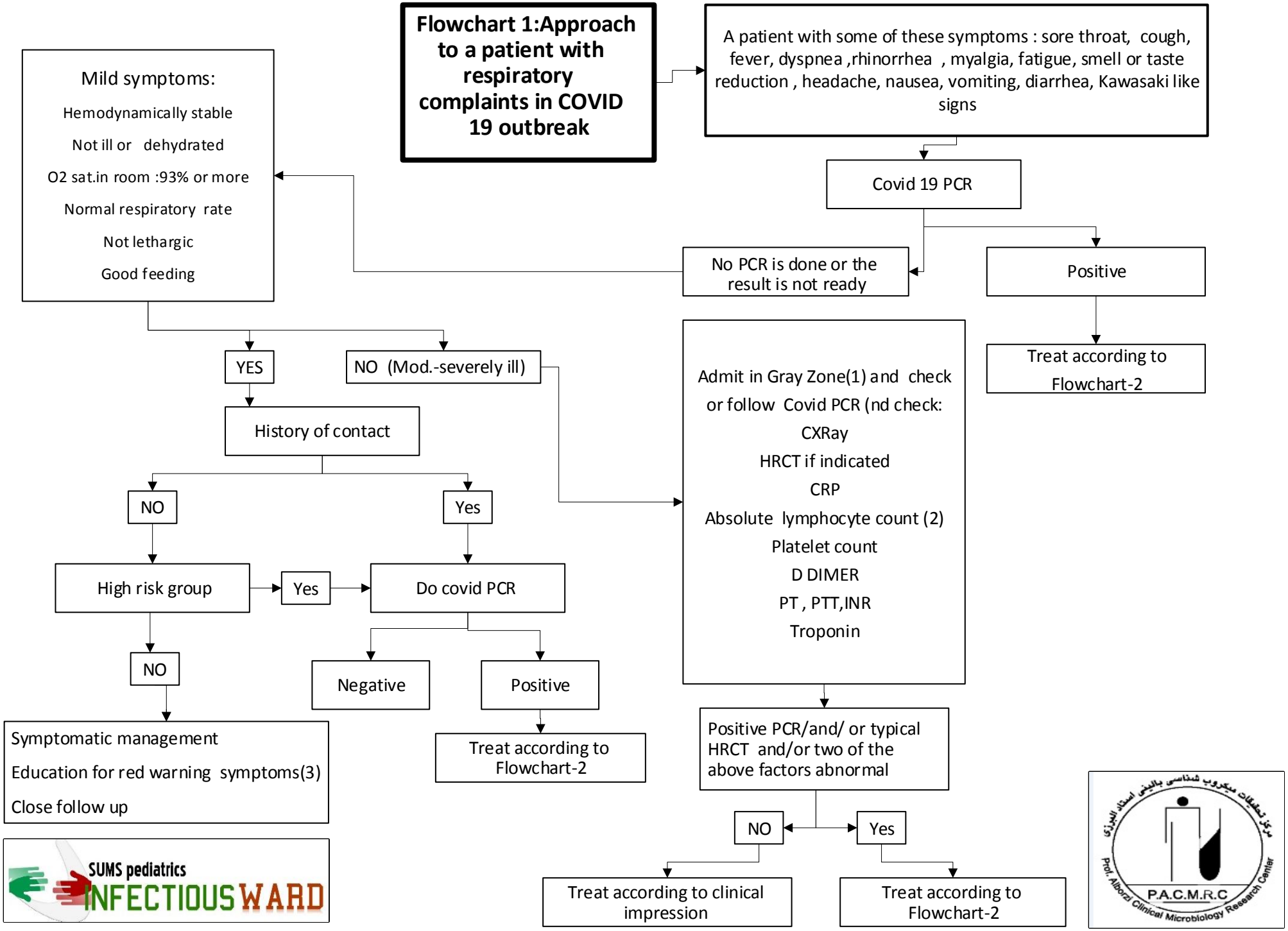
Flowchart 1:Approach to a patient with respiratory complaints in COVID 19 outbreak
A patient with some of these symptoms : sore throat, cough, fever, dyspnea ,rhinorrhea , myalgia, fatigue, smell or taste reduction , headache, nausea, vomiting, diarrhea, Kawasaki like signs
Covid 19 PCR
Positive
Treat according to Flowchart-2
No PCR is done or the result is not ready
Mild symptoms:
Hemodynamically stable
Not ill or dehydrated
O2 sat.in room :93% or more
Normal respiratory rate
Not lethargic
Good feeding
YES
NO (Mod.-severely ill)
History of contact
NO
Yes
High risk group
Yes
Do covid PCR
NO
Negative
Positive
Symptomatic management
Education for red warning symptoms(3)
Close follow up
Treat according to Flowchart-2
Admit in Gray Zone(1) and check or follow Covid PCR (nd check:
CXRay
HRCT if indicated
CRP
Absolute lymphocyte count (2)
Platelet count
D DIMER
PT , PTT,INR
Troponin
Positive PCR/and/ or typical HRCT and/or two of the above factors abnormal
NO
Yes
Treat according to clinical impression
Treat according to Flowchart-2
SUMS pediatrics
INFECTIOUS WARD
P.A.C.M.R.C
Prof. Alborzi Clinical Microbiology Research Center

Flowchart 2: Approach to a patient with COVID 19 infection

A patient with acute COVID-19 infection

History & physical exam. Initiate isolation precautions

Determine disease severity

Asymptomatic Exposed(pre-symptomatic)

Positive SARS-CoV-2 PCR without significant clinical signs and symptoms

Imaging is not recommended

No specific lab testing is recommended .
However, in those with underlying comorbidities, lab studies Should be individualized on case –by – case basis

Discharge from triage ,home-quarantine
Supportive care.
Assure hydration
If already prescribed continue NSAIDS, ACE- I and angiotensin Receptor blockers(ARBs), or steroids
Antivirals not recommended.
Anticoagulation not recommended.
Consider supplements(4)
Educate parents regarding warning symptoms(3)
Antibiotic therapy if indicated (5)

Mild

Fever, fatigue ,headache, nasal congestion ,sore throat cough, diarrhea, vomiting myalgia ,No respiratory distress. No O2 requirement (Spo2 ≥ 93%). Adequate hydration

Imaging is not recommended(6)

No specific lab testing is recommended .
However, in those with underlying comorbidities, lab studies Should be individualized on case –by – case basis

Discharge from triage ,home-quarantine
Supportive care.
Assure hydration
If already prescribed continue NSAIDS, ACE- I and angiotensin Receptor blockers(ARBs), or steroids
Antivirals not recommended.
Anticoagulation not recommended.
Consider supplements(4)
Educate parents regarding warning symptoms(3)
Antibiotic therapy if indicated (5)

Moderate

Lower respiratory tract symptoms, including:
Tachypnea(7),fever. Inadequate hydration
No o2 requirement(Spo2 ≥ 93%)

CXR is recommended. Chest CT in Certain circumstances (8)

Initial labs (9)
CBC with differential
CRP; ESR; D dimer
PT / INR, PTT
Fibrinogen, LDH, Troponin
Procalcitonin (10)
Ferritin (11), VBG
Serum Lactate

Oxygen if needed
Antibiotic therapy if indicated.(5)
Consider Favipiravir(12)
Consider Remdesivir (13)
Anticoagulation therapy with Prophylactic dose (14)

Severe

Lower respiratory tract symptoms ,including: tachypnea. Spo2 ≤ 90% (without supplemental o2). Pao2/Fio2< 300mmHg. Need for supplemental oxygen via regular nasal cannula or high –flow nasal cannula

CXR and Chest CT is recommended.(8)

Initial labs (15)
CBC with differential, PT/ PTT , Fibrinogen, D dimer, CRP, ESR, Procalcitonin, LFT, LDH, Ferritin, Triglycerides , Troponin ,CKMB. If ferritin>500 mcg /ml: consider cytokine panel(IL-6, NK cell activity)

Antibiotic therapy if indicated (5)
Anticoagulation therapy (14)
Observe for signs of critical illness
Dexmethasone (16)
Remdesivir is a suggested (13)
Consider convalescent plasma (17)
Consider Immunomodulation (Tocilizumab)(18)

Critical

Lower respiratory tract symptoms, including :Tachypnea ,grunting ,with need for invasive or non-invasive mechanical ventilation
Acute Respiratory Distress Syndrome
.Septic shock

Chest CT is recommended.(8)

Initial labs (19)
CBC with differential, PT/ PTT , Fibrinogen, D dimer, CRP, ESR, Procalcitonin, LFT, LDH, Ferritin ,Triglycerides ,Troponin, CKMB
If ferritin>500 mcg /ml: obtain Cytokine panel(IL-6, NK cell activity)

Admit to pediatrics intensive care unit(PICU)
Antibiotic therapy if indicated.(5)
Anticoagulation (14)
Consider Steroids(20)
Consider convalescent plasma (17)
Consider Immunomodulation (Tocilizumab) (18)
Consider interferon-beta (21)

Appendix: Approach to a patient with respiratory complaints in COVID 19 outbreak

(1) If unstable admit in pediatric ICU

(2) Age-related lymphopenia defines as below:

- Between2-6 years less than 1800 (10^9/lit), and
- Over six years less than 1,500 (10^9/lit) ; see figure 1 in full version PDF file for other age group

3) The following signs and symptoms necessitate revisit of the child:

- Extremely sleepy or irritable
- Trouble breathing
- Repeated vomiting and or severe diarrhea
- Redness or swelling in anybody area
- Drinking very little or not at all
- Decreased urination
- Fever lasting longer than three days
- Seizure

(4) Consider following supplements:

- Vitamin C
- Zinc
- Vitamin D3 (consider prophylactic dose in all patients, and therapeutic dose in those with Vitamin D deficiency)
- Antipyretics
- Analgesics
- Anti-emetics

(5)Routine empiric antibiotics are not recommended; however, empirical antibiotics may be considered if there is clinical suspicion of bacterial infection (especially in

patients with moderate, severe, or critical disease). Antibiotics may also be considered in children <5 years of age.[1]

- If secondary bacterial pneumonia or sepsis is suspected, administer empiric antibiotics, re-evaluate daily, and, if there is no evidence of bacterial infection, de-escalate or stop antibiotics
- Consider antibiotics in the presence of leukocytosis, and or elevated serum procalcitonin, and or lactate level, or positive cultures or when the patient deteriorates.

(6) Indication for radiologic evaluations in "Mild" group
(Chest x-ray is recommended as a primary imaging modality)

- Underlying comorbidities including:

1. Asthma
2. Cystic fibrosis
3. Congenital heart disease
4. Immunosuppressed state (malignancy, transplantation, corticosteroid use, chemotherapy, neonates)
5. Bronchopulmonary dysplasia
6. Chronic infections (tuberculosis and HIV)

(7) Abnormal Respiratory Rates by Age
Age: Respiratory Rate per minute
0-2 months > 60
2-12 months > 50
1-6 years > 40
> 6 years > 30

(8) Chest CT should be considered in this group if the outcome will impact clinical decision making

- Evaluation of any changes in chest imaging findings
- Potential complications
- Comorbidities

[1] https://bestpractice.bmj.com/topics/en-gb/3000168/pdf/3000168/Coronavirus%20disease%202019%20%28COVID-19%29.pdf

Common pulmonary involvement:
Ground-glass opacity in isolation or co-existing with other findings (e.g., consolidation, interlobular septal thickening, crazy-paving pattern); bilateral, peripheral/ subpleural, posterior distribution with a lower lobe predominance.[2]

(9)In this stage, severe lymphopenia and a marked increase in CRP/ESR may be seen. Also, abnormal PT/PTT, D-dimer, LDH, and ferritin level is seen. In some cases, a decrease in eosinophils may be observed.

(10)Raised serum procalcitonin levels could be in favor of bacterial co-infection

(11)Monitoring ferritin should begin on day 4 of illness.

(12)Favipiravir; Pediatric Dosing[3]:

Favipiravir dosing is in patients ≥ 12 months of Age &body weight ≥10kg

Body weight	**Favipiravir 200 mg Tablet**
10-15 kg	**Loading Dose**: One tablet PO BID for One day Maintenance from Day2: Half tablet (100 mg) PO BID
16-21 kg	**Loading Dose:** Two tablets PO BID One day Maintenance fromDay2: One Tablet PO BID
22-35 kg	**Loading Dose:** 3 Tablets PO BID for One day Maintenance from Day2: One tablet PO TID
36-45 kg	**Loading Dose:** Four tablets PO BID for One day Maintenance from Day2: Two tablets PO BID
46-55 kg	**Loading Dose:** Five tablets PO BID for One day Maintenance from Day2: Two tablets qAM, thee Tablets qPM
For >55 kg	Can use adult dosing if age ≥16 years, if age <16years use dosing of 46-55 kg range

Treatment duration: 7 to 14 days

[2] https://bestpractice.bmj.com/topics/en-gb/3000168/pdf/3000168/Coronavirus%20disease%202019%20%28COVID-19%29.pdf
[3] Lancet. 2015 Feb 14;385(9968):603-604. doi: 10.1016/S0140-6736(15)60232-X.

13)Remdesivir

Optimal clinical timing: before 4_{th} day of symptoms[4]
Dosing:

Body weight	Recommended dosage form	Loading dose (on Day 1)	Maintenance dose (from Day 2)
3.5 kg to less than 40 kg	**Remdesivir Lyophilized Powder for Injection Only**	5 mg/kg	2.5 mg/kg
40 kg and higher	Remdesivir Lyophilized Powder for Injection or Remdesivir Injection	200 mg	100 mg

(14)Venous thromboembolism (VTE) management in different COVID phenotypes[5,6,7,8]

Exposed (pre-symptomatic), Asymptomatic case, and mild phenotype:
VTE prophylaxis not recommended.

Patients with moderate phenotype who need hospitalization:

- Anticoagulation therapy with prophylactic dose (Table 1).

Table 1. Standard dose thromboprophylaxis

For Any age :
 	
***If normal renal function and no contraindications**
	Chemoprophylaxis (Enoxaparin)
	• **<2 mo:**
	  ○ **0.75 mg/kg/dose SC q12 h**
	• **≥ 2 mo:**
	  ○ **Wt<40 kg:**
	  ▪ **0.5 mg/kg/dose SC q12 h**

[4] https://www.nature.com/articles/s41390-020-1053-9
[5]Kashe S et al. Pediatr Res. 2020 Jul 7. doi: 10.1038/s41390-020-1053-9
[6] Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JC, Fogerty AE, Waheed A, Goodarzi K, Bendapudi P, Bornikova L, Gupta S, Leaf D. COVID and Coagulation: Bleeding and Thrombotic Manifestations of SARS-CoV2 Infection. Blood. 2020 Jun 3.
[7]https://www.chop.edu/clinical-pathway/covid-disease-clinical-pathway
[8]https://www.connecticutchildrens.org/wp-content/uploads/2020/05/COVID19-VTE-Prevention.pdf

	○ **Wt ≥40 kg:** ▪ **40 mg SC qd** ▪ **Titrate to Anti-Xa 0.2-0.4 units/mL**
*** If renal impairment (CrCl < 30mL/min) consider unfractionated heparin (UFH)** †	

†See supplemental material for dosing and adjustment.

Severe phenotype:

- Start standard thromboprophylaxis (Table 1)
- Switch to intensified dose thromboprophylaxis (Table 2) if D-dimer is >500 (5ng/ml) and Ferritin> 500 ng/ml and those with the worsening clinical situation.
- Consider therapeutic dose anticoagulation (Table 3) if D-Dimer > 2500 ng/ml, Platelet count> 450 x10^9/L and CRP elevation>100 mg/dL.

Table 2. Intensified dose thromboprophylaxis

For Any age: ***If normal renal function and no contraindications**	**Chemoprophylaxis (Enoxaparin)** • **<2 mo:** ○ **1 mg/kg/dose SC q12 h** • **≥ 2 mo:** ○ **Wt<40 kg:** ▪ **0.75 mg/kg/dose SC q12 h** ○ **Wt ≥40 kg:** ▪ **40 mg q12 h** ▪ **Titrate to Anti-Xa 0.4-0.8 units/mL**
*** If renal impairment (CrCl < 30mL/min) consider unfractionated heparin (UFH)** †	

Critically ill phenotype:

- Start intensified dose thromboprophylaxis (Table 2).
- Start therapeutic dose anticoagulation (Table 3) if D-Dimer > 2500 ng/ml, Platelet count> 450 x10^9/L and CRP elevation>100 mg/dL.

Table 3. Therapeutic dose anticoagulation

High-risk of VTE: **-critically ill** ***Normal renal function and** **No contraindications**	• **Anticoagulation with therapeutic dose** ○ **Consider Enoxaparin:** ▪ **<2 mo: 1.5 mg/kg/dose SC q12 h** ▪ **≥ 2 mo:** ▪ **Wt<40 kg:** ▪ **1 mg/kg/dose SC q12 h** ▪ **Wt ≥40 kg:** ▪ **40 mg q12 h** ○ **Titrate to Anti-Xa 0.6-1.1 units/mLTitrate to Anti-Xa 0.6-1.1 units/mL**

*** If renal impairment (CrCl < 30 mL/min) consider unfractionated heparin (UFH)†**

† See supplemental material for dosing and adjustment.

On Discharge:

1. At least two weeks of prophylactic or therapeutic anticoagulation
2. Obtain imaging to evaluate thrombosis and its treatment

(15) At this stage, laboratory symptoms may include severe lymphopenia, increase in D-dimer, ferritin > 500 ng/dL, LDH> 245 U/l, and increased liver enzymes and triglycerides. There may also be an increase in brain natriuretic peptide (BNP), N-terminal pro-b-type natriuretic peptide (NT-pro-BNP), troponin, high IL6 level, CRP> 100, thrombocytopenia, and a significant decrease in eosinophil count.

(16) Dexamethasone

Systemic steroids should be avoided for patients with mild or moderate disease (no oxygen support) unless there is another indication.

• Recommended dose and duration: 6 mg (0.15 mg/kg once daily) IV or PO for 10 days

The best time for prescription

<7 days from symptom onset[10], Optimal clinical timing: days 4–7 of symptoms when ferritin > 500[11]

(17)The best time for prescription

<7 days from symptom onset in moderate COVID-19 patients, Optimal clinical timing: days 4−7 of symptoms[12]

Indications

• Convalescent plasma can be considered for patients with severe/critical COVID-19 with positive SARS-CoV-2 PCR from at least one site.

Table 4. Dosing and Administration	
Adult or child > 40 kg	**1-2 units of plasma (200-500 mL) over 1-2 hours**

[10]https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/remdesivir/

[11]https://www.nature.com/articles/s41390-020-1053-9

[12]https://www.nature.com/articles/s41390-020-1053-9

Child < 40 kg	**10-15 ml/kg over 1-2 hours**

(18) Tocilizumab

Patients must have the following documented[15]

- A positive test for SARS-CoV-2
- AND
- Serum IL-6 level > 25 pg/mL (5-fold above normal range)
- AND
- One or more of the following:
    1. Hemodynamic instability despite intravenous fluid resuscitation and high dose vasoactive support OR
    2. Worsening respiratory dysfunction including increased FiO2 requirement via high-flow nasal cannula, or need for invasive or non-invasive mechanical ventilation OR
    3. Rapid clinical deterioration, including evidence of cardiomyopathy or arrhythmia

Dose[16,17]

Tocilizumab: IV infusion over 1 hour dosed by total body weight:

- Patient weight < 30 kg: 12 mg/kg IV
- Patient weight > 30 kg: 8 mg/kg IV (max 800 mg)

If no improvement with 1st dose of tocilizumab within 12-18 hours, consider:

- Steroids: Methylprednisolone 2 mg/kg/day, duration TBD in consultation with DIRT but should generally be limited to a few days as possible
- The second dose of tocilizumab (same dose as above)

(19) Common laboratory findings:

Severe lymphopenia, high IL6 level, D-dimer > 1000, ferritin > 1000 ng/dl, high troponin level, high NT-pro-BNP level, severe cytopenia, increased liver enzymes > 5-fold of normal limits, severe thrombocytopenia, increased BUN/Cr, disseminated intravascular coagulation (DIC)

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[15] https://www.chop.edu/clinical-pathway/covid-disease-immunomodulation-covid-19-associated-cytokine-release-syndrome-crs

[16] https://www.connecticutchildrens.org/wp-content/uploads/2020/07/Therapies-for-COVID-19.pdf

[17] https://www.chop.edu/clinical-pathway/covid-disease-immunomodulation-covid-19-associated-cytokine-release-syndrome-crs

(20)Corticosteroid therapy can be considered in children with COVID-19 ARDS and for patients with fluid- and catecholamine-refractory septic shock.
If used, intravenous methylprednisolone is recommended with the following dose/schedule for ARDS and septic shock; modifications to weaning schedule can be considered based on clinical course.

Table 5. Intravenous Methylprednisolone Dosing/Schedule for ARDS

	mg/kg/dose	Interval
Days 1-5	**1**	**Every 12 hours**
Days 6-10	**0.5**	
Days 11-12	**0.25**	
Days 13 -14	**0.125**	

Septic Shock IV Hydrocortisone Dosing
BSA-based dosing:
Hydrocortisone 100 mg/m2 load, then 100 mg/m2/day divided q4 hours IV

Mg/kg-based dosing:
Hydrocortisone 2 mg/kg IV load (max 100 mg), then 2 mg/kg/day divided q4 hours IV

(21)Interferon-beta-1α (<10 years):
The best time for prescription
<7 days from symptom onset in moderate COVID-19 patients, Optimal clinical timing: days 4−7 of symptoms[19]

For children >10 years:
A full dose should be given to children weighing ≥50 kg

For children <10 years:
INF-beta-1α=$\frac{Child's\ Body\ weight}{50} x$ 0.0625 mg (2 million units [0.25 mL])
[Repeat calculated dose every other day.]

INF-beta-1α=0.0625 mg (2 million units [0.25 mL])

[19]https://www.nature.com/articles/s41390-020-1053-9

[Repeat calculated dose every other day].[20]

[20]https://www.uptodate.com/contents/treatment-and-prognosis-of-pediatric-multiple-sclerosis