400 mg IV once
- 65-84.9 kg: 600 mg IV once
- 85 kg: 800 mg IV once

Can repeat dose in 12 hours for maximum of 2 doses total if continued clinical decompensation at the discretion of ID consult

Criteria for use in COVID patients in the ICU failing to respond to steroids and meeting all the below criteria:

- Persistent fever defined as 38.0°C for at least 6 hours not subsiding
- ARDS defined as PaO2/FiO2 < 150
- Laboratory criteria:
  - Ferritin ≥ 1000 ug/L (or doubling within 24 hours), D-Dimer ≥ 5 mg/L (persistent or rising), AND LDH ≥ 500 (persistent or rising)

    OR
  - IL-6 ≥5x upper normal limit

Patients who don't meet all 3 criteria above may still be appropriate for tocilizumab per collaborative discussion with the Infectious Disease COVID Team and ICU team

Exclusion criteria: Document Patient has satisfied these criteria below

- Pregnant or lactating women
- ALT / AST > 5 ULN
- Neutrophils <0.5
- Platelets < 50
- Definite diagnosis of rheumatic immune-related diseases
- Long-term oral anti-rejection or immunomodulatory drugs
- Hypersensitivity to tocilizumab or any excipients
- Patients with active pulmonary tuberculosis, with definite bacterial and fungal infections

Appendix 2: PEEP tables

PEEP Table, Proning study (Guerin, et al.)

$F_iO_{2\,(\%)}$	30	40	50	50	60	70	70	70	80	90	90	100
PEP (cm H_2O)	5	5	8	10	10	10	12	14	14	14	18	18-24

PEEP table, ARDSnet study

Allowable combinations of PEEP and FiO_2†

Lower-PEEP group														
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24
Higher-PEEP group (before protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0	
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22–24	
Higher-PEEP group (after protocol changed to use higher levels of PEEP)														
FiO_2	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0				
PEEP	12	14	14	16	16	18	20	22	22	22–24				

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