June 25, 2020

From: COVID-19 Scientific Research Committee

To: COVID-19 Pandemic Response Team

Dear Committee:

The Scientific Research Committee was asked to review literature surrounding therapeutic treatment of COVID-19 in pediatric patients.

As a committee, we believe the documented algorithm is thought to be the most up to date, comprehensive and scientifically current treatment algorithm. The committee supports the adaptation of the algorithm prepared and approved by the Chief Medical Officer approval board.

Sincerely,

COVID-19 Scientific Committee

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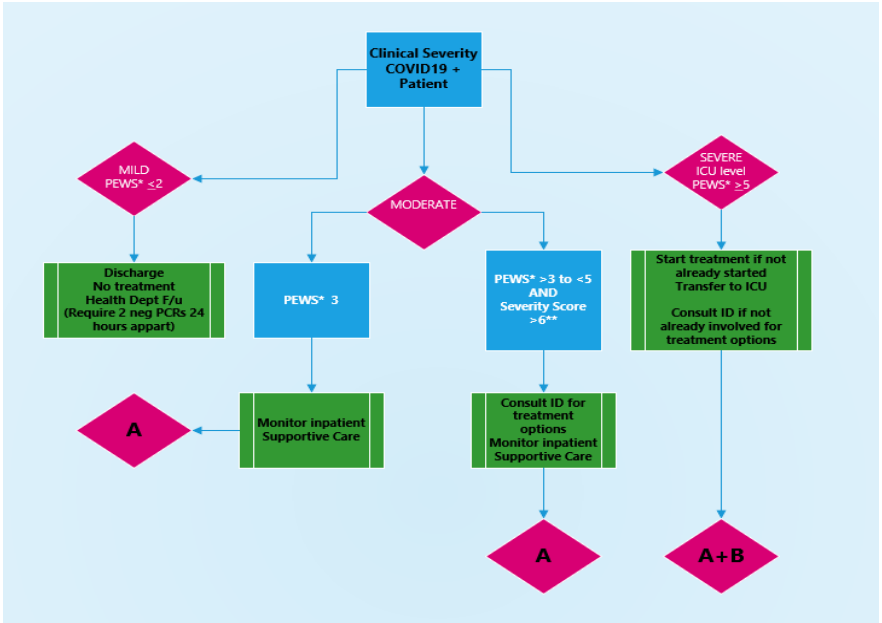
COVID-19 Pediatric Inpatient Treatment Plan



***Pediatric Early Warning Score (PEWS)**

Add 2 points for ¼ hourly nebulized treatments, persistent vomiting post-op

	0	1	2	3
BEHAVIOR	Playing/ appropriate	Sleeping	Irritable	Lethargic/ confused OR reduced response to pain
CARDIOVASCULAR	Pink or capillary refill 1-2 seconds	Pale or capillary refill 3 second	Grey or capillary refill 4 seconds OR tachycardia of 20 above normal rate	Grey and mottled or capillary refill 5 seconds or above OR tachycardia of 30 above normal rate OR bradycardia
RESPIRATORY	Within normal parameters, no retractions	>10 above normal parameters, using accessory muscles OR 30+ % FIO2 OR 3+ liters/ minute	>20 above normal parameters, retractions OR 40+% FIO2 OR 6+ liters/ minute	5 below normal parameters with retractions and/or grunting OR 50% FIO2 OR 8+ liters/min

****Pediatric Infection Severity Score**

(3 points)

Chest radiograph with bilateral infiltrates or CT scan findings suggestive of COVID19 infection (rounded ground glass opacities or ground glass opacities with consolidation)

(1 points each)

Lymphopenia (<45% or <1500/microL)
CRP > 3
Procalcitonin > 0.05
Transaminitis

(2 points)-Fever > 101F

(3 points)-Hypoxia (spO2 < 90%) of unknown etiology

Treatment Options

A.
Supportive care (IV fluids, anti-pyretics, anti-emetics, etc)
Consider dexamethasone 0.15 mg/kg/dose (max 6mg IV daily) for patients with hypoxia (if dexamethasone not available consider alternate steroid)

B.
If eligible for Remdesivir (restricted to ID)
Add dexamethasone 0.15 mg/kg/dose (max 6mg IV daily), if dexamethasone not available consider alternate steroid

Also to consider Interleukin-6 Receptor Antagonists (i.e. Tocilizumab, Sarilumab)
Immunoglobulin (IVIG)-possibly indicated for clinically confirmed Multisystem Inflammatory Syndrome in Children (MIS-C)

Please refer to APPENDIX 1 for further details

Hydroxychloroquine: There are insufficient clinical data to recommend either for or against the use of hydroxychloroquine for the treatment of COVID-19

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Last Updated: 6-25-20

General Recommendations:

- All patients should receive supportive care (IV fluids, antipyretics, antiemetics, etc.)
- If clinically stable, consider discharge for family quarantine.

Other considerations:

- **Corticosteroids:**
  - Corticosteroids are not routinely recommended for viral pneumonia or ARDS. However, early studies indicate a reduction of mortality with low dose dexamethasone in patients requiring respiratory support. Consider alternative steroid in the case of shortage.
- **ACE I/ARB:**
  - The HFSA, ACC and AHA emphasize the lack of experimental or clinical data on these class of drugs in COVID-19 and recommend that patients currently taking these medications for known beneficial indications (HTN, nephrotic syndrome, for example) be advised to continue them. They advise against adding/removing beyond what would be done in standard practice and urge individualized treatment decisions based on patient's clinical presentation and hemodynamics
- **Hydroxychloroquine:**
  - Hydroxychloroquine: There are insufficient clinical data to recommend either for or against the use of hydroxychloroquine for the treatment of COVID-19
- **NSAIDs:**
  - There is no evidence for or against the management of fever with NSAIDs. Acetaminophen is preferred for management of fever, but each clinical scenario should be carefully evaluated.
- **Nebulized respiratory medications for patients:**
  - Nebulized respiratory medications should be avoided in non-intubated patients unless otherwise indicated in patients with bronchospasms to further prevent the spread of the COVID-19oIf indicated, inhalers (MDIs) with spacers are preferred for non-intubated patients
  - If indicated, nebulized medications with a closed circuit may be used in intubated patients
  - For COVID-19 negative, non-intubated patients, nebulized respiratory medications are preferred over MDIs
- **Immunoglobulin (IVIG):**
  - Possibly indicated for pediatric multisystem inflammatory syndrome that are clinically diagnosed.

Treatment Options:

	Treatment for Hospitalized Patients	Duration of treatment
A	Supportive care (IV fluids, anti-pyretics, anti-emetics, etc) Consider dexamethasone 0.15 mg/kg/dose (max 6mg IV daily) for patients with hypoxia. Consider alternative steroid in the case of shortage.	N/A
A+B	If eligible for Remdesivir* (restricted to ID) Add dexamethasone** 0.15 mg/kg/dose (maximum 6mg IV daily). Consider alternative steroid in the case of shortage. Also, to consider Interleukin-6 Receptor Antagonists (i.e. Tocilizumab, Sarilumab) Immunoglobulin (IVIG)-possibly indicated for clinically confirmed Multisystem Inflammatory Syndrome in Children (MIS-C)	*5-10 days **10 days
• **It is NOT recommended to use hydroxychloroquine for prophylaxis at this time.** • **IVIG should be reserved for a case by case consideration in the most severe patients and/or confirmed Multisystem Inflammatory Syndrome in Children (MIS-C)**		

Drug	Dosing	Formulations	Monitoring	Adverse Effects	Notes
Remdesivir (compassionate use only, restricted to ID)	Remdesivir (restricted to ID) Youngest child tested included down to 0 days of age and at least 2 kg per protocol. Loading dose 5 mg/kg/dose (max 200 mg) and maintenance 2.5 mg/kg/dose (max 100 mg) IV daily	**IV infusion**	CMP Daily CBC with differential PT/INR Daily Urinalysis If possible CoV PCR Physical and vital signs at least daily	• Transient elevations in ALT and AST • Dose-dependent, reversible kidney injury and dysfunction	**See inclusion/exclusion criteria below. Contact pharmacy to initiate request.**
Immunoglobulin	2 gm/kg/dose IV once. Use ideal body weight to calculate.	**IV Infusion**	Hypersensitivity CBC with differential CMP	•Hemolytic Anemia •Hypotension/Hypertension •Anaphylaxis •Headache- aseptic meningitis	**Run over 12 hours so max of 1.8 ml/kg/hr rate recommended.**
Tocilizumab	8 mg/kg/dose IV x 1 (max dose 400 mg), May repeat in 12 hours if no improvement	**IV infusion** (DO NOT USE Subcutaneous formulation for IV)	Hypersensitivity CBC with differential CMP	•Hepatitis •Hypotension/Hypertension •Anaphylaxis •Headache •Very rarely bowel perforation •Neutropenia & thrombocytopenia	See considerations for use below
Dexamethasone	0.15mg/kg/dose once daily (maximum 6 mg per day)	**IV/PO**	N/A	Hyperglycemia	N/A

Interleukin-6 Receptor Antagonist (i.e. Tocilizumab) Considerations for Use:

For severe patients with progressive clinical deterioration.
If high-risk for developing cytokine storm (at least 2 of the following):

- IL-6 ≥3x upper normal limit
- If IL-6 level not available, may use the following as a marker
    - CRP ≥ 100 mg/L
    - D-dimer >1 mg/L

Laboratory Monitoring for patients with COVID-19 on treatment:

- CRP/Procalcitonin at baseline and then every 2-3 days x 4
- D-dimer at baseline and then every 2-3 days x 4
- CMP at baseline and then every 2-3 days x 4
- If patient receives tocilizumab, repeat IL-6 level on day 1 after dose of tocilizumab

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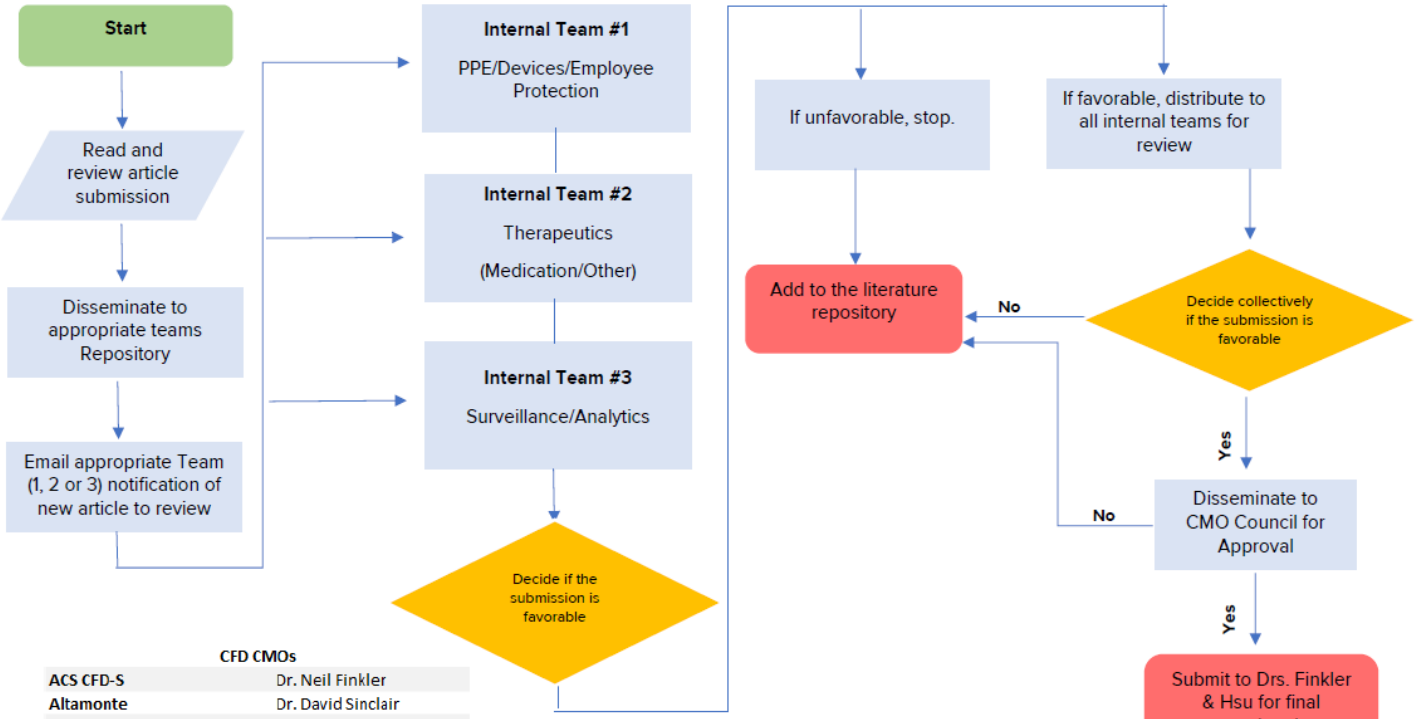
Revisions:

6-24-20

Added Dexamethasone treatment for patients with severe illness and/or patients with moderate illness with hypoxia

Disclaimer: The Scientific Committee was formed under the Medical Management Branch of the COVID-19 Pandemic Response Team. The committee's goal is to create a repository, interrogate research literature as it pertains to the treatment of COVID-19 and provides a rapid approval process. The algorithm below is the decision-making process that governs our decisions.

Scientific Subcommittee Approval Process



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Celebration	Dr. Jay Ball
Mission Control	Dr. Sanjay Pattani
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Orlando	Dr. Victor Herrera
Children's	Dr. Michael Keating
Heart of Florida / Lake Wales	Dr. Vincent Carifi
Winter Park	Dr. Jennifer Keehbauch
Kissimmee	Dr. Dennis DeLeon

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Internal Team #2	Drs. Parikh & Smith
Internal Team #3	Drs. Parikh & West
	Drs. Mansfield & Herrera to be added

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