Philippine Pediatric Society
Pediatric Infectious Disease Society of the Philippines

INTERIM GUIDELINES ON THE SCREENING, CLASSIFICATION, AND MANAGEMENT OF PEDIATRIC PATIENTS WITH SUSPECTED OR CONFIRMED CORONAVIRUS DISEASE 2019 (COVID-19)

Version 5, 08 January 2022

INTRODUCTION

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 continues to greatly impact the lives of everyone all over the world. As the total number of reported cases increase globally, the number of pediatric cases have also steadily increased over the past two years. Although children have been shown to comprise a smaller percentage of cases compared to adults and have been less likely to have severe disease, they are still vulnerable, and prevention and treatment remains paramount. The emergence of the highly transmissible Omicron variant of SARS-CoV-2 will also require a heightened response from all those who care for children. The scientific and clinical knowledge generated to address this challenge continues to aid in addressing the demands brought by the pandemic and has developed at a rapid pace.

This rapid advice is the fifth version released by the Philippine Pediatric Society and the Pediatric Infectious Disease Society of the Philippines. It is intended to guide pediatricians, general and family practitioners, and other healthcare professionals caring for children on how to assess and treat pediatric patients with suspected or confirmed COVID-19. These guidelines were formulated based on information available at the time of its release.

This update is a shortened version and contains the following updates: a modified triage algorithm which takes into account the need to screen patients with symptoms and exposure; a revised severity criteria; new treatment indications for monoclonal antibodies, Tocilizumab, Baricitinib; thromboprophylaxis; and therapeutics for Multisystem Inflammatory Syndrome in Children (MIS-C). Sections with no recent updates, and for which the advice remains the same, e.g, infection prevention and control, discharge from isolation, can be accessed in the fourth version. Pediatric COVID-19 vaccination is continuously evolving and is being advocated for in various venues by PPS and PIDSP.

DISEASE SEVERITY CLASSIFICATION CRITERIA

A child for whom the diagnosis of COVID-19 is considered should further be classified according to disease severity. Table 1 lists criteria for severity based on the WHO COVID-19 clinical management living guidance with modifications following the latest PCAP Clinical Practice Guidelines.

Table 1. COVID-19 Disease Severity

Severity		Definition
Mild disease	**No pneumonia**	Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.
Moderate disease	**Pneumonia**	Child with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest indrawing) and no signs of severe pneumonia, including SpO_2 ≥ 95% on room air Tachypnea (in breaths/min): • 3months old to 12months old: ≥50 breaths per minute • 1year old to 5years old: ≥40 breaths per minute • 5-12years: ≥30 breaths per minute • ≥12years: ≥20 breaths per minute While the diagnosis can be made on clinical grounds, chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications.
Severe disease	**Severe pneumonia**	Child with clinical signs of pneumonia (cough or difficulty in breathing) + at least one of the following: ▪ Central cyanosis or SpO_2 < 95%; severe respiratory distress (e.g. fast breathing, grunting, very severe chest indrawing); general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions ▪ Tachypnea (in breaths/min): • 3months old to 12months old: ≥50 breaths per minute • 1year old to 5years old: ≥40 breaths per minute • 5-12years: ≥30 breaths per minute • ≥12years: ≥20 breaths per minute
Critical disease	**Acute respiratory distress syndrome (ARDS)**	**Onset**: within 1 week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms. **Chest imaging**: (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules. **Origin of pulmonary infiltrates**: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. ECG) to exclude hydrostatic cause of infiltrates / edema if no risk factor present.

Critical disease		**Oxygenation impairment in adolescents/adults**: a) Mild ARDS: 200 mmHg < PaO_2/FiO_2 ≤ 300 mmHg (with PEEP or CPAP ≥ 5 cmH_2O) b) Moderate ARDS: 100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg (with PEEP ≥ 5 cmH_2O) c) Severe ARDS: PaO_2/FiO_2 ≤ 100 mmHg (with PEEP ≥ 5 cmH_2O) **Oxygenation impairment in children**: note OI and OSI, use OI when available. If PaO_2 not available, wean FiO_2 to maintain SpO_2 ≤ 97% to calculate OSI or SpO_2/FiO_2 ratio: • Bilevel (NIV or CPAP) ≥ 5 cmH_2O via full face mask: PaO_2/FiO_2 ≤ 300 mmHg or SpO_2/FiO_2 ≤ 264 • Mild ARDS (invasively ventilated): 4 ≤ OI < 8 or 5 ≤ OSI < 7.5 • Moderate ARDS (invasively ventilated): 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3 • Severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥ 12.3
	Sepsis	**Adolescents/adults**: acute life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia. **Children**: suspected or proven infection and ≥ 2 age-based systemic inflammatory response syndrome (SIRS) criteria, of which one must be abnormal temperature or white blood cell count.
	Septic shock	**Adolescents/adults**: persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L. **Children**: any hypotension (SBP < 5th centile or > 2 SD below normal for age) or two or three of the following: altered mental status; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and heart rate < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or weak pulse; fast breathing; mottled or cool skin or petechial or purpuric rash; high lactate; reduced urine output; hyperthermia or hypothermia
	Acute thrombosis	Acute venous thromboembolism (i.e. pulmonary embolism), acute coronary syndrome, acute stroke.

Critical disease	**MIS-C (WHO Classification)**	Preliminary case definition: children and adolescents 0–19 years of age with fever > 3 days **AND** two of the following: rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet); hypotension or shock; features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP); evidence of coagulopathy (by PT, PTT, elevated D-dimers), acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain); **AND** elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin. **AND** no other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes. **AND** evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19. See scientific brief, 15 May 2020 WHO: Multisystemic inflammatory syndrome in children and adolescents temporally related to COVID-19

Notes:
If altitude is higher than 1000 m, then the correction factor should be calculated as follows: PaO2/FiO2 x barometric pressure/760

When PaO_2 is not available, $SpO_2/FiO_2 \leq 315$ suggests ARDS (including in non-ventilated patients).

Oxygenation Index (OI) is an invasive measurement of the severity of hypoxemic respiratory failure and may be used to predict outcomes in pediatric patients. It is calculated as follows: percentage of fraction of inhaled oxygen multiplied by the mean airway pressure (in mmHg), divided by the partial pressure of arterial oxygen (in mmHg). Oxygen saturation index (OSI) is a non-invasive measurement and has been shown to be a reliable surrogate marker of OI in children and adults with respiratory failure. OSI replaces PaO_2 with oxygen saturation as measured by pulse oximetry (SpO_2) in the OI equation.

SIRS criteria: abnormal temperature (> 38.5°C or < 36°C); tachycardia for age or bradycardia for age if < 1 year; tachypnea for age or need for mechanical ventilation; abnormal white blood cell count for age or > 10% bands.

DIAGNOSTIC TESTING

1. SARS-CoV 2 TESTING

A. Molecular-based assays

Nucleic acid amplification testing (NAAT) using the **reverse transcriptase polymerase chain reaction (RT-PCR)** is the standard method for diagnosing SARS-CoV-2 infection. Appropriate specimens include samples collected from the upper (pharyngeal swabs, nasal swabs, nasopharyngeal secretions) and/or lower airways (sputum, airway secretions, bronchoalveolar lavage fluid). RT-PCR testing using nasopharyngeal swab (NPS) and oropharyngeal swab (OPS) remains to be the most sensitive test for COVID-19.

RT-PCR is recommended at or shortly after the onset of illness for symptomatic patients, or at least five (5) to seven (7) days after exposure for presumed asymptomatic close contacts or pre-symptomatic close contacts.

Neonates born to mothers with suspected or confirmed COVID-19, regardless of whether there are signs and symptoms of infection in the neonate, must be tested using RT-PCR (NPS/OPS) at the 24th hour of life, and preferably a repeat at the 48th hour of life. Should the neonate not be tested, the observation period is 14 days from date of birth or 7 days from the time of onset of symptoms, if any. Neonates not tested must be treated as positive for the duration of the 14-day observation. The management of infants born to COVID-19 positive mothers is discussed in the Philippine Obstetrical and Gynecological Society (POGS)-Philippine Pediatric Society (PPS) Care of Suspect/Confirmed COVID-19 Newborns Interim Guidelines.

B. Antigen Tests

Antigen tests detect the presence of viral proteins (antigens) expressed by the SARS-CoV-2 virus in a sample, usually obtained through *nasal or nasopharyngeal swabs*. After collection, the sample is placed into an extraction buffer or reagent, and the extract is allowed to interact with antibodies that are either (1) embedded into a lateral flow immunochromatographic test device (rapid antigen test); or (2) processed through a laboratory-based automated assay machine. The use of saliva as a specimen for rapid antigen test is NOT recommended in patients suspected of COVID-19 infection.

The PSMID Living CPG states that rapid antigen test is recommended for use under ALL these conditions in patients suspected of COVID-19 infection: a) symptomatic, AND b) at the early phase (≤ 7 days) from onset of symptoms, AND 3) using specific brands that demonstrated sensitivity ≥ 80% and specificity ≥ 97-100%. The main advantages offered by antigen tests are relatively lower costs and faster turnaround times. Although both antigen and RT-PCR tests perform best at points in time when viral load is highest, antigen tests are usually less sensitive. In contrast, the specificity of antigen tests are generally as high as the RT-PCR. The use of the rapid antigen test alone is also not recommended for use in diagnosing COVID-19 in asymptomatic patients suspected of COVID-19 infection.

The DOH allows the use of rapid antigen tests to confirm COVID-19 infection in close contacts living in communities and closed or semi-closed institutions with confirmed outbreaks and in remote settings where RT-PCR is not immediately available. For symptomatic close contacts, antigen testing can be used as a confirmatory test as well. For asymptomatic close contacts, antigen test can be used provided that the negative result are confirmed with RT-PCR or be subjected to repeat antigen testing within 48 hours after the first negative test results. Antigen tests are most useful during the acute phase of the disease when the viral load is high, which is within 5 days after onset of symptoms. The SARS-CoV-2 RT-PCR remains to be the standard diagnostic test for COVID-19.

C. Antibody (Serologic) Tests

Specific antibodies (IgM and IgG) are produced after SARS-CoV-2 infection and can be detected by a variety of methods from the blood, e.g., lateral flow immunochromatographic assay (LFIA), enzyme linked immunosorbent assay (ELISA), chemiluminescence immunoassay (CLIA), etc. Determining unique viral protein targets to reduce cross-reactivity to other coronaviruses is a challenge and can affect test sensitivity and specificity. Antibody tests may be utilized in the following situations: 1) provide evidence of previous infection with SARS-CoV-2, but not for the diagnosis of acute infection; 2) as part of work-up for multisystem inflammatory syndrome in children (MIS-C); and 3) for studies of population seroprevalence to understand the epidemiology of SARS-CoV-2. Antibody testing is not recommended to determine immunity to COVID-19 following vaccination or to assess the need for vaccination.

2. ANCILLARY LABORATORY TESTS

A. Complete blood count (CBC)

The WBC count is generally normal, however, lymphocytopenia has been frequently reported in early disease, while leukocytosis has been associated with severe disease. Appearance of significant lymphopenia may coincide with worsening clinical status and increase in inflammatory markers. Platelet count may be normal or high. However, thrombocytopenia has been reported in several case reports of COVID-19 patients presenting with fever, initially assessed to have dengue fever based on positive serology. The presentation of fever and thrombocytopenia is important to recognize in the local setting where dengue fever is common.

B. Inflammatory markers

General recommendations on the use of biomarkers based on currently available evidence state that no investigations are warranted for children who are asymptomatic or in the mild disease without comorbidity categories. Children in higher categories may require basic laboratory workup and any additional biomarkers as appropriate.

Associations of inflammatory markers with COVID-19 progression and severity have been reported in several studies; however, inconsistencies in final interpretations remain due to evidence of heterogeneity among studies. Although most cases of COVID-19 have mild symptoms and good prognosis, it is imperative to identify useful markers that provide additional objective information to identify patients who need to be monitored and treated early. Among the inflammatory markers investigated, C-reactive protein (CRP), procalcitonin, erythrocyte sedimentation rate (ESR), and interleukin-6 were found to be positively correlated with severe COVID-19 disease. CRP is known to be a sensitive acute-phase response inflammatory marker, as well as indicator of infection and tissue damage. Increase in CRP levels have positive correlation with COVID-19 severity. Increased procalcitonin levels may be seen in patients with severe COVID-19 without bacterial co-infection; however, a rapid rise or significantly elevated procalcitonin may also indicate secondary bacterial infection. Significant increase in PCT was reported to be associated with higher risk of severe infection. ESR, although a non-specific inflammatory marker, was found to be in higher levels in severe COVID-19 groups. However, studies mostly involved older age groups, as ESR levels increases with age. IL-6 has been reported to be secreted by pathogenic T-cells upon COVID-19 infection, which may explain its dramatic increase in severe COVID-19 disease. IL-6 may be a good marker to monitor therapeutic response. However, many hospitals and laboratories in the Philippines do not have routine capability to detect IL-6 compared to other inflammatory markers mentioned above.

Biomarkers such as lactate dehydrogenase (LDH), creatine kinase (CK), and cardiac troponin I, may be elevated in myocardial, lung, hepatic, or renal injury. These biomarkers need to be used judiciously as routine use may be misleading. Other inflammatory markers such as coagulative parameters (e.g., D-dimer) have prognostic values in predicting mortality. Associations with serum ferritin still need further studies.

Overall, laboratory abnormalities are usually uncommon in most children with acute COVID-19, as these elevations are predominantly confined to those with severe COVID-19 disease and multisystem inflammatory syndrome in children (MIS-C).

3. IMAGING STUDIES

Chest x-ray is the recommended first line imaging modality in children suspected to have COVID-19 presenting with respiratory symptoms. Typical findings of pediatric COVID-19 include bilateral distribution peripheral and/or subpleural ground glass opacities and/or consolidation; these imaging findings are commonly seen with COVID-19 pneumonia in children however, differential diagnosis also includes other viral or atypical pneumonia. However, this modality has limited sensitivity and specificity, hence, a negative chest x-ray does not exclude pulmonary involvement in patients with laboratory-confirmed COVID-19, nor does it indicate absence of infection in cases of suspected COVID-19 not yet confirmed by RT-PCR.

Other imaging modalities. A Chest CT scan is not recommended as the initial diagnostic test in pediatric patients suspected to have COVID-19. Chest CT scan findings of COVID-19 in the pediatric population are not pathognomonic but may be suggestive of the diagnosis in the appropriate clinical setting. It may be considered in patients with a worsening clinical course who are not responding appropriately to therapy, or to further investigate a specific pulmonary condition. Chest ultrasound on the other hand has been used as an alternative to chest x-ray and chest CT scan in the diagnosis of pneumonia in COVID-19 patients due to its ease of use at point-of-care, absence of radiation exposure, and lower cost than CT scan. The PSMID Living CPG suggests against the routine of CT scan and lung ultrasound for diagnosing COVID-19 among suspected patients with COVID-19.

PHARMACOLOGIC INTERVENTIONS FOR CHILDREN WITH COVID-19

Since the SARS-CoV-2 is a newly detected virus and COVID-19 cases were only diagnosed in January 2020, there is limited data on the treatment and prevention of this illness in children. There have been numerous observational research, randomized controlled trials, and even systematic reviews for specific treatments for COVID-19 in adults. Ethically, new drugs are tested first in adults before testing them in children unless there is an important reason, such as if the disease is only seen in children. For this review, data from children were collected when available, and adult research results were heavily relied upon.

The Committee has categorized the therapies according to when they should be used due to the severity of illness. Those recommended for use should be used routinely for that category, and experimental options should only be used in the context of a clinical trial or for compassionate use as specified. Treatment of mild and moderate COVID-19 is mainly supportive, and most of the recommendations in this chapter are for those in the severe and critical category, including MIS-C.

The use of experimental drugs should be discussed with the child's parents or legal guardian, carefully explaining these investigational drugs' potential clinical benefits and potential adverse reactions. The clinician should obtain a signed informed consent form.

Table 2. Recommended therapy for severe and critical COVID-19

DRUG and Indication	Dosing Regimen / Duration	Contraindications	Adverse Effects
CORTICOSTEROIDS (CS) Patients classified as severe & critical COVID-19	**Dexamethasone**: 0.15 mg/kg IV once daily (max. dose: 6mg) Up to 10 days or until discharge *Alternative CS if IV dexamethasone is not available:* 1. **Methylprednisolone**: 0.8 mg/kg IV once daily (max dose: 32mg) OR 2. **Hydrocortisone**: < *1 month:* 0.5 mg/kg IV every 12 hrs for 7 days followed by 0.5 mg/kg IV once daily for 3 days ≥ *1 month:* 1.3 mg/kg IV every 8 hrs (max dose 50mg; max total daily dose 150mg) *Alternative oral CS:* **Dexamethasone** PO: 0.15mg/kg orally once daily (max. dose: 6mg) OR **Prednisolone**: 1 mg/kg orally once daily (max dose: 40mg)	• Systemic fungal infection • Systemic infection, unless specific anti-infective therapy is employed • Hypersensitivity to the active ingredient or any other component	• Adrenal suppression • Immunosuppression (reactivation of latent infections, secondary infections) • Hyperglycemia • Psychiatric disturbances • Increased blood pressure • Peripheral edema • Myopathy (particularly if used with neuromuscular blocking agents) • Hypernatremia • Avascular necrosis • Adrenal insufficiency

DRUG and Indication	Dosing Regimen / Duration	Contraindications	Adverse Effects
TOCILIZUMAB (use Tocilizumab plus systemic steroids) Patients showing rapid respiratory deterioration and/or requiring high doses of oxygen and with elevated markers of inflammation	8 mg/kg (*patients ≥ 30 kg*) or 12 mg/kg (*patients < 30 kg*) as a single dose (maximum: 800 mg/dose) in combination with corticosteroids If clinical improvement does not occur, a second dose may be given ≥8 hours after the first dose	• Known hypersensitivity to Tocilizumab or any component of the formulation PRECAUTIONS: • Immunocompromised patients, particularly those who have recently received other biologic immunomodulating drugs • Alanine transaminase levels >5 times the upper limit of normal • A high risk for gastrointestinal perforation • An uncontrolled serious bacterial, fungal, or non-SARS-CoV-2 viral infection • Absolute neutrophil counts <500 cells/µL • Platelet counts <50,000 cells/µL • Known hypersensitivity to the drug	• Serious and potentially fatal infections (including active tuberculosis and other opportunistic infections) • Increased serum cholesterol • Constipation (6% to 13%) • Neutropenia • Hepatic: Increased serum AST and ALT • Injection site reaction • Infusion-related reaction

Table 3. Experimental therapy for mild-moderate COVID-19 in children

DRUG and Indication	Dosing Regimen / Duration	Contraindications	Adverse Effects
BAMLANIVIMAB + ETESEVIMAB Child AND non-hospitalized patient, AND laboratory confirmed SARS-CoV-2 infection, AND mild to moderate COVID-19, AND within 10 days of symptom onset, AND high risk for progressing to severe COVID-19 and/or hospitalization *cardiovascular disease, chronic lung disease, chronic metabolic disease, chronic kidney disease, chronic liver disease, and immunocompromised conditions	**Administered together as a single intravenous (IV) infusion** *1 to 12 kg:* Bamlanivimab 12 mg/kg and etesevimab 24 mg/kg *> 12 to 20 kg:* Bamlanivimab 175 mg and etesevimab 350 mg *> 20 to < 40 kg:* Bamlanivimab 350 mg and etesevimab 700 mg *≥ 40 kg:* Bamlanivimab 700 mg and etesevimab 1400 mg	Severe hypersensitivity (e.g., anaphylaxis) to bamlanivimab, etesevimab, or any component of the formulation	Fever, chills, dizziness, dyspnea, urticaria, pruritus, flushing, nausea, and vomiting
CASIRIVIMAB + IMDEVIMAB Child/adolescent >12 years and weighing >40 kg, AND non-hospitalized patient AND laboratory confirmed SARS-CoV-2 infection, AND mild to moderate COVID-19, AND within 10 days of symptom onset, AND high risk for	Casirivimab and imdevimab are packaged separately but are only authorized for administration together as a single IV infusion; the authorized dosage is 600 mg of casirivimab and 600 mg of imdevimab infused over at least 60 minutes	Severe hypersensitivity (e.g., anaphylaxis) to casirivimab, imdevimab, or any component of the formulation.	Fever, chills, dizziness, dyspnea, urticaria, pruritus, flushing, nausea, and vomiting

progressing to severe COVID-19 and/or hospitalization mAb therapies are NOT authorized for use in patients hospitalized for COVID-19 (unless admitted to the hospital for reasons other than COVID-19 and otherwise meet EUA criteria for treatment)			

Note: *With the emergence of the Omicron VOC, the recent US NIH Treatment guidelines state that "if the Delta VOC still represents a significant proportion of infections in the region and other options are not available or are contraindicated, patients can be offered bamlanivimab + etesevimab or casirivimab + imdevimab, with the understanding that this treatment would be ineffective if they are infected with the Omicron VOC. In those aged ≥12 years and weighing ≥40 kg who live in areas with a high prevalence of the Omicron VOC, Sotrovimab should be administered as soon as possible and within 10 days of symptom onset". However, Sotrovimab is not yet available in the Philippines.*

Table 4. Experimental therapy for severe and critical COVID-19 in children

DRUG and Indication	Dosing Regimen / Duration	Contraindications	Adverse Effects
REMDESIVIR Hospitalized and requires supplemental oxygen (but does not require oxygen delivery through a high flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO)	*≥ 12 years and weighing ≥ 40 kg:* Remdesivir 200 mg IV over 30-120 min on Day 1, 100 mg IV on Day 2 to Day 5 *3.5 kg to < 40 kg:* Remdesivir 5 mg/kg IV over 30-120 min on Day 1, followed by 2.5 mg/kg once daily on Day 2 to Day 5 Duration: 5 up to 10 days	• eGFR is <30 mL/min • ALT levels increase to > 5 times the upper limit of normal (ULN)	• Nausea • ALT and AST elevations • Hypersensitivity • Increases in prothrombin time • The drug vehicle is SBECD (sulfobutyletherbeta-cyclodextrin), associated with renal toxicity, SBECD accumulation may occur in patients with moderate or severe renal impairment
BARICITINIB (use in combination with Remdesivir) Hospitalized children, in whom corticosteroids cannot be used, aged ≥2 years with COVID-19 who require supplemental O_2, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)	*Children 2 to < 9 years:* 2 mg PO once daily combined with remdesivir *Children ≥ 9 years and adolescents*: 4 mg PO once daily combined with remdesivir Duration: 14 days or until hospital discharge, whichever is first	Hypersensitivity to baricitinib or any component of the formulation	• Increased AST and ALT • Thromboembolism • Thrombocythemia
CONVALESCENT PLASMA Consider in a clinical trial, consult with an Infectious Disease specialist	8-10ml/kg, with a maximum of 600ml, as slow infusion over 1-4 hours	• Previous reactions to plasma infusion • With IgA deficiency • Pregnant or breastfeeding • If with previously repeated transfusions	• Fever • Hypersensitivity reaction • Circulatory overload • Transfusion-related acute lung injury

Table 5. Anti-coagulation for COVID-19

DRUG and Indication	Dosing Regimen / Duration	Contraindications	Adverse Effects
Prophylactic anti-coagulation (in consultation with Hematology) 1. Hospitalized COVID-19 symptomatic patients with plasma D-dimer levels ≥5 times the upper limit of normal values, *or* 2. Hospitalized COVID-19 symptomatic patients with presence of at least 1 clinical risk factor (see Note below) for hospital-associated venous thromboembolism (VTE) **Treatment dose is not recommended unless with diagnosis of thrombosis**	For prophylaxis: LMWH for stable patients: *> 2 months to <18 years:* Enoxaparin 0.5-0.75 mg/kg/dose (max: 30 mg/dose) SQ Q12 ≥ *18 years:* Enoxaparin 40 mg SQ Q24 UFH For unstable patients: Heparin: 10-15 units/kg/hour IV, no loading dose needed	Active bleeding is an absolute contraindication Relative contraindications: Platelet count < 20,000-50,000/µL, fibrinogen activity <100 mg/dL by Clauss method, recent major bleeding, and concomitant aspirin administration at doses > 5 mg/kg/day;	Active bleeding Elevation of serum AST and ALT Fever Local site reactions Thrombocytopenia and anemia Ecchymosis

Note: Clinical risk factors for hospital-associated venous thromboembolism: 1. Pubertal, post-pubertal, or age >12 years, 2. Obesity (ie, BMI >95th percentile), 3. Active malignancy, nephrotic syndrome, cystic fibrosis exacerbation, sickle cell disease vaso-occlusive crisis, or flare of underlying inflammatory disease (eg, lupus, juvenile idiopathic arthritis, inflammatory bowel disease), 4. Congenital or acquired cardiac disease with venous stasis or impaired venous return, 5. Status-post splenectomy for underlying hemoglobinopathy, 6. Known thrombophilia (eg: protein S, protein C, or antithrombin deficiency; factor V Leiden; factor II G20210A; persistent antiphospholipid antibodies), 7. Central venous catheter, 8. Mechanical ventilation, 9. Prolonged length of stay (eg, anticipated >3 days), 10. Complete immobility (Braden Q Mobility Score = 1), 11. Previous history of VTE, 12. First-degree family history of VTE before age 40 years or unprovoked VTE, 13. Receiving estrogen-containing oral contraceptive pill

Table 6. MIS-C Treatment

(in addition to supportive treatment including fluid resuscitation, inotropes, and empiric antibiotics for those in shock as necessary; a multi-specialty team including Cardiology, Hematology, Rheumatology, and Infectious Disease specialists should be involved)

DRUG and Indication	Dosing Regimen / Duration	Contraindications	Adverse Effects
CORTICOSTEROIDS	Methylprednisolone 1-2 mg/kg/dose (max: 30 mg/dose) IV q12h initially then shift to oral corticosteroids once with defervescence or after 3-5 days, tapered off over three to four weeks High-dose pulse glucocorticoids (10-30 mg/kg/day IV) is recommended in patients who do not respond to IVIG and low-dose corticosteroids, especially those on high-dose multiple inotropes (adapted from American College of Rheumatology)	• Systemic fungal infection • Systemic infection, unless specific anti-infective therapy is employed • Hypersensitivity to the active ingredient or any other component	• Adrenal suppression • Immunosuppression (reactivation of latent infections, secondary infections) • Hyperglycemia • Psychiatric disturbances • Increased blood pressure • Peripheral edema • Myopathy (particularly if used with neuromuscular blocking agents) • Hypernatremia • Avascular necrosis • Adrenal insufficiency
INTRAVENOUS IMMUNOGLOBULIN (IVIG) with corticosteroids	2 g/kg over 8-12 hours (max 100 g)* *Assess cardiac function and fluid status before giving IVIG; should only be administered when cardiac function is restored	• History of anaphylaxis to human Ig • IgA deficient patients with antibodies against IgA and a history of hypersensitivity	• Hypersensitivity reaction, including anaphylaxis • Infusion reactions: headache, chills, myalgia, wheezing, tachycardia, lower back pain, nausea, hypotension • Renal failure • Thromboembolism • Aseptic meningitis syndrome • Hemolysis • Transfusion-related acute lung injury • Transmission of infectious pathogens

DRUG and Indication	Dosing Regimen / Duration	Contraindications	Adverse Effects
Anti-coagulation	ASA 3-5 mg/ kg/ dose (max: 81 mg/ dose) PO OD until normalization of platelet count and confirmed normal coronary arteries at ≥ 4 weeks after diagnosis MIS-C patients with a coronary aneurysm z-score ≥10.0, an ejection fraction <35%, or those with documented thrombosis should be treated with low dose aspirin and therapeutic anticoagulation with enoxaparin; consult with Cardiology and Hematology (adapted from American College of Rheumatology)	• Platelet count < 100,000/µL • Active bleeding or significant bleeding risk	Active bleeding

There is no evidence for or against multivitamins and minerals as prevention or treatment of COVID-19 in children. Nutritional support may be given upon the attending physician's discretion with doses not exceeding the Recommended Dietary Allowance.

***Disclaimer*:** Recommendations were made based on the best available evidence at the time of its release. As the knowledge on this disease is still evolving, these recommendations may change as more evidence becomes available.

ALGORITHM ON THE SCREENING, CLASSIFICATION, AND MANAGEMENT OF PEDIATRIC PATIENTS WITH COVID-19
(V5, 8 Jan 2022)

SCREEN

TRIAGE

*Any **ONE** of the following*:*

Fever	Cough	Sore throat	Dyspnea	Coryza	General weakness
Anorexia	Nausea/ vomiting	Diarrhea	Myalgia	Headache	Altered mental status

** Clinical symptoms of COVID-19 are non-specific and can mimic any viral illness.*

+ *Any **ONE** of the following:*

CLASSIFY

EXPOSURE EVALUATION
- **Residing in** or **travel** to areas with community transmission or local communities under quarantine within the last 14 days
- **Close contact** with sick individuals (proven or highly suspected of COVID-19)

CLINICAL EVALUATION
- There is **rapid progression** of symptoms
- **Worsening** symptoms **despite** compliance to standard treatment and **no etiology** determined

LABORATORY EVALUATION
- **Laboratory examination** results and **imaging studies** may aid in assessing severity of symptoms and need for further management

YES

COVID-19 SUSPECT CASE

- MODERATE
- SEVERE
- CRITICAL
- ASYMPTOMATIC
- MILD

See Table 1. COVID-19 Disease Severity Classification Criteria

NO

CONSIDER ALTERNATIVE DIAGNOSIS

MANAGE

ADMIT
1. Admit to isolation room / critical area
- Ensure that staff uses PPE
- Observe safety precautions

2. Refer to a specialist

3. Do the following:
- SARS-CoV-2 testing
- Ancillary laboratory tests as appropriate
- Follow pharmacologic management according to disease classification

HOME ISOLATION
- Supportive treatment
- Prevention of virus transmission
- *Note:* If the child has **comorbidities**, admit for observation if close follow-up is not possible

MANAGE
- Treat present problem accordingly
- Treat other pre-existing conditions (if present)
- Screen for comorbidities that may be contributory and/or causative of the current complaint
- Home quarantine if not admitted

RE-EVALUATE
Is there **non-improvement** or **worsening status** after 2-3 days? If **YES** → bring the patient to the hospital

This algorithm is designed to guide clinicians in the approach to potential pediatric COVID-19 cases and does not replace clinical judgment and proper assessment; common sense must prevail at all times.

ALGORITHM ON THE SCREENING, CLASSIFICATION, AND MANAGEMENT OF PEDIATRIC PATIENTS WITH COVID-19

(V5, 8 Jan 2022)

DIAGNOSTIC TESTING

SARS-CoV 2 TESTING

Type of test	When to test	Samples used
RT-PCR	• At or shortly after onset of illness for symptomatic patients • If asymptomatic, at least 5 to 7 days after exposure to a COVID-19 case • For neonates born to COVID-19 positive mothers, test at 24th hour of life, and preferably a repeat at the 48th hour of life	• Nasopharyngeal swab • Oropharyngeal swab • Saliva • Nasal swab • Throat swab
Rapid Antigen Test	• During the early phase (≤ 7 days) from onset of symptoms • To confirm COVID-19 infection in close contacts during outbreaks when RT-PCR is not immediately available • A negative RAT should be confirmed with an RT-PCR in settings or situations wherein COVID-19 is highly suspected Note: Use RAT brands that demonstrate sensitivity ≥ 80% and specificity ≥ 97%	• Nasal swab • Nasopharyngeal swab • Combined nasopharyngeal and oropharyngeal swab • Saliva and sputum NOT recommended
Antibody test	• NOT for diagnosis of acute infection, provides evidence of previous infection with SARS-CoV-2 • Work-up for multisystem inflammatory syndrome in children (MIS-C) • NOT recommended to determine immunity to COVID-19 following vaccination or to assess the need for vaccination	• Blood

ANCILLARY LABORATORY TESTS

MILD/ ASYMPTOMATIC	MODERATE	SEVERE/CRITICAL	MIS-C
None	CBC Optional: CRP Liver and renal function tests Chest x-ray	CBC CRP, ESR, PCT Liver and renal function tests, LDH, electrolytes PT/PTT, D-dimer, fibrinogen Ferritin IL-6 ABG Chest x-ray Optional: Chest CT scan Chest ultrasound	CBC CRP, ESR, PCT Liver and renal function tests, LDH, electrolytes PT/PTT, D-dimer, fibrinogen Ferritin IL-6 BNP, Troponin, CKMB Chest x-ray 2D Echo ECG

Note: The ancillary laboratory tests and imaging listed are the suggested minimum diagnostic work-up; additional testing may be done depending on symptoms or organ involvement noted.

ALGORITHM ON THE SCREENING, CLASSIFICATION, AND MANAGEMENT OF PEDIATRIC PATIENTS WITH COVID-19

(V5, 8 Jan 2022)

TREATMENT

PHARMACOLOGIC MANAGEMENT ACCORDING TO DISEASE CLASSIFICATION

MILD/MODERATE

- Supportive care

Experimental therapeutic options: (see table 3 for dosages)

- **Bamlanivimab + Etesevimab**

  Indications: For children with confirmed mild to moderate COVID-19, non-hospitalized, within 10 days of symptom onset, and high risk for progressing to severe COVID-19 and/or hospitalization

- **Casirivimab + Imdevimab**

  Indications: For ≥12 years old and weighing > 40kg with confirmed mild to moderate COVID-19, non-hospitalized, within 10 days of symptom onset, and high risk for progressing to severe COVID-19 and/or hospitalization

SEVERE

- Supportive care
- **Dexamethasone**

  0.15 mg/kg IV once daily (max 6mg), up to 10 days or until discharge

  If not available, use alternative corticosteroids [see table 2]
- **Tocilizumab**

  8 mg/kg (patients ≥30 kg) or 12 mg/kg (patients <30 kg) as a single dose (max 800 mg) in combination with corticosteroids

  [If clinical improvement does not occur, a 2nd dose may be given ≥8 hours after 1st dose]

Experimental therapeutic option:

- **Remdesivir**
  - ≥ 12 years and ≥ 40 kg: 200 mg IV over 30-120 min on D1, 100 mg IV OD on D2 to D5
  - 3.5 kg to < 40 kg: 5 mg/kg IV over 30-120 min on D1, 2.5 mg/kg IV OD on D2 to D5
  - Duration: 5-10 days

CRITICAL

Experimental therapeutic options:

- **Baricitinib** (use in combination with Remdesivir)
  - 2 to < 9 years: 2 mg PO once daily
  - ≥9 years: 4 mg PO once daily
  - Duration: 14 days or until discharge, whichever is first
- **Convalescent plasma**

  8-10ml/kg, max 600ml, as slow infusion over 1-4 hours [clinical trial use]

Others:

1. Nutritional support
2. Thromboprophylaxis [see table 5 for indications and contraindications]

   LMWH for stable patients:

   > 2 mos to < 18 yrs: **Enoxaparin** 0.5-0.75 mg/kg/dose (max 30 mg/dose) SQ q12

   ≥ 18 yrs: **Enoxaparin** 40 mg SQ q24

   UFH For unstable patients:

   Heparin 10-15 units/kg/hour IV, no loading dose needed

Multisystem Inflammatory Syndrome in Children (MIS-C)

- **Corticosteroids**

  Methylprednisolone 1-2 mg/kg/dose (max 30 mg/dose) IV q12h initially, then shift to PO once afebrile or after 3-5 days, then taper off over 3-4wks

  OR

  IVIG + Corticosteroids

  2 g/kg IVIG over 8-12 hours (max 100 g)
- **Aspirin** 3-5 mg/kg/dose (max 81 mg/dose) PO OD if with documented coronary artery aneurysm, until normalization of platelet count and confirmed normal coronary arteries at ≥4 weeks after diagnosis
- **Thromboprophylaxis** (if indicated)

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