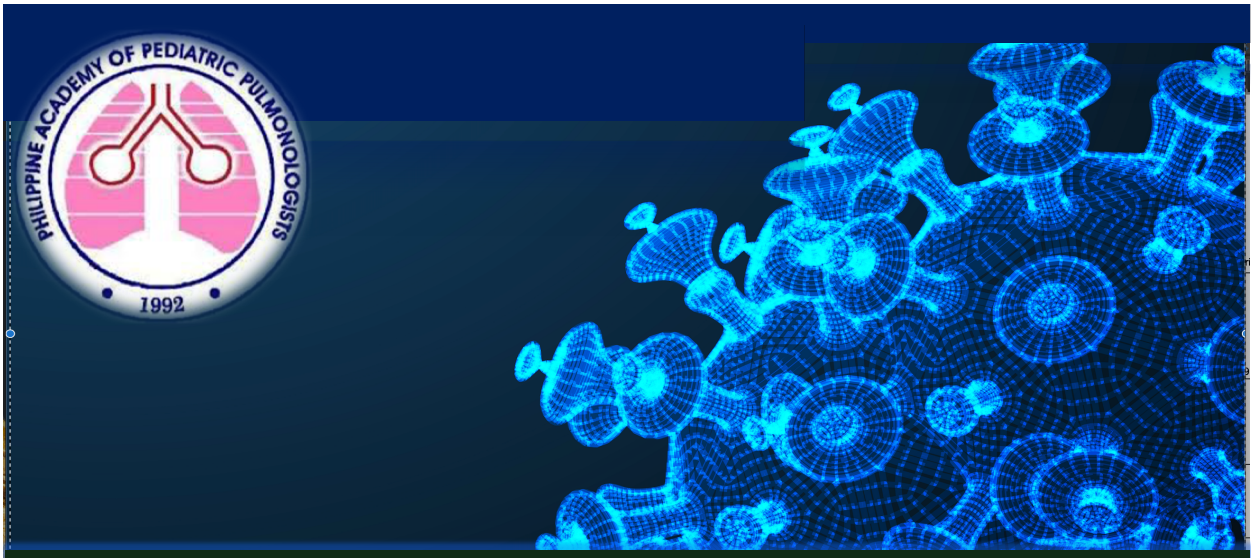
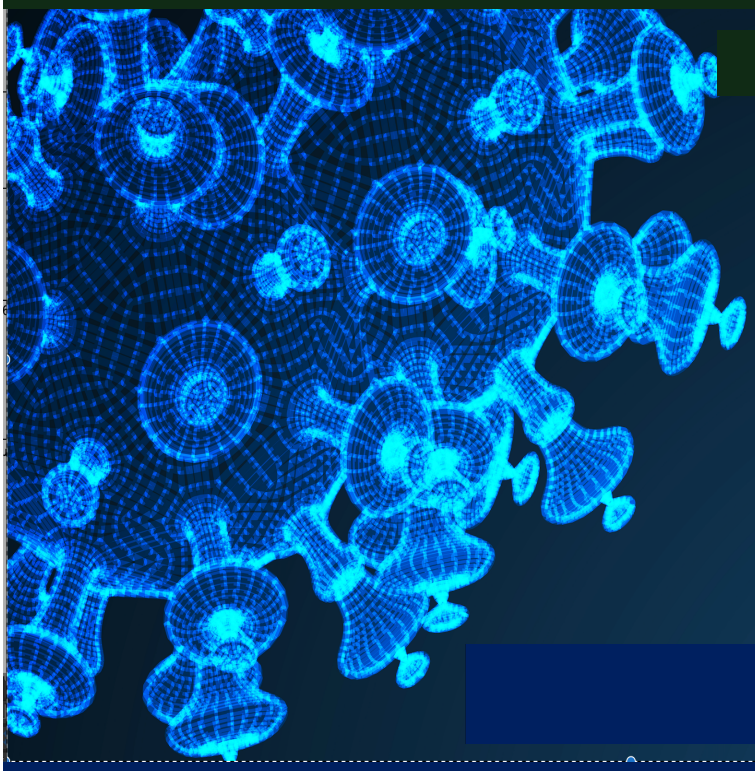


Philippine Academy of Pediatric Pulmonologists

INTERIM GUIDELINES ON PULMONARY CARE IN PEDIATRIC COVID-19



May 8, 2021 Edition

PAPP COVID TASK FORCE

Philippine Academy of Pediatric Pulmonologists (PAPP)

May 8, 2021

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EXECUTIVE SUMMARY

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus. There are few data on the clinical presentation of COVID-19 in specific populations, such as infants and children. While clinical data available to date are based largely on the disease experience in China, Europe, and the United States, the pediatric literature on COVID-19 is still in its infancy. Acquisition of new data in the regional, national, and international guidance is still rapidly evolving.

This guidance was made from meager resources available in children and will serve as a foundation for optimized respiratory supportive care for pediatric COVID-19 patients. The purpose of this document is to complement with the WHO, CDC and the other subspecialty guidelines in providing respiratory care for children with acute respiratory infections when COVID-19 is suspected. This guidance should be used alongside with infection prevention control guideline.

This novel virus involves the respiratory system in the progressive stage of the disease. The considerations in management of pediatric patients with respiratory involvement both in the home and hospital setting are highlighted throughout the text. These recommendations are not meant to replace clinical judgment or specialist consultation but rather to strengthen clinical management of these patients and to provide up-to-date guidance. Best practices for optimized respiratory supportive care like aerosolized procedures, proning in children, and airway clearance therapies, performing special pulmonary procedures and concurrent disease management of asthma, childhood TB and Chronic Lung Disease among pediatric COVID-19 patients.

We recognize the unsettling nature of these changing recommendations and we want to provide pediatric health care providers with more data to better understand the shifting landscape surrounding respiratory care in COVID-19. The evidence is rapidly changing and this guidance will be updated to reflect the same as evidence becomes available.

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Philippine Academy of Pediatric Pulmonology COVID Task Force
Committee Chair

Guideline Methodology

This Guideline was prepared in accordance with the general rules of WHO Rapid Advice Guidelines and DOH Manual for Clinical Practice Guideline Development 2018.

The End-User of The Guideline

The guideline is intended for clinicians involved in the care of pediatric patients with suspected or confirmed to have COVID-19.

Declaration of Conflict of Interests

Written inquiry for financial interests of relevant personal was conducted after the first meeting prior to the start of this guideline. Relevant financial as well as nonfinancial interests were surveyed and disclosed and subsequently assessed in consensus conference in order to minimize potential bias in guideline development. Finally, there is no conflict of interests for all the personnel participating to prepare this guideline.

Literature Searching and Preparation of Evidence and Updates

Draft of the proposed scope and list of potential priority topics was performed. This was subsequently refined to the list of priority topics and identifying key issues. The Pediatric Pulmonology COVID task Force Committee members concentrated on the management of respiratory care and the topic list was utilized to formulate the key questions. These questions were used as a guide in the search of evidence and are developed using the PICO format. In addition, we have an independent literature searching team to search available indirect evidence from systematic reviews and/or RCTs (randomized controlled trials), of the existing evidence. We addressed topics or questions covered by the guideline, then its quality assessed. If there is a lack of higher-level quality evidence, our panel considered observational studies and case series.

Literature search included new guidelines and systematic reviews in pediatric COVID-19. The bibliographic databases and concepts were defined with search terms that include both medical subject headings (MeSH) and text words. We also searched following websites: the WHO (https://wwwwho.int/), The Centers for Disease Control and Prevention (CDC) (https://www.cdc.gov/) and the Philippine Department of Health, (DOH) https://www.doh.gov.ph).

This is the third update document of which followed the May 25, 2020 and September 30,2020 editions. A new search for pediatric COVID 19 specific updates on the respiratory management were done by the committee members until April 30 2021.

In light of the changing recommendations, a Homecare Chapter for suspected and confirmed children with COVID-19 was included. The registry of Pediatric COVID-19 patients in PAPP affiliated institutions previously gathered have now grown in number providing a better insight of the characteristics of pediatric COVID-19 patients locally. These institutions include: Philippine General Hospital, Philippine Children's Medical Center, St. Luke's Medical Center, Chong Hua Hospital, Makati Medical Center, Philippine Heart Center and the University of Santo Tomas Hospital. The guidance from respective PAPP Task Force Committees in the Special Situations and Special Pulmonary Procedures has also been updated as a collective effort of the PAPP to provide respiratory care guidance to clinicians attending to children afflicted with the disease. Inclusion of new recommendations in TB and Asthma during this pandemic are added to this edition.

Grading the Evidences and Recommendations

We accorded to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) basic approaches and rules and particularly considered experts' evidence to assess the quality of a body of evidence to make recommendations.

The quality of evidence reflects whether the extent to which our confidence estimating the effect is adequate to support a particular recommendation. The level of evidence was categorized as "high quality", "moderate quality", "low quality", or "very low quality";

The recommendations were classified as "strong" or "weak." In specific recommendations, we used "*should" or "strongly recommend*" for **strong** recommendations; whereas, "*suggest" or "consider"* was used for **weak ones**.

Updating the Guideline

The evidence is rapidly changing and this guidance will be updated to reflect the same as evidence becomes available. Please take note that this rapid advice will have to undergo revisions and editing as new evidence will set in before it will be published in the final form. The final articles registered in this document were those that were warranted valid enough for citation (systematic reviews and meta-analyses) in Pediatric COVID-19 were prioritized among other articles as they grant the most accurate findings) available during the past 12 months of this pandemic.

Acknowledgement

The Philippine Academy of Pediatric Pulmonologists COVID Task Force hereby acknowledge the following people, committee and organizations for their contribution to the chapters on Pulmonary Care in Special Situations and Special Pediatric Pulmonary Procedures in the update of this interim guideline on Pulmonary Care In Pediatric Covid :

- Philippine Academy of Pediatric Pulmonologists Asthma Committee
  Chair: Rozaida R. Villon MD FPPS FPAPP
- The PAPP Task Force in Childhood TB 2019-2021
  Chair: Agnes R. Mendoza MD FPPS FPAPP
- The PAPP Task Force in Pediatric Bronchoscopy
  Chair: Marion O. Sanchez MD FPPS FPAPP
- The PAPP Committee on Pre-Operative Evaluation
  Chair: Christine Q. Sua MD FPPS FPAPP
- The PAPP Committee on Pulmonary Function Testing
  Chair: Maria Isabel M. Atienza MD FPPS FPAPP
- The PAPP Committee on Sleep
  Chair: Beverly Dela Cruz MD FPPS FPAPP FPSSM
  Joint Statement for Sleep Study recommendations from the
  Philippine Society of Sleep Medicine (PSSM),
  Philippine Neurological Association (PNA),
  Philippine College of Chest Physicians (PCCP)
  Philippine Academy of Pediatric Pulmonology (PAPP)
  Philippine Academy of Sleep Surgery (PASS) of the Philippine Society of Otolaryngology – Head and Neck Surgery (PSO-HNS)

Update Points of this Edition

Chapter 1

- Updated data on epidemiologic features of COVID-19 in the Philippines
- Survey of Pediatric COVID19 from 7 Training Institutions under the Philippine Academy of Pediatric Pulmonologists (PAPP) are updated which include their clinical presenting symptoms and imaging results.
- Updated recommendations on the diagnosis of MIS-C related to COVID19
- Inclusion of the discussion of the Pediatric Post Acute Sequelae of COVID-19 (PASC) or Long Haul COVID-19
- Inclusion of the Clinical Diagnosis and Management Algorithm

Chapter 2

- New chapter on Homecare of MILD Pediatric COVID19 patients
- Inclusion of the respiratory precautions of a child when brought out into the community

Chapter 3

- Pediatric Respiratory Management in COVID-19 updated evidence for recommendations
- Specific recommendation updates Intubation and managing of the difficult airway
- Respiratory Management of Hypoxemia in COVID-19 Algorithm

Chapter 4

- Inclusion of recent evidence and review of SARS CoV2 transmission affecting aerosolized therapies during the COVID-19 pandemic
- Additional precautions in aerosol therapy among spontaneously breathing pediatric COVID-19 on HFNC/NIV
- Updated practice points in the limited use of nebulization among suspected and confirmed children with COVID-19
- Inclusion of the Aerosol Therapy in Pediatric COVID-19 Algorithm

Chapter 5

- Inclusion of the new statement on ending of isolation recommendation based on the new local and international guidelines
- Inclusion of the Home care advise post discharge from isolation and hospitalization

Chapter 6

- Updated data on the Pediatric Pulmonary Care in Special Situations in Asthma
- New Childhood TB recommendations on TB screening should a pediatric patient receive COVID-19 vaccination.

Chapter 7

- Additional recommendations in the Pediatric Pre-operative Risk evaluation for care in children during the COVID19 pandemic are included

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Recommendations at a Glance

Recommendation 1

Children presenting with any of the following: fever, cough sore throat, shortness of breath and/or gastrointestinal symptoms without any plausible etiology should be further investigated for possible exposure to COVID–19 and be considered as COVID suspect.
(Strong recommendation, Moderate-grade of evidence)

Recommendation 2

Consider the diagnosis of Post-acute COVID-19 Syndrome in children as it may also occur in the pediatric age group and the most common symptoms are tiredness/weakness, fatigue, chest pain, palpitation, headache, dizziness, abdominal pain, muscle pain, rash. There was also significant prevalence of neuropsychiatric symptoms like lack of concentration, difficulty in doing everyday tasks and processing information as well as short term memory loss.
(Weak recommendation, Low-grade of evidence)

Recommendation 3

Consider the use of laboratory tests to support the diagnosis and monitor COVID-19 patients especially in evaluating for co-infections and multi-organs dysfunctions.
(Weak recommendation, Low-grade of evidence)

Recommendation 4

- Chest Imaging should be requested
  - For medical triage of patients with suspected COVID-19 who present with **Moderate to severe** clinical features and a high pre-test probability of disease in resource limited settings
  - When a child requires hospitalization, or is suspected of having hospital acquired pneumonia, CXR is the most appropriate step in imaging evaluation
- Chest x-ray should not be requested in patients with suspected early stages of pediatric COVID-19 and mild clinical features at outpatient setting unless they are at risk for disease progression

(Strong recommendation, low-moderate grade of evidence)

Recommendation 5

The following should be the structured reporting of CXR finding for pediatric COVID-19 patients[76].

- **Typical Findings of Pediatric COVID-19**
  Bilateral distribution peripheral and/or subpleural GGOs and/or consolidation.
- **Indeterminate Findings of Pediatric COVID-19**
  Unilateral peripheral or peripheral and central GGOs and/or consolidation, bilateral peribronchial thickening and/or peribronchial opacities, or multifocal or diffuse GGOs and/or consolidation without specific distribution.
- **Atypical Findings of Pediatric COVID-19**
  Unilateral segmental or lobar consolidation, central unilateral or bilateral GGOs and/or consolidation, single round consolidation i.e., round pneumonia with or without air bronchogram, pleural effusion, or lymphadenopathy.
- **Negative for Pediatric COVID-19**
  No CXR findings suggestive of pneumonia

(Strong Recommendation, Moderate-Grade Evidence)

Recommendation 6

Chest CT scan may be considered in the following situations:[76]

1. **Mild clinical features of COVID-19:**
   If there is clinical progression, inadequate clinical improvement, or when an alternative diagnosis (such as concern for pulmonary embolism) necessitates further evaluation.
2. **Moderate – Severe clinical features of COVID-19 in a without resource-constrained environment:**
   If the outcome will impact clinical decision (i.e., imaging findings would affect how closely a patient is clinically followed and possibly followed with imaging to assess for change or potential complication)
3. **Moderate – Severe clinical features of COVID-19 in a resource-constrained environment:**
   When there is unavailability of testing or lengthy turn-around time of results that would avert rapid triage decisions, imaging may be used as an initial step to evaluate for findings suggestive of COVID-19 (presumed positive) versus findings suggestive of an alternative diagnosis. Considering the limited sensitivity of chest radiography, low-dose technique chest or pediatric patients closely following the as-low-as-reasonably-achievable (ALARA) principle, may be considered either initially or following unrevealing chest radiography results.

(Strong recommendations, moderate grade evidence)

Recommendation 7

Chest ultrasound can be considered as an alternative to CXR and Chest CT in the diagnosis of pneumonia in COVID-19 patient. It is a tool that could be used at bedside avoiding the need for shifting infected patients to the Radiology suite.

(Weak recommendations, low grade evidence)

Recommendation 8

Supplementary tests that may be done that will aid in the diagnosis of MIS-C would include rapid antibody test and chest radiographs.

The three main thoracic imaging findings may be observed in pediatric patients with MIS-C associated COVID-19 are heart failure, ARDS pattern and pulmonary embolus.[78]

(Weak recommendation, Moderate-grade evidence)

Recommendation 9

We strongly recommend the strict adherence to the set guidelines for local or regional level for home care management among pediatric patients suspected or confirmed to have MILD COVID-19 to reduce SARS-CoV-2 transmission.

Recommendation 10

We strongly recommend the giving of FDA approved supportive care measures pediatric patients suspected or confirmed to have MILD COVID-19 as follows:

1. Support treatment for fever lysis will be through good hydration and antipyretic use of Paracetamol at 10-15mg/kg /dose *(Strong recommendations, strong grade evidence)*

2. Aerosol Therapy is to be administered only when bronchospasm is observed, the recommended device for aerosol therapy is the use of the pMDI with a valve holding chamber unless the patient qualifies for the limited indications for nebulization. *(Strong recommendations, moderate to strong grade evidence)*

(Strong recommendation, Strong-grade evidence)

Recommendation 11

We strongly recommend that caregivers of children with MILD COVID-19 should be counseled about signs and symptoms of clinical deterioration that should prompt urgent re-evaluation.
(Strong recommendations, moderate to strong grade evidence)

Recommendation 12

1. We strongly recommend, that well children less than 2 years old *should not* wear masks or face shields when are they are out in the community or with people not living in the same household.[118,119]
While older children (2 -11 years old) needing to be out from the home or be with people not in the same household, use masks and face shields with adult supervision.
Children above 12 years old follow mask and face protection advise for adults.

2. For the subgroups of children with disabilities, developmental disorder or specific conditions where mask wearing interferes with the health condition, a case-to-case basis recommendation from their medical provider is warranted. [118,119,120]
(Strong recommendations, moderate to high grade evidence)

3. Children should not wear a mask when playing sports or doing physical activities such as running, jumping or playing on the playground, so that it does not compromise their breathing.
(Strong recommendations, moderate to high -grade evidence)

Recommendation 13 [64, 124,126]

The use of High Flow Nasal Cannula (HFNC), CPAP/BiPAP and Non Invasive Ventilation (NIV) theoretically increase the risk of viral spread through aerosol generation. Therefore, we suggest to observe the following precautions.

1. Preferably in an appropriate Airborne Infection Isolation Room (AIIR)
2. Use of a surgical mask over HFNC to reduce droplet spread
3. Use an appropriate viral exhalation filter for CPAP/BiPAP
4. Healthcare providers shall be in proper Personal Protective Equipment (PPE)

(Strong recommendation, high quality evidence)

Recommendation 14 [22, 128,129,130]

Children with suspected or confirmed severe COVID-19 will need supplemental oxygen to achieve target sp02 ≥94%. We suggest to use

1. Supplemental oxygen therapy by Low Flow Nasal Cannula (LFNC) may be started, with a surgical mask worn over the patient's face to reduce droplet spread, when oxygen saturations (sp02) are < 90%. If patient continues to be hypoxemic, oxygen delivery via face mask with reservoir bag should be initiated. Titrate supplemental oxygen based on patient's saturation
2. Patients that remain hypoxemic with increased work of breathing should be escalated to High Flow Nasal Cannula (HFNC) if available.
3. Those with progressive respiratory distress or with no HFNC available, continuous positive airway pressure (CPAP) or a bi-level non-invasive ventilation (NIV), may be used.

(Strong recommendation, low quality evidence)

Recommendation 15

In low-resource settings or in facilities where ventilators are not available, we suggest that an improvised CPAP (iCPAP), using locally available equipment, may be used.

(Weak recommendation, moderate-high grade quality evidence)

Recommendation 16

We strongly recommend an appropriate environment for airway management of suspected or confirmed COVID-19 pediatric patients as follows;

1. The use of a negative pressure ventilation room is ideal to minimize exposure to aerosols and droplets from pediatric COVID-19 patients
2. Normal pressure rooms with closed doors are an alternative setting in low-resource facilities
3. The use of airway devices providing 6L/min or more of oxygen shall be discouraged as this procedure is considered aerosol-generating, unless it is performed under an AIIR.
4. Strict hand hygiene and compliance to the minimum PPE requirement is necessary in handling pediatric COVID-19 patients
5. Double gloving as a standard practice for handling pediatric COVID-19 patients

(Strong recommendation, high quality evidence)

Recommendation 17

We strongly recommend intubation in the following cases:

1. SpO2/FiO2 ratio < 221 in pediatric patients on bi-level NIV or CPAP. [124]
   (Strong recommendation, Moderate quality evidence)
2. If there is no improvement in oxygenation (target SpO_2 92-97% and FiO_2) within 60 minutes on NIV or CPAP.[124] *(Strong recommendation, Moderate quality evidence)*
3. Patients with hypoxaemic respiratory failure and hemodynamic instability, multiorgan failure or abnormal mental status. *(Strong recommendation, high quality evidence)*

Recommendation 18

Pre-oxygenation with 100% FiO2 for 5 minutes using face mask with reservoir bag is preferred for suspected or confirmed COVID-19 patients.

When possible, avoid the use of Bag Valve Mask (BVM) to reduce exposure to aerosols. However, if its use is absolutely necessary for pre-oxygenation, it is strongly recommended to follow safety measures to minimize aerosolization:[129,130]

a. Two-Person technique/Two handed vice grip, use of a viral filter, and gentle ventilation
b. A clear drape should be placed over the patient's face to minimize aerosolization.

(Strong recommendation, low grade evidence)

Recommendation 19 [64,129,130, 136]

Rapid Sequence Intubation (RSI) is should be the treatment of choice for endotracheal intubation of suspected or confirmed COVID-19 patients as inadequate sedation and paralysis can produce coughing during laryngoscopy, which is an aerosol-generating procedure. It is strongly recommended that cuffed endotracheal tubes be used to avoid peritubal leak and dissemination of secretions. *(Strong recommendation ,high grade evidence)*

Recommendation 20

The suggested lung protective strategies for children with Pediatric ARDS related to COVID-19 are as follows:

1. Low tidal volume (3-6 ml/Kg IBW) if poor respiratory compliance
   Low tidal volume (5-8ml/Kg) if better preserved respiratory compliance
2. Initial Positive End Expiratory Pressure (PEEP) of 8-10cmH20 individualized for each patient's phase of ARDS and should be titrated when there is refractory hypoxemia. Maximal PEEP in younger children is 15cmH2.[64,129]
3. Target plateau pressure (< 28 cm H20)
4. Permissive hypercapnia (pH 7.15 – 7.30)

(Weak recommendation, moderate to high quality evidence)

Recommendation 21

Prone positioning may be considered as part of treatment regimen for pediatric COVID-19 patients with moderate to severe ARDS.

(*Weak recommendation, low quality evidence)*

Recommendation 22

The use of pMDI for the delivery of B2 agonists via spacer or valve holding chamber (VHC) should be done as means of drug delivery over nebulizers among non-intubated children suspected or confirmed to have COVID-19 with signs of bronchospasm.

(Strong recommendations, low grade evidence)

Recommendation 23

The use of pressurized metered dose inhaler (pMDI) over nebulization is strongly recommended among mechanically ventilated COVID-19 suspect or confirmed children.

(Strong recommendation, low grade evidence)

Recommendation 24

It is strongly recommended that for suspected or confirmed COVID-19 children presenting with bronchospasm

1. **initial dose of salbutamol 2 puffs** for children ≤ 5 year old;
   4 puffs for children 6 to 11 year old and adolescent (100 mcg/actuation) delivered is strongly recommended.
2. If symptoms persist after initial bronchodilator: **a further 2–6 puffs of salbutamol for < 5-year-old; 4 to10 puffs (> 6-year-old); should be repeated every 20 minutes** until good clinical response is achieved.

(*Strong, recommendation, low-grade evidence)* [171, 105]

Recommendation 25

In ventilator-supported children, clinicians can consider using bidirectional in-line adapter when administering pMDI. This should be connected to the inspiratory limb of the ventilator tubing before the Y-piece. Unidirectional in-line and elbow adapters may be used as alternatives but are less effective. *(Weak recommendation, low-grade evidence* [166,173]

Recommendation 26

The use of nebulization for the delivery of B2 agonists among children having bronchospasm should only be used for limited specific situations under strict aerosol generating procedure protective measures and must be avoided as much as possible.
(Strong recommendation, low grade evidence)

Recommendation 27

For airway clearance procedures, we strongly recommend the following strategies among pediatric COVID-19 patients:

1. Ensuring adequate oxygenation, keeping the respiratory tract unobstructed
2. Appropriate inhalation therapy
3. Appropriate reassessment of airway patency
4. Non-invasive/invasive respiratory support and mechanical ventilation
5. Judicious use of fluids and vasoactive medications

(Strong recommendations, high grade evidence)

Recommendation 28

We strongly recommend that based on the Department of Health (DOH) updated guidelines for discharge and ending isolation[200]:

(1) Patients with at least moderate severity of COVID-19 illness (moderate, severe or critical) who have fulfilled **at least 21 days** of **isolation**, inclusive of 3 days of being asymptomatic can be discharged.
(2) Patients with mild symptoms and completed **at least 10** days of isolation from start of illness inclusive of 3 days of being asymptomatic can be discharged.
(3) Patients with positive SARS-CoV-2 PCR test but were asymptomatic, and remain asymptomatic for **at least 10 days** from the day the specimen was collected can discontinue isolation after 10 days.
(4) Close contacts of patients with COVID-19 who are asymptomatic and remain to be so for **at least 14 days** from date of exposure can discontinue quarantine.

We also recommend that in line with the DOH recommendations, a patient should be cleared by a licensed physician as a pre-requisite to discharge; and that repeat testing for COVID-19 is not required as part the aforementioned medical clearance. Once discharge criteria are met, confirmed cases of COVID of any disease severity can be labeled as recovered. [200]

Recommendation 29A PEDIATRIC ASTHMA RECOMMENDATIONS

1. Asthma patients on maintenance medications are advised to continue treatment as prescribed
2. Monitor asthma symptom control and risk factors for poor asthma outcomes which may require adjustment of medications.
3. Nebulization is discouraged because it can generate aerosol particles which increase the spread of the SAR-CoV2 virus. Inhaled medications must be administered using pressurized metered dose inhaler (pMDI) via spacers or valve holding chambers.
4. In limited situations when nebulization is absolutely necessary, the use of appropriate infection control measures should be strictly followed.
5. Single patient device use must be observed at all times.
6. Pediatricians may use the asthma action plan to educate guardians/parents in identifying asthma symptoms while at home and guide corresponding action to specific clinical situations.
   Please see the Asthma Action Plan below
7. When available, COVID-19 vaccination is recommended for pediatric patients with asthma. Usual vaccine precautions should apply.
8. Routine spirometry testing is not advisable to decrease the risk of viral transmission. Should this be done infection strict contact and airborne precautions must be instituted.

Recommendation 29b

The administration of existing medications for asthma controller medications should be continued for pediatric patients with asthma during the COVID-19 pandemic.
(Strong recommendations, moderate grade evidence)

Recommendation 30. CHILDHOOD TB RECOMMENDATIONS

1. Preventive measures should be observed by a patient with pediatric TB and the healthcare staff attending to them.
   (*Strong recommendations, very low grade evidence)*
2. TB testing should continue during the COVID-19 pandemic.
   (Strong recommendations, low-moderate grade evidence)
3. When COVID-19 vaccine be given to the pediatric age group, testing with TST or IGRA must be done before or at the same time during COVID-19 vaccination, otherwise, delay the test ≥4 weeks after the completion of COVID-19 vaccination.[217]
   (Strong recommendations, moderate grade evidence)
4. In COVID-19 patients with Latent TB Infection, TB preventive therapy (TPT) should be initiated and completed, with options on shorter rifamycin- containing preventive regimens.
   (Strong recommendations, low-moderate grade evidence)

Recommendation 31 RECOMMENDATIONS IN CHILDREN WITH CHRONIC LUNG DISEASE DURING THE COVID-19 PANDEMIC

Children with chronic lung conditions should continue to seek medical consults for regular follow-ups via remote consultation (Telemedicine /Video conference) and should be given preventive vaccination like pneumococcal and influenza vaccines.
(Strong recommendations, low to moderate grade evidence)

Recommendation 32 PERFORMANCE OF BRONCHOSCOPY THIS COVID-19 PANDEMIC

1. Contact precautions (face shield, masks and gloves) are integral components of PPE strategy to prevent the transmission of this disease, and N95 respirators or powered air purifying respirators (PAPR) represent additional precautions and must be worn by all health care workers.
   (Strong recommendation, moderate grade evidence)
2. Proper training on donning and doffing should be provided to healthcare workers.
   Proper personnel instruction on wearing PPE step-by-step should be made available at the changing area. *(Strong recommendation, moderate grade evidence)*
3. All patients undergoing bronchoscopy must undergo SARS-CoV-2 RT-PCR swab test. The validity of the results should be 3 days *(Strong recommendation, moderate grade evidence)*
4. Elective and non-emergent procedures may be deferred upon the discretion of the bronchoscopist and thoroughly discussed with the attending physician.
   (Weak recommendation, moderate grade evidence)
5. The number of healthcare workers assisting in the operating room/ bronchoscopy suite should be limited. *(Strong recommendation, moderate grade evidence)*
6. The decision to perform elective bronchoscopy from patients recovered from COVID-19 infection will need to be individualized based on disease severity, duration of illness, and a negative SARS-CoV2 RNA test from at least two consecutive nasopharyngeal swab specimens collected 24h apart (total of two negative specimens). The exact time to perform bronchoscopy is still unknown, but it would be reasonable to wait at least 30 days from resolution of symptoms.
   (*Weak recommendations, moderate grade evidence)*

Recommendation 31 PEDIATRIC PRE-OPERATIVE EVALUATION IN CHILDREN

1) All children scheduled for surgery or other procedures that require general anesthesia, deep sedation or moderate sedation should be screened and tested for SARS-CoV-2.
   (*Strong recommendations, moderate grade evidence)*
2) Pre-operative / pre-procedure screening will include clinical signs and symptoms of COVID-19 and significant exposure to confirmed COVID-19 persons.
   (Strong recommendations, moderate grade evidence)
3) Assessment of patients before surgery should include the questionnaire concerning exposure to a COVID-19 patient in the past 14 days or having COVID-19-related symptoms within the prior 2 weeks. *(Strong recommendation, low-moderate grade evidence)*
4) SARS-CoV2 PCR is the recommended screening test for asymptomatic patients scheduled for surgery/procedure. *(Strong recommendation, moderate grade evidence)*
5) The timing of SARS-CoV-2PCR testing should be done as close to the time of the procedure as possible and preferably done 48 hours prior to the procedure.
   (Strong recommendations, high grade evidence)
6) The use of antigen-detecting rapid diagnostic tests and the antibody testing for SARS-CoV2 are not recommended as pre-operative screening tools.
   (Strong recommendations, low grade evidence)
7) Radiographic imaging such as chest x-ray and/ or chest CT scan is not recommended as a screening or diagnostic tool for COVID-19.
   (Strong recommendations, low grade evidence)

8) Timing of urgent and elective surgeries:
   a. If the patient travelled to a country/locality with sustained community transmission, delay the surgery for 14 days following return, even if asymptomatic.
   b. If the patient has been in direct contact with a confirmed COVID-19 + patient, delay the surgery for 14 days following last contact, even if asymptomatic.
   c. If the patient presents with influenza-like illness or unexplained cough at the time of procedure, defer the surgery until they have recovered.

   (Strong recommendations, moderate-high grade evidence)

9) The timing of elective surgery after recovery from COVID-19 utilizes both symptom- and severity-based categories. Suggested wait times from the date of COVID-19 diagnosis to surgery are as follows:
   a. Four weeks for an asymptomatic patient or recovery from only mild, non-respiratory symptoms.
   b. Six weeks for a symptomatic patient (e.g., cough, dyspnea) who did not require hospitalization.
   c. Eight to 10 weeks for a symptomatic patient who is diabetic, immunocompromised, or hospitalized.
   d. Twelve weeks for a patient who was admitted to an intensive care unit due to COVID-19 infection.

Recommendation 34 PULMONARY FUNCTION TEST (PFT)

Pulmonary Function Tests in children during the COVID-19 pandemic is vital for the management of children with respiratory conditions. The tests must be performed with the following measures to reduce the risk of SARS-CoV2 transmission:

1. Routine PFT should not be performed. The PFTs should be limited to those patients for whom the results would be essential for making immediate treatment decisions.
2. A PFT Laboratory waiting area must be established for the purpose of triage and screening of patients, caregivers, and laboratory staff.
3. The PFT laboratory must ensure the use of Personal Protective Equipment (PPE) for patients, caregivers, and laboratory staff.
4. The testing environment and equipment must have optimal cleaning and disinfection as provided by the institutional infection control standards.
5. PFT Procedures:
   - Tidal breathing test must be performed first before any ventilation maneuvers.
   - A single-patient use pressurized metered-dose inhaler (pMDI) via a spacer should be the preferred device for the administration of Salbutamol in children.
   - Methacholine challenge tests and aerosol treatments must be avoided.

   (Strong recommendations, moderate-high grade evidence)

Recommendation 35 POLYSOMNOGRAPHY (SLEEP STUDY)

In performing Sleep Studies, the necessary the necessary triage and screening of consultations prior to the set schedule of the test strict infection control measures are imposed upon the patient, sleep technologist and the sleep center as a facility to prevent transmission of SARS-CoV-2. The quarantine level status set by the Philippine Interagency Task Force for Emerging Infectious Disease (IATF- EID) should guide the sleep laboratory on its operation. *(Strong recommendations, moderate to high grade evidence)*

Chapter 1

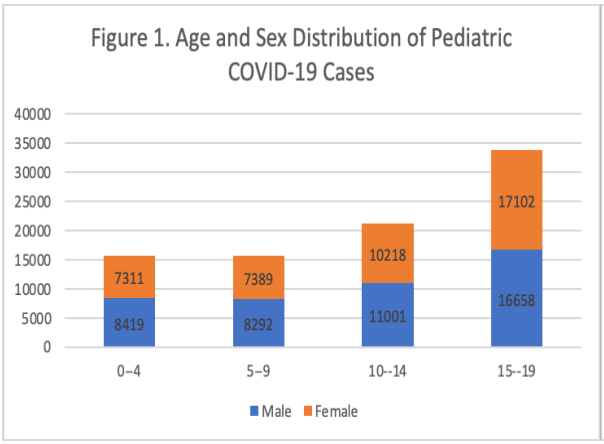
1. PEDIATRIC COVID-19

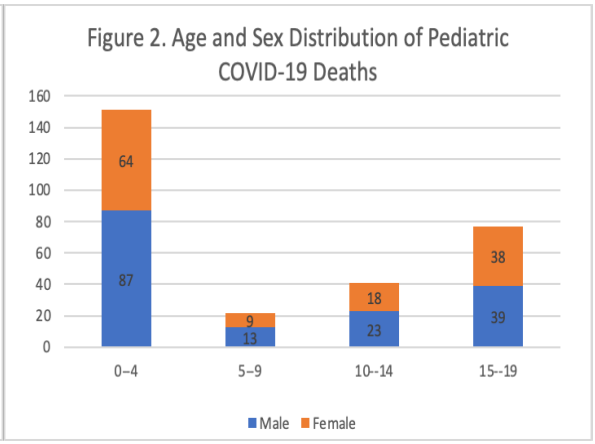
1.1. Local Epidemiologic Features

1.1.1. Pediatric Burden of Disease

As of April 30, 2021, there are 150,110,310 confirmed cases of COVID-19 with 3,158,792 deaths globally[1], including 1,037,460 confirmed cases and 17,234 deaths coming from the Philippines.[2]

The burden of COVID-19 in the pediatric age group is observed to be not as severe as in the adult population. As of April 18, 2021, the Department of Health (DOH) has recorded 86,390 (9.3%) cases in children out of 926,052 total cases, with majority (33,760; 39.1%) of them belonging to ages 15 to 19 years and the least number of cases belonging to ages 5 to 9 (15,681; 18.2%) and 0 to 4 years (15,730; 18.2%). Males (51%) and females (49%) were almost equally affected[3] (Figure 1). In contrast to the low number of COVID-19 cases in the youngest age groups, more than half (151; 51.9%) of deaths were seen in children 0 to 4 years old[3] (Figure 2). This is consistent with the current situation in other countries and is not unique to our local setting. In a systematic study by Kitano, et al, age-specific deaths presented as case fatality rate (CFR) (10.03 per 1,000,000 children) and ICU admissions shown as ICU admission rate (16.84 per 1,000,000 children) were found to be highest among children 0 to 4 years old, specifically in infants under 1 year old.[4] Furthermore, the highest pediatric morbidity and mortality from COVID-19 were seen in low-to-middle-income countries.[4]

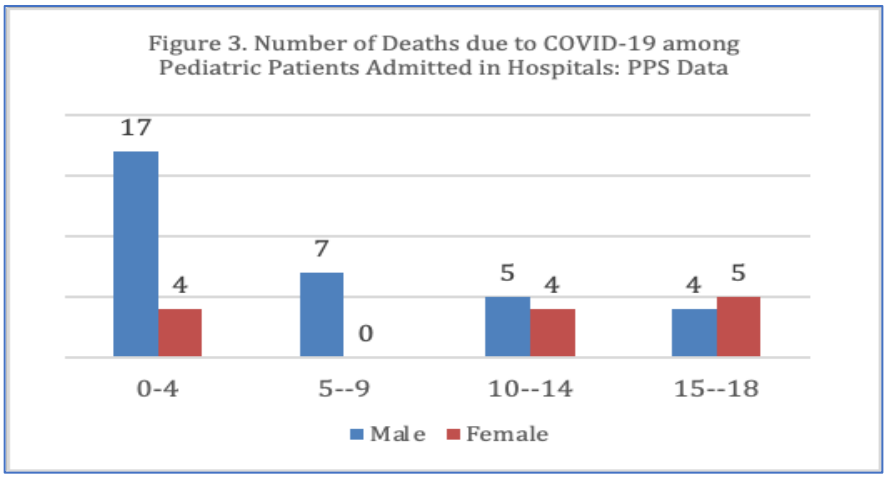




The local pediatric CFR of 0.34% (291 pediatric deaths out of 86,390 confirmed pediatric cases) as of April 18, 2021 is considerably lower compared to 1.85% (15,504 adult deaths out of 837,439 adult cases) in adults,[3] but on an international scale, the pediatric CFR in the Philippines is 7-8x higher than the global rate (0.45% vs 0.06%).[4]

Patients under 19 years of age have mostly been spared from severe disease, with an observed low number of admissions since the beginning of the pandemic. Based on the Philippine Pediatric Society (PPS) registry of COVID-19 cases from January to December 2020, there were 776 pediatric admissions, majority (42%) of whom were children 0 to 1 year old, 13% were 5- to 9-year-olds, 19% were 10- to 14-year-olds, and 20% were adolescents 15 to 18 years old. Among the children who were admitted for COVID-19, there were 46 (5.9%) deaths during the same time period and the death-to-cause ratio was found to be highest (2.7%) among 0- to 4-year-olds, decreasing in frequency with increase in age, with a rate of 0.9% among 5- to 9-year-olds, and 1.2% among both 10- to 14-year-olds and 15- to 18-year-olds. More deaths were seen in males (56.2%).[5] (Figure 3).

These figures do not represent the actual Philippine situation of COVID-19 in children due to lack of available complete national data; however, majority of health care institutions that deliver tertiary level of care in the country particularly among the young report to PPS, hence these data may give an overview of the severity of COVID-19 in children locally.



1.1.2. Clinical Features

The clinical features of pediatric COVID-19 in the local setting are comparable to those seen in other countries. In terms of presenting symptoms, fever (42.7%) and cough (28.2%) were the most frequently reported, while a large proportion of patients were found to be asymptomatic (14.5%). This is based on a survey of pediatric COVID-19 cases from 7 of the largest pediatric pulmonary referral hospitals in the country accredited by the Philippine Academy of Pediatric Pulmonologists (PAPP) (Table 1). Other less common

symptoms reported, such as bleeding, unilateral weakness, edema, increased sleeping time, and behavioral change were accompanying symptoms of another primary disorder and may or may not be related to COVID-19. A large systematic review by Hoang, et al, also showed similar clinical symptoms across nations. Fever (59.1%) and cough (55.9%) were the most common manifestations in children, followed by rhinorrhea and nasal congestion (20.0%), myalgia and fatigue (18.7%), sore throat (18.2%), dyspnea (11.7%), abdominal pain and diarrhea (6.5%), nausea and vomiting (5.4%), pharyngeal erythema (3.3%), decreased oral intake (1.7%), and rash (0.25%), with a large number (19.3%) reporting no symptoms.[6]

Table 1. Clinical Symptoms: PAPP Data

Symptoms	Frequency	%*
Fever	59	37.8
Cough	38	24.4
Vomiting	24	15.4
Diarrhea	18	11.5
Abdominal pain	13	8.3
Rhinorrhea	11	7.1
Dyspnea	10	6.4
Rash	8	5.1
Poor intake	6	3.8
Fatigue	5	3.2
Convulsion	5	3.2
Nausea	4	2.6
Extremity pain	4	2.6
Decreased sensorium	4	2.6
Body malaise	4	2.6
Headache	3	1.9
Cyanosis	3	1.9
Sore throat	2	1.3
One-sided weakness	2	1.3
Hematuria	2	1.3

Edema	2	1.3
Melena	1	0.6
Increased sleeping time	1	0.6
Gross bleeding	1	0.6
Behavioral change	1	0.6
Anosmia	1	0.6
Ageusia	1	0.6
Asymptomatic	19	12.2
*% was calculated based on 154 cases with data on clinical symptoms		

Table 2. Chest Radiograph and CT Scan Findings: PAPP Data

Characteristic	Frequency	%
Chest X-ray*		
No Pneumonia	59	38.0
Type of Parenchymal Opacity		
Consolidation	34	23.9
Ground glass	49	24.6
Infiltrates	16	11.3
Distribution		
Peripheral predominant	6	4.2
Perihilar predominant	35	24.6
Neither peripheral nor perihilar predominance	35	24.6
Right lung	11	7.7
Left lung	4	2.8
Bilateral lung	54	38.0
Upper zone predominance	7	4.9
Lower zone predominance	20	14.1
No zonal predominance	40	28.2
Other Features		
Pleural effusion	8	5.6
Pulmonary nodules	6	4.2
Chest CT Scan		
Total chest CT Scans done**	20	13.9
Consolidation and/or ground glass opacity***	19	95.0

*%was calculated based on 142 cases with chest x-ray
**% was calculated based on 144 cases with data on CT scan
***% was calculated based on 20 cases with CT scan results

1.2. Etiology, Pathogenesis, Incubation Period

1.2.1. Etiology

In December 2019, a cluster of patients with pneumonia of unknown etiology were identified in Wuhan, China. The virus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is an enveloped positive stranded RNA virus. It can be spherical or elliptical in shape. Its size is about 60 to 140 nm with distinctive spikes about 9 to 12 giving it the appearance of a solar corona. It is under a large family of Coronaviradae viruses with the genus Betacoronavirus. To date, there are seven CoVs known to infect humans, two of which caused outbreaks in Guandong, China in 2002 (SARS- CoV) and in Saudi Arabia in 2012 (MERS-CoV). Its genome has 82% similarity with SARS CoV hence designated the name SARS-CoV-2.[7]

The disease it caused is called coronavirus disease 2019 (COVID-19). Its symptoms included flu-like illness which are relatively mild, but it is highly contagious (R_0= 2.2 to 3.5), spreading via air droplets.[8] Besides being highly contagious, it was apparent that the infection could be transmitted from an asymptomatic individual. This contributed further to the difficulty by which the disease can be contained. Severe disease can be seen in extremes of ages, in the elderly and infants especially those with co-morbidities.

New Variants

Multiple variants of the virus that causes COVID-19 have been documented globally during this pandemic. In early October 2020, a new variant was originally detected in South Africa which was called B.1351. Likewise, the United Kingdom (UK) identified a variant called B.1.1.7 which was first detected in the US at the end of December 2020 and was also identified in many countries around the world.[9] In a preliminary report by Davies et al, they assessed the relative transmissibility of the UK variant and it was estimated to be 43–82% more transmissible than pre-existing variants of SARS-CoV-2.[10] Zhao et al reconstructed the variant-specified instantaneous reproduction number of the UK variant and found out that the 501Y variant is 52% (95% confidence interval: 46, 58) more transmissible than the 501N variant.[11] It has also been associated with increased risk of death compared to other variant viruses as reported by a study in the UK in which Grint et al found out a consistently higher absolute risk of death by 28 days in patients infected with variant B.1.1.7 but more data are needed to confirm this finding.[12] Furthermore, another variant which was first detected in the US at the end of January 2021 was P.1 which was first identified in travelers from Brazil, who were tested during routine screening at an airport in Japan, in early January. This Brazil variant has a set of additional mutations that may alter its ability to be recognized by the antibodies. The ability of these variants to spread rapidly than the predominant viruses is

because of one specific mutation called D614G and based on epidemiologic evidence the variants with this specific mutation spread more quickly without mutation. This mutation was one of the first documented in the US in the initial stages of the pandemic, after having initially circulated in Europe.[3]

In children aged 18 years old and younger, the clinical impact of the UK variant regarding acute respiratory COVID-19 is yet to be fully defined. Gupta et al findings in the King's College Hospital, London have found no evidence of more severe disease in children during the second wave, implying that infection with the UK variant does not result in a significantly different clinical course to the original strain.[13]

Table 3. Number of COVID-19 cases in the Philippines caused by SARS-COV2 variants *(as of April 10, 2021)*

VARIANT	NUMBER OF CASES
P.1	1
B.1.1.7	170
B.1.351	192
P.3	19

Table 3 above shows the number of cases caused by SARS-COV1 variants as reported by the Philippines' Department of Health, the University of the Philippines-Philippine Genome Center and the University of the Philippines-National Institutes of Health Further studies of these variants are needed to determine their effects on the transmissibility and severity of the disease.[14]

1.2.2. Pathogenesis[15]

The structure of the Coronavirus S protein is an important factor that will help the virus enter the host cells. The envelope spike glycoprotein (S1) binds to the cellular receptor of Angiotensin Converting Enzyme 2(ACE2) for SARS-CoV and SARS-CoV-2. ACE2 is present in epithelium in the nose, mouth, lungs, heart, blood vessels, kidneys, liver and gastrointestinal tract. In the lungs, ACE2 is highly abundant in type 2 pneumocytes, an important cell type present in chambers within the lung called alveoli, where oxygen is absorbed, and waste carbon dioxide is released.

Belouzard et al. found that a critical proteolytic cleavage event occurred at SARS-CoV S protein at position (S2) mediated the membrane fusion and viral infectivity. After cell entry, the viral RNA genome is released into the cytoplasm and is translated into two polyproteins and structural proteins, after which the viral genome begins to replicate. During this process of rapid viral replication, the affected pneumocytes will be damaged,

subsequently stimulating the body's humoral and cellular immunity, which are mediated by virus-specific B and T cells. Inflammatory mediators (Interleukin 1, Interleukin 6 and Tumor Necrosis Factor Alpha) will be released causing vasodilation and increased capillary permeability. This in turn may lead to alveolar edema and atelectasis leading to impaired gas exchange and eventual hypoxemia.

The main pathogenesis of COVID-19 infection is rapid RNAemia, which leaves the host cells or the immune cells ineffective and activates towards the hyperinflammatory side. It results in the overproduction of pro-inflammatory cytokines and chemokines. This brings about cytokine storm which will trigger a violent attack, this time, on respiratory cellular structures which include the pneumocytes and the endothelial cells, leading to organ failure, and finally leading to death in severe cases.

Table 4. Theories on why children fare better than adults in SARS-CoV-2 infection [96]

1. Prevention of virus exposure	Early isolation and movement restriction - Closing schools and day-care centers during the epidemic
2. Appropriate infection handling	▪ Trained immunity (strong innate response) due to: - Live vaccines (BCG, live virus vaccines) - Frequent virus infections Children are susceptible to a wide variety of viral illnesses. Presence of these viruses on epithelial surfaces can limit infection of SARS-CoV-2 through competition. Also, cross-reactive antibodies resulting from other viral infections, including non–SARS coronaviruses, may be partially protective against SARS-CoV-2 ▪ High ACE-2 expression metabolizing angiotensin-2 ▪ Lack of immune senescence Natural involution of the thymus over time leads to a decline in circulating naïve T cells. Due to this normal process, immune systems in adults are less able to be adaptive than those of children ▪ Good lung regeneration capacity
3. Absence of high risk factors	▪ Absence of ageing related co-morbidities (Hypertension, Diabetes) ▪ Less degree of obesity, smoking ▪ Pro-inflammatory cytokines are more prominent in adults

1.2.3. Incubation Period

The incubation period for COVID-19 is thought to extend to 14 days, with a median time of 4-5 days from exposure to symptoms onset.[16]

Based on data from the first cases in Wuhan and investigations conducted by the China CDC, the incubation time could be generally within 3 to 7 days and up to 2 weeks as the longest time from infection to symptoms was 12.5 days (95% CI, 9.2 to 18). This data also showed that this novel epidemic doubled about every seven days. There is currently no data on the specific incubation period of SARS-CoV2 among pediatric patients, though a current study suggests the median incubation to be at 5.1 days (95% CI, 4.5-5.8 days) and the development of symptoms start within 11.5 days (95% CI, 8.2-15.6 days) of infection.[16] There is also an implication that, under conservative assumptions, 101 out of every 10,000 cases will develop symptoms after 14 days of active monitoring or quarantine[16.]

1.2.4. Mode of Transmission of COVID-19

Inhalation of respiratory droplets is the major transmission route for COVID-19 infection in children[17,18.] Therefore, having close contact with adults positive to COVID-19 is the most common mode of infection in children [17,18.] There is no risk of vertical transmission of COVID-19 from infected pregnant mothers to their fetuses [17.]

The World Health Organization (WHO) believes that further evidence is needed to assess the possibility of aerosol transmission. Commonly performed medical procedures that are often considered aerosol-generating procedures (AGPs) and may increase the likelihood of transmission include open suctioning of the airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g., BiPAP, CPAP), bronchoscopy, manual ventilation, nebulizer administration and high flow O2 delivery[19]. The possibility of aerosol transmission outside of these procedures may occur in enclosed spaces, prolonged exposure (more than 15 minutes) and if the infectious individual has high concentrations of aerosols during increased exhalation such as when he/she exercises, shouts or sings.[20]

Children are unlikely to be the main drivers of COVID-19 infection. They may seem to have high viral load when they get infected but they have simpler airway structure as compared to adults. Fewer alveoli and terminal bronchioles equate to lower airspeed and less airway collapse.[96] In a research done by Posfay-Barbe et al, among 40 pediatric COVID-19 patients, 79% of households had an infected adult first before the child.[21] On the other hand, only 8% of households had a child who had the infection first before the adults. More studies need to be done to prove further whether children can effectively transmit the virus to other individuals.

1.3. Clinical Presentation of COVID-19

1.3.1. Early Recognition and Clinical Presentation

The main symptoms in children are fever, flu-like illness (nasal obstruction, runny nose), dry cough, myalgia and fatigue. Some children only present with low to moderate grade fever in their entire course of disease, and some do not have fever at all.[22,23] It is important for pediatric providers to not only have an appropriate suspicion of COVID-19, but also to continue to consider and test for other diagnoses, such as influenza.

Recommendation 1

Children presenting with any of the following: fever, cough sore throat, shortness of breath and/or gastrointestinal symptoms without any plausible etiology should be further investigated for possible exposure to COVID–19 and be considered as COVID suspect.

(Strong recommendation, Moderate-grade of evidence)

Table 5. Clinical Manifestations

Signs and Symptoms	Physical examination
Fever range is usually > 38^0C Cough Nasal Congestion or Rhinorrhea Sore throat Gastrointestinal symptoms Shortness of breath Fatigue Headache Myalgia Poor Feeding or poor appetite	Tachypnea and tachycardia Minimal rales or wheezing *Other findings*: Digital swelling Cutaneous manifestations Kawasaki disease-like manifestations (gastrointestinal symptoms, conjunctivitis, rashes and mucosal changes).

Rationale

Fever and cough remain as the most common symptoms of pediatric COVID - 19, amongst all epidemiological studies around the globe. Fever range is usually above 38^0C (38.1^0C to 39^0C)[17,18]. Median duration of fever is 1 day but can last up to 3 days.[24] Characteristic type of cough is usually dry. Other symptoms are variable when it comes to rate of occurrence. These may include shortness of breath, gastrointestinal symptoms, rhinorrhea and sore throat[17,18]. Systematic reviews and meta-analyses are often affected by the heterogeneity of the study population. Subgroup analysis by age may point out to some differences in symptomatology.

Infants: Fever and cough are still the most common symptoms, but it is worth mentioning that this age group has the most number of cases of severe disease. This age group also has the highest mortality and high incidence of viral (influenza and RSV) and bacterial co infection[6,25].

Younger children (<5 y/o): This is the age group that is commonly infected from clustering. Fever and cough are usual but gastrointestinal symptoms particularly vomiting and abdominal pain are well documented in this age group[26, 27].

Older children and adolescents: less likely to be symptomatic but this age group in children are the most infected and most likely to infect[28]. They are most likely to report headache, anosmia[29,30]. They are prone to develop rashes as well. Depression and anxiety have been reported. If gastrointestinal symptoms are present, the most common presentation would be diarrhea.[27]

Physical examination may reveal tachypnea and tachycardia[18]. Auscultatory findings may reveal minimal rales or wheezing[18,27]. Recently, there have been reports of dermatologic manifestations in children especially amongst teens with mild disease. The cutaneous manifestations consisted of an acral eruption of erythemo-violaceous papules and macules, with possible bullous evolution or digital swelling (*see Figure 4*). These are benign self-limiting lesions that would tend to appear late in the course of disease.[27]

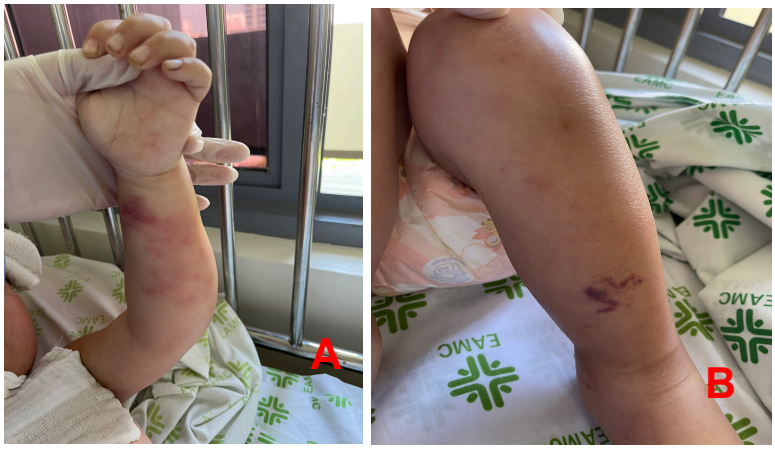


Figure 4.
Erythematous violaceous maculopapular rashes seen on forearms (A) and legs (B) of a 4y/o male with COVID-19 pneumonia. With permission.

1.3.2. Multisystem Inflammatory Syndrome in Children with COVID-19 (MIS-C)[31]

There had been increasing pediatric patients presenting with a multisystem inflammatory syndrome, the clinical presentation of which overlaps with Kawasaki disease (KD), toxic shock syndrome, and severe sepsis. In late April 2020, the National Health Service (NHS) in the United Kingdom, followed by the New York City Department of Health and Mental Hygiene, released alerts of increasing cases of pediatric patients with symptoms of fever, gastrointestinal symptoms, and signs of shock. They were termed as **Multisystem Inflammatory Syndrome in Children or MIS-C.**

Some are positive for RT-PCR for SARS-CoV-2 while others are positive for serum IgG for SARS-CoV-2. Still, some are negative for both but has a history of exposure to a COVID-19 infected adult. The syndrome has been theorized to be a hyperinflammatory reaction from a previous COVID-19 infection two to four weeks before symptoms of Kawasaki-like illness occur.[32]

Many have evidence of cardiac inflammation, with or without coronary arterial dilation. Since those initial reports, the Royal College of Pediatrics and Child Health, Center for Disease Control (CDC) and the WHO have all released initial case definitions for this entity. While slightly different, they all include the presence of fever, elevated inflammatory markers, and manifestations of effect on more than one organ system.

Pathophysiologic mechanism involves the activation of both T and B cell inflammatory pathway triggered by a superantigen (SAg) complex encoded by the SAR CoV2 spike protein. This super antigen complex is highly similar in sequence and three-dimensional structure to a fragment of the superantigenic Staphylococcal Enterotoxin B (SEB), which is known to interact with the TCR and CD28. SEB triggers large-scale T-cell activation and proliferation, resulting in massive production of a proinflammatory cytokine profile typical of Toxic shock syndrome[33].

They tend to occur in older children with a mean age of 10 years old but can occur in as young as 4 years of age. There seems to be no sexual predilection. When compared to severe pediatric COVID-19, MIS-C children have more severe cardiovascular involvement than respiratory involvement. They may occur even in a healthy child. Severe COVID 19 on the other hand, is predominantly a respiratory disease superimposed with an underlying condition such as congenital heart disease, oncologic diseases and immunodeficiency syndromes[34]. When it comes to laboratory results, MIS-C would also have higher neutrophil to lymphocyte count and elevated acute phase reactants such as CRPs when compared to severe COVID-19[35].

When compared to a non-COVID-19 related Kawasaki disease, they have lower platelet counts, lower lymphocyte counts, elevated D-dimer levels and higher values of acute phase reactants like ESR, CRP and Procalcitonin.[35] They have more frequent cardiac involvement, particularly myocarditis and pericarditis hence resulting to higher levels of cardiac enzymes (Troponin, pro BNP). Hypotensive episodes are also prominent. Moreover, greater number of these patients required a second line of treatment after one IV Immunoglobulin infusion. Generally intravenous steroids are used. Outcome is generally good. Few cases of MIS-C patients who progress to pediatric ARDS were also reported.[36]

Table 6. WHO preliminary case definition of Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19[37]
Children and adolescents 0–19 years of age with fever ≥ 3 days
AND two of the following: 1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet). 2. Hypotension or shock. 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP), 4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers). 5. Acute gastrointestinal problems (diarrhea, 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.

1.3.3. WHO COVID-19 Case Definitions[38]

Suspected Case

A. A person who meets the clinical AND epidemiological criteria

Clinical Criteria:

- Acute onset of fever AND cough; **OR**
- Acute onset of ANY THREE OR MORE of the following signs or symptoms:
  - Fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status.

AND

Epidemiological Criteria:

- Residing or working in an area with high risk of transmission of virus: closed residential settings, humanitarian settings such as camp and camp-like settings for displaced persons; anytime within the 14 days prior to symptom onset; **OR**
- Residing or travel to an area with community transmission anytime within the 14 day prior to symptom onset; **OR**
- Working in any healthcare setting, including within health facilities or within the community; anytime within the 14 days prior of symptom onset

B. A patient with severe acute respiratory illness: (SARI: acute respiratory infection with history of fever or measured fever of ≥ 38ºC; and cough; with onset within the last 10 days; and requires hospitalization)

C. Asymptomatic person not meeting epidemiologic criteria with a positive SARS-CoV-2 Antigen-RDT

Probable Case

A. A patient who meets clinical criteria above AND is a contact of a probable or confirmed case, or linked to a COVID-19 cluster

B. A suspect case with chest imaging showing findings suggestive of COVID-19 disease

C. A person with recent onset of anosmia (loss of smell) or ageusia (loss of taste) in the absence of any other identified cause.

D. Death, not otherwise explained, in an adult with respiratory distress preceding death AND was a contact of a probable or confirmed case or linked to a COVID-19 cluster.

Confirmed Case

A. A person with a positive Nucleic Acid Amplification Test (NAAT)

B. A person with a positive SARS-CoV-2Antigen-RDT AND meeting either the probable case definition or suspect criteria A or B

C. An asymptomatic person with a positiveSARS-CoV-2Antigen-RDT who is a contact of a probable or confirmed case

Children with symptoms that meet the case definition for suspected COVID-19 should immediately be given a medical mask and directed to a single room and be kept together with caregivers wherever possible (if caregivers also have suspected or confirmed COVID-19 infection). Aside from their medical, nursing and nutritional needs, mental and psychosocial health should also be taken into account. If a single room is not possible, then patients should be grouped with similar clinical diagnosis and epidemiological risk factors, with a spatial separation (at least 1 m between patients). Suspected cases should not be cohorted together with confirmed cases, there should be a transition area for probable cases who have pending RT-PCR swab results.

1.4. COVID-19 Disease Severity[64]

Mild disease		Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.
Moderate disease	**Pneumonia**	Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including SpO2 ≥ 90% on room air. Child with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest indrawing) and no signs of severe pneumonia. Fast breathing (in breaths/min): < 2 months: ≥ 60 2–11 months: ≥ 50 1–5 years: ≥ 40 >5 years: ≥30 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**	Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the following: ▪ Respiratory rate > 30 breaths/min ▪ Severe respiratory distress ▪ SpO2 < 90% on room air Child with clinical signs of pneumonia (cough or difficulty in breathing) + at least one of the following: ▪ Central cyanosis or SpO2 < 90% ▪ 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 ▪ Fast breathing (in breaths/min): < 2 months: ≥ 60 2–11 months: ≥ 50 1–5 years: ≥ 40 >5 years: ≥ 30 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.
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, echocardiography) to exclude hydrostatic cause of infiltrates/oedema if no risk factor present. Oxygenation impairment in adults: • Mild ARDS: 200 mmHg < PaO2/FiO2a ≤ 300 mmHg (with PEEP or CPAP ≥ 5 cmH2O) • Moderate ARDS: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg (with PEEP ≥ 5 cmH2O) • Severe ARDS: PaO2/FiO2 ≤ 100 mmHg (with PEEP ≥ 5 cmH2O) Oxygenation impairment in children: note OI and OSI. Use OI when available. If PaO2 not available, wean FiO2 to maintain SpO2 ≤ 97% to calculate OSI or SpO2/FiO2 ratio. • Bilevel (NIV or CPAP) ≥ 5 cmH2O via full face mask: PaO2/FiO2 ≤ 300 mmHg or SpO2/FiO2 ≤ 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	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	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.
	MIS-C	*(Refer to Table 5)*

Source: WHO January 25,2021 Living Guidance in the management of COVID-19 [64]

A. Mild Disease in Pediatric COVID-19

Patients presenting with mild disease are the subset of cases that are deemed to be the drivers of viral transmission by having symptoms that are too nonspecific to be tagged as COVID-19 at the onset, making these patients escape suspicion leading to risky behaviors and activities on the part of both the patients and the people around them. It is important to repeatedly inform the general public to disclose all symptoms no matter how seemingly insignificant and monitor them closely and to implement strict isolation procedures. In an ideal set-up, all cases of COVID-19 should be admitted in a government or hospital facility to cut transmission risk, but resource limitations make this improbable and impractical. Home care management, therefore, is the next best management strategy for those with mild disease. (see chapter 2)

B. Moderate Disease in Pediatric COVID-19

The difference of moderate COVID-19 from mild COVID-19 is the presence of pneumonia. Once a child presents with pneumonia, his/her risk for pneumonia-related mortality increases, as described in the paper PAPP Perspective: Update in the Evaluation and Management of Pediatric Community-acquired Pneumonia, 2016. These patients must be admitted in a hospital for closer monitoring and instituting the standard of care for pneumonia.

C. Severe to Critical Disease in Pediatric COVID 19

Clinically, it would be difficult to differentiate the manifestations of a sick child presenting with severe pneumonia, a critically ill child suffering from septic shock and a child with pediatric acute respiratory distress syndrome (pARDS). All will have some form of respiratory distress that may be related to a direct lung injury caused by an infectious process such as pneumonia, an uncontrolled inflammatory cascade causing alveolar edema and decreased lung compliance secondary to ARDS or the distress could be due to a compensatory mechanism from a metabolic acidosis brought about by severe sepsis. Notably, however, by following WHO classification for disease severity, we will be guided to appropriate management and increase chance of recovery.

Risk factors for severe disease include obesity, chronic respiratory diseases, cardiovascular diseases, neurologic diseases, immune disorders and metabolic diseases[39].

Pediatric Acute Respiratory Distress Syndrome in COVID-19

A study done in New York, USA revealed that 76.9% (10/13) of patients admitted at the pediatric ICU had ARDS. Six patients required invasive ventilation. Lung protective strategies for mechanical ventilation in ARDS were insufficient in these patients by day 3 with a median PEEP requirement of 10 cm water, resulting in a median peak pressure of 35 cm water.[40]

Central to the pathophysiology of ARDS is the presence of fibrin-rich exudates (hyaline membranes) due to activation of coagulation and inhibition of fibrinolysis. Upregulation of procoagulant activity in the alveolar compartment has been proposed as the driving force for intra-alveolar fibrin deposition and has been implicated in the development of ARDS. Concentrations of D-dimer, a proteic fragment present in the blood resulting from clot degradation commonly found in patients with suspected thrombotic disorders, are significantly increased in the edema fluid of patients with ARDS.

Table 7: Pediatric Acute Respiratory Distress Syndrome (PALICC Guidelines)[41,84]

<table>
<tr><td>Age</td><td colspan="4">Exclude patients with perinatal-related lung disease</td></tr>
<tr><td>Timing</td><td colspan="4">Within 7 d of known clinical insult</td></tr>
<tr><td>Origin of edema</td><td colspan="4">Respiratory failure not fully explained by cardiac failure or fluid overload</td></tr>
<tr><td>Chest imaging</td><td colspan="4">Chest imaging findings of new infiltrates consistent with acute pulmonary parenchymal disease</td></tr>
<tr><td rowspan="3">Oxygenation</td><td>Non-invasive mechanical ventilation</td><td colspan="3">Invasive mechanical ventilation</td></tr>
<tr><td>PARDS
(No severity classification)</td><td>Mild ARDS</td><td>Moderate ARDS</td><td>Severe ARDS</td></tr>
<tr><td>Full face mask, bi level ventilation or CPAP ≥ 5 cm H_2O:
PF ratio ≤ 300
SF ratio ≤ 264</td><td>4 ≤ OI < 8 or
5 ≤ OSI < 7.5</td><td>8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3</td><td>OI ≥ 16 or
OSI ≥ 12.3</td></tr>
<tr><td>Cyanotic Heart Disease</td><td colspan="4">Standard criteria above for age, timing, origin of edema, and chest imaging with an acute deterioration in oxygenation not explained by underlying cardiac disease</td></tr>
<tr><td>Chronic Lung Disease</td><td colspan="4">Standard criteria above for age, timing, and origin of edema with chest imaging consistent with new infiltrate and acute deterioration in oxygenation from baseline that meet oxygenation criteria above</td></tr>
<tr><td>Left Ventricular Dysfunction</td><td colspan="4">Standard criteria for age, timing, and origin of edema with chest imaging changes consistent with new infiltrate and acute deterioration in oxygenation that meet criteria above not explained by left-ventricular dysfunction</td></tr>
</table>

Early studies proposed that widespread pulmonary vascular thrombosis was a consistent feature of ARDS, and increased serum levels of D-dimers and pulmonary vascular endothelialitis, thrombosis, and angiogenesis have been observed in patients with COVID-19. Furthermore, dysregulation of other factors related to coagulation (eg, low vitamin K-dependent protein C and increased plasminogen activator inhibitor 1) has been associated with very high mortality in ARDS.[42]

Moreover, lung involvement in COVID pARDS may not always be bilateral hence PALICC, which omits bilaterality in its criteria would be more appropriate. It is also more sensitive in the pediatric age group as compared with other criteria.[43,44,45]

The common radiographic findings and clinical presentations are further discussed in section 1.7 Radiographic findings in Pediatric COVID-19.

Post-Acute Sequelae of COVID-19 (PASC)

It is now recognized that Long COVID syndrome is clinically known as Post-Acute Sequelae of COVID-19 (PASC). Other terms which have been used in the past months have included Post-acute COVID-19, long COVID, post-COVID, long haul COVID.

Post-acute COVID-19 was defined as persistent symptoms and/or delayed or long-term complications of SARS-CoV-2 infection beyond 4 weeks from the onset of symptoms. It is divided into two categories, the subacute or ongoing symptomatic COVID-19, which includes symptoms and abnormalities present from 4–12 weeks beyond acute COVID-19 and the chronic or post-COVID-19 syndrome, which includes symptoms and abnormalities persisting or present beyond 12weeks of the onset of acute COVID-19 and not attributable to alternative diagnoses.[46]

To mention the findings in adult cases in this new disease complication due to COVID-19, the persistence of symptoms can occur from 8 - 12 weeks and these manifestations include muscle weakness in 63%, sleep difficulties in 26%, anxiety and depression in 23%, decreased quality of life in 23%.[47] In 70% of the survivors, hair loss, memory impairment, breathlessness, cough and fatigue were observed, whereas 39% was unable to return to work because of ongoing symptoms.[48] Long-COVID was characterized by symptoms of fatigue, headache, dyspnea and anosmia and was associated with increasing age, BMI and female sex.[49]

Carfi et.al., has comparable findings as well, wherein 71.4% of 143 adult patients have persistent symptoms 60 days after follow -up, 32% had 1-2 symptoms, while 55% have more than 3 symptoms. High proportion of individuals complained of fatigue (53.1%), dyspnea (43.4%), joint pain, (27.3%) and chest pain (21.7%).[50]

In 158 recovered adult patients in Karachi, Pakistan, 94.9% experienced at least one post-COVID-19 symptom, with fatigue (82.9%) being the most prevalent post-discharge manifestation. COVID-19 disease with moderate severity compared to mild severity was a predictor of persistent COVID-like symptoms after discharge.[51,52]

In another cohort study, DLCO of <80%, functional impairment based on the Short Physical Performance Battery [SPPB] score, and posttraumatic stress symptoms were found 4 months after discharge from the hospital.[53] Similarly, Huang et.al. study demonstrated that 76% of adult patients had persistent symptoms for 6 months and was more evident in patients that were on HFNC, NIV or IMV and among females. Thirty four percent (34%) was noted to have a low DLCO and was higher in patients that were on HFNC, SIMV or IMV[47].

In a retrospective cohort analysis of 1946 adult patients with clinical or laboratory diagnosis of COVID-19, radiological changes persisted in more than 50% of cases after 6 weeks of follow-up[51]. Severe post-COVID-19 syndrome was defined as ongoing respiratory symptoms and/or moderate functional impairment in daily activities; single-organ and multiorgan impairment 10 or more symptoms. Mild organ impairment was seen in the heart (26%), lungs (11%), kidneys (4%), liver (28%), pancreas (40%) and spleen (4%), with single organ and multiorgan impairment in 70% and 29%, respectively.[54]

Data on long COVID-19 in children is congruous to that in adults. Buonsenso et al., gathered data from the 'Long COVID Kids Rapid Survey' wherein 510 children were included in the study and 56.3% were female. Persistence of symptoms was observed with a mean of 8.2 months. Most frequent symptoms were tiredness and weakness (87.1%), fatigue (80.4%), headache (78.6%), abdominal pain (75.9%), muscle and joint pain (60.6%), post-exertional malaise (53.7%), rash (52.4%). Children who had at least four symptoms were observed in 94.9%. Moreover, 25.3% have suffered constant COVID-19 infection symptoms, 49.4% have had periods of apparent recovery and then recurrence of symptoms, and 19.0% had a prolonged period of wellness followed by symptoms. Only 10.0% of children have returned to previous levels of physical activity. There was also a significant prevalence of neuropsychiatric symptoms, among them were lack of concentration (60.6%), difficulty in doing everyday tasks (40%) and processing information (32.7%) and short-term memory issues (32.7%).[55]

A similar pattern of symptoms was noted in a case report of 5 Swedish children by Ludvigsson. Those children aged 9-15 years old had symptoms 6-8 months after their clinical diagnosis of COVID-19. All of them complained of fatigue, dyspnea, heart palpitations or chest pain, headaches, difficulties concentrating, muscle weakness, dizziness and sore throats months from initial diagnosis.[56] In addition, persistent symptoms 28 were seen in 96% of female. During the acute illness, the post COVID syndrome group had more chest pain, fatigue, fever, olfactory impairment, headache and diarrhea compared to those who fully recovered.[57]

The etiology and pathophysiology of late sequelae may reflect organ damage from the acute infection phase, manifestations of a persistent hyperinflammatory state, ongoing viral activity associated with a host viral reservoir, or an inadequate antibody response. Other factors linked to persistent symptoms are physical deconditioning at baseline or after a long disease course, pre-COVID-19 comorbidities, and psychological sequelae following a long or difficult disease course as well as those relating to lifestyle changes due to the pandemic. The persistent sequelae of COVID-19 possibly represent multiple syndromes resulting from distinct pathophysiological processes along the spectrum of disease.[58]

Post-acute COVID-19 is a multisystem disease, occurring sometimes even in mild acute illness. Aside from close monitoring after discharge, a multi-disciplinary approach is essential in the management of these patients. Referral to specialists if there are clinical concern along with respiratory, cardiac, or neurological symptoms is indicated. Physical, psychological, and psychiatric aspects of rehabilitation is also paramount in those who have neuropsychiatric sequelae and those who have functional impairment.[59,60]

Recommendation 2 [58 59 60]

Consider the diagnosis of Post-acute COVID-19 Syndrome in children as it may also occur in the pediatric age group and the most common symptoms are tiredness/weakness, fatigue, chest pain, palpitation, headache, dizziness, abdominal pain, muscle pain, rash. There was also significant prevalence of neuropsychiatric symptoms like lack of concentration, difficulty in doing everyday tasks and processing information as well as short term memory loss

(Weak recommendation, Low-grade evidence)

1.5. Diagnostic Confirmation

1) Real-Time Reverse Transcriptase (RT)-PCR determination of SARS CoV-2 from oropharyngeal or nasopharyngeal specimen remains as the reference standard for the diagnosis of pediatric COVID-19. Viral load is not parallel with clinical severity[61]. Sensitivity is 95% (95% CI: 0.69 to 0.99) while specificity is 99% (95% CI: 0.92 to 1.00) using combined nasopharyngeal and oropharyngeal swab[62].

The ideal time to collect the specimen from symptomatic children would be done immediately during the first days of being symptomatic. It is worth noting however that the highest sensitivity for the test occurs at the 3rd day of onset of symptoms. Moreover, viral yield will start to diminish 10 days after being symptomatic. The asymptomatic children with exposure, on the other hand, are no longer advised to be tested. If done, the best timing would be 4 days after the exposure[63,64]. The average number of days before negative conversion in children is 12 days or 4 to 5 days after symptoms resolve[23].

RT PCR using blood sample can also be done and if positive may be indicative of viremia, hence severe disease[18,65]. If the receiving laboratory is capable, fecal and salivary samples can also be tested however, accuracy is less as compared to nasopharyngeal swabs. Sensitivity and specificity of saliva RT-PCR was 87.7% (95% CI 78.5%-93.9%) and 98.5% (95% CI 96.8%-99.5%) when done in children[66].

As of the time of this writing, WHO does not recommend testing with other samples other than nasopharyngeal swab as the sole basis for diagnosis, but recent US CDC guidelines included saliva as specimen alternative for RT-PCR. Studies have shown that getting salivary samples is feasible even for children as young as 3 years of age. Some studies would even suggest that salivary samples can correlate better than nasopharyngeal samples when it comes to clinical and immunological profiles of children with COVID-19 infection.[67] Moreover, this has the advantage of being able to conserve personnel and PPE since collection may be done at home. However, DOH maintains

that nasopharyngeal and oropharyngeal swab specimens remain as the standard specimen for the diagnosis of COVID-19 through RT-PCR testing. Saliva can be an alternative but clinical correlation should be done[68].

Indications for nasal/oropharyngeal swab for RT-PCR for SAR CoV2[70]

1. For symptomatic children
2. If the child has been in close contact, such as within 6 feet of a person with documented SARS-CoV-2 infection for at least 15 minutes even if asymptomatic Because of the potential for asymptomatic and pre-symptomatic transmission, it is important that contacts of individuals with SARS-CoV-2 infection be quickly identified and tested. Pending test results, the child should be isolated at home. Even if the child has a negative test, he/she should still self-isolate for 14 days.
3. If the child lives in a high SARS-CoV-2 transmission zone and attended a public or private gathering of more than 10 people (without universal mask wearing and/or physical distancing)
4. If for public health reasons, the public health official(s) or healthcare provider may advise specific people, or groups of people, to be tested. This advice should be followed (e.g., prior to a medical procedure such as elective surgery or as a school or workplace requirement).

2) Serology: Rapid antibody test using lateral flow immunoassay to detect IgM and IgG can be used to determine past infection but not current or active disease with an overall testing sensitivity of 88.66% and specificity of 90.63%.

The greatest value of serology test would be in children suspected to have a post infectious syndrome caused by SARS-CoV-2 infection (Multisystem Inflammatory Syndrome in Children; MIS-C). Since MIS-C occurs after the infectious state, the yield of attaining a positive RT-PCR during this time will be low but antibodies are usually present[71].

Serology can also be useful in patients in whom there is high index of suspicion, but RT-PCR test turns out to be negative. One specimen can be taken during the acute phase and another in the convalescent phase, 2-4 weeks later. If antibodies become present at the latter stage, then there is seroconversion, diagnosis is confirmed[72].

3) Rapid Antigen Testing - antigen tests are immunoassays that detect the presence of a specific viral nucleocapsid protein. Sensitivity is highly variable from 0-94% but specificity is consistently high at > 97%[73]. Most rapid antigen tests for COVID-19 use a sandwich immunodetection method employing a simple-to-use lateral flow test format.

A positive test would mean active viral infection. However, the absence of gene amplification process makes it less sensitive as compared to RT-PCR. The specimen used would still be the nasopharyngeal or oropharyngeal swab. Its advantage would be a faster turnaround time (15 minutes) and lower expense. Up to present time, the Department of Health only allows the use of rapid antigen tests for diagnostic testing of close contacts in communities and closed or semi-closed institutions with confirmed outbreaks and in remote settings where RT-PCR is not immediately available[74].

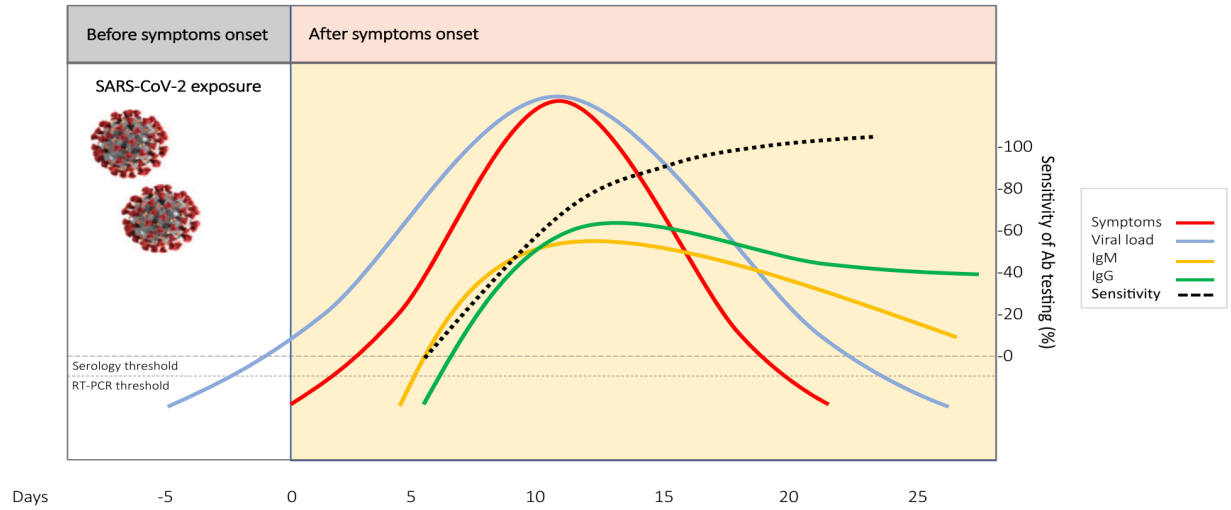


Figure 5. *Variation of the Levels of SARS-CoV-2 RNA and Antigen, IgM and IgG after infection.* The time relationship between viral load, symptoms and positivity on diagnostic tests. The onset of symptoms (day 0) is usually 5 days after infection (day –5). At this early stage corresponding to the window or asymptomatic period, the viral load could be below the RT-PCR threshold and the test may give false-negative results. The same is true at the end of the disease, when the patient is recovering. Seroconversion may usually be detectable between 5–7 days and 14 days after the onset of symptoms. Image reprinted from "A systematic review and clinical guide to molecular and serological in-vitro diagnostic assays" by A. La Marca (2020) Reproductive biomedicine online, 41(3), 483–499. Copyright © 2020 Published by Elsevier Ltd

1.6 Ancillary Laboratory Examinations in Pediatric COVID-19

Recommendation 3

Consider the use of laboratory tests to support the diagnosis and monitor COVID – 19 patients especially in evaluating for co-infections and multi-organ dysfunctions. *(Weak recommendation, Low-grade of evidence)* [6,22,23]

Table 8. Summary of laboratory findings for COVID 19 in children:[6,69]

1. Complete Blood Count – maybe normal, mild leukopenia and lymphopenia, slight thrombocytopenia
2. C Reactive Protein (CRP) - may be elevated
3. Erythrocyte Sedimentation Rate (ESR) – may be elevated
4. Procalcitonin – maybe elevated especially in severe cases with bacterial co infection
5. LDH – maybe elevated

Table 9. Other tests that may indicate end organ involvement and severe disease: [6,69]

1. Alanine transferase (ALT)
2. Aspartate aminotransferase (AST)
3. PT, PTT
4. Creatinine Kinase-MB
5. arterial blood gas
6. D-dimer
7. Serum Ferritin
8. possible biomarkers for critical disease: IL-6 and Il10

Unlike adults, most laboratory findings are equivocal in children[6,18]. There is also no single laboratory test that is indicative of COVID-19 infection in children except for RT-PCR.

CBC: Leukopenia, and lymphopenia have been reported. A handful of sick children may reveal lymphopenia (less than 1500 x 10^9), but still, a normal CBC is the most likely finding[18]. Contrary to adult data where lymphopenia is usually predictive of an unfavorable outcome, lymphopenia in children is not that prominent[75]. Mild thrombocytopenia is also commonly seen in children[18].

Inflammatory Markers: CRP, ESR may be elevated by as much as 30 to 100%. Procalcitonin may be used to determine secondary bacterial infection which is common among severe cases[69].

Liver Function Tests: Alanine Aminotransferase (ALT), Aspartate aminotransferase (AST). Elevated liver enzymes (ALT, AST) are observed in up to one third of patients[69].

Serum Electrolytes and Renal Function Tests: These may be normal but are deranged in critical patients. Creatinine and Blood Urea Nitrogen (BUN) are also increased and need to be monitored.

Lactate Dehydrogenase (LDH): LDH may increase and is a predictive factor for early recognition of lung injury[29,69.]

Serum Ferritin: elevation indicates cytokine storm syndrome or organ damage[29].

CKMB: Recently, pediatric COVID - 19 has been linked to myocarditis therefore requesting for cardiac enzymes such as CK-MB in patients with tachycardia without any known cause may be prudent[23].

Biomarkers for critical disease : IL-6 and IL-10 maybe increased in severe cases[6,69]. Further studies are needed.

Other tests:

In areas where other possible causes of fever such as Dengue or Malaria are prevalent, validated rapid diagnostic tests can be done to rule out such diseases versus COVID – 19. However, one must remember, that COVID – 19 may cross react with Dengue rapid tests. Serial CBC would therefore be more reliable to diagnose Dengue. A positive Dengue rapid test on the other hand, does not automatically exclude COVID- 19. RT-PCR for COVID 19 should be done in such cases[64].

If Tuberculosis is a consideration, tuberculin skin test and other diagnostics such as sputum AFB or Gene Xpert may be performed as long as protocol for aerosol generating procedures are implemented (e.g., to be done in an open area outside the home and away from others or in an open, well-ventilated space – preferably outside of the health facility far from any individual). Bacterial coinfection may be present. Sputum culture can be done. Again, while strictly adhering to safety protocols[66]. *(further discussion on Pediatric TB can be seen in Chapter 5 Section 5.2.)* Clinical presentation of sepsis overlaps with severe COVID-19. In such cases, where sepsis should be ruled out, requesting for blood culture and sensitivity would be prudent[66].

1.7 Chest Imaging in Pediatric COVID-19 Patient

Recommendation 4
Chest Imaging should be requested

- For medical triage of patients with suspected COVID-19 who present with **Moderate to severe** clinical features and a high pre-test probability of disease in resource limited settings
- When a child requires hospitalization, or is suspected of having hospital acquired pneumonia, CXR is the most appropriate step in imaging evaluation

Chest x-ray should not be requested in patients with suspected early stages of pediatric COVID-19 and mild clinical features at outpatient setting unless they are at risk for disease progression [76,77]

(Strong Recommendation, Low- moderate grade evidence)

1.7.1 Chest Radiography

A. Indication of Chest Imaging

CXR is frequently used as the first imaging in the evaluation of pediatric patient presenting with cough, fever and difficulty of breathing. The findings on CXR are not specific, it is insensitive in mild or early COVID-19 infection.

According to the American College of Radiology (ACR) appropriate criteria, imaging is not indicated in a well appearing immunocompetent child > 3 months of age who does not require hospitalization. However, if the child is not responding to outpatient management, requires hospitalization, or is suspected of having hospital acquired pneumonia, CXR is considered the most appropriate first step in imaging evaluation.[76] Initial chest radiographs should be considered in pediatric patients with suspected COVID-19 presenting with moderate to severe acute respiratory illness symptoms. However, due to limited sensitivity and specificity, a negative CXR 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. Chest X-ray imaging had a median sensitivity of 25% and median specificity of 90% for identifying lung opacities identified on same day chest CT scan.[77]

B. Common Radiographic Findings in Pediatric Patients with COVID-19

1. Bilateral distribution peripheral and/ or subpleural ground-glass opacities (GGOs) and “halo sign” or consolidation were the most common feature
2. Local or bilateral patchy shadowing
3. Viral pneumonia-like change[17,18]

C. Structured Reporting of CXR findings for Pediatric COVID-19 patients

Recommendation 5
The following should be the structured reporting of CXR finding for pediatric COVID-19 patients[76]

Typical Findings of Pediatric COVID-19
Bilateral distribution peripheral and/or subpleural GGOs and/or consolidation.

Indeterminate Findings of Pediatric COVID-19
Unilateral peripheral or peripheral and central GGOs and/or consolidation, bilateral peribronchial thickening and/or peribronchial opacities, or multifocal or diffuse GGOs and/or consolidation without specific distribution.

Atypical Findings of Pediatric COVID-19
Unilateral segmental or lobar consolidation, central unilateral or bilateral GGOs and/or consolidation, single round consolidation i.e., round pneumonia with or without air bronchogram, pleural effusion, or lymphadenopathy.

Negative for Pediatric COVID-19
No CXR findings suggestive of pneumonia

(Strong Recommendation, Moderate-Grade Evidence)

In a systematic review and meta-analysis done by Chang et al, the most common radiographic features among 31% patchy consolidation and 48% of these patients were halo signs with ground glass opacities, and in 27% of the patients, there was no definite lung lesion[17]. Similarly, ground glass opacity was seen in 33% of diagnosed children. Local or bilateral patchy shadowing was seen in 18.7% and 12.3%, respectively[18]. Viral pneumonia-like changes were seen in 70.4% children undergoing chest imaging.[18,79]

In a study done by Winant et al., it has been suggested that there are three imaging phases of typical acute pediatric COVID-19 infection: early, progressive, and developed phases. As there is significant clinical and imaging variation between patients, there is no known timeline for demarcating these phases. Typically, the "halo" sign, which indicates a rim of ground-glass opacity surrounding a nodule or consolidation is often noted in the early phase (reported in up to half of the cases), often progressing to ground-glass (progressive phase), and ultimately developing into a confluent consolidation (developed phase).[78]

Similarly, according to Feng Pan et al., in stage1 (early stage, 0–4 days after the onset of initial symptoms), GGO was the main radiologic demonstration and is distributed subpleural in the lower lobes unilaterally or bilaterally. In stage 2 (progressive stage, 5–8 days after the onset of initial symptoms), the infection rapidly extends to a bilateral multilobe distribution with diffuse GGO, crazy-paving pattern, and consolidation. In stage 3 (peak stage, 9–13 days after the onset of the initial symptoms), the lungs' involved area slowly increased to peak involvement, and dense consolidation became more

prevalent.Imaging findings seen are diffuse GGO, crazy-paving pattern, consolidation, and residual parenchymal bands.[79]

In the International Expert Consensus Statement on Chest Imaging in Pediatric COVID- 19 from United States, Spain, Hong Kong, Brazil, South Africa, and United Emirates they cited similar findings typical of COVID-19 pneumonia as multiple unilateral and bilateral opacities with peripheral and lower lung zones predominance seen both on CXR and Chest CT.[76]

Table 10. Structured CXR Reporting for Pediatric COVID-19 patients

Classification	Rationale	CXR Finding(s)	Suggested Reporting Language
Typical	Commonly reported CXR findings of COVID-19 pneumonia in children	▪ Bilateral distribution peripheral and/or subpleural GGOs and/or consolidation	Imaging findings are commonly seen with COVID-19 pneumonia in children. Differential diagnosis also includes other viral or atypical pneumonia.
Indeterminate	Non-specific CXR findings of pediatric COVID-19 pneumonia	▪ Unilateral peripheral or peripheral and central GGOs and/or consolidation ▪ Bilateral peribronchial thickening and/or peribronchial opacities ▪ Multifocal or diffuse GGOs and/or consolidation without specific distribution	Imaging findings can be seen with COVID-19 pneumonia in children. However, they are non-specific and differential diagnosis includes both infectious and non-infectious etiologies.
Atypical	Uncommon or not reported CXR findings of pediatric COVID- 19 pneumonia	▪ Unilateral segmental or lobar consolidation ▪ Central unilateral or bilateral GGOs and/or consolidation ▪ Single round consolidation (i.e., round pneumonia ± air bronchogram) ▪ Pleural effusion Lymphadenopathy	Imaging findings are atypical or uncommonly reported in cases of COVID-19 pneumonia in children. Recommend consideration of alternative diagnosis.
Negative CXR = Chest Xray ; GGO = Ground glass opacity; COVID - 19 = Coronavirus Disease of 2019	No CXR findings suggestive of pneumonia in children	▪ No CXR findings suggestive of pneumonia	No CXR findings present to suggest pneumonia (Note: CXR has limited sensitivity for COVID- 19, especially in early stages).

CXR = Chest Xray ; GGO = Ground glass opacity; COVID -19 = Coronavirus Disease of 2019

Chest Xray Images in Pediatric COVID-19[76]

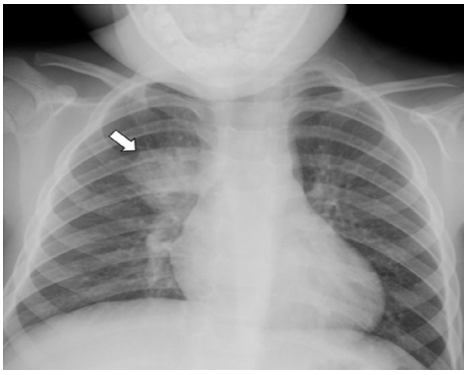


Figure 6A. A case of 16-year-old female with tuberous sclerosis and positive COVID-19 RT-PCR test. Chest radiograph shows bilateral lower lung zone-predominant consolidation(arrow) and ground-glass opacities, which is typical CXR findings of pediatric COVID-19 pneumonia.[76]

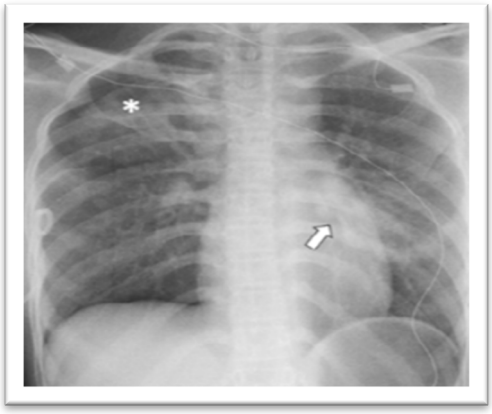


Figure 6B. A case of 4-year-old male with fever and respiratory distress. Chest radiograph shows a round consolidation (arrow) in the medial right upper lung zone which is atypical for pediatric COVID-19 pneumonia. This patient's round pneumonia was due to bacterial

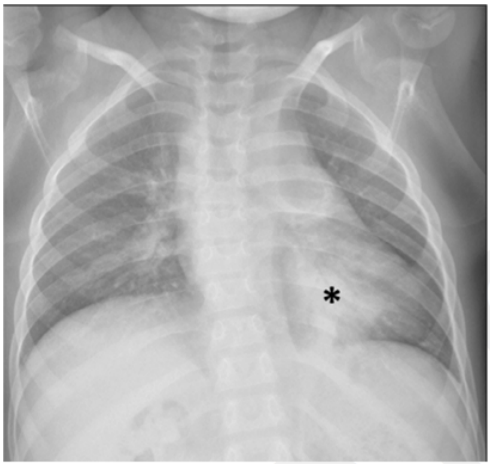


Figure 6C. A case of 15-year-old female with asthma and positive COVID-19 RT-PCR test who presented with fever and respiratory distress. Chest radiograph shows ground-glass opacities in both peripheral (asterisk) and central (arrow) distribution, which are indeterminate CXR findings of pediatric COVID-19 pneumonia. Also noted is right apical pneumothorax[76]

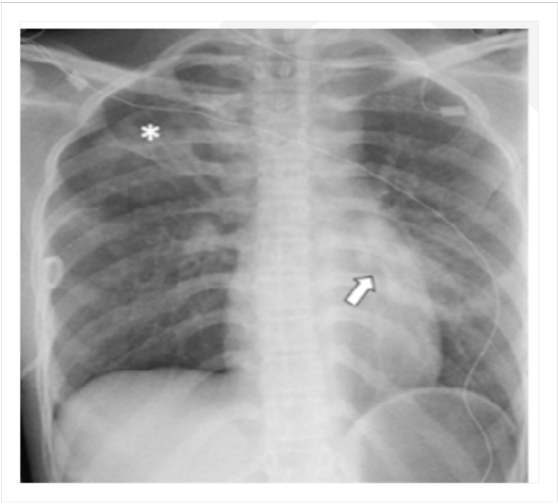


Figure 6D. 9-year-old female with renal transplant and positive COVID-19 RT-PCR test who presented with respiratory distress. Frontal chest radiograph shows consolidation (asterisk) in the left lower lobe, which is atypical for pediatric COVID-19 pneumonia.[76]

1.7.2 Chest Computed Tomography

The estimated positive predictive value of Chest CT for COVID-19 is 92% while the negative predictive value is 42% in a population with high pretest probability. This suggests that CT may not be useful as a screening test in the earlier stages of COVID-19[80]. The American College of Radiology indeed does not recommend the use of Chest CT as the first line screening test to diagnose COVID-19 and emphasized that chest CT should be reserved for symptomatic hospitalized patients with specific clinical indications. Despite scarce data on imaging literature in pediatric COVID-19, imaging findings in children tend to have milder presentation compared with adults.[76] In a study done by Chen Z et.al., among 98 COVID-19 positive patients in all age groups, CT findings in children <18 years of age demonstrated a lower total number and smaller size of pulmonary lesions in contrast with adults.[81] Furthermore, a comparison study of CT findings between 14 pediatric patients and 47 adults, with RT-PCR–confirmed COVID-19 infections showed that pediatric patients had a significantly lower rate of positive CT findings, lower number of pulmonary lobes involved, and lower overall semi-quantitative lung score.[82]

Recommendation 6

Chest CT scan may be considered in the following situations:[76]

1. **Mild clinical features of COVID-19:**
   If there is clinical progression, inadequate clinical improvement, or when an alternative diagnosis (such as concern for pulmonary embolism) necessitates further evaluation.

2. **Moderate – Severe clinical features of COVID-19 in a without resource-constrained environment:**
   If the outcome will impact clinical decision (i.e., imaging findings would affect how closely a patient is clinically followed and possibly followed with imaging to assess for change or potential complication)

3. **Moderate – Severe clinical features of COVID-19 in a resource-constrained environment:**
   When there is unavailability of testing or lengthy turn-around time of results that would avert rapid triage decisions, imaging may be used as an initial step to evaluate for findings suggestive of COVID-19 (presumed positive) versus findings suggestive of an alternative diagnosis. Considering the limited sensitivity of chest radiography, low-dose technique chest or pediatric patients closely following the as-low-as-reasonably-achievable (ALARA) principle, may be considered either initially or following unrevealing chest radiography results.

(Strong recommendations,moderate grade evidence)

There are three distinct clinical situations wherein Chest CT may be recommended in children at the time of initial presentation, similar to the recent Fleischner Society consensus statement for adult patients. These situations include pediatric patients presenting with (1) mild clinical features of COVID-19, (2) with moderate-to-severe clinical features of COVID-19 in a without resource-constrained environment, and (3) with moderate-to-severe clinical features of COVID-19 in a resource-constrained environment.[76]

1.7.3 Radiographic Findings in COVID –19 Pediatric ARDS

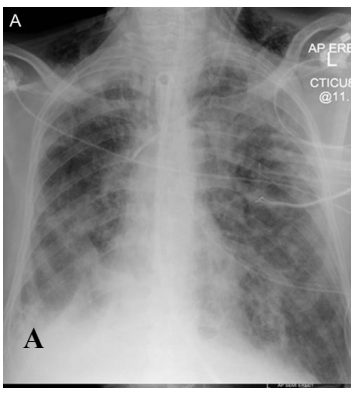
Based on the Berlin ARDS Definition, chest radiograph criterion include bilateral opacities consistent with pulmonary edema that are not fully explained by effusions lobar/lung collapse, or nodules/masses on chest radiograph, there is also absence of cardiomegaly and septal lines.[83]

However, The Pediatric Acute Lung Injury Consensus Conference (PALICC) definition for pediatric ARDS (PARDS) eliminated the requirement for bilateral radiographic findings, although evidence of new infiltrate(s) consistent with the acute pulmonary parenchymal disease is still required.[84]

CT has been shown to be helpful, not only as a confirmatory and problem-solving tool, but emerging studies have shown the potential for classifying and prognosticating ARDS. The classical CT appearance of acute phase ARDS is that of opacification that demonstrates an antero-posterior density gradient within the lung, with dense consolidation in the most dependent regions, merging into a background of widespread ground-glass attenuation and then normal or hyperexpanded lung in the non-dependent regions (see Figure 6). Ground-glass opacification on CT is a non-specific sign that reflects an overall reduction in the air content of the affected lung. In the case of acute ARDS, this is likely to represent edema and protein within the interstitium and alveoli. Another important observed feature in acute ARDS is bronchial dilatation within areas of ground-glass opacification.[85]

A case report of pediatric COVID – 19 shows interlobular and intralobular septal thickening and rounded ground-glass opacities, predominantly in a peripheral distribution in both lungs; small peripheral or subpleural areas of subsegmental collapse or consolidation are noted, particularly at the bases.[86]

Lung ultrasound findings may facilitate the diagnosis in acute respiratory failure (ARF) patients. In particular, ARDS presents multiple B lines, typically with a non-homogeneous non-gravity-dependent distribution, pleural thickening, subpleural consolidations, decreased or abolished lung sliding, spared areas especially in anterior regions and in the early stage of the disease.[44]



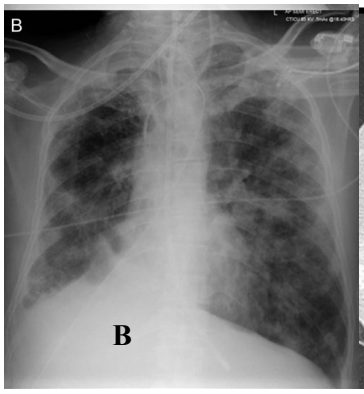


Figure 7A: Chest radiograph of patient with ARDS shows bilateral infiltrates. There is bilateral consolidation and a right pleural effusion. B: Chest radiograph of the same patient shows persistent bilateral infiltrates after 7 days[85]

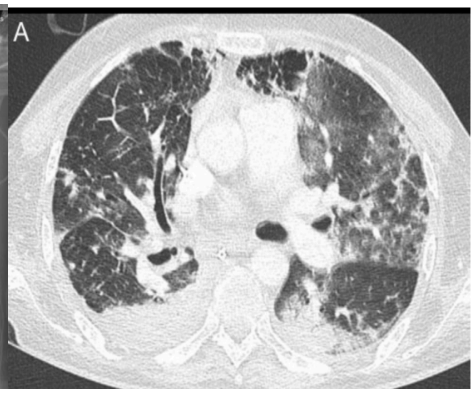


Figure 7B Computed tomogram shows bilateral dependent consolidation in a patient with ARDS, as well as ground-glass opacities in the non-dependent lung[85]

Table 11. Structured Reporting for CT Findings for Pediatric COVID-19 Patients

Classification	Rationale	CT Finding(s)	Suggested Reporting Language
Typical	Commonly reported CT findings of COVID-19 pneumonia in children	▪ Bilateral, peripheral and/or subpleural GGOs and/or consolidation in lower lobe predominant pattern ▪ "Halo" sign (early)	Imaging findings are commonly seen with COVID-19 pneumonia in children. Differential diagnosis also includes other viral or atypical pneumonia, hypersensitive pneumonitis, and eosinophilic lung disease. In addition, fungal infection in immunocompromised children when "halo" sign is present.
Indeterminate	Non- specific CT findings of pediatric COVID- 19 pneumonia	▪ Unilateral peripheral or peripheral and central GGOs and/or consolidation ▪ Bilateral peribronchial thickening and/or peribronchial opacities ▪ Multifocal or diffuse GGOs and/or consolidation without specific distribution "Crazy paving" sign	Imaging findings can be seen with COVID-19 pneumonia in children. However, non-specific and differential diagnosis includes infectious and non- infectious etiologies.

Classification	Rationale	CT Finding(s)	Suggested Reporting Language
Atypical	Uncommon or not reported CT findings of pediatric COVID- 19 pneumonia	▪ Unilateral segmental or lobar consolidation ▪ Central unilateral or bilateral GGOs and/or consolidation ▪ Discrete small nodules (centrilobular, tree-in-bud) ▪ Lung cavitation ▪ *Pleural effusion ▪ Lymphadenopathy	Imaging findings are atypical or uncommonly reported in cases of COVID-19 pneumonia in children. Recommend consideration of alternative diagnosis.
Negative		▪ No CT findings suggestive of pneumonia	No CT findings present to suggest pneumonia (Note: CT may be negative in the early stages of COVID-19).

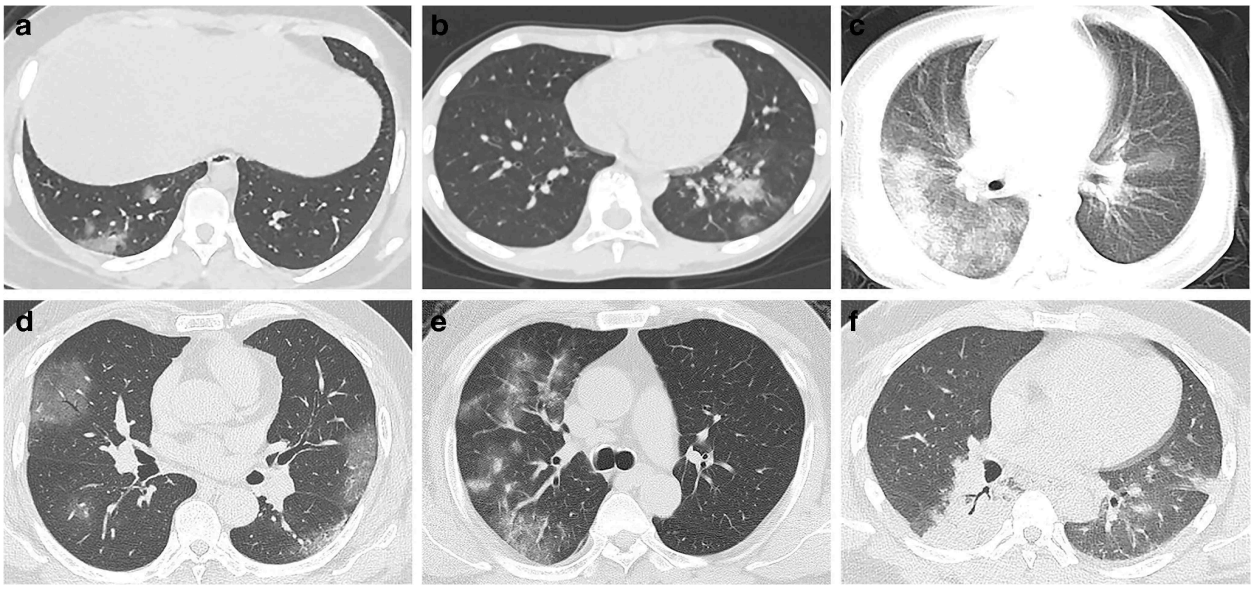


Fig 8a Chest CT imaging of coronavirus disease 2019 (COVID-19) pneumonia in children and adults. a Female, 14 years old. Chest CT showed scattered GGO in the inferior lobe of the right lung, located subpleural or extended from subpleural lesions. **b** Male, 10 years old. Chest CT showed consolidation with halo sign in the inferior lobe of the left lung surrounded by GGO. **c** Male, 1 year old. Chest CT showed diffused consolidations and GGO in both lungs, with a "white lung" appearance of the right lung. **d** Male, 49 years old. Chest CT showed multiple subpleural GGO in both lungs. **e** Male, 64 years old. Chest CT showed multiple GGO and consolidations in the right upper lobe. **f** Male, 34 years old. Chest CT showed diffused consolidation in the right lower lobe and left lung with fewer GGO surrounded[87].
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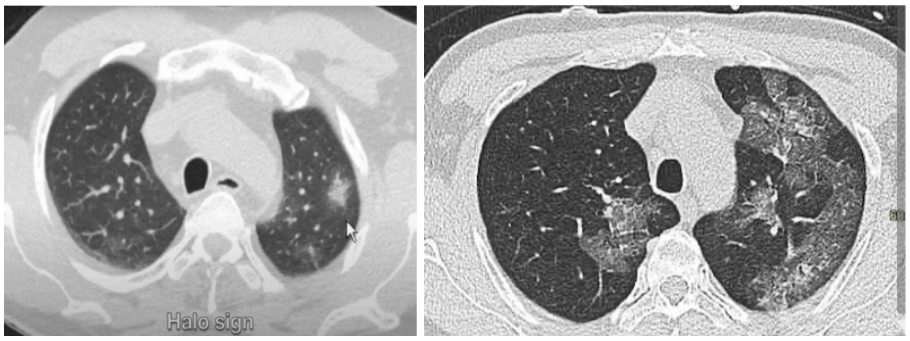


Fig 8b A) Focal consolidation with a rim of surrounding ground glass opacity "halo sign" B) Bilateral ground-glass opacities C) Thickened interlobular and intralobular lines in combination with a ground glass pattern called "crazy paving" [87]*Published with permission from Authors.*

1.7.4 Chest Ultrasound

Recommendation 7

Chest ultrasound can be considered as an alternative to CXR and Chest CT in the diagnosis of pneumonia in COVID 19 patients. It is a tool that could be used at bedside avoiding the need for shifting infected patients to the Radiology suite [88] [89]

(Weak Recommendation, Low-Grade Evidence)

Through the years, chest ultrasound has been proven to be a useful tool for the evaluation of a wide variety of chest diseases particularly when pleural cavity is involved. Lung Ultrasound (LUS) is commonly used in the emergency department at the bedside for early diagnosis of non-COVID pneumonia. It is a highly sensitive and specific technique considered as an alternative to chest radiography or Chest CT scan. Chest CT scan performedin COVID-19 patients and showed a strong correlation with chest ultrasound[88]

<u>The well-known advantages of LUS are the following:</u>[89]

1. Portability, bedside evaluation
   It is a tool that could be used at bedside avoiding the need for transferring infected patients to the Radiology suite.
2. Safety
3. Low risk of further infection spreading within the health care personnel.
4. Low cost and no radiation exposure as compared to Chest CT.

Ultrasonographic Features of SARS-CoV-2 Pneumonia:[90]

1. Thickening of the pleural line with pleural line irregularity
2. B lines in a variety of patterns including focal, multi- focal, and confluent
3. Consolidations in a variety of patterns including multifocal small, non-translobar, and translobar with occasional mobile air bronchograms
4. Appearance of A lines during recovery phase Pleural effusions are uncommon.

Chest ultrasound performed on COVID-19 pneumonia patients and showed thickened pleural lines, B lines organized in different patterns & patchy consolidation; Ultrasound along with Chest CT was done demonstrating an association with CT findings of GGO and consolidation. These findings confirm the important Role of chest ultrasound in the management of patients with SARS COV-2 allowing to rapidly diagnose and monitor COVID-19 pneumonia and its evolution towards ARDS.[91]

The LUS on patients with COVID-19 was performed using 12-zone method (Table 12) The observational patterns occurred across a continuum from mild alveolar interstitial pattern to lung consolidation. The findings of LUS features of SARS COV-2 pneumonia/ARDS are related to the stage of the disease and the severity of lung injury and co-morbidities. The predominant pattern is of varying degrees of interstitial syndrome and alveolar consolidation, the degree of which is correlated to lung injury. However, articles on its use in diagnosing COVID-19 pneumonia especially in children were very limited. Data are preliminary and further studies are necessary to confirm the role of lung US in the diagnosis and management of COVID-19 pneumonia in children.

Table 12. CT and Ultrasonographic Features of COVID-19 Pneumonia[90]

Lung CT	Lung ultrasound
Thickened pleura	Thickened pleural line
Ground glass shadow and effusion	B lines (multifocal, discrete, or confluent)
Pulmonary infiltrating shadow	Confluent B lines
Subpleural consolidation	Small (centomeric) consolidations)
Translobar consolidation	Both non-translobar and translobar consolidation
Pleural effusion is rare.	Pleural effusion is rare
More than two lobes affected	Multilobar distribution of abnormalities
Negative or atypical in lung CT images in the super-early stage, then diffuse scattered or ground glass shadow with the progress of the disease, further lung consolidation	Focal B lines is the main feature in the early stage and in mild infection; alveolar interstitial syndrome is the main feature in the progressive stage and in critically ill patients; A lines can be found in the convalescence

Images on Ultrasound as point of care for pediatric COVID-19 [92]

Figure 8 Series: Pediatric Ultrasound Findings

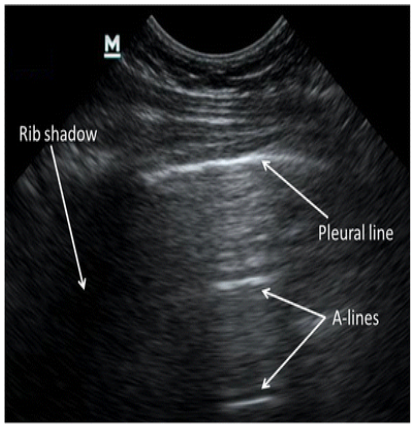


Figure 9A: **Normal Ultrasound in children :** note the A lines

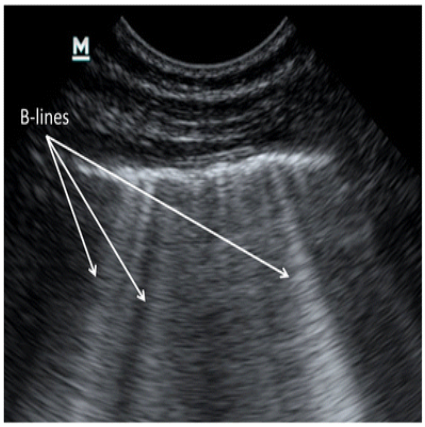


Figure 9B. **Pathologic Ultrasound**: note the B lines in a child with Pneumonia

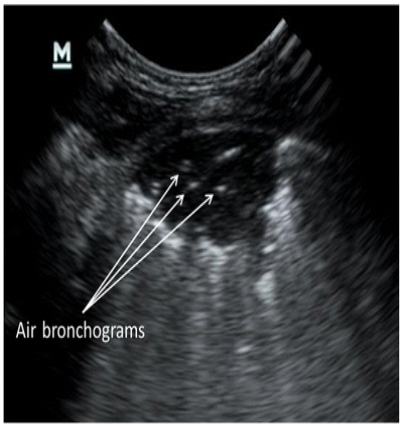
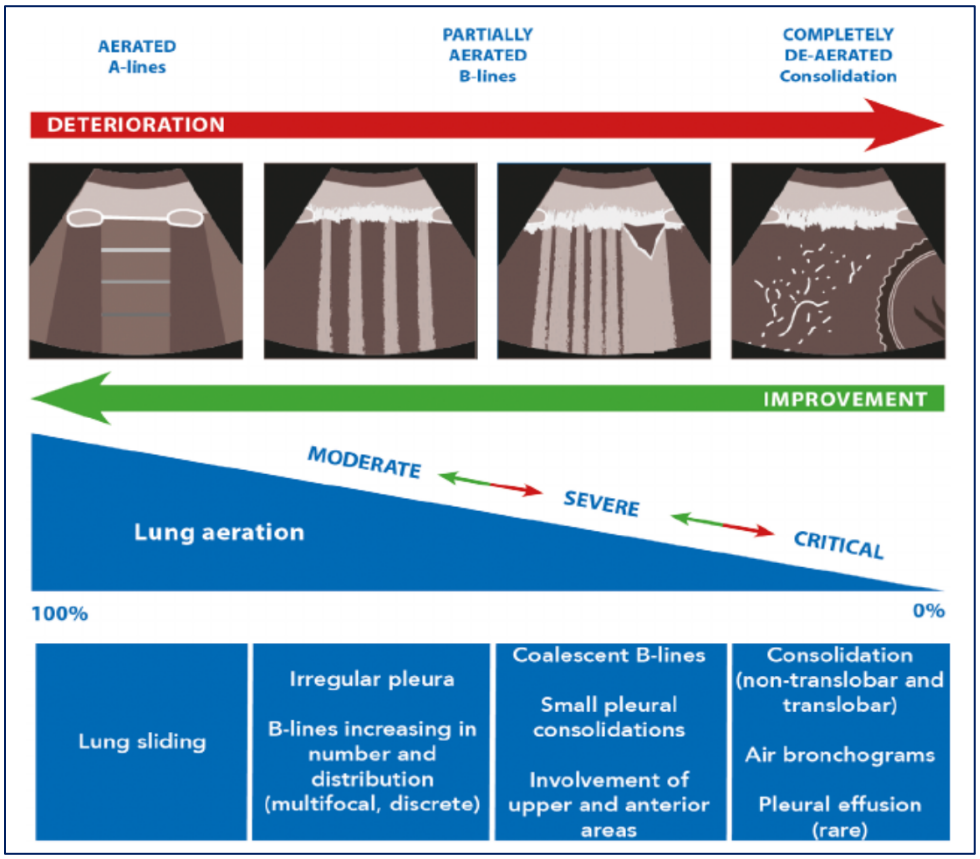


Figure 9C : **Pathologic Ultrasound:** note the Air Bronchograms

Figure 10. Ultrasound Guide for Pediatric COVID-19[93]



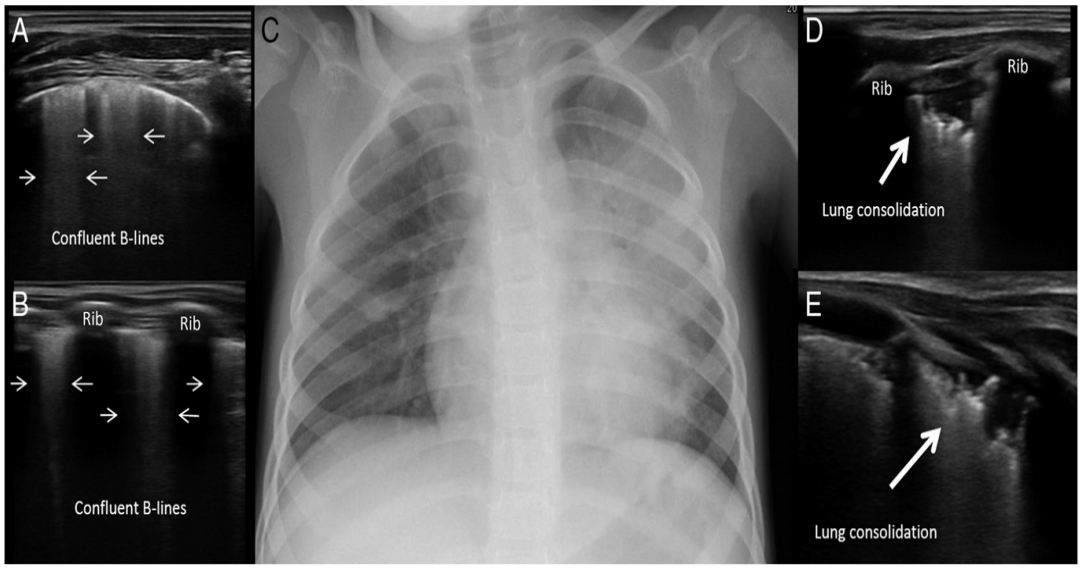


Fig 11- Chest Xray and Chest Ultrasound correlation . See **A and B,** Multiple confluent B-lines (thin arrows). **C**, Chest radiography with left upper lobe consolidation and right central ground-glass opacities. **D** and **E,** A lung consolidation (thick arrows) at LUS. [94]

1.7.5. Post-Recovery Follow-up Chest Imaging in Pediatric COVID-19 Patients[76]

The decision to do a repeat a chest imaging should be based both on the severity of disease (mild vs moderate-to-severe) and the presence (or absence) of clinical symptoms (i.e., dyspnea, decreased exercise tolerance) at the time of follow-up.

A repeat imaging on follow-up is not recommended in asymptomatic patients with mild COVID-19. However, it may be considered in asymptomatic individuals with an initial moderate-to-severe course depending on the level of clinical concern for long-term lung injury. It may also be appropriate for pediatric patients with prior COVID-19 infection with persistent or worsening symptoms regardless of initial disease severity to assess for postinfectious lung injury.

1.7.6. Main Thoracic Findings in Children with MIS-C and COVID-19[78]

The data is scarce regarding the radiological findings in MIS-C. Radiologists from the Boston Children's Hospital and Medical School and Children's Hospital at Montefiore and Montefiore Medical School came up with an analytical review of the clinical and imaging findings of pediatric MIS-C associated with COVID-19 compared with typical acute pediatric COVID-19 infection, which also highlighted thoracic imaging. The main radiologic difference between typical pediatric COVID-19 and MIS-C associated with COVID-19 is the location of imaging abnormalities. In a typical pediatric COVID-19 infection, the pulmonary parenchyma is primarily affected, demonstrating bilateral peripheral and subpleural airspace opacities. Extrapulmonary abnormalities are rare and usually not found in typical acute pediatric COVID-19 infection. On the other hand, pediatric MIS-C associated with COVID-19 is defined as a systemic hyperinflammatory state with multiple organ system involvements, often with prominent cardiovascular abnormalities, such as heart failure, cardiomegaly, pulmonary edema, and pleural effusions. Moreover, the hyperinflammatory state of MIS-C associated with COVID-19 may play a big part in a prothrombotic coagulopathy state predisposing to thromboembolic complications, including pulmonary emboli. Furthermore, it is often associated with adenopathy, rare, and not usually observed in typical pediatric COVID-19 infection. Lastly, ARDS, a common thoracic imaging pattern in late-stage adult COVID-19 infection, can also be seen in some pediatric MIS-C cases but is not common in typical pediatric COVID-19 infection.

Children with MIS-C associated with COVID-19 have been observed to present with hypoxic respiratory failure and ARDS imaging findings. Chest radiographs demonstrate bilateral multifocal ground-glass and consolidative airspace opacities. A small number of pediatric patients with MIS-C associated with COVID-19 demonstrating an ARDS pattern and airspace opacities on imaging were asymmetrical.[93]

Recommendation 8

Consider supplementary tests that may be done that will aid in the diagnosis of MIS-C would include rapid antibody test and chest radiographs.

The three main thoracic imaging findings may be observed in pediatric patients with MIS-C associated COVID-19 are heart failure, ARDS pattern and pulmonary embolus.[78]
(Weak recommendation, Moderate-grade evidence)

Table. 13. Differences in Imaging Findings between MIS-C Associated with COVID-19 and Typical COVID-19 in Children.[78]

	MIS-C associated with COVID-19	Typical COVID-19
Pulmonary Findings	Pulmonary edema ARDS, possibly asymmetric	Bilateral, lower lobe predominant peripheral/subpleural GGO and/or consolidation
Pleural findings	Pleural effusions	None known at the time of publication
Cardiovascular findings	Heart failure/left ventricular systolic dysfunction Pericardial effusion Pulmonary embolism* Coronary artery dilatation	None known at the time of publication
Extrathoracic Findings	Mesenteric lymphadenopathy Hepatomegaly Gall bladder wall thickening Echogenic renal parenchyma Ascites	None known at the time of publication

MIS-C = Multisystem Inflammatory Syndrome in Children; COVID-19 = Coronavirus Disease 2019; ARDS = Acute respiratory Distress Syndrome; GGO = Ground-glass Opacity ; *Segmental pulmonary embolism has been observed so far.

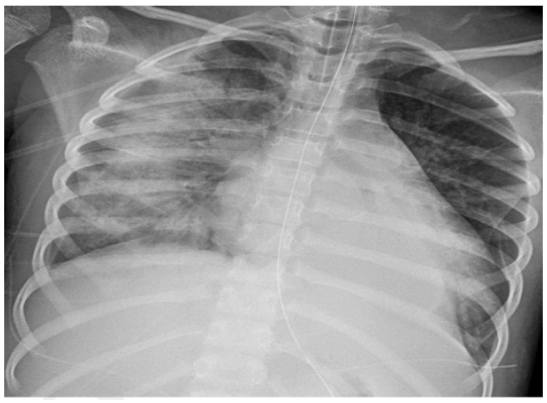


Figure 12a. *7-year-old male, with MIS-C associated with COVID-19, who presented with symptoms of fever, sore throat vomiting , abdominal pain, truncal rash, and hypotension. Frontal chest radiograph shows cardiomegaly, pulmonary edema, and small bilateral pleural effusions*[78] *Published with Permission*

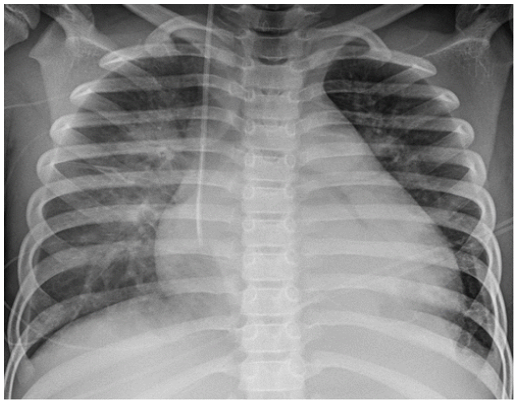


Figure 12b. *8-year-old female, who presented MIS-C associated with COVID-19, with fever, sore throat, vomiting, diarrhea, abdominal pain, back pain and fatigue. The patient ultimately progressed to develop hypoxic respiratory failure, hypotension, myocarditis, and acute kidney injury. Frontal chest radiograph shows an ARDS pattern with asymmetric, right greater than left, hazy opacities, and dense consolidative opacity in the left lung base, and cardiomegaly.*[78]
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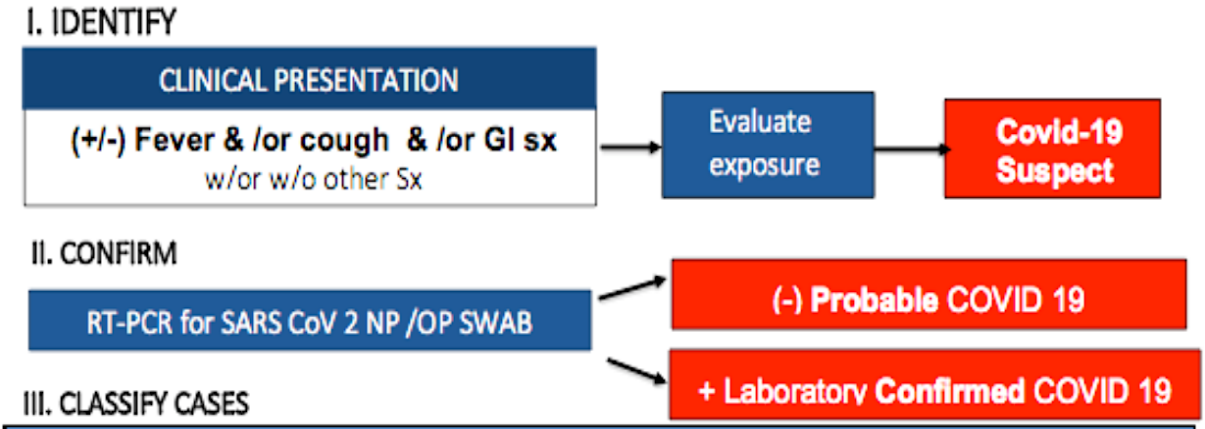
Algorithm in the Clinical Classification and Respiratory54 Management In Pediatric COVID-19



Symptomatic			
MILD	**Moderate**	**Severe**	**Critical**
	PNEUMONIA		
	NON SEVERE	**SEVERE**	**ARDS**
Acute URTI Fever, cough, Flu like +/- fever or only GI sx ie nausea, vomiting, abdominal pain and diarrhea rash Congested pharynx no auscultatory abnormalities	**Pneumonia** fast breathing: < 2 months: ≥ 60 2–11 months: ≥ 50 1–5 years: ≥ 40 +/- wheezing No hypoxemia	**Pneumonia with Early severe respiratory distress** Fever, +/- cough, +/- GI Sx Dyspnea, + central cyanosis Grunting, chest indrawing O_2 sat < 90% at room air	**Respiratory failure,** +/- shock MODS Encephalopathy, Myocardial injury or heart failure, Acute kidney injury Liver Injury Coagulation dysfunction
	Chest Xray CT scan CBC CRP ESR Procalcitonin	Chest Xray CT scan ALT AST PT PTT LDH Creatinine, BUN serum electrolytes CK-MB D Dimer Arterial Blood gases Serum Ferritin	Chest Xray CT scan ALT AST PT PTT LDH Creatinine, BUN serum electrolytes CK-MB D Dimer Arterial Blood gases Serum Ferritin

Chapter 2

2. HOMECAREDURINGTHECOVID-19PANDEMIC

2.1. HOME CARE FOR CHILDREN WITH MILD COVID-19

2.1.1 Home Care Management

Recommendation 9

We strongly recommend the strict adherence to the set guidelines for local or regional level for home care management among pediatric patients suspected or confirmed to have MILD COVID-19 to reduce SARS-CoV-2 transmission.

(Strong recommendation, Strong-grade evidence)

Home-based care for mild COVID-19 is a suitable management strategy to achieve a reduction in viral transmission in resource-limited settings in the face of an endless number of, and at times rapid rise of cases. It is not only applicable to low-to-middle income countries, but also to a developed country such as Korea, which has already adapted this practice effectively [97].

The success of home care management depends on correct implementation of set guidelines. This is a shared responsibility between the patient, the caregiver, other household members, and the health care worker. Table 14 summarizes and outlines the important points stated in the WHO interim guidance for home care:

Table 14. Home Care for Patients with Suspected or Confirmed COVID-19 and Management of their Contacts[98]

Site of Care	Person/s Responsible	Responsibilities
Initial: **Emergency department** **OPD** **Health centers**	• Health care worker	1. Implement Infection Prevention and Control (IPC) recommendations for health workers. (see appendix A) 2. Evaluate the child as to: ▪ Clinical presentation ▪ Presence of risk factors for poor outcome: comorbidities, epidemiologic ▪ Need for supportive care and monitoring

		3. Evaluate the home setting ▪ Assess the suitability of the home for isolation and provision of care ▪ Factors to consider: • Presence of household members as support network • Living conditions and alternatives available • Address the health needs of the patient and other household members • Knowledge of household members about COVID-19 and its transmission • Knowledge of the family on when to call for medical assistance and the presence of means for communication • Economic impact and financial provider • Health facility and health professional who is responsible for follow-up 4. Ensure proper home monitoring of the patient with COVID-19 ▪ Establish lines of communication between the caregiver and a health care worker or public health personnel (i.e. barangay health worker)
Continuing: Home	• Caregiver • Household member • Patient	1. Adhere to IPC recommendations for health workers (see appendix A) 2. Implement IPC advice for caregivers providing care at home (see appendix B) 3. Do proper patient monitoring and regularly communicate with a health worker.

Practice Points

- Patients suspected or confirmed to have mild COVID-19 are recommended to be isolated to contain the virus. This can be done at a designated health facility, community facility, or at home.[64,97]

- Rapid Implementation of infection control measures for Suspected or Confirmed Mild COVID-19 at Initial Site of Care[64] by:
    - Facilitating immediate isolation/separation where a patient is to be isolated in a separate room from other household members.

    - Applying standard precautions for all patients by ensuring correct and continuous use of face masks even at home except for children younger than 2 years old. Proper respiratory hygiene, appropriate PPE use, cleaning and disinfecting of equipment and the surrounding environment after each patient use, and proper

hazardous waste disposal. For hand hygiene, use an alcohol-based hand rub if hands are not visible dirty or soap and water and disposable paper towels before and after PPE handling.

- Applying of contact and droplet precautions for suspected and confirmed COVID-19 patients by limiting patient movement and ensure proper medical mask use inside or outside their care area. Health workers should use gloves, gown, medical mask, and eye protection.

- In areas with high endemicity for certain diseases such as malaria or dengue, febrile patients should be evaluated for such infections regardless of the presence of respiratory signs and symptoms. Coinfection with COVID-19 may occur.[64]

- The decision where to monitor a COVID-19 patient should be made on a case-by-case basis, depending on the clinical presentation, requirement for supportive care, presence of risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household.[64]

- If managed at home in self-isolation, refer to WHO guidance on home care for patients with COVID-19 presenting with mild symptoms and management of their contacts.[64, 98]

The health worker responsibilities include clinical evaluation of the patient and evaluation of the home setting to look for safety and logistical issues. It is the duty of the health care worker to educate the caregiver on proper home monitoring, anticipating and recognizing danger signs, and ensuring that a follow-up care will be in place before sending the patient for home care. Upon meeting the requirements for effective home care, the responsibility is now directed to the caregiver, especially for younger children, and extended to the child-patient and the health worker for continuing care.

A study by Ilesanmi, et al, found that home-based care of COVID-19-positive patients was associated with higher likelihood of familial viral transmission. The reason for this was the poor IPC practices in their setting in Nigeria.[99] . Korea, on the other, has been successful in limiting viral transmission through the government's strict facility isolation policy, which recently has allowed for home-based care, due to the general public's adherence to infection control guidelines[97]. Therefore, to effectively implement this management strategy, the guidelines set above must be strictly followed.[64,97,98]

2.1.2 SUPPORTIVE MANAGEMENT

Recommendation 10

We strongly recommend the giving of FDA approved supportive care measures pediatric patients suspected or confirmed to have MILD COVID-19 as follows:

1. Support treatment for fever lysis will be through good hydration and antipyretic use of Paracetamol at 10-15mg/kg /dose
(Strong recommendations, strong grade evidence)

2. Aerosol Therapy is to be administered only when bronchospasm is observed, the recommended device for aerosol therapy is the use of the pMDI with a valve holding chamber unless the patient qualifies for the limited indications for nebulization.
(Strong recommendations, moderate to strong grade evidence)

A. Hydration and Antipyretics

Since most of the pediatric population with COVID-19 are asymptomatic and some with mild symptoms only, we only monitor and give supportive management at home.

The preferred antipyretic treatment is paracetamol at 10-15 mg/kg/dose given every four to six hours (4-6hours).[64,100] Venturini et al advised Ibuprofen in case of dehydration, vomiting and diarrhea, as it is associated with an increased risk of kidney failure. [101]On the other hand a statement from WHO said that there is moderate to high evidence showing little or no difference between ibuprofen and paracetamol among children with fever regarding effects on death from all causes, hospitalization, acute renal failure, and acute gastrointestinal bleeding.[100]

If with fever, it also important to ensure that adequate hydration is provided to the child by asking parents to give the plenty of liquids to child.[98]

B. Home Aerosol Therapy in SARS-CoV2 Confirmed Children with MILD disease

We are made aware that children may have mild versions of COVID-19 infection[21], yet this does not preclude the fact that children are not virus carriers. To consider the risk of viral load and transmissibility of the SARS-CoV2 in children , a study by Yonker, of 192 children with confirmed SARS-CoV2 carry high levels of virus in their upper airways, particularly early in an acute SARS-CoV-2 infection, yet they display relatively mild or no symptoms. However, there was no age correlation with viral load, indicating that infants through young adults can carry equally high levels of virus.[102] These findings suggests

that, regardless of disease susceptibility, children with Mild COVID-19 can carry high viral loads and may infect others.

The COVID-19 pandemic has widely shifted the practice of giving aerosolized treatments from nebulization to the use of inhalers (pressurized metered dose inhaler (pMDI) or Dry powdered inhalers) which are as effective in aerosol drug delivery as nebulization[103] for children with chronic respiratory conditions such as bronchial asthma.[103, 104, 105, 106] This has been due to the possible risk of SARS-CoV2 transmission because of the potential to generate a high volume of respiratory aerosols that may be propelled over a longer distance than is involved in a natural dispersion pattern.[107] Simply put ,nebulizers can increase the dispersal of aerosolized particles from the infected patient with COVID-19.[108] This risk is of SARS CoV2 dispersion of virus laden particles is more plausibly noted if the nebulized equipment is contaminated.[108,109,110] Thus, aerosol treatments should be avoided unless necessary during this pandemic.

Events of bronchospasm in a COVID-19 suspected or confirmed child in home isolation warrants re-evaluation of the patient's disease severity status by the medical healthcare professional. This is done thru telemedicine or coordinated health team ER evaluation as it is prudent not be disregard the symptoms of bronchospasm as a plain asthma exacerbation only in a SARS-CoV2 infected child. Seen below are the practical steps recommended when giving nebulized drug during home isolation for children with MILD COVID-19.

Practice Points for Aerosol Treatment in patients with MILD COVID-19 [106, 111, 112]

1. Home nebulization should be avoided as much as possible in suspected or confirmed COVID-19 patients isolated at home.
2. If a confirmed COVID-19 child shows sign of bronchospasm, and available resource at the home is by nebulizer delivery, drug dose and administration must be done per instructions of the medical professional and to be done in a well- ventilated area . (*Please see Chapter 4.1.4 in the Limited use of nebulization in COVID-19)*
3. Immediate reassessment of the patient by medical practitioner should be done via telemedicine or thru a coordinated health team ER consult immediately after the bronchospasm event.

2.1.3 Respiratory Anticipatory Management and Monitoring

Recommendation 11

We strongly recommend that caregivers of children with MILD COVID-19 should be counselled about signs and symptoms of clinical deterioration that should prompt urgent re-evaluation.

(Strong recommendations, moderate to strong grade evidence)

Remarks

- Regular evaluation should be done for children with suspected or confirmed COVID-19 presenting with mild symptoms managed at home. Close monitoring of symptoms and a pulse oximetry if available to self-monitor the oxygen saturation, are recommended.

  It is important to teach caregiver responsible for the child to monitor the child's *respiratory rate*) and hypoxemia as follows: ≥50 breaths per minute for three (3) months to twelve (12) months old; respiratory rate of ≥40 breaths per minute for one (1) to five (5) years old; ≥30 breaths per minute for children more than 5 years old (oxygen saturation ≤93%). [113,114]

- Caregivers who are in good health and most familiar of the SARS-CoV2 infected child, should be counseled about symptoms of clinical deterioration, which may occur suddenly after about one week of symptom onset. Red flag symptoms that should prompt urgent re-assessment (either in person or teleconsultation, depending on the circumstances) include the following: [64,98 ,113, 115]
- If these suspected or confirmed children with COVID-19 develop any of these symptoms, they should seek urgent care through the established COVID-19 care pathway or with assistance from the local barangay heath care teams (BHERTS) or alternative delivery platforms such as home-based, phone, telemedicine or community outreach teams to assist with monitoring may be considered.[56,114, 116,117]

2.1.4. Discharge from Home Isolation (Please see Chapter 5 for further discussion)

2.2 Respiratory Precautions Among Children in the Community during the COVID-19 Pandemic

2.2.1 Use of Masks in Children in the Community

Children should stay at home and avoid unnecessary exposure to others leading to distance learning and sports restrictions during this pandemic. However, if a child is brought to the community or happen to need exposure to people not living in their household, infection prevention for both the child and other individuals is done by wearing a facemask along with other non-pharmaceutical interventions like physical distancing at 2-meter distance and avoidance of hand exposure to possible contaminated surfaces.[118,119,120] Health professionals must teach families how children should be wearing these masks to ensure their safety under the family members' care.

Recommendation 12

1. We strongly recommend, that well children less than 2 years old *should not* wear masks or face shields when are they are out in the community or with people not living in the same household.[118,119]

   While older children (2 -11 years old) needing to be out from the home or be with people not in the same household, use masks and face shields with adult supervision. Children above 12 years old follow mask and face protection advise for adults.

2. For the subgroups of children with disabilities, developmental disorder or specific conditions where mask wearing interferes with the health condition, a case-to-case basis recommendation from their medical provider is warranted. [118,119,120]

   (Strong recommendations, moderate to high grade evidence)

Remarks

Children may be less efficient transmitters of SARS-CoV2 than adults due to their inherent simpler airway structure (fewer alveoli and terminal bronchioles), lower exhaled airspeed, and less airway collapse than older children and adults. [96,121,122] Interestingly, they are reported to have a viral load that is greater than that of adults[102,123] and can transmit SARS-CoV2 infection.[21,102] In general, the efficacy of masks in reducing transmission depends on a variety of factors, including fit, time worn, and filtration efficacy. Higher filtration efficacy masks (e.g., N95 masks) are much more effective at filtration of aerosols than lower efficiency masks (e.g., surgical masks),[124] but these do not currently exist in sizes for children and are poorly tolerated for long periods of time.[96]

The American Academy of Pediatrics (AAP) and the Centers for Disease Control (CDC) recommendations that children 2 years old and older can be taught the minimum infection control practices like hand washing and physical distancing, including wearing a cloth face cover. [118,119] World Health Organization states that if children less than five years of age (2-3 years old) are to wear masks in the community, consistent supervision, including a direct line of sight supervision by a competent adult, needs to be ensured times. These precautions ensure the correct use of the mask and prevent any potential harm associated with mask-wearing to the child. [120] Home use of face masks also may be particularly valuable in households that include medically fragile or at-risk adults and children.[118] During the COVID-19 pandemic, plans for the safe return of children to school, child care, and other group settings must include the universal use of face masks by children 2 years of age and older and the adults with whom they interact.[125]

On the Use of Face Shields

Current laboratory testing standards only assess face shields for their ability to provide eye protection from chemical splashes and should not be considered as an equivalent to masks with respect to respiratory droplet protection and/or source control. [126] In the

context of non-availability or difficulties wearing a non-medical mask (in persons with cognitive, respiratory or hearing impairments, for example), face shields may be considered as an alternative, noting that they are inferior to masks with respect to droplet transmission and prevention. If face shields are to be used, ensure proper design to cover the sides of the face and below the chin.[127]

The WHO and UNICEF advise that when physical distance cannot be maintained, and in special situations where it is not practical to wear a mask (for example, among children with hearing loss or other disabilities or health conditions that limit compliance with wearing fabric or medical masks and consequently their utility), face shields may be used while taking the following considerations into account: [120]

- The face shield is an incomplete physical barrier and does not provide the filtration layers of a mask.
- The face shield should cover the entire face, be wrapped around the sides of the face and extend to below the chin.
- Reusable face shields must be properly cleaned (with soap or a detergent and water), disinfected (with 70-90% alcohol) and stored after each use. Face shields that will withstand the use of disinfectants without damaging their optical properties should be selected.
- Maintaining physical distance of at least 1 m (3.3 feet) should be maintained where feasible, with ongoing promotion of frequent hand hygiene and respiratory etiquette.
- Caution should be taken to avoid injury when children don, wear, and doff face shields.

2.2.2. Use of Masks During Play and Exercise in Children in the Community

Promoting behaviors to lower spread of SARS CoV2 in children at play or those engaging in youth sports is necessary. It is imperative to encourage all other important public health measures to family members caring for the children:[119,120,127]

- Require the consistent and correct use of the masks when physical distancing is not possible, and the exercise is nonvigorous, a cloth face mask should be worn.
- maintaining physical distancing of at least a 1-meter by limiting the number of playing children
- reminding children of the need to have clean hands while providing access to hand hygiene facilities.
- Instruct children to remove masks when it is wet. Sweat produced during exercise can make the mask wet more quickly making it difficult to breath and promote bacteria growth.

- Reminders should be given to caregivers ,family members or coaches that masks should not be placed on[119]
    - Babies or children younger than 2 years old
    - Anyone who has trouble breathing
    - Anyone who is unconscious, incapacitated, or otherwise unable to remove the mask without assistance

- Vigorous exercise in a closed environments /confined space may contribute to the transmission of COVID-19 and should be limited.[127]
- Masks should not be worn in water sports (e.g., swimming, diving) or in activities where they could pose a risk for accidents due to catching on equipment or sudden impairment of vision during the a sport (e.g., gymnastics, cheer).
- Among sports athletes, risk often increases when players are not actively engaged in activity, for instance when they are taking a break or socializing. Ensure that masks are used at all times.
- Special considerations may be appropriate when there is an increased risk of heat-related illness. The Centers for Disease Control present the other consideration for young athletes' participation in youth sports (CDC), will include reducing physical closeness, minimizing sharing of equipment gear, limiting travel outside of the local area, identifying small groups, and keeping them together while spectators are to space out by 6 feet during games.[127] Parental and sports coaching staff guidance are essential during these activities as well.

2.2.2 Aerosol Therapy in the Home Among Children not suspected for COVID-19

At home, should children with no known SARS-CoV2 infection have bronchospasm possibly due to asthma or other causes the use of the equally effective pMDI with VHC or spacers are strongly recommended.[103] On the other hand, home nebulization may be done in SARS-CoV2 negative children, preferably in a well-ventilated area in the home like the porch or a room with open windows. [111,112]

Fast air exchanges can lessen aerosol suspension in the air surrounding the patient, as recommended in the newly published WHO Roadmap, a new guidance on achieving proper air ventilation in the healthcare, public, and home setting allowing actions and building setting steps for better air exchange in facilities where aerosol procedures occur during the COVID-19 pandemic. [193] A new guidance on steps on achieving proper air ventilation in the healthcare, public and home setting allowing actions. and building setting steps for better air exchange in facilities where aerosol procedures take place during the COVID-19 pandemic. Then again, the best approach for prevention of transmission during this COVID-19 pandemic is to consider all individuals to be possible carriers of the disease [109,110]

Practice Points for home Aerosol treatment among children *without* COVID-19

- Any child who could tolerate the use of a pMDI with appropriate spacer or DPI format for aerosol treatment should be prescribed with such drug forms and spacer devices. (please see Chapter 4 for further discussion on Aerosol Therapy, indications, techniques of use and care of pMDI in children)
- Care and proper cleaning of aerosol therapy devices per manufacturer's advise should be taught to caregivers
- Repeated bronchospasm events and use of aerosol treatment in a SARS-CoV2 (-) child warrants immediate evaluation with a physician.

Chapter 3

3. RESPIRATORY SUPPORT FOR COVID-19 PATIENTS

3.1 Management of Hypoxemia in the Spectrum of the COVID-19 Illness

A. Precaution

Recommendation 13. [64, 124,126]

The use of High Flow Nasal Cannula (HFNC), CPAP/BiPAP and Non-Invasive Ventilation (NIV) theoretically increase the risk of viral spread through aerosol generation. Therefore, we suggest to observe the following precautions.

1. Preferably in an appropriate Airborne Infection Isolation Room (AIIR)
2. Use of a surgical mask over HFNC to reduce droplet spread
3. Use an appropriate viral exhalation filter for CPAP/BiPAP
4. Healthcare providers shall be in proper Personal Protective Equipment (PPE)

(Strong recommendation, high quality evidence)

Remarks

Contact and airborne precautions should be observed for suspected and confirmed COVID-19 patients especially when performing aerosol-generating procedures. If feasible, they should be admitted in well-ventilated single rooms but when not possible, patients should be cohorted in adequately ventilated areas with bed space at least 1meter apart.[64]

B. First line Approach

Children with severe respiratory distress should receive emergency airway management and oxygen therapy to target SpO2 > 94%. The use of nasal prongs or nasal cannula is preferred in young children, as they may be better tolerated. Oxygen support for infants may start at 1 to 2 LPM, young children at 2 to 4 LPM and 5 to 6LPM for older children and adolescent.[128,129] Supplemental oxygen should be titrated based on the patient's saturation. Other parameters to be monitored are respiratory rate and heart rate, hemodynamic parameters, and sensorium. Close monitoring should be done to detect clinical deterioration so respiratory support can be escalated immediately.

The High Flow Nasal Cannula (HFNC) use may reduce the need for intubation compared with standard oxygen therapy. Previous recommendations suggest the use of HFNC for patients with SPO2/FiO2 ratio of < 264.[130] Emerging data suggest that its use may be safe in patients with mild-moderate and non-worsening hypercapnia. However, evidence-based guidelines on HFNC do not exist, and reports on HFNC in

patients infected with other coronaviruses are limited. In using HFNC, choose an appropriate sized nasal cannula, only 50% after the nares diameter to permit leak of excessive pressure, and there should be a wider distance of the prongs to avoid pinching the nasal septum.[131]

Recommendation 14. [22, 128,129,130]

Children with suspected or confirmed severe COVID-19 will need supplemental oxygen to achieve target sp02 ≥94%. We suggest to use

1. Supplemental oxygen therapy by Low Flow Nasal Cannula (LFNC) may be started, with a surgical mask worn over the patient's face to reduce droplet spread, when oxygen saturations (sp02) are < 90%. If patient continues to be hypoxemic, oxygen delivery via face mask with reservoir bag should be initiated. Titrate supplemental oxygen based on patient's saturation

2. Patients that remain hypoxemic with increased work of breathing should be escalated to High Flow Nasal Cannula (HFNC) if available.
3. Those with progressive respiratory distress or with no HFNC available, continuous positive airway pressure (CPAP) or a bi-level non-invasive ventilation (NIV), may be used.

(Strong recommendation, low quality evidence)

Next is to choose the appropriate delivery settings. The optimal maximal flow for HFNC is not known. In most studies, the flow rate used varied from 2 to 8 L/min and was adjusted individually to minimize the patients' work of breathing and SpO2 values. Initially,[129] flow rates can be started at 1 to 2 L/kg/min. (*Refer to Table 15) T*he use of CPAP or a bi-level NIV, on the other hand, is recommended for patients with SPO2/FiO2 ratio >221 and < 264.[130] The rationale is that a higher pressure level might be obtained when using CPAP/NIV.

Table 15. Oxygen flow settings for high-flow nasal cannula use in infants and children

Weight (in kg)	Initial FR (LPM)	Maximum FR (LPM)
< 5	6	8
5 - 10	8	15
10 – 20	15-20	20
20 - 40	25-30	40
>40	25-30	40-60

The rationale of using a surgical mask to be worn over the patient's face when giving any form of respiratory support is to prevent droplet spread during aerosol-generating procedures. In a study by Hui et al., substantial exposure to exhaled air occurs within 0.3-0.42 meters from patients receiving oxygen support via nasal cannula. This aerosol exposure increases to 1 meter from patients receiving NIV even in an isolation room with negative pressure,[132] hence, surgical masks can reduce such spread. [133] The Center for Disease Control and Prevention (CDC) and the American Academy of Pediatrics recommendations for COVID-19 stating that face coverings should not be worn by children ages 2 years and below because of the danger of suffocation, is meant for children going out into the community. [118,119]

The recommendation of using surgical masks while on any respiratory support in this chapter is meant for all children with hypoxemia, needing oxygen supplementation in a health care setting undergoing close clinical monitoring.

Recommendation 15

In low-resource settings or in facilities where ventilators are not available, we suggest that an improvised CPAP (iCPAP), using locally available equipment, may be used.

(Weak recommendation, moderate-high grade quality evidence)

Remarks

In the latest WHO recommendation, the bubble nasal CPAP may be used as this is more readily available alternative for newborns and children with severe hypoxemia in situations where mechanical ventilation might not be available.[64.] The iCPAP is much like the Pediatric Bubble CPAP (*figure 14*), a simple and effective means of generating airway pressure by bubbling expired air or oxygen through a fixed amount of water.[134]

In order to address the demand for standard ventilators, an improvised CPAP system using a facemask has been considered which provides a potentially more benign form of breathing assistance than invasive ventilation. In a pilot study among adults with ARDS, it was shown that limited experimentation with higher pressure values could be reliably maintained by this device.[135]

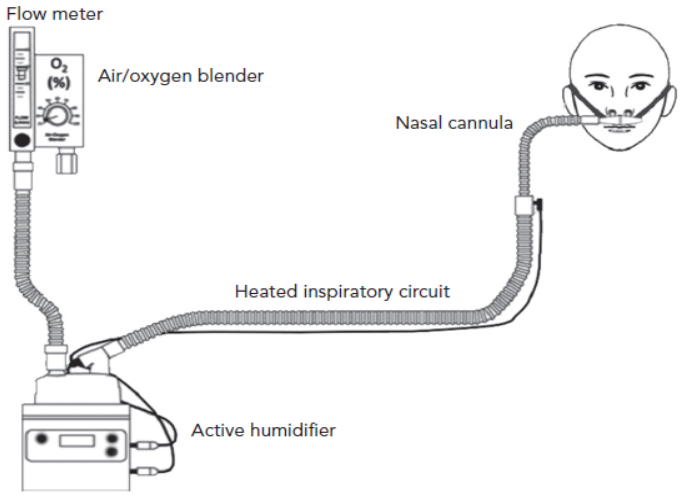


Figure 13. High Flow Nasal Cannula (HFNC) from: High Flow Nasal Cannula Oxygenation revisited in COVID-19. https://www.cfrjournal.com/journals/editions/cfr-volume-6-2020. Reprinted with permission.

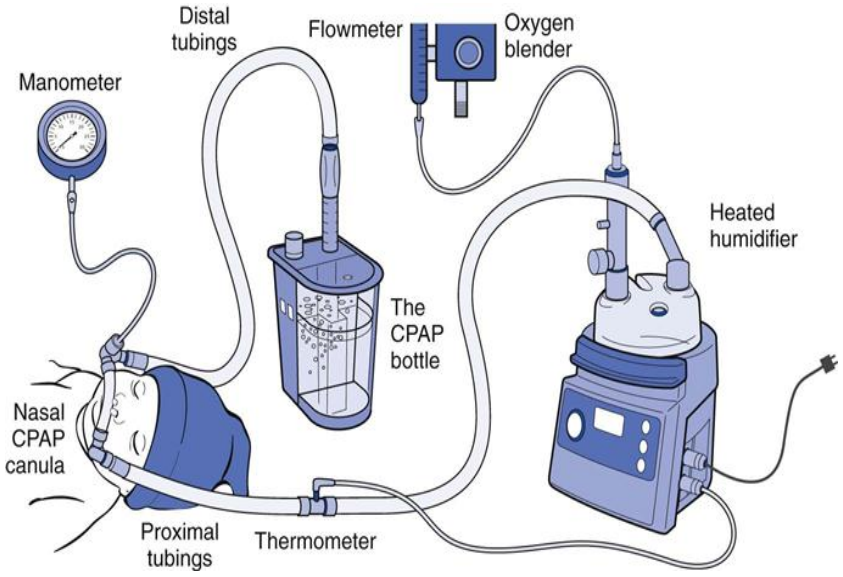


Figure 14. Diagram of Bubble CPAP delivery system. DiBlasi, R. M. (2016). Neonatal and Pediatric Mechanical Ventilation. In *Thoracic Key.* Retrieved from https://thoracickey.com/neonatal-and-pediatric-mechanical-ventilation/. Reprinted with permission

3.2 Airway Management and Tracheal Intubation Specific to COVID-19

Recommendation 16

We strongly recommend an appropriate environment for airway management of suspected or confirmed COVID-19 pediatric patients as follows;

1. The use of a negative pressure ventilation room is ideal to minimize exposure to aerosols and droplets from pediatric COVID-19 patients
2. Normal pressure rooms with closed doors are an alternative setting in low-resource facilities
3. The use of airway devices providing 6L/min or more of oxygen shall be discouraged as this procedure is considered aerosol-generating, unless it is performed under an AIIR.
4. Strict hand hygiene and compliance to the minimum PPE requirement is necessary in handling pediatric COVID-19 patients
5. Double gloving as a standard practice for handling pediatric COVID-19 patients

(Strong recommendation, low quality evidence)

Recommendation 17

We strongly recommend intubation in the following cases:

1. SpO2/FiO2 ratio < 221 in pediatric patients on bi-level NIV or CPAP.
   (Strong recommendation, Moderate quality evidence)

2. If there is no improvement in oxygenation (target SpO_2 92-97% and FiO_2) within 60 minutes on NIV or CPAP.[124]
   (Strong recommendation, Moderate quality evidence)

3. Patients with hypoxaemic respiratory failure and haemodynamic instability, multiorgan failure or abnormal mental status.
   (Strong recommendation, high quality evidence)

B. Indication for Intubation

Oxygenated patients may continue to have increased work of breathing or hypoxemia hence may require mechanical ventilation. Those receiving trial of HFNC and/or NIV should be closely monitored and be cared for by personnel capable of performing endotracheal intubation in case the patient acutely deteriorates or does not improve with initial respiratory support.[64] Monitoring SpO2/FiO2 ratio in patients on non-invasive respiratory and the oxygenation saturation index (OSI) or the oxygenation index (OI) in invasively ventilated children for disease severity grading. The level of FiO2 should be guided by targeting SpO2 > 97% to allow for valid measurement of the SpO2/FiO2 ratio and the OSI.

Upon initiation of intubation, preoxygenation must be optimized with 100% Fi02 for five (5) minutes using a face mask with reservoir. Place the patient's bed up, the head elevated, use of end expiratory airway valves and airway adjuncts. The "two person/two handed vice grip" technique will ensure a better seal of the mask around the mouth. A clear drape placed over the patient's face can help minimize aerosolization.[133, 136]

Figure 15. Two-handed vice grip during BVM (right).
from Australian Safe Airway Society
Consensus Statement. Reprinted with permission

One person manages the mask and the airway, while the second person squeezes the bag to ventilate the chest. The person responsible for the mask stands at the head of the bed and places his thumbs on the top surface of the mask. The remaining fingers are then used to grip the mandible on either side. The mask is squeezed between the thumbs and the fingers to create a seal and at the same time the mandible is elevated to open the airway. This technique is considerably easier, but again, the physicians must be constantly checking that air is flowing easily into the patient and that the chest is rising and falling.

Recommendation 18

Pre-oxygenation with 100% FiO2 for 5 minutes using face mask with reservoir bag is preferred for suspected or confirmed COVID-19 patients.

When possible, avoid the use of Bag Valve Mask (BVM) to reduce exposure to aerosols. However, if its use is absolutely necessary for pre-oxygenation, it is strongly recommended to follow safety measures to minimize aerosolization:[129,130]

a. Two-Person technique/Two handed vice grip, use of a viral filter, and gentle ventilation
b. A clear drape should be placed over the patient's face to minimize aerosolization.

(Strong recommendation, low grade evidence)

Tracheal intubation is a high risk procedure to physiologically compromised COVID19 patients as well as healthcare providers. This should ideally be performed by the most skilled and experienced person to increase first pass success rate and to minimize attempts. If available, the use of video laryngoscopy is recommended over direct laryngoscopy since it has the advantage of improving the view during intubation as well as a longer distance between the intubation field and the operator thereby reducing the risk of transmission. [137]

Recommendation 19 [64,129,130, 136]

Rapid Sequence Intubation (RSI) is should be the treatment of choice for endotracheal intubation of suspected or confirmed COVID-19 patients as inadequate sedation and paralysis can produce coughing during laryngoscopy, which is an aerosol-generating procedure.

It is strongly recommended that cuffed endotracheal tubes be used to avoid peritubal leak and dissemination of secretions.

(Strong recommendation,high grade evidence)

(1) video laryngoscopy
(2) fiberoptic intubation through a supraglottic airway device (i.e. LAM)
(3) combined video laryngoscopy and fiberoptic bronchoscopy and lastly
(4) an invasive airway, front of the neck airway (FONA). [136]

3.3 Ventilator Management and Strategies

Preliminary pediatric data shows that severe COVID-19 disease appears uncommon in young children although those < 1 year of age may experience greater disease.

Recommendation 20

The suggested lung protective strategies for children with Pediatric ARDS related to COVID-19 are as follows:

1. Low tidal volume (3-6 ml/Kg IBW) if poor respiratory compliance
   Low tidal volume (5-8ml/Kg) if better preserved respiratory compliance
2. Initial Positive End Expiratory Pressure (PEEP) of 8-10cmH20 individualized for each patient's phase of ARDS and should be titrated when there is refractory hypoxemia. Maximal PEEP in younger children is 15cmH2.[64,129]
3. Target plateau pressure (< 28 cm H20)
4. Permissive hypercapnia (pH 7.15 – 7.30)

(Weak recommendation, moderate to high quality evidence)

For mechanically ventilated patients, FiO2 can be titrated to maintain SpO2 of 92 – 96% but for patients with severe disease, the minimal acceptable SpO2 should be 88%. [130] A lower level of plateau pressure (<28cmH2O) is targeted, and a lower target of pH is permitted (7.15–7.30). The tidal volumes should be adapted to disease severity:3–6 mL/kg PBW in the case of poor respiratory system compliance, and 5–8 mL/kg PBW with better preserved compliance.

In the early phase of respiratory failure with COVID19, patients exhibit critical hypoxemia but lung compliance is maintained. In such cases, a PEEP of 8-10cmH20 may be started, given that the recruitability is low and risk of hemodynamic failure increases at higher level. On the other hand, during the later phase, the pathophysiology may change to typical ARDS requiring a higher PEEP. [138]

In patients with moderate to severe ARDS, a trial of higher PEEP is suggested but requires individualization as well as taking into consideration the risk versus benefit in each patient. Individualized titration of PEEP in refractory hypoxemia is recommended a refractory hypoxemia defined PaO2/FiO2 150; OI$\geq$12; OSI $\geq$10 and FiO2 > 0.6 is present. The patient's hemodynamics must be monitored closely with increasing PEEP.[64,129]

In younger children, maximal PEEP pressures are 15cmH20, although high driving pressure may more accurately predict increased mortality in ARDS compared with high tidal volume or plateau pressure, data from RCTs of ventilation strategies that target driving pressure are not currently available.[64]

3.4. Prone Positioning for Mechanically Ventilated Confirmed Covid-19 Children

Recommendation 21

Prone positioning may be considered as part of treatment regimen for pediatric COVID-19 patients with moderate to severe ARDS.
(*Weak recommendation, low quality evidence)*

The Pediatric Mechanical Ventilation Consensus Conference (PEMVECC) and European Society for Pediatric and Neonatal Intensive Care (ESPNIC) recommends early and prolonged prone positioning of moderate to severe ARDS among children with suspected and proven COVID-19.[130] While the World Health Organization (WHO) Interim guidance on the management of COVID-19 states that prone positioning may be considered for pediatric patients with severe ARDS . A comprehensive Cochrane review involving 24 studies involving hospitalized infants and children with Acute Respiratory Distress Syndrome (ARDS) who were made to use proning as part of their management was published by Gilles, et al. Among the outcome measures there was improvement in

oxygen saturation, arterial oxygen, and oxygenation index. [139] Kache, et al. suggests prone positioning as one of the treatment considerations in children with ARDS and severe hypoxemia due to COVID-19 requiring mechanical ventilation in the PICU setting.[129] The suggested indications and contraindications for proning in mechanically ventilated children with COVID-19 were adapted from previous proning studies and is stated in **Table 16**.

Table 16. Indications for Prone Positioning

- PEDIATRIC COVID-19 patient
- On invasive mechanical ventilation with attached ETT or tracheal tube access
- Received mechanical ventilation for at least 24 hours at the Acute Phase of ALI/ARDS
- *Patient has the Pediatric ARDS (PARDS) Baseline Criteria (PALLIC Guidelines)[85]*
    1. Onset within 7 days of known clinical insult
    2. New pulmonary infiltrates on CXR/CT Scan
    3. Absence of cardiac failure
    4. Sudden deterioration in oxygenation

    * Exclusion: Perinatal Lung disease
- Patient has moderate to Severe Pediatric ARDS based on
    * Moderate PARDS : OI 8-16 / OSI 7.5-12.3
    * Severe PARDS : OI ≥16 / OSI ≥12.3

Contraindications for Prone Positioning

- Hemodynamic instability despite the administration of adequate inotropic agents.
- Patients with bronchospasms
- Patients with tracheal lesions (congenital tracheomalacia, tracheal infections)
- Unstable spinal cord injuries.
- Increased intracranial pressure
- Recent abdominal or thoracic injuries or surgeries
- Inability to tolerate Proning (*eg*, pelvic fracture, unstable long bone fracture).
- Patients without consent for proning

As to the duration of proning, a study by Relvas, et al evaluated the changes in oxygenation index (OI), one of the oxygenation measures for pediatric ARDS patients; among 40 critically ill children placed in prone positioning over a prolonged time interval of 18-24 hours, the authors noted improvement in the oxygenation index compared with prone positioning with shorter time durations (6-10 hrs).[41] A case report and clinical experience report of the First Affiliated Hospital in China stated that that they ceased doing the proning procedure once the patient demonstrated improvement of PaO2/FiO2 ratio to > 150. [140,141]

There are no standard proning techniques for children with COVID-19 related ARDS . A team coordinated approach with pre-positioning turning [142,143] and post positioning protocol have been described[142,143,144] Based on the proning positioning protocol for children with ARDS developed by Curley, et al, preparation and assessment are important during the procedure [41] recommend a coordinated health care team to perform the proning procedure on children with ARDS, involving 2-4 health personnel during the proning turn, which is described as follows for separate age groups of children: smaller children are first elevated then turned 45 degrees; while use of bed linens for proning of bigger children may be done.[141] The authors recommend that precautions during performing the proning procedure should be observed to secure placement of the endotracheal tubes and other patient devices such as intravenous lines.[41]

An adapted list of preparation and prone positioning steps for proning among mechanically ventilated COVID-19 confirmed children below (*see Table 17)* using data gathered from local institution practices in child proning. Providing adequate sedation and preoxygenation with a fraction of inspired oxygen (FiO2) of 1 is recommended before moving the patient to prevent transient hemodynamic instability, and desaturation is included.

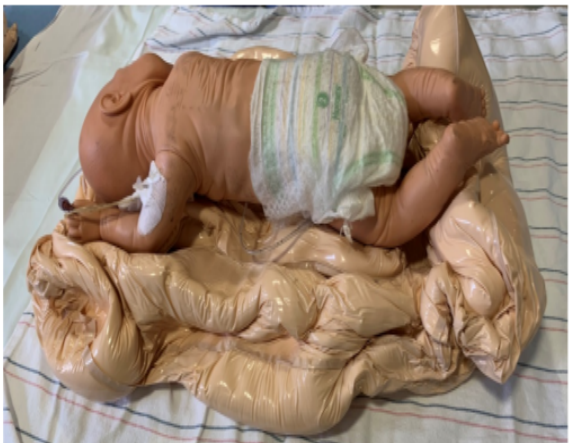


Figure 16 Child on Prone. & Figure 17 Infant on Prone*. The main goal is to have a free floating abdomen and adjustments to Z Flo sizes (or cushions) or additional pillows may be done. Adapted with permission from Tracy Fulkerson,BSN RN CCRN*

Table 17. The Prone Positioning Steps for Mechanically Ventilated Pediatric COVID-19 patients

1. Prepare cushions available in the PICU unit: memory foam (egg-crate material) or rolled blankets to cushion the head, the chest Moreover, the pelvis to allow free movement of the patient's abdomen.
2. Identify the Pediatric Proning team dependent on the patient size:
    - Physician: in-charge of the airway access and possible re-intubation
    - At least 2 nurse team assigned to facilitate the roll/turning of the patient
    - One (1) nurse assigned to support midsection and (1) to the lower extremities
    - Once identified team lead (physician) discusses turning technique for the patient

    SUPINE – PRONE TURN TECHNIQUE:

    * It is Important to plan to do the turn TOWARDS the ventilator side WITHOUT disconnecting the ventilator support from the patient to ensure safety & avoidance of aerosolization.

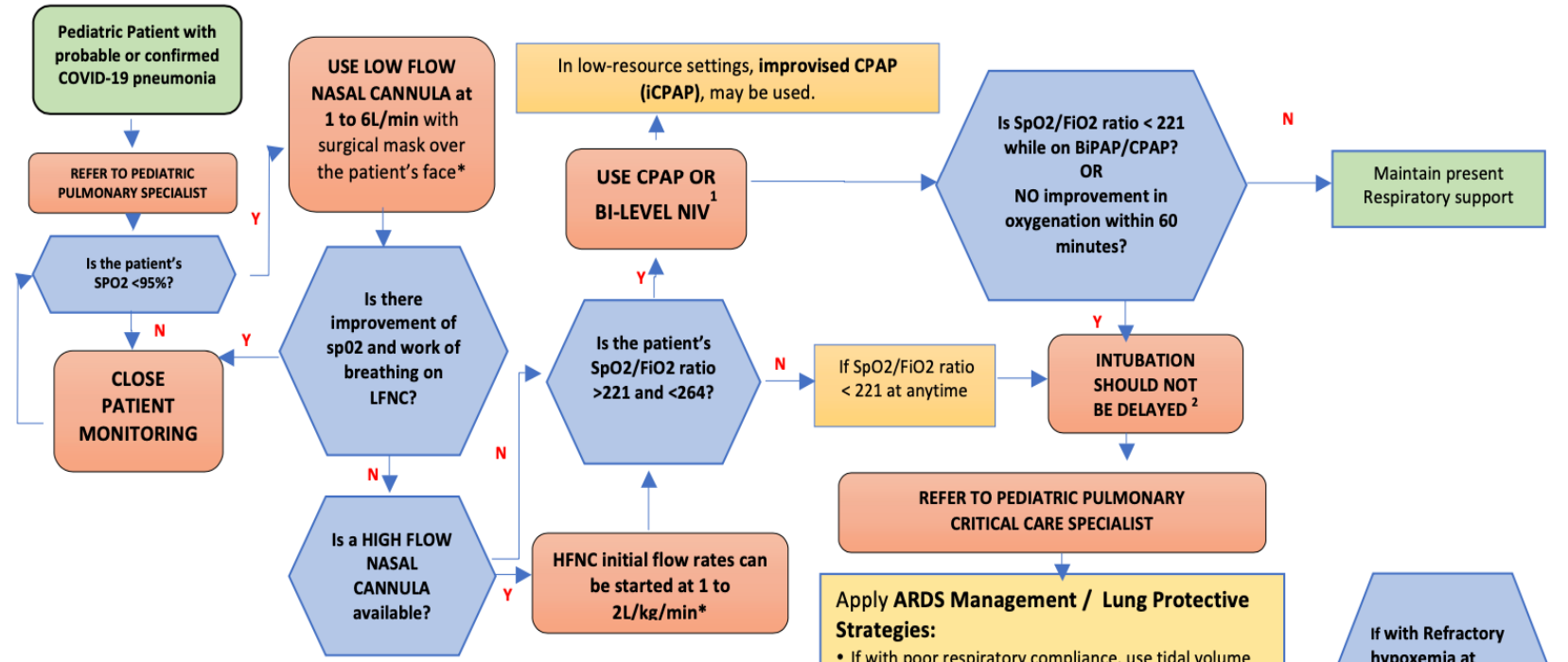
    Smaller Children (nfants/ Toddlers) : body elevated, turned to side (about 45degrees) Placed on prone over prepared cushions

    Bigger Children: Turn by log roll using linens draped around each side of the patient; initially move towards the edge of the bed away from the ventilator, then turn to side (about 45 degrees) , place on prone using drape linens with prepared cushions placed on designated areas

    PRONE – SUPINE TURN TECHNIQUE:

    - Smaller Children (infants/ Toddlers) : body elevated, turned to side (about 45 degrees) Place on SUPINE with the head and shoulder supported then elevate bed to 30 degrees head elevation
    - Bigger children: initially move towards the edge of the bed nearest from to the ventilator, then turn to side (45 degrees),turn patient to SUPINE by log roll using draped linens from each side of the patient. Adjust patients position to elevate head part to 30 degrees elevation
3. Ensure team members wear complete PPE during each procedure. Do hand washing.
4. Cap the nasogastric tube, secure the Foley Bag Catheter
5. Move ECG electrodes to the lateral aspects of the patient's trunk. Reposition tubing/lines to allow sufficient mobility of the proning team and patient during the turn.
6. Consider giving scheduled sedation or Neuromuscular blockade agents (NMA) before each turn
7. Apply cover or plastic drape over the patient's head
8. Suction the oropharynx, recheck ETT level placement and secure plasters; reposition drape
9. Team lead then reviews turning techniques out loud, the team prepares for turning on his count
10. During the turn, the team, should be mindful to keep the head aligned with the patient's body to ensure avoidance of disconnection from the ventilator and any untoward injuries
11. Once the patient is in a prone position, recheck ETT level /IV line placement and patency, remove the drape
12. Gently place the patient's head on the side over a cushion lined with an underpad for draining oro-nasal secretions, then one elbow is folded over the head level, the other stretched, a cushion supporting the upper shoulders, hips and the abdomen is repositioned in a suspended placement to achieve a "swimmer's position" of the *patient as seen in Figure 16 and Figure 17*
13. Place patient on prone for at least 12 hours per day. Proning may be extended for 18-24 hours during the early course of the disease trajectory.[32]
14. Assess patient tolerance to the prone position for around 10-15 minutes.
    *If well tolerated; move the ECG leads to the chest of the patient support pressure points with gel pads or watered gloves continue monitoring, feeding and care
15. *To return to the supine position*, do handwashing, recheck that PPE worn by the team should be level 4 PPE for AGMP procedures. Team lead reviews the prone to supine procedure aloud.
16. Recheck and secure airway patency and Iv access, reposition the ECG lead, cap NGT
17. Place drape over the patient's head part, wipe oral secretions if any
18. Gently turn patient from PRONE to SUPINE while supporting the mid-torso and leg portion of patient
19. Recheck airway access, patency and secure ETT and attachments. Ensure proper placements of IV access ECG monitor leads, pulse oximeter.
20. Adjust patient to most comfortable position with head part elevated to 30 degrees. Continue care. Repeat cycle till patient has achieved *PaO2/FiO2 ≥150; OI < 12; OSI < 10*[32]. If not tolerated, do not proceed with proning.

ALGORITHM 2. Respiratory Management of Pediatric Patient with Probable or Confirmed COVID-19 Pneumonia



Notes:

* Titrate supplemental oxygen based on patient's saturation

[1] If HFNC, CPAP/BiPAP or NIV should be instituted, suggest to observe the following precautions:

- Patient preferably in an appropriate **Airborne Infection Isolation Room** (AIIR)
- Use of a **surgical mask over HFNC** to reduce droplet spread
- Use an appropriate **viral exhalation filter** for CPAP/BiPAP
- Healthcare providers shall be in **proper PPE**

[2] The **use of Bag Valve Mask (BVM)** prior to intubation is **not advised.** However, if the bag/mask ventilation is necessary for pre-oxygenation, it is strongly recommended to do the **Two-Person Technique/Two-Handed Vice Grip**, with use of a **viral filter**, and **gentle ventilation**.

Another option for pre-oxygenation, if time allows, is to use **100% FiO2 for 3–5 minutes**, using a **well-fitting mask with reservoir**, preferably using a closed circuit.

Rapid Sequence Intubation (RSI) should be the procedure of choice for endotracheal intubation. Use of **cuffed endotracheal tubes** is recommended to avoid peri-tubal leak and dissemination of secretions.

Chapter 4

AIRWAY THERAPIES AND RESPIRATORY MECHANICS

4.1 Aerosol Therapy : Its related benefits and risks

Inhaled medications are the mainstay of therapy for many pediatric pulmonary diseases. [145]In the science of aerosol drug delivery, a “medical aerosol” is any suspension of liquid (nebulizer or pMDI) or solid drug particles (pMDI or DPI) in a carrier gas. [146]The common types of aerosol generator devices for the pediatric group include nebulizers, pressurized metered-dose inhaler (pMDI), dry powder inhaler (DPI), liquid soft mist liquid inhalers (SMI) [147, 148, 105.] Much evidence was found on the equally efficacious function of these aerosol generators (nebulizers, PMDI and DPI) when used to delivery bronchodilators and aerosolized steroids in children in acute care and for long term treatments.[130,145,149,150,151]

Nebulizers operate by converting liquid formulations into fine breathable droplets.[152] While pMDI and SMI are portable, hand-held drug delivery system that uses a pressurized propellant to create and reliably deliver a specific amount of medication, a metered dose, with each actuation. A valved-holding chamber (VHC) is used with pMDIs to improve aerosol delivery and lower oropharyngeal deposition and address its limitation of poor hand-breath coordination [147,153] No propellants are used with the DPI but this requires high inspiratory flow rate needed to disperse the drug particles and draw the drug from the device and is often used in older adolescents.[166]

The primary advantage of inhaled aerosol therapy is treating the lung directly with smaller doses, resulting in fewer side effects than with oral delivery. The disadvantages presented to patients are related to the inhaled drug components, type of aerosol generator device, technique of use and environment.[147] Care providers, bystanders and even other patients are exposed to secondhand aerosol drugs and the risk of inhaling pathogens during aerosol therapy has been reported. [153,154,155.] Infection can be minimized with the implementation of an infection control management system including use of masks, filters, and ventilation systems.[156]

In the present COVID-19 pandemic, there are currently no approved medications for aerosol therapy in the treatment of COVID-19,[157] however, children in all the severity forms of COVID-19 with signs and symptoms of bronchospasm will need aerosol drug delivery to address this problem.

While respiratory organisms transmitted thru droplets and aerosols are generated by tidal breathing, talking, coughing, and sneezing.[108,158,159] SARS-CoV-2 can be transmitted by all these methods and is viable in particles that remain suspended in air.[125] Increased risk of transmission SARS-CoV-2 has been associated with aerosol generating

procedures like endotracheal intubation, bronchoscopy, open suctioning, nebulization, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from the ventilator, noninvasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation.[109]

It is important to note that medical aerosols generated during aerosol treatment by inhalers and nebulizers, such as those containing bronchodilators, anti-inflammatory agents, mucokinetics, antivirals, antibiotics, and prostanoids, do not contain pathogens unless the nebulizers are contaminated by the patient or HCW.[108,109] Although there is no evidence to show that aerosols get contaminated in the lungs before exhalation also because when an aerosol droplet combines with contaminated mucous membrane, it can no longer be airborne and be a part of an aerosol.[160] The greater risk occurs on exhalation of patient-generated bioaerosols with pathogens while medical aerosols get released as fugitive emissions into the environment during expiration [110, 161]

Nebulized therapies however are classified as a "possible aerosol generating procedure" by the WHO [64] as well as the CDC based on SARS-CoV epidemic in 2009 data from the SARS-CoV epidemic. [19,20.] In an experimental study by Tang et al. in the early part of COVID-19 pandemic to emphasize the risks of nebulization indoors, demonstrated the risk of using nebulizers without filters via face mask in a room even with the recommended 12 Air Changes/Hour (ACH).[162] A report on SARS-CoV2 states that its infectivity is maintained at a respirable particle size over short distances, in contrast to either betacoronavirus [163] and is found to be resilient in aerosol form.[163, 164]

The reluctance among clinicians to continue the wide use of nebulization was felt [112, 165] with the knowledge that AGMPs performed in an infected person allows aerosols to traverse farther distances [108] as illustrated in the figure below.

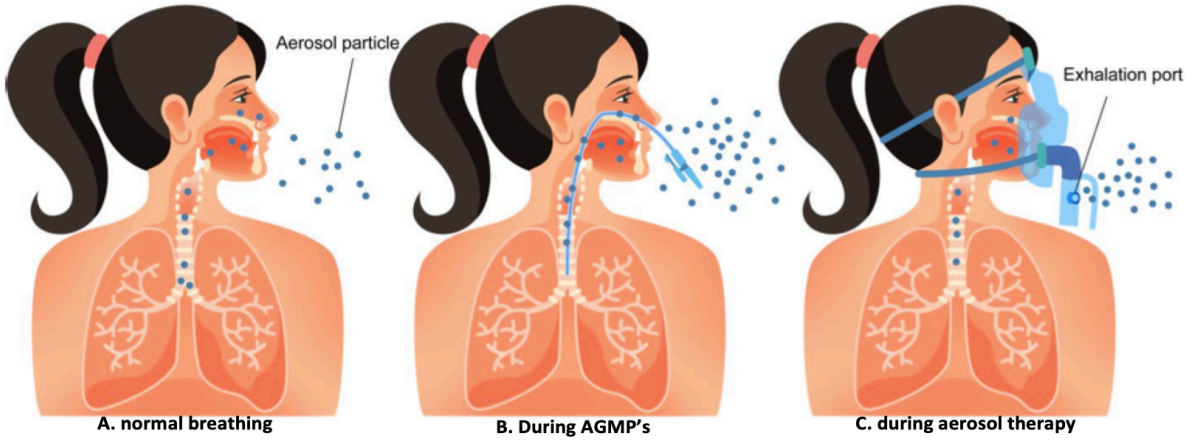


Figure 18. : Illustration to show difference between aerosol "generating" versus aerosol "dispersing" procedures.
Panel A shows that small amount of aerosols generated during normal breathing travel short distances before evaporation.
Panel B shows a burst of aerosols generated during procedures that provoke coughing such as suctioning, intubation or bronchoscopy. In **Panel C,** administration of therapeutic aerosols by nebulizer, NIV or use of HFNC could disperse aerosols from the patient as a jet to a greater distance.
Source: Dhand R, Li J. Coughs and Sneezes: their role in transmission of respiratory viral infections, including SARS-CoV-2 Am J Respir Crit Care Med. 2020.[108] permission requested

COVID-19 is exceedingly communicable. Contaminated aerosols may expose healthcare professionals to the virus, poor compliance with infection control and prevention may lead to occupationally acquired infection. Therefore, it is imperative to assume all patients may be infected [109] and all caregivers and healthcare workers need to effectively wear their PPE. In the optimal setting, the clinician attending to a child with COVID-19 should be able to decide which aerosol treatment fits best to the patient's needs and teach the caregivers and or older patients the proper technique of administration to ensure optimal drug delivery to the lungs. Always bear in mind to do inhaled treatments only when necessary and with abundance of caution.

4.2 Aerosol Therapy Among Hospitalized Spontaneously Breathing Children

Recommendation 22

The use of pMDI for the delivery of B2 agonists via spacer or valve holding chamber (VHC) should be done as means of drug delivery over nebulizers among non-intubated children suspected or confirmed to have COVID-19 with signs of bronchospasm.

(Strong recommendations, low grade evidence)

Among children with COVID-19 who are experiencing bronchospasm , the preferred device recommended for use is the pMDI with the age appropriate spacer or valve-holding chamber during this pandemic please see table 18 below

Table 18 Choosing an inhaler device suited for age for suspected or confirmed COVID-19 children

	AGE			
	0-3 years old	***4-5 years old***	***6 years old to 11 years***	***13 years old & above***
Preferred device	pMDI plus dedicated spac	pMDI plus dedicated spacer	pMDI with VHC, DPI or breath actuated pMDI	
Alternate device only when necessary	Nebulizer	Nebulizer	Nebulizer	
Interface	Tightly sealed Face mask	Tightly sealed Face mask or Mouthpiece	Mouthpiece	Mouthpiece

Combined reference: GINA 2020 Report & Arzu Ari and James B. Fink. Journal of Aerosol Medicine and Pulmonary Drug Delivery. PR 2016.95-106

The rationale for pMDI use recommendations in children with COVID-19 is its enclosed design with lesser risk of contamination of the internal component while needing no drug handling preparations [147,166] with low emitted dose (100 µL/actuation) producing less aerosol mass with shorter treatment times.[166]

Practice Points

- Avoid unnecessary aerosol drug delivery to patients with COVID-19.
- Use pMDIs with valve holding chambers for aerosol drug delivery instead of nebulizers if the patient is awake and can perform specific breathing patterns (tidal breathing) among spontaneously breathing children suspected or confirmed to have COVID-19.
  The selection of device is best based upon. [148,151]
  1) the pediatric patient's pathophysiology and the severity of the lung disease,
  2) the pharmacological aspects of the various drugs that can be used for the treatment,
  3) about the technical qualities of the delivery devices and
  4) about the abilities of the child and parents.
- It is important to note that drug delivery success depends on the proper technique in using the chosen device[104,105] *(Further discussion regarding the use of device techniques in Section 4.5.2.)*

4.3 Aerosol Therapy Among Non-intubated Children on Non-Invasive Ventilation

Noninvasive ventilation (BIPAP/CPAP) is considered an aerosol generating medical procedure[64] and has been implicated for aerosolized nosocomial transmission during the SARS outbreak and is considered a high plausible risk of SARS-CoV2 transmission in healthcare [167] thus safety precautions must be well observed. It has been suggested that drug delivery among children with COVID-19 on High Flow Nasal Cannula (HFNC) or mechanical ventilation uses the vibrating mesh nebulizers (VMN) as an option.[148,168] Aerosol therapy is possible through HFNC with lower aerosol dispersion than ordinary open oxygen masks.[154] The practitioner should strongly consider the device and interface available for use in the institution of care, availability of negative pressure rooms or well ventilated single patient rooms, and full PPE supply in each practice setting before initiating aerosol therapy among children suspected and confirmed with COVID-19.

Practice Points

1) Avoid unnecessary aerosol drug delivery to patients with COVID-19 on non-invasive ventilation.
2) Continue to provide a surgical mask cover for patients on high flow oxygen therapy by HFNC.

3) Use pMDIs with valve holding chambers for aerosol drug delivery instead of nebulizers when feasible (see Section 3.2 for further discussion).
4) In suspected or confirmed COVID-19 patients on HFNC or NIV needing nebulization, make sure that the interface device is well fitted. Use in-line or closed system nebulization with filters by the mesh nebulizers attached to the inlet of the humidifier ventilator circuit [168] keep the viral filter at the expiratory end of the single limb noninvasive ventilator circuit, and ventilator limb to reduce secondhand aerosol exposure. [166,168]
5) If a patient is on HFNC, DO NOT discontinue HFNC for any conventional aerosol drug delivery. Never place an aerosol mask over HFNC to deliver aerosol by pMDI or nebulizers. Gas flows may be reduced *only if the patient can tolerate it*.[168]
6) The procedure must be done in a negative pressure room if feasible, or in a well ventilated single patient room with healthcare workers using PPE level 4 for AGMP, limiting one person in the said room with the patient during the procedure while maintaining 1meter distance from the patient.
7) In older children who respond to HFNC support and aerosol therapy, aerosol medications can be given by pMDI using spacer or valve holding chamber with a mouthpiece, this method has been successfully done among local COVID-19 adolescent and adult patients.

4.4. Aerosol Therapy Among Intubated Mechanically Ventilated Suspected or Confirmed COVID-19 Children

If life-threatening bronchospasms or patient response is not optimal with pMDI delivery, consider an alternate aerosol therapy option by giving bronchodilators via inline closed-system mesh nebulizers among mechanically ventilated patients. To provide the aerosol treatment, position the nebulizer device before the humidifier tank without removing the virus filter over the exhalation end of the nebulizer for mechanically ventilated patients.[109,153] The Australian Physiotherapy management of COVID-19 recommends (e.g., PariSprint with inline viral filter) [170].However, should this device be unavailable in local settings, clinicians should consider using pMDI delivered via actuator devices connected to the ventilator circuit. (*Further details in next section 4.5B.)*

Recommendation 23

The use of pressurized metered dose inhaler (pMDI) over nebulization is strongly recommended among mechanically ventilated COVID-19 suspect or confirmed children.

(Strong recommendation, low grade evidence)

Practice Points for Mechanically Ventilated Patients with COVID-19

1. Avoid unnecessary aerosol drug delivery to mechanically ventilated patients with COVID-19.
2. Use pMDIs with valve holding chambers for aerosol drug delivery instead of nebulizers In cases warranting nebulization, use in-line, or closed system nebulization if the patient with COVID-19.
3. Should nebulization be done, keep the Viral/ HEPA filter should be placed at the expiratory end of the ventilator limb to reduce secondhand aerosol exposure.
4. Avoid regular breaking of the circuit to lessen released of secretions from the ventilator circuit. If this is needed, clamping of the ventilator tubings before tube detachment and aseptically administer the drug for aerosol treatment may be done.[64]
5. Proper personal protective equipment must be worn during the aerosol generating procedure in an Airborne Infection Isolation Room (AIIR) room or in the hospital COVID-19 designated ward isolation section.

4.5. Pressurized metered dose inhaler (pMDI) and Administration Techniques

4.5.1. Salbutamol Dose for Pressurized Metered Dose Inhaler (pMDI) for Non-intubated and Intubated Children

Recommendation 24

It is strongly recommended that for suspected or confirmed COVID-19 children presenting with bronchospasm

1. **initial dose of salbutamol 2 puffs** for children ≤ 5 year old;
   4 puffs for children 6 to 11 year old and adolescent (100 mcg/actuation) delivered is strongly recommended.
2. If symptoms persist after initial bronchodilator: **a further 2–6 puffs of salbutamol**
   for < 5-year-old; 4 to10 puffs (> 6-year-old); should be repeated every 20 minutes until good clinical response is achieved.

(*Strong, recommendation, low-grade evidence)* [171, 105]

There is no direct evidence on the dosage of salbutamol in treating bronchospasm specific for children with COVID-19. Based on evidence extrapolated from studies and current guidelines for asthma, administration of four puffs (0.4 mg) of salbutamol may be explored as a means of bronchodilation for pediatric COVID-19 who are not intubated and presenting with bronchospasm.

The optimal dose for pMDI is not well established. However, most studies used nominal dosage ratios between pMDI and nebulizer from 1:1 to 1:13 to determine the

dose needed by pMDI to achieve effectiveness comparable to the standard nebulizer doses.[103] A double- blind, randomized, placebo-controlled trial by Colacone et al., found out that 0.4 mg albuterol pMDI achieved similar bronchodilation to that of 2.5 mg albuterol by nebulization (1:6 ratio).[171] In another study by Schuh and co-workers, done in children with mild acute asthma comparing initial albuterol treatment with low dose pMDI (2 puffs), high dose pMDI (6 to 10 puffs), and via nebulizer (0.15 mg/kg), showed that there was no significant difference in terms of improvement of FEV1 (p=0.12), clinical score, respiratory rate, or O2 saturation. Neither the low dose nor the high dose MDI groups had any side effects. [172]

The Global Initiative for Asthma 2021 recommends a dose of 2-6 puffs for children ≤ five years old and 4-10 puffs for children ≥ six years old.[105] Doses may be repeated every 20 minutes until a good clinical response is achieved based on the GINA guidelines. This is based on several experimental trials using repeated treatments at short intervals (4 puffs every 10-15 minutes). The number of treatments required was adjusted depending on each patient's response, as there is the uncertainty of aerosol delivery from different devices.[103] The drug delivery with pMDI per actuation is only 10–20% of the drug prescribed dose. Hence, the proper technique of administration is crucial to ensure optimal drug delivery to the lungs.

There is no direct evidence of salbutamol dosages in treating bronchospasm specific for intubated children with COVID-19. Evidence was extrapolated from infants with bronchopulmonary dysplasia, adults with COPD, in vitro, and in vivo animal studies.

Infants' breathing pattern with high respiratory rate and low tidal volume decreases the time available for aerosol deposition, thereby reducing drug delivery into the lungs. Hence, for ventilator-supported infants, the administration of one or two puffs of albuterol pMDI with the chamber is sufficient for routine therapy. In certain situations, such as severe airway obstruction or when administration technique is not optimal, increasing the dose to achieve clinical response may be needed. Titrating the dose, as opposed to using a standard dose, may be used as an alternative to achieve maximal bronchodilatation.[173,174]

4.5.2. Pressurized metered dose inhaler (pMDI) Administration Techniques

A. <u>SPONTANEOUSLY BREATHING CHILDREN</u>

<u>Steps on how to use pMDI in Non-intubated children:</u>

1. Remove the mouthpiece cover and shake the inhaler thoroughly.
2. Prime the pMDI into the air if it is new or has not been used for several days.*
3. Assemble the apparatus and check for foreign objects.
4. Keep the canister in a vertical position.
5. Sit up straight or stand up.
6. Breathe all the way out.
7. Follow the instructions below based on the type of device interface used:

For Salbutamol HFA, prime with 2 puffs when it is new and when not used for 14 days.

With the mouthpiece:

a. Place the mouthpiece of the spacer between their teeth and seal their lips. Make sure that their tongue is flat under the mouthpiece and does not block the pMDI.
b. Actuate the pMDI as they begin to breathe in slowly. Also make sure to inhale slowly if the device produces a "whistle" indicating that inspiration is too rapid.
c. Move the mouthpiece away from the mouth and hold their breath for 10 seconds. If they cannot hold their breath for 10 seconds, then hold for as long as possible.

With the mask:

a. Place the mask completely over the nose and mouth and make sure it fits firmly against the face.
b. Hold the mask in place and actuate the pMDI as the child begin to breathe in slowly. Make sure to inhale slowly if the device produces a "whistle" indicating that inspiration is too rapid.
c. Hold the mask in place while the child takes six normal breaths (including inhalation and exhalation), then remove the mask from the child's face.
d. Wait 15–30 seconds if another puff of medicine is needed.
e. Repeat steps above until the dosage prescribed by the patient's physician is reached.
f. If taking a corticosteroid, rinse the mouth after the last puff of medicine, spit out the water, and do not swallow it.
g. Replace the mouthpiece cover on the pMDI after each use.

Note. Reprinted from Pulmonary disease aerosol delivery devices: a guide physicians, nurses, pharmacists, and other health care professional, 3rd ed. (p.36), by K. Gregory, L. Wilken, & M. Hart, 2017. Copyright [2017] by the American Association for Respiratory Care. Permission requested.

B. INTUBATED CHILDREN

Steps on how to use pMDI in ventilator-supported children:

1. Position patient in a semi-recumbent position (head of bed elevated to 20-30º).
2. Suction ETT and airway secretions using a closed suction catheter.
3. Shake pMDI and warm to hand temperature.
4. Place pMDI in the bidirectional in-line adapter connected to the inspiratory limb of the ventilator circuit about 15 cm from the ETT.
5. Remove the heat and moisture exchanger (HME), if used. Do not disconnect humidifier.
6. Ensure that there is no leak in the circuit.
7. Actuate pMDI at the beginning of inspiration.
8. Wait for at least 15 seconds between actuations; deliver total dose.
9. Observe the response.

Note. Adapted from "How should aerosols be delivered during invasive mechanical ventilation," by R. Dhand, 2017, Respiratory care, 62(10):1343–1367. Adapted with permission.

Remarks

The efficiency of drug delivered through pMDI varies widely. Thus, the importance of proper administration technique to ensure optimal drug delivery to the lungs. Studies have shown that aerosol deposition is influenced by the size of the endotracheal tube (ETT), heat and humidity, ventilator mode and settings, patient position, and location of the pMDI in the ventilator circuit.

The efficiency of aerosol deposition is lower with narrow ETT (<6 mm) due to impaction. A 40% to 60% reduction in drug delivery was observed when the internal diameter of the ETT was reduced from 6 to 4 mm.[175] Drug losses within the ETT may be minimized by placing the aerosol generator at a distance from the ETT rather than attaching it directly.[176]

When the aerosol is exposed to humidity, the particle size increases; thus, a greater amount of aerosol is lost, reducing drug delivery by 40% to 50%. A pediatric mechanical ventilation model showed that when humidity was changed from 54% to 100%, the mass median aerodynamic diameter (MMAD) of an hydrofluoroalkane formulation increased from 1.2 μm to 2.8 μm.[175] However, removing the humidifier is not routinely recommended as more time would be added to each treatment because it requires the disconnection of the ventilator circuit and allowing it to dry. Moreover, even with a humidified circuit, a significant effect was noted with as few as 4 puffs.[177]

Shaking of pMDI before administration was found to be important. The failure to shake a pMDI canister that has been standing overnight may decrease total emitted and respirable dose by as much as 25% and 35%, respectively.[178]

Ventilator mode and settings may influence drug delivery. Studies have shown that higher tidal volume, longer inspiratory time, and slower inspiratory flow rate improve aerosol delivery.[179,180] Moreover, drug delivery is improved when a pMDI is synchronized with a simulated spontaneous breath compared with a controlled ventilator breath of similar tidal volume. Significant results were also obtained when pMDI actuation is synchronized at the beginning of inspiration. Failure to synchronize would result in the reduction of inhaled drug mass by 35%.[181]

In ventilator-supported patients who are unable to sit upright during aerosol administration, several studies showed significant bronchodilator response when pMDI is administered in a semi-recumbent position with the head of the bed elevated to 20° to 30°.[177,182,183]

4.6 Different Types of Chamber/Adapters Used To Connect the Metered Dose Inhaler (MDI) Canister to The Ventilator Circuit

Recommendation 25
In ventilator-supported children, clinicians can consider using bidirectional in-line adapter when administering pMDI. This should be connected to the inspiratory limb of the ventilator tubing before the Y-piece. Unidirectional in-line and elbow adapters may be used as alternatives but are less effective.

(Weak recommendation, low-grade evidence [166,173]

Remarks

Actuator devices are adapters used to connect the pMDI canister to the ventilator circuit. The use of these devices can be considered to enable more efficient delivery of pMDI in intubated children. Several types are commercially available including chamber adapters (cylindrical and reservoir) and non-chamber adapters (inline and elbow) [*Figure 19*].

Chamber adapter requires removal of the adapter after delivery of the drug. Hence, this is not recommended for intubated COVID-19 patient. This procedure will lead to aerosol transmission of the virus.

Non-chamber adapters are recommended in the delivery of pMDI in intubated COVID-19 patients. As with bidirectional in-line adapter, it has a higher delivery efficiency when compared with unidirectional in-line adapter and is comparable with chamber spacers in performance.[184] The advantage of bidirectional in-line adapter over chamber adapters is that it is small hence dead space volume is expected to be minimal. This device can stay in-line, thereby avoiding disruption of the ventilator circuit prior to aerosol therapy.[184,185] Because of the aforementioned advantages, clinicians should consider using bidirectional in-line adapter to deliver pMDI for ventilator-supported patients to minimize the risk of aerosol transmission of the virus.

Connecting the pMDI and chamber in the inspiratory limb of the ventilator circuit before the Y-piece increases aerosol deposition with improved potential for clinical response. This was demonstrated in an in-vitro adult model of mechanical ventilation wherein they quantified the emitted dose of albuterol delivered distally to an ETT from three different positions. pMDI and chamber placed in the inspiratory limb 15 cm from the Y-piece (17.0±1.0%) showed the highest aerosol deposition when compared to placing the pMDI between ETT and Y-piece (7.6±1.3%), and 15 cm from the ventilator before the inlet of the humidifier (2.5±0.8%).[173]

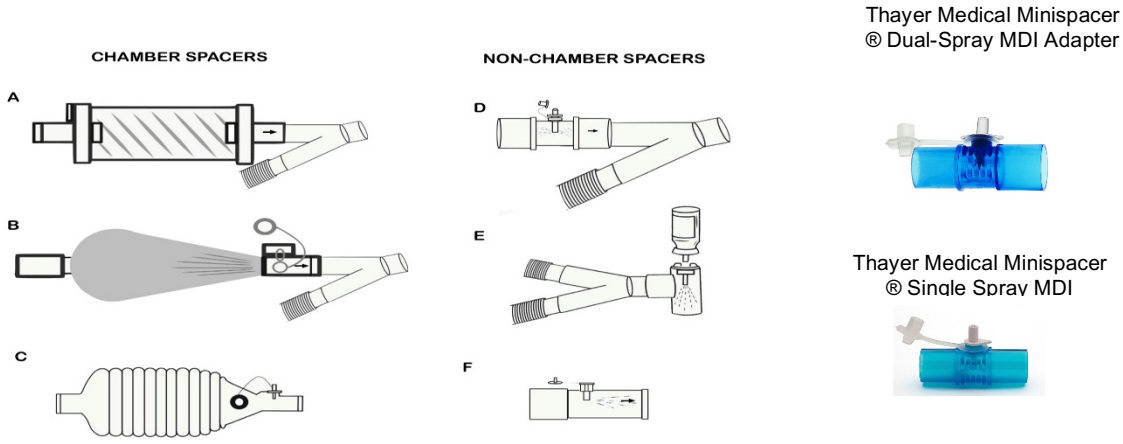


Figure 19. Different types of chamber/adapters used to connect the metered dose inhaler (MDI) canister to the ventilator circuit.
A, non-collapsible cylindrical chamber; **B**, aerosol cloud enhancer (ACE) spacer, with which the MDI flume is directed away from the patient; **C**, collapsible cylindrical chamber; **D**, bidirectional in-line adapter; **E**, elbow adapter; **F**, unidirectional in-line adapter. Modified from "Bronchodilator therapy in mechanically ventilated patients," by J.B. Fink, M.J. Tobin, & R, Dhand, 1999, *Respiratory care,* 44(1):53– 69. Modified with permission.

4.7. The Limited Use of Nebulizers Among Covid-19 Children

Recommendation 26
The use of nebulization for the delivery of B2 agonists among children having bronchospasm should only be used for limited specific situations under strict aerosol generating procedure protective measures and must be avoided as much as possible.

(Strong recommendation, low grade evidence)

The Limited Indications of Nebulization include[106]
1. Severe life-threatening respiratory distress,
2. Patients with compromised ventilation,
3. Uncooperative patients,
4. Children with poor response to pMDI

The full scope of the function and comparison of the different aerosol generators especially nebulizers are not included in this document, however, we would like to highlight the difference in their inherent designs implicating the plausible infection risks when these devices get contaminated with the exhaled breath of SARS-CoV2 infected persons or by breaks in aseptic technique during drug administration.

Nebulizers are divided into jet nebulizers (JN), electronic (ultrasonic) nebulizers and the vibrating mesh nebulizers (VMN).[146,147,152] The produced aerosol is from the liquid medication transformed into a 1-5 µm sized aerosol particle range to allowing deposition to the lower airways.[147] Nebulizers are under potential short-range aerosol transmission

sources.[107] Notably, aerosol plumes are seen as "smoke leak "from the mask's exhalation vents during nebulizer use. Fugitive aerosol release were reported hazards of nebulization, these are medical aerosols generated by aerosol devices, whereas bioaerosols are produced by patients.[110]

Jet nebulizers (JN) have an open cup design positioned below the gas pathway it is not impossible that contamination of the nebulizer cup with the virus-laden exhaled breath or cough droplet secretions from a COVID-19 patient could occur. Ultrasonic nebulizers were also reported to be potential sources of bacterial outbreaks [186],[187] Mesh nebulizers (VMN, has a mesh to separate its medication from the patient's interface reducing contamination risks during exhalation. Mesh nebulizers separate the medication from the patient interface through the mesh and have less residual volume (<0.5 mL) than jet nebulizers with a residual volume of ~2 mL, such liquids could potentially allow microbial growth in these devices.[147]

Fugitive-aerosol-emissions represent a potential-risk to both healthcare-providers and acute-care-environment.[161] This has been the main concern during the SARS-CoV epidemic whereby evidence of viral transmission to bystanders where seen[19, 188,189] Jet nebulizers are reported to disperse contaminated SAR-CoV aerosols to nearby surfaces where exhaled air leakage through the side vents of the jet nebulizer.[188.] Lesser fugitive aerosols were emitted during nebulization with the non-portable VMN than the jet nebulizers.[154] In a recent study examining the release of simulated patient derived bioaerosol, effect on positive end expiratory pressure during nebuliser refill during mechanical ventilation of a simulated patient and reported that JN and VMNs produced but the least emissions were noted with the use of VMN.[157] Breath-actuated nebulizers are jet nebulizers designed to increase aerosol drug delivery to patients by generating aerosol only during inspiration, has reduce fugitive emissions compared with nebulizers that operate continuously during the breathing cycle.[190]

The pMDI and DPI delivery systems are presented as having reduced risk compared with other medical aerosols may be because drug is enclosed and less open to contamination than open cup nebulizers, and the low emitted dose (100lL/actuation) produces less aerosol mass with shorter treatment times. [153,191] Characteristics of drug formulation can precipitate cough with both nebulizers and inhalers.[192] While exhaling into valved holding chambers (VHC) might decrease the dispersion of exhaled bioaerosol to the environment[110] though experimental studies for SARS-CoV-2 are still unavailable.

The choice of aerosol therapy for children confirmed or suspected of COVID-19 need the mindful understanding of the benefits and risks to the patient. If the patient needs inhaled drug therapy, in a format other than the pMDI,or DPI, or soft mist inhaler , nebulization should be done under controlled conditions to mitigate the risks of second hand exposure of fugitive emissions and surface contamination from the procedure. The following are the suggestions on how to perform nebulization when indicated during this pandemic.

Precautions in the limited use of nebulization during the COVID19 pandemic:

Pre- nebulization

- ✓ Prepare a well ventilated room with a minimum of 6-12 air changes per hour these can be achieved with window opening or a portable HEPA unit can be placed in the room.[193] In the healthcare settings ,in cases of patients in cohort groups admitted in the COVID19 ward, they need to be moved to a negative pressure room if available or to a separate well ventilated room for delivery of nebulization.
- ✓ There should be only one patient in the room. For young children, limit to one person who will accompany the patient who is a healthy adult and is wearing a sealed surgical mask.
- ✓ For caregivers who will administer the inhaled drug, thoroughly wash hands before drug administration. For Healthcare workers, first wash hand thoroughly, don personal protective equipment (PPE) for aerosol and droplet protection, including an N95 mask, face shield, gown, and gloves
- ✓ Incorporation of the doctor prescribed liquid medication to the nebulization cup should be done aseptically. In mechanically ventilated patients follow previously discussed precautions.
- ✓ Have the patient sit upright.
- ✓ Preferably use the mouthpiece as interface and place a filter on the exhalation part of a nebulizer *(see Figure 2*0a *& 20b)* to provide protection from infection and reduce secondhand aerosol breathing in hospitals and outpatient clinics. A surgical mask maybe placed over the patient during the procedure especially those coughing and crying children during the procedure.
- ✓ Single patient device use is recommended.

During nebulization

- ✓ During nebulization, all non-essential personnel should leave the room and should not enter the room for three hours to allow removal of infectious particles.
- ✓ Should the HCW need to stay in the room, a distance of 3 feet away from the patient is advised.
- ✓ If the patient requires a break from nebulization, turn off the nebulizer then complete the entire dose prescribed by the doctor.

After nebulization

- ✓ Discard remaining residual liquid from the nebulizer cup. Clean and disinfect the nebulizer equipment per manufacturer's advice and dispose the non-reusable parts after each procedure.[194] Clean room surfaces promptly after each procedure as SARS-CoV2 are found in hospital objects and medical equipment.
- ✓ Wash hands thoroughly after leaving the patient

In local hospital settings, the procurement of aerosol generators with lesser risks of viral transmission like pressurized metered-dose inhalers and the respective interface and adaptor supplies is needed. Nebulizer s like the vibrating mesh nebulizer models for those with NIV or mechanically ventilated COVID-19 patients must be prioritized. It was stated that pMDI and DPI delivery systems are the most convenient and provide the lowest cost dose, they should be the first choice of clinicians,[195] and these must be given to those who can tolerate its use. As the pandemic trudges on, it is still best to minimize aerosol treatment among confirmed or suspected COVID-19 patients unless necessary. Should caregivers attend to children needing such this should be done with adherence to the above stated precautions until robust data proves this recommendation otherwise.

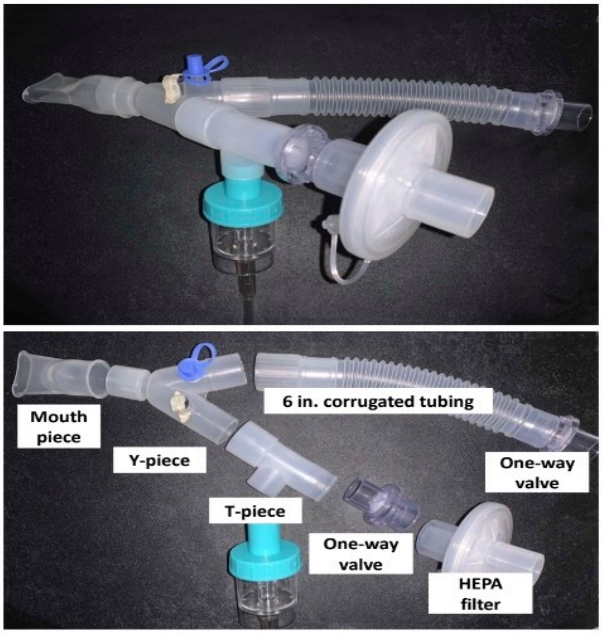
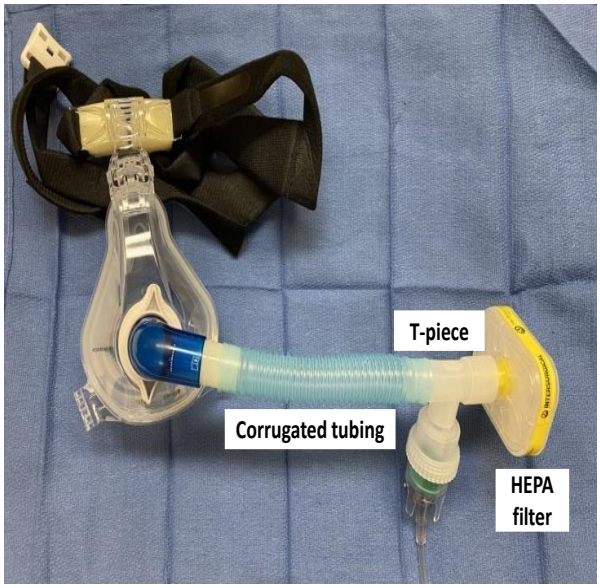


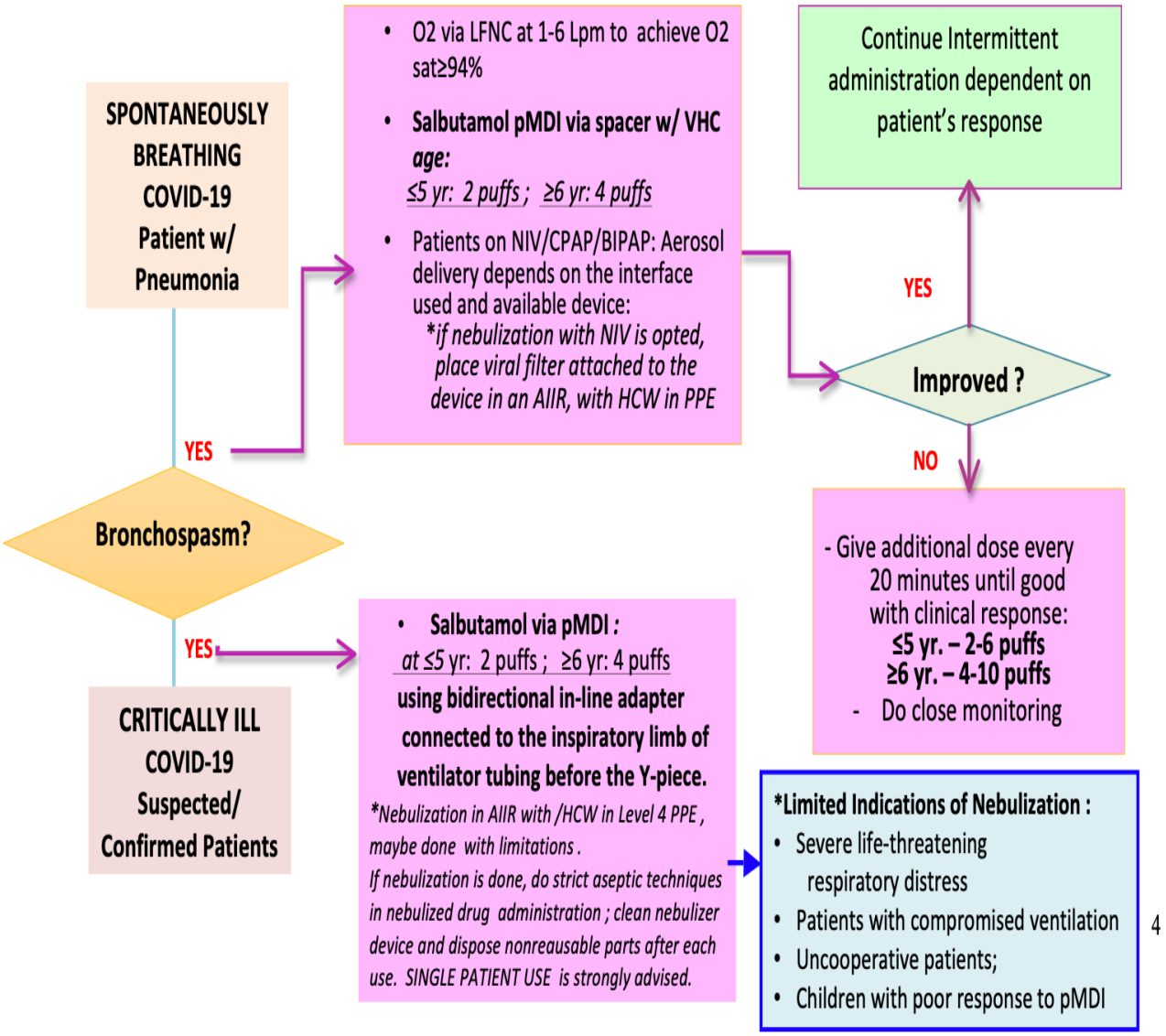
Figure 20a. *Nebulizer attached with HEPA filter for a cooperative patient via a mouthpiece. This is a suggested set-up for COVID-19 patients and is an adjunct to the safety practice points during the limited use of nebulization as stated above.*



Weingart, S. (2020, March 27). COVID Airway Management Thoughts. Retrieved from https://emcrit.org/emcrit/covid-airway-management/

Figure 20b. *HEPA filter in a single limb circuit for a patient with non-invasive ventilation via a face mask.*

ALGORITHM 3. AEROSOL THERAPY FOR COVID-19 SUSPECTED/CONFIRMED CHILDREN *WITH BRONCHOSPASM*



4

4.8 Airway Clearance Therapies

Recommendation 27
For airway clearance procedures, we strongly recommend the following strategies among pediatric COVID-19 patients:

1. Ensuring adequate oxygenation, keeping the respiratory tract unobstructed
2. Appropriate inhalation therapy
3. Appropriate reassessment of airway patency
4. Non-invasive/invasive respiratory support and mechanical ventilation
5. Judicious use of fluids and vasoactive medications

(Strong recommendations, high grade evidence)

Remarks

Thomas, et. al. highlighted key concepts in the principles of physiotherapy among patients with confirmed or suspected COVID-19. Based on the authors, physiotherapy management should be evaluated on a case-to-case basis based on the patient's medical indications; patients who may benefit from physiotherapy include COVID-19 patients with copious airway secretions which they not be able to clear on their own, high-risk patients with neuromuscular disorders and other co-morbid illnesses which result in increased mucus production or weak cough, as well as mechanically ventilated patients with inadequate airway clearance.COVID-19 patients may also be referred for respiratory physiotherapy if they have severe symptoms of pneumonia or with chest imaging findings showing consolidation.[170]

Positioning, active cycle of breathing, manual and/or ventilator hyperinflation, percussion and vibrations, positive expiratory pressure therapy, cough maneuvers, and airway suctioning are some examples of respiratory physiotherapy techniques that may be useful in aiding airway clearance for Covid-19 patients.[170] Other respiratory support techniques stated by Barentz, et al include breathing control, thoracic expansion exercises, and respiratory muscle strength training. However, the authors emphasized that because of aerosolization and exposure risks, these interventions should only be provided when clinically indicated.[196] A position paper by the Italian Association of Respiratory Physiotherapists also state similar precautions because aerosolization risk.[197] The said paper recommends that airway clearance procedures may be done only when needed and are not frequently required in COVID-19 patients.

Because of risk of aerosolization while performing respiratory physiotherapy procedures for COVID-19 patients, the risks versus benefits should be carefully measured before proceeding with these interventions on a case-to-case basis. Examples of potentially aerosol-generating respiratory physiotherapy procedures include the following: cough-generating procedures, techniques for gravity-assisted drainage or techniques and manual procedures such as expiratory vibrations, percussion or manually-assisted cough and use of positive-pressure breathing devices. Open suctioning, nasopharyngeal or oropharyngeal suctioning, manual hyperinflation, sputum induction and mobilization techniques which result in coughing of the patient likewise pose risks of aerosolization.[170]

In a report of 2 mechanically ventilated pediatric patients with COVID-19, Schaan, et al reported benefits of airway clearance techniques. For one patient, the following maneuvers were performed: compression/decompression, prolonged slow expiration, manual hyperinflation (MH) with self-inflating bag and bag squeezing) were performed, with the goals of maintaining pulmonary expandability and bronchial toilette; while for the second patient, chest physiotherapy, including airway clearance through aspiration of endotracheal tube, and compression/decompression techniques were used. Both patients showed improvement in ventilation and functional status.[198] Similarly, in a review by Magalhaes, airway clearance therapies should be only performed when strictly indicated [199] The WHO recommends that in patients with excessive secretions or difficulty clearing secretions, consider application of airway clearance techniques. These should be performed only if deemed medically appropriate and appropriate infection prevention control measures are in place. [64]

It is recommend that airborne precautions should be observed for health care workers performing aerosol-generating interventions among patients with COVID-19, this include use of the following personal protective equipment (PPE): N95/P2 mask, long-sleeved, fluid-resistant gown, face shield or goggles, gloves, hair cover and liquid-impermeable shoes.[147]

Chapter 5

5.1. Discharge and Ending Isolation of Pediatric COVID-19 Patients

Recommendation 28

We strongly recommend that based on the Department of Health (DOH) updated guidelines for discharge and ending isolation[200]:

(1) Patients with at least moderate severity of COVID-19 illness (moderate, severe or critical) who have fulfilled **at least 21 days** of **isolation**, inclusive of 3 days of being asymptomatic can be discharged.
(2) Patients with mild symptoms and completed **at least 10** days of isolation from start of illness inclusive of 3 days of being asymptomatic can be discharged.
(3) Patients with positive SARS-CoV-2 PCR test but were asymptomatic, and remain asymptomatic for **at least 10 days** from the day the specimen was collected can discontinue isolation after 10 days.
(4) Close contacts of patients with COVID-19 who are asymptomatic and remain to be so for **at least 14 days** from date of exposure can discontinue quarantine.

We also recommend that in line with the DOH recommendations, a patient should be cleared by a licensed physician as a pre-requisite to discharge; and that repeat testing for COVID-19 is not required as part the aforementioned medical clearance. Once discharge criteria are met, confirmed cases of COVID of any disease severity can be labeled as recovered. [200]

Remarks

Based on the Department of Health (DOH) Revised Omnibus Interim Guidelines on the Prevention, Detection Isolation, Treatment and Reintegration Strategies for COVID-19 released last November 20, 2020, [200] repeat testing for COVID-19 is no longer required as part of the discharge criteria and should not be a requirement for the granting of medical clearance.

Close contacts of patients with COVID-19 who were asymptomatic for at least 14 days starting from the date of exposure can discontinue quarantine without the need for any test. Upon discharge and discontinue of quarantine, physicians should still advise recovered patients to be vigilant against the disease and to observe minimum health standards of proper wearing of face masks and face shields, social distancing, frequent handwashing and ample ventilation.

Discontinuation of Transmission Based Precautions [64,143]

Among patients with mild to moderate illness who are not severely immunocompromised, symptom-based strategy include the following: (1) at least 10 days have passed since symptoms first appeared and (2) at least 24 hours have passed since

last fever without the use of fever-reducing medications and (3) COVID-19 Symptoms have improved. Furthermore, "for patients who are **not severely immunocompromised and who were asymptomatic** throughout their infection, transmission-based precautions may be discontinued when at least 10 days have passed since the date of their first positive viral diagnostic test." [143] Among patients with severe to critical COVID illness who are severely immunocompromised, that the recommended duration for Transmission-Based Precautions was changed to at least 10 days and up to 20 days after symptom onset for patients. Another pertinent update with regards to the discontinuation of transmission-based precautions is to consider consultation with infection control experts.[143]

Home Care Precautions

As discussed in Chapter 2, caring for a COVID patient at home, will require caregivers to observe hand hygiene, wearing of face masks, cleaning or disinfecting the home, setting aside bedding and utensils for the patient's own use, as well as avoiding contact with bodily fluids or secretions and using gloves while handling dishes of the patient.[144] Home isolation will include separation with avoidance of exposure from other household members , however, if this is not possible and the patient is in a shared space, good air flow should be ensured, windows can be maintained open to improve ventilation. Having visitors over at the home of the patient should also be avoided. [144-145]

Current guidelines on discharge and isolation are evolving based on the local protocols and recent available scientific evidence, knowledge and understanding of this novel disease, hence these recommendations may also change over time.

5.2 Home Care Post Discharge

Post-acute COVID-19 Syndrome has been reported in children who recovered from the illness. It is important for clinicians to consider this newly evolving disease complication of COVID-19 in these children.[55-57] Caregivers should be made aware that the spectrum of symptoms like tiredness/weakness, fatigue, chest pain, palpitation, headache, dizziness, abdominal pain, muscle pain, rash are included in this complication. Proper and timely management can be made if symptoms are identified which may also include short term memory loss and other neuropsychiatric manifestations.

The child who has recovered from COVID-19 after clearance from their attending physician should continue their chronic medications as prescribed. Vaccinations for age need to be received as per discretion of the attending physician of these children . Those who require physiotherapy and home oxygen support are suggested to continue these therapies with close medical follow up.

Chapter 6

6. PULMONARY CARE IN SPECIAL SITUATIONS OF PEDIATRIC COVID-19

6.1. ASTHMA IN CHILDREN DURING THE COVID-19 PANDEMIC

Recommendation Points for Asthma in Children
By the Philippine Academy of Pediatric Pulmonologists Asthma Committee

Recommendation 29A

1. Asthma patients on maintenance medications are advised to continue treatment as prescribed
2. Monitor asthma symptom control and risk factors for poor asthma outcomes which may require adjustment of medications.
3. Nebulization is discouraged because it can generate aerosol particles which increase the spread of the SAR-CoV2 virus. Inhaled medications must be administered using pressurized metered dose inhaler (pMDI) via spacers or valve holding chambers.
4. In limited situations when nebulization is absolutely necessary, the use of appropriate infection control measures should be strictly followed.
5. Single patient device use must be observed at all times.
6. Pediatricians may use the asthma action plan to educate guardians/parents in identifying asthma symptoms while at home and guide corresponding action to specific clinical situations. Please see the Asthma Action Plan below
7. When available, COVID-19 vaccination is recommended for pediatric patients with asthma. Usual vaccine precautions should apply.
8. Routine spirometry testing is not advisable to decrease the risk of viral transmission. Should this be done infection strict contact and airborne precautions must be instituted.

Recommendation 29B

The administration of existing medications for asthma controller medications should be continued for pediatric patients with asthma during the COVID-19 pandemic.
(Strong recommendations, moderate grade evidence)

6.1.1 Use of Inhaled Corticosteroids as Asthma Controller Medication

Remarks

Asthmatic patients have not been shown to have increased risk of COVID-19 infection and death. However, an increased risk of COVID-19 death was found to be associated with those recently given oral corticosteroids for acute attacks. Therefore, medications and strategies to maintain good asthma control, reduce risk of severe exacerbations as well as

need for oral corticosteroids is of utmost importance. Discontinuing controller medications, such as ICS, for asthmatic patients may lead to poor symptom control thereby increasing the risk for complications of COVID-19 leading to associated need for interaction with the health care system.

6.1.2. Use of Systemic Corticosteroids During an Acute Exacerbation

Patients with COVID-19 infection and a concomitant acute exacerbation of asthma and COPD should receive prompt treatment with short term systemic glucocorticoids as indicated by usual guidelines. Delaying therapy can increase the risk of a life-threatening exacerbation.

There is currently no evidence to suggest that short-term use of systemic corticosteroids to treat asthma exacerbations increases the risk of developing severe COVID-19, Overall, the known benefits of systemic glucocorticoids for acute exacerbations of asthma and COPD outweigh the potential harm in COVID-19. [202]

The short course of oral corticosteroids (OCS) doses include: (GINA Report 2020)

Children less than 5-year-old

a. A dose of OCS equivalent to prednisolone 1–2 mg/kg/day, with a maximum of 20 mg/day for children under 2 years of age and 30 mg/day for children aged 2–5 years,
b. A course of 3–5 days being sufficient in most children of this age, and can be stopped without tapering but the child must be reviewed after discharge from the emergency room department.

Children 6-year-old to 11-year-old

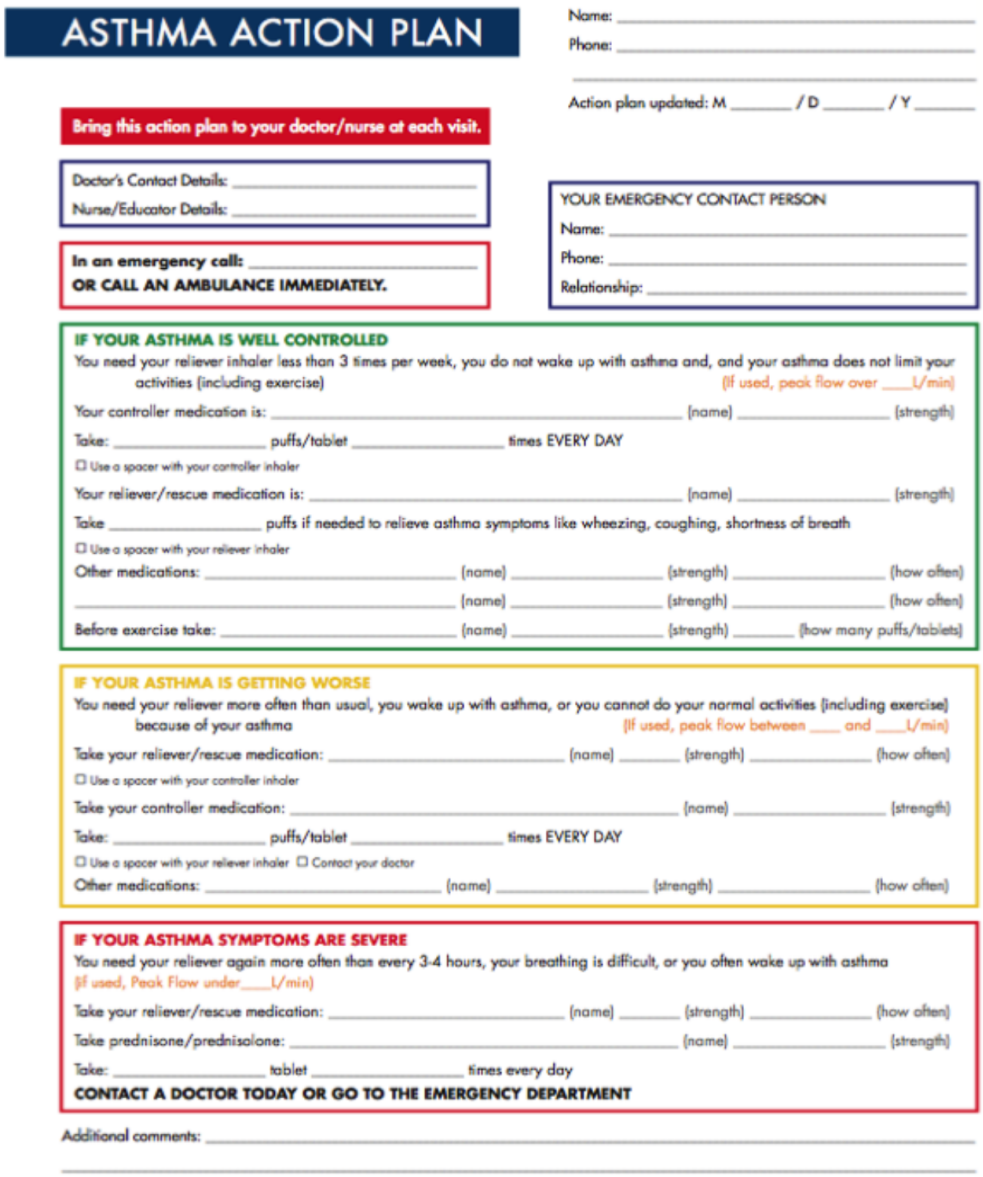
a. For children 6–11 years, the recommended dose of OCS is 1–2 mg/kg/day to a maximum of 40 mg/day, usually for 3–5 days. Patients should contact their doctor if they start taking OCS.
b. Dose of 40–50 mg/day usually for 5–7 days for patients who:
    - Fail to respond to an increase in reliever and controller medication for 2–3 days.
    - Deteriorate rapidly or who have a PEF or FEV1 <60% of their personal best or predicted value.
    - Have a history of sudden severe exacerbations.

When indicated inhaled medications during exacerbations or bronchospasms, the preferred mode of aerosol therapy will be the use of pressurized metered-dose inhalers (pMDIs) over nebulizer use to limit transmission of potentially viable COVID-19 aerosolized droplets to susceptible bystander hosts.

6.1.3 The Asthma Action Plan

The GINA 2020 and the GINA 2021 Report recommends the provision of a written Asthma Action Plan for each child with asthma. This helps patients to recognize and respond appropriately to worsening asthma. It should include specific instructions for the patient about changes to reliever and controller medications, how to use oral corticosteroids (OCS) if needed and when and how to access medical care.[104-105]

Figure21: ASTHMA ACTION PLAN



ASTHMA ACTION PLAN

Name: _____
Phone: _____
_____
Action plan updated: M _____ / D _____ / Y _____

Bring this action plan to your doctor/nurse at each visit.

Doctor's Contact Details: _____
Nurse/Educator Details: _____

In an emergency call: _____
OR CALL AN AMBULANCE IMMEDIATELY.

YOUR EMERGENCY CONTACT PERSON
Name: _____
Phone: _____
Relationship: _____

IF YOUR ASTHMA IS WELL CONTROLLED
You need your reliever inhaler less than 3 times per week, you do not wake up with asthma and, and your asthma does not limit your activities (including exercise) (If used, peak flow over ____L/min)
Your controller medication is: _____ (name) _____ (strength)
Take: _____ puffs/tablet _____ times EVERY DAY
☐ Use a spacer with your controller inhaler
Your reliever/rescue medication is: _____ (name) _____ (strength)
Take _____ puffs if needed to relieve asthma symptoms like wheezing, coughing, shortness of breath
☐ Use a spacer with your reliever inhaler
Other medications: _____ (name) _____ (strength) _____ (how often)
_____ (name) _____ (strength) _____ (how often)
Before exercise take: _____ (name) _____ (strength) _____ (how many puffs/tablets)

IF YOUR ASTHMA IS GETTING WORSE
You need your reliever more often than usual, you wake up with asthma, or you cannot do your normal activities (including exercise) because of your asthma (If used, peak flow between ____ and ____L/min)
Take your reliever/rescue medication: _____ (name) _____ (strength) _____ (how often)
☐ Use a spacer with your controller inhaler
Take your controller medication: _____ (name) _____ (strength)
Take: _____ puffs/tablet _____ times EVERY DAY
☐ Use a spacer with your reliever inhaler ☐ Contact your doctor
Other medications: _____ (name) _____ (strength) _____ (how often)

IF YOUR ASTHMA SYMPTOMS ARE SEVERE
You need your reliever again more often than every 3-4 hours, your breathing is difficult, or you often wake up with asthma
(If used, Peak Flow under____L/min)
Take your reliever/rescue medication: _____ (name) _____ (strength) _____ (how often)
Take prednisone/prednisolone: _____ (name) _____ (strength)
Take: _____ tablet _____ times every day
CONTACT A DOCTOR TODAY OR GO TO THE EMERGENCY DEPARTMENT

Additional comments: _____
_____

6.1.4 Asthma and vaccines[105]

Annual influenza vaccination is recommended for asthmatic patients, more so during this pandemic. For COVID-19 vaccination, once already available for the pediatric population, it is recommended to be given as the benefits outweigh possible risks. An interval of fourteen (14) days between both vaccines is recommended.

PULMONARY TUBERCULOSIS IN CHILDREN DURING COVID-19 PANDEMIC

By The PAPP Task Force in Childhood TB 2019-2021

Tuberculosis (TB) is one of the top ten ranking communicable disease causing death globally.[203] Worldwide, approximately 10M people were ill with TB, 11% of which were children.2 Childhood TB have caused significant illness and death in TB endemic countries wherein at least 550,000 children get sick with TB yearly.

Pulmonary TB accounts for 70-80% of these.[204] In 2018, most TB cases take place in South East Asia (44%), Africa (24%), Western Pacific (18%), Eastern Mediterranean (8%), America (3%) and Europe (3%). Two thirds of the world's population of TB comprise of eight countries represented by India (27%), China (9%), Indonesia (8%), Philippines and Pakistan (both 6%), Nigeria and Bangladesh (both 4%) and South Africa (3%).[205] While the Philippines at 8%, is one of one of the ten countries accounting for about 80% of the global gap between the number of cases reported (7M) and the number of incidence (10M) in 2018, this gap is primarily due to inability to access health care services (under-reporting) or are inadequately diagnosed (under-diagnosis).[206,207]

Recommendation 30

1. Preventive measures should be observed by a patient with pediatric TB and the healthcare staff attending to them.
   (*Strong recommendations, very low grade evidence)*

2. TB testing should continue during the COVID-19 pandemic.
   (Strong recommendations, low-moderate grade evidence)

3. When available COVID-19 vaccine be given to adolescents, testing with TST or IGRA must be done before or at the same time during COVID-19 vaccination, otherwise, delay the test ≥4 weeks after the completion of COVID-19 vaccination.[217]
   (Strong recommendations, moderate grade evidence as appraised)

4. In COVID-19 patients with Latent TB Infection, TB preventive therapy (TPT) should be initiated and completed, with options on shorter rifamycin- containing preventive regimens.
   (Strong recommendations, low-moderate grade evidence)

6.2.1.a Actions to be taken by person with TB during COVID-19 pandemic.[208, 209]

1. Social distancing as "reverse-quarantine" (a person with weakened immunity/ high risk person is kept away from exposure to people with probable/ suspect and/or confirmed COVID-19) by staying at home as much as possible.
2. Regular use of masks, and maintain hygiene such as disinfection of hands with at least 60% ethanol or 70% isopropanol, of surfaces, and proper waste management (i.e. yellow bag for infectious wastes).
3. Avoid touching face, mouth, eyes, nose with unwashed hands.
4. Observe cough etiquette.
5. Home-based treatment. Strict compliance to one's TB treatment by securing multiple months of TB medicines made available at home. TB patients will more likely start TB treatment at home. It is important to limit TB transmission among household especially during the first few weeks.
6. Avoid hospital visits if possible as not to congest as well as prevent possible exposure to COVID-19.
7. Maintain communication with your TB doctor/ nurse/ health facility by phone or other digital technology available to manage unforeseen conditions such as adverse reactions and occurrence of comorbid conditions, counsel on nutritional and mental health issues and the need to restock medicines.

6.2.1.b. Actions to be taken by staff working in TB laboratories, healthcare facilities and community healthcare workers during COVID-19 pandemic.[208,209]

1. Reduce TB follow up visits.
   a. Spreading appointments to avoid exposure to other clinic attendees.
   b. Maximize use of communication technologies such as mobile and/ or computers using accessible virtual telehealth platforms to conduct case-findings, diagnosis, contact investigations as well as maintain treatment support.
   c. Limit visits only during follow-up testing as scheduled.
2. Provide sufficient amount of TB medicines. Dispense TB medicines for consumption until the next planned visit or until end of treatment if no follow up visit is needed. This will avoid interruption of TB treatment and unnecessary visits.
3. Special precautions on sputum collection and transport.
   a. Done preferably at home in open spaces away from others.
      If not possible at home, sputum collection must be in an open, well-ventilated space outside the health facility with the staff far from the patient during the sputum collection.
4. Infection prevention control measures.
   a. Bio-safety cabinets are preferred when available.
   b. Consistent proper hand washing.
   c. Use of personal protective equipment (gloves, N95 mask, goggles, face protection shields, hazmat suits).
   d. Regular disinfection of surfaces.
   e. Staff distancing.
   f. Well ventilated workspaces.
   g. Safe transportation.

6.2.2. TB Testing must continue during COVID-19 pandemic [208]

The diagnosis for both TB and CoVID-19 are equally important. Concurrent testing for both TB and COVID-19 is indicated depending on the clinical signs and symptoms, simultaneous exposure to both disease and/or presence of a risk factor for poor outcomes to either disease.[208] TB and COVID-19 have similarities and differences. Both are spread by close contact between people and both involve the lungs presenting with cough, fever, and difficulty of breathing. They differ in the size of droplet nuclei, determining its infectiousness, and the mode of transmission. While droplet nuclei of 1-5 μ in diameter containing TB bacilli remain suspended in air for hours and people gets infected upon its inhalation, COVID-19 with 0.1μm in diameter, on the other hand, is transmitted by droplet and airborne transmission, directly from an infected person and indirectly through fomites.[210]

Further on, COVID-19 has an acute onset, which may present initially as dry cough among mild uncomplicated cases, while TB occurs in a more chronic pattern. The transmission of COVID-19 may be within a few days to two weeks within the

household or congregate setting while in TB, its course can take several months. TB diagnosis in a COVID-19 patient may be considered when patient clinically presents with hemoptysis, persistent fever, night sweats or weight loss in addition to history of TB exposure or previous TB disease.

As a person infected with COVID-19 cannot rule out TB disease especially in high TB burden countries, simultaneous testing for both diseases to prevent missed TB cases has been recommended by the WHO. It is worth taking into consideration, despite minimal evidences for now, that the presence of TB puts the person at high risk for severe COVID19 illness and death.[211,212,213,214,215]

During this trying time of COVID-19 pandemic, WHO strongly reiterates the scaling up of access to rapid molecular tests such as Xpert MTB/Rif assays and GeneXpert Ultra assay as the initial test to the diagnosis of pulmonary TB and drug-resistant TB which replace smear microscopy and culture.[216]

6.2.3. When testing with TST or IGRA cannot be done before or at the same time during COVID-19 vaccination, delay these tests to a minimum of 4 weeks after the completion of COVID-19 vaccination but not canceled.[217]

Testing for TB infection with either the tuberculin skin test (TST) or an interferon release assay (IGRA) do not alter the safety or the effectiveness of COVID-19 vaccine. COVID-19 vaccination is not likely to cause false positive TB test done at the same time as or 4 weeks after COVID-19 vaccination if an adolescent visiting the pediatric clinic need TST or IGRA testing and is also scheduled to receive COVID-19 vaccine,

When delay in at least 4 weeks cannot be followed, (like for example admission to long-term care or for people at high risk for progression to TB disease), a false negative TST or IGRA cannot be excluded. Retesting negative TST or IGRA tests > 4 weeks after the completion of COVID-19 vaccination is recommended. If TST was the initial test, boosting could be a factor if the result of the repeat test is positive. As of this writing however, there are yet no guidelines for COVID vaccination for children younger than 18yo in the Philippines.

6.2.4. In COVID-19 patients with Latent TB infection, TB preventive therapy (TPT) must be initiated and completed, with options on shorter rifampicin- containing preventive regimens.[208, 218]

The *WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment* considers the primary intervention for latent TB infection is TB preventive therapy (TPT) to avert progression into an active TB disease. TB infection will develop into TB disease over a lifetime in 5-10% and TB preventive therapy decreases the probability of progressing to TB disease by 60-90%.[219]Forum of International Respiratory Societies (FIRS) strongly advocates TB prevention as an essential step towards ending TB.[220]

Recommended approach to diagnose TB in children*

1. History of exposure
2. Clinical signs and symptoms of at least 2 weeks duration of cough, unexplained fever, unexplained weight loss, and night sweats

**Clinical diagnosis is more relied upon especially in young children.*

Diagnostic tests indicated in the evaluation of presumptive TB**

1. Chest radiograph
2. Tuberculin skin testing 5TU - for less than 2 years old
3. Interferon Gamma Release Assay (IGRA) - for 2year old and above
4. HIV test

- Routinely done in assessment of a child with suspected TB.
- HIV is a risk factor for TB disease and a susceptibility for a severe TB disease;

* Antiretroviral therapy (ART) initiated at once when positive

** Lack of availability of TB diagnostic test should not delay the diagnosis of TB in children.

Diagnostic tests for bacteriological confirmation of TB in children and adolescents with presumptive TB***

1. Xpert MTB/Rif assay

- Specimen: sputum, nasopharyngeal aspirate, gastric aspirate and stool
- Higher sensitivity and specificity than DSM; detects rifampicin resistant TB. (or presumptive MDRTB)

2. Xpert MTB/Rif Ultra assay (new, 2019)

- Specimen: sputum, nasopharyngeal aspirate, gastric aspirate and stool
- Higher sensitivity than Xpert MTB/Rif; also detects rifampicin resistance
- A rapid test recommended during COVID19 pandemic

3. Xpert MTB/XDR (new, 2020)

- Detects resistance to isoniazid and fluoroquinolones; a rapid test recommended during COVID19 pandemic

4. Direct smear microscopy

- Specimen: expectorated sputum, gastric aspirate
- Low sensitivity and yield among young children, becomes higher among adolescents

5. Culture and drug susceptibility testing

- Gold standard with highest sensitivity however, in children, reaches only as much as 50% sensitivity; detects resistance to wide range of drugs

*** Bacteriologic confirmation must be done when possible, but a negative diagnostic test does not exclude TB in children.

Pulmonary TB As the initial diagnostic test for TB and rifampicin-resistant detection in children with signs and symptoms of Pulmonary TB, WHO strongly recommend using:

1. Xpert MTB/Rif in sputum *(moderate certainty for test accuracy),* in nasopharyngeal aspirate, gastric aspirate and stool *(low certainty for test accuracy)* rather than DSM/ culture and phenotypic DST.[216]
2. Xpert Ultra in sputum (*low certainty for test accuracy)* and in nasopharyngeal aspirates (*very low certainty of evidence for test accuracy)* rather than the DSM/ culture and phenotypic DST.[216]

TB Meningitis As the initial diagnostic test for TB and rifampicin-resistant detection in adults and children with signs and symptoms of TB meningitis, WHO strongly recommends using Xpert MTB/Rif (*moderate certainty for accuracy)* or Xpert Ultra (*low certainty for accuracy)* in cerebrospinal fluid (CSF) rather than DSM/culture.[216]

Extrapulmonary TB (EPTB) As the initial diagnostic test for EPTB in adults and children with signs and symptoms of EPTB, WHO has conditional recommendation for Xpert MTB/Rif in pleural fluid *(moderate certainty for accuracy),* in lymph node aspirate, peritoneal fluid, synovial fluid and urine *(low certainty of evidence for test accuracy)* and in pericardial fluid, lymph node biopsy *(very low certainty).*[216]

Five (5) Recommended TB Preventive treatment options

1. Six or nine months of daily isoniazid (6H or 9H)*
2. Three months of weekly rifapentine plus isoniazid (3HP)*
3. Three months of daily isoniazid plus rifampicin (3HR)*
4. One months of daily rifapentine plus isoniazid (1HP)**
5. Four months daily rifampicin (4R)**

* Strong recommendation, moderate to high certainty in the estimates of effect.
** Conditional recommendation, low to moderate certainty in the estimates of effect.

TB Preventive treatment for PLHIV

1. Thirty-six months of daily IPT***

MDR-TB Preventive treatment

1. Six months of daily levofloxacin

*** In settings with high TB transmission, adults and adolescents PLHIV with unknown or positive LTBI test and unlikely to have active TB disease; conditional recommendation, low to moderate certainty in the estimates of effect.

Table 19A : Recommended dosages for TB preventive treatment*

Regimen	Age < 10 years	Age > 10 years
6 or 9 months of daily isoniazid (6H, 9H)	10 mg/kg/day (range 7-15mg)	5 mg/kg/day
4 months daily rifampicin (4R)	15 mg/kg/day (range, 10-20 mg)	10 mg/kg/day
3 months of daily rifampicin plus isoniazid (3HR)	(R) 15 mg/kg/day (range, 10-20mg) (H) 10 mg/kg/day (range, 7-15 mg)	10 mg/kg/day 5 mg/kg/day

**WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment.[198]*

Table 19B : Rifapentine -containing TB Preventive Treatment*

	Age 2 - 14 years		Age above 14 years	
	Isoniazid, 100mg	**Rifapentine, 150mg**	**Isoniazid, 300mg**	**Rifapentine, 150mg**
3 months weekly rifapentine plus isoniazid **(12 doses, 3HP)**	10-15 kg: 3 16-23 kg: 5 24-30 kg: 6 31-34 kg: 7 >34 kg: 7	10-15 kg: 2 16-23 kg: 3 24-30 kg: 3 31-34 kg: 5 >34 kg: 5	30-35 kg: 3 36-45 kg: 3 40-55 kg: 3 56-70 kg: 3 >70 kg: 3	30-35 kg: 6 36-45 kg: 6 40-55 kg: 6 56-70 kg: 6 >70 kg: 6
1-month daily RPT plus INH (28 doses, 1HP)	Age > 13 years (regardless of weight band) Isoniazid, 300mg/day Rifapentine, 600mg/day			

**WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment[218].*

Table 19C : Levofloxacin-containing TB Preventive Treatment (TPT)*

	Age < 15 years	Age > 14 years by body weight:
6 months daily levofloxacin (MDR-TB preventive treatment)	**(range, approx. 15-20 mg/kg/day)** **5-9 kg: 150mg/day** **10-15 kg: 200-300 mg/day** **16-23 kg: 300-400 mg/day** 24-34 kg: 500-750 mg/day	**<46 kg: 750mg/day** >45 kg: 1 gram/day

**WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment.[218]*

Isoniazid and Rifampicin can be used in individuals of all ages. 3HP regimen is recommended only for children ages 2 years and older as there are limited data on the efficacy and safety of Rifapentine in children less than 2 years. Pyridoxine (vitamin B6) must be given to children and adolescents at risk for peripheral neuropathy when taking isoniazid (i.e. malnutrition, chronic alcohol dependence, HIV infection, renal failure, diabetes, pregnant or breastfeeding).

TPT regimens are generally safe though adverse reactions may be observed with isoniazid (i.e. hypersensitivity reactions, gastrointestinal disturbance, peripheral neuropathy and asymptomatic increase serum liver enzymes or hepatotoxicity) and rifampicin and rifapentine (i.e. hypersensitivity reactions, cutaneous reactions, gastrointestinal disturbance and hepatotoxicity) which may be manifested as anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark- colored urine, pale stools, jaundice, confusion and drowsiness. In such cases, the healthcare provider must be contacted upon and if fails to do so, patient should stop treatment immediately. All efforts must be taken to seek the healthcare provider's advice. Rifampicin-resistant TB (RR-TB) are usually treated with 6 months fluoroquinolone unless Isoniazid-susceptibility in the index case has been confirmed, in which case IPT may be equally effective.[209]

Surveillance of adherence towards completion of TPT is essential and may be done through an electronic application for mobile phones created by WHO. This could also be used for early identification of patients developing active TB disease while on TPT or even those who have completed TPT. For those with MDR-TB exposures, closely monitor their clinical progression to active TB disease for at least 2 years after the exposure regardless whether MDR-TB preventive treatment was given or not.[218]

6.2.5 In patients with active TB disease co-infected with COVID-19, TB treatment must be continued.

Access to TB Diagnosis and treatment must be continuously available, monitored and engaged upon during the COVID-19 pandemic. The services for TB diagnosis and treatment must be available during the COVID-19 pandemic with strict implementation of WHO basic infection prevention and control.

Table 20: Current Recommendation on TB treatment Regimens in Children[221]

TB Category	Intensive Phase	Continuation Phase
Smear or Xpert-negative pulmonary TB; Intrathoracic lymph node TB; Tuberculous peripheral lymphadenitis	2RHZ	4RH
Non-severe forms in high prevalence for HIV	2RHZE	4RH
Extensive pulmonary disease; Smear or Xpert	2RHZE	4RH

positive pulmonary TB; Severe forms of EPTB other than TB meningitis and osteoarticular TB		
TB meningitis; Osteoarticular TB	2RHZE	10RHR
R-Rifampicin; H-Isoniazid; Z-Pyrazinamide; E- Ethambutol		

Table 21: Current recommendation on TB treatment regimens for drug-susceptible TB in adolescents [221]

TB Category	Intensive Phase	Continuation Phase
All forms of TB except TB Meningitis and TB osteoarthritis	2HRZE	4RH
TB meningitis and Osteoartiicular TB	2HRZE	10RH

Table 22: Recommendation on daily TB treatment in FDC for young children [221]

Weight	Number of Tablets		
	Intensive Phase (2 months)		Continuation Phase (4 months)
	RHZ (75/50/150 mg)	E (100 mg)	RH (75/50 mg)
4 – 7 kg	1	1	1
8 - 11 kg	2	2	2
12 - 15 kg	3	3	3
16 - 24 kg	4	4	4

Note: Older children and adolescents with body weight >25 kg can be given with FDC formulation as in adult dosages in mg/kg (RHZE 150/75/ 400/275 and RH 150/75).

Source: National Tuberculosis Control Program Manual of Procedures 6th edition,2020. Department of Health[221]

6.2.7 . Once MDRTB is suspected or confirmed in a child or adolescent, a referral to a specialist is needed for further management

Among children or adolescents with confirmed multi-drug resistant TB, the authors of this document would advise referral to the Pulmonary and Infectious disease specialist for the specific needs of close treatment monitoring and management in this pediatric group.

6.3. PATIENTS WITH CHRONIC LUNG DISEASES OR DISEASES WITH PROMINENT RESPIRATORY COMPONENT AND THE COVID-19 PANDEMIC

Recommendation 31
Children with chronic lung conditions should continue to seek medical consults for regular follow-ups via remote consultation (Telemedicine /Video conference) and should be given preventive vaccination like pneumococcal and influenza vaccines.

(Strong recommendations, low to moderate grade evidence)

At the start of the COVID-19 pandemic, various countries have adopted strategies to protect people considered to be "vulnerable" to COVID-19 infection. This includes individuals that are immunocompromised, those with specific types of cancer, severe respiratory conditions and other rare diseases.[222] Underlying medical conditions associated with increased risk of severe disease were based on adult data, however, protective strategies have been applied across all ages.[223]

The SARS-CoV-2 infections in children with risk factors and underlying diseases (chronic respiratory diseases such as cystic fibrosis, severe asthma, bronchopulmonary dysplasia as well as cardiac diseases, primary and secondary immunodeficiencies, underlying malignant diseases, malnutrition, etc.) are rarely reported in pediatric analyses.[224,225]

Table 23 Children who may be at increased risk of severe illness from COVID-19

- Cystic fibrosis
- Primary ciliary dyskinesia
- Significant bronchiectasis
- Chronic lung disease of prematurity with oxygen dependency
- Severe asthma
- Interstitial lung disease
- Obliterative bronchiolitis
- Children receiving additional daytime and/or night time oxygen
- Life dependent on long term ventilation (via tracheostomy or non – invasive ventilation)
- Neuromuscular disease on long term ventilation
- Significant underlying neurodisabilities and lung infection risk
- Significant lung disease relating to underlying systemic diseases such as rheumatological disease

Source: British Paediatric Respiratory Society[197]

The majority of patients with COVID-19 (81%) present with mild symptoms (fever, cough, and dyspnea), while 14% have respiratory distress and hypoxemia, and 5% will develop respiratory failure. It is unknown whether patients with ILD have different or more severe manifestations. [226] Another study meanwhile stated that due to structural lung changes, immunosuppressive therapy, diffusion impairment with a frequently existing need for

supplemental oxygen and advanced age, patients with interstitial lung disease (ILD) are a COVID-19 risk group.[227]

Patients with pulmonary arterial hypertension (PAH), belong to the risk patient group; however, there are no data on the clinical course of COVID-19 in patients with PAH. There is no reliable information on whether sleep apnea patients have an increased risk for SARS-CoV-2 infection, or are subject to a greater risk of a severe course of the disease.[227]

The risk of a severe course of COVID-19 is increased in patients suffering with neuromuscular disorders (NMD) due to the following comorbidities: muscular weakness of the chest and diaphragm, use of ventilator supports and/or presence of tracheostomy, weak airway clearance, cardiac involvement, rhabdomyolysis, comorbidities , steroid and immunosuppressant treatments.[228]In contrast to the data from adults, the majority of underlying medical conditions do not appear to place children at significantly increased risk of either developing COVID-19 disease or experiencing severe symptoms and complications if infected.[220]

Patient suspected to have ILD, an initial consultation preferably by videoconferencing may be done. Patients with ILD who notice a new fever or mid change in respiratory symptoms should have a lower threshold than the general population for assessment, potentially using telemedicine to determine whether an emergency room visit is necessary.[229] Patients with risk factors for severe COVID-19 should have a lower threshold for a more comprehensive assessment of COVID-19 and for other causes of respiratory worsening.

a) Primary care providers should continue to refer patients with suspected ILD to tertiary referral centers where they can be seen using virtual platforms or in-person consultations where appropriate. Multidisciplinary ILD conferences involving other clinicians, radiologists, and pathologists should continue to be conducted virtually to help minimize delays in diagnosis.[230]
b) To minimize direct contact between physicians and thus the risk of infection transmission, alternative (e.g.digital) forms of communication should also be considered for multidisciplinary case discussions. Alternatives such as video chats can be considered for routine follow ups.[227]
c) Patients with chronic lung diseases may protect themselves from serious infections or, in the case of an infection, may reduce the risk of a severe course of the illness-by completion of the vaccination status with pneumococcal vaccine and Influenza vaccine.[227]

Chapter 7

GUIDANCE IN PERFORMING SPECIAL PEDIATRIC PULMONARY PROCEDURES DURING THE COVID 19 PANDEMIC

7.1. INTERIM GUIDELINES ON THE PERFORMANCE OF BRONCHOSCOPY IN THE COVID-19 PANDEMIC

By the PAPP Task Force in Pediatric Bronchoscopy

RECOMMENDATION 32 *231,232,233*

1. Contact precautions (face shield, masks and gloves) are integral components of PPE strategy to prevent the transmission of this disease, and N95 respirators or powered air purifying respirators (PAPR) represent additional precautions and must be worn by all health care workers. *(Strong recommendation, moderate grade evidence)*

2. Proper training on donning and doffing should be provided to healthcare workers. Proper personnel instruction on wearing PPE step-by-step should be made available at the changing area. *(Strong recommendation, moderate grade evidence)*

3. All patients undergoing bronchoscopy must undergo SARS-CoV-2 RT-PCR swab test. The validity of the results should be 3 days.
(Strong recommendation, moderate grade evidence)

4. Elective and non-emergent procedures may be deferred upon the discretion of the bronchoscopist and thoroughly discussed with the attending physician.
(Weak recommendation, moderate grade evidence)

5. The number of healthcare workers assisting in the operating room/ bronchoscopy suite should be limited. *(Strong recommendation, moderate grade evidence)*

6. The decision to perform elective bronchoscopy from patients recovered from COVID-19 infection will need to be individualized based on disease severity, duration of illness, and a negative SARS-CoV2 RNA test from at least two consecutive nasopharyngeal swab specimens collected 24h apart (total of two negative specimens). The exact time to perform bronchoscopy is still unknown, but it would be reasonable to wait at least 30 days from resolution of symptoms.
(*Weak recommendations, moderate grade evidence)*

Remarks

Bronchoscopy plays an integral part in the diagnosis and management of most pediatric respiratory diseases. However, there is a need to emphasize that it is not routinely indicated for the diagnosis of COVID-19. In light of the COVID pandemic, several revisions had to be put into perspective given the nature of bronchoscopy being a high aerosol generating procedures which could mitigate risk to health care workers if appropriate. Its utility during the pandemic must be justifiable to ensure appropriate and utmost protection both to the patient and health care workers.

Any part of the content of this interim guideline on the performance of bronchoscopy during the COVID pandemic may be subject to revision every year or so depending on new international recommendations that may be available.

7.2. INTERIM PRE-OPERATIVE / PRE-PROCEDURAL GUIDELINES DURING THE COVID-19 PANDEMIC

By the PAPP Committee on Pre-Operative Evaluation

The General Principles in requesting for preoperative/pre-procedural testing for SARS-CoV-2 are:

Patients who are infected with the virus have been reported to have a higher perioperative morbidity and mortality when undergoing surgical procedures.[234] Asymptomatic patients may have the potential of transmitting the virus. Viral transmission may occur up to three days before patients become symptomatic.[235]

<u>Pre-operative COVID-19 Screening and Testing</u>

All children scheduled for surgery or other procedures that require general anesthesia, deep sedation or moderate sedation should be screened and tested for SARS-CoV-2. 234,[236,237]

Pre-operative/ pre-procedure symptom screening of COVID-19 will include symptoms and significant exposure. Symptoms include, but are not limited to, the presence of any of the following: subjective or measured fever, cough, shortness of breath, sore throat, muscle aches, diarrhea, fatigue, nasal congestion, headache, loss of smell, altered sense of taste, new onset of rash.

Recommendation 33 PEDIATRIC PRE-OPERATIVE EVALUATION IN CHILDREN

1) All children scheduled for surgery or other procedures that require general anesthesia, deep sedation or moderate sedation should be screened and tested for SARS-CoV-2.
(*Strong recommendations, moderate grade evidence)*

2) Pre-operative / pre-procedure screening will include clinical signs and symptoms of COVID-19 and significant exposure to confirmed COVID-19 persons.
(Strong recommendations, moderate grade evidence)

3) Assessment of patients before surgery should include the questionnaire concerning exposure to a COVID-19 patient in the past 14 days or having COVID-19-related symptoms within the prior 2 weeks.
(Strong recommendation, low-moderate grade evidence)

4) SARS-CoV2 PCR is the recommended screening test for asymptomatic patients scheduled for surgery/procedure. *(Strong recommendation, moderate grade evidence)*

5) The timing of SARS-CoV-2PCR testing should be done as close to the time of the procedure as possible and preferably done 48 hours prior to the procedure.
(Strong recommendations, high grade evidence)

6) The use of antigen-detecting rapid diagnostic tests and the antibody testing for SARS-CoV2 are not recommended as pre-operative screening tools. *(Strong recommendations, low grade evidence)*

7) Radiographic imaging such as chest x-ray and/ or chest CT scan is not recommended as a screening or diagnostic tool for COVID-19.
(Strong recommendations, low grade evidence)

8) Timing of urgent and elective surgeries:
   a. If the patient travelled to a country/locality with sustained community transmission, delay the surgery for 14 days following return, even if asymptomatic.
   b. If the patient has been in direct contact with a confirmed COVID-19 + patient, delay the surgery for 14 days following last contact, even if asymptomatic.
   c. If the patient presents with influenza-like illness or unexplained cough at the time of procedure, defer the surgery until they have recovered.

(Strong recommendations, moderate-high grade evidence)

9) The timing of elective surgery after recovery from COVID-19 utilizes both symptom- and severity-based categories. Suggested wait times from the date of COVID-19 diagnosis to surgery are as follows:
   a. Four weeks for an asymptomatic patient or recovery from only mild, non-respiratory symptoms.
   b. Six weeks for a symptomatic patient (e.g., cough, dyspnea) who did not require hospitalization.
   c. Eight to 10 weeks for a symptomatic patient who is diabetic, immunocompromised, or hospitalized.
   d. Twelve weeks for a patient who was admitted to an intensive care unit due to COVID-19 infection.

Significant exposure is history of travel to or residence in an area with local transmission, or exposure to contacts who are confirmed positive for COVID-19 for the past 14 days.[238] Patients will then be classified based on the guideline of the Philippine Pediatric Society and Pediatric Infectious Disease Society of the Philippines.[238]

If the patient is SYMPTOMATIC, non-emergent procedure / surgery should be postponed or cancelled. If the patient is ASYMPTOMATIC, proceed with COVID-19 testing. The recommended method of testing for SARS-CoV-2 is detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR) testing. The reported sensitivity of SARS-CoV-2 testing is approximately 70% to 90%, meaning that up to 30% of infected patients will be reported as free of the virus.[239]Clinicians must be mindful that a negative test does not negate the possibility that an individual is infected.

Timing of RT-PCR testing

Patients should undergo SARS-CoV2 PCR testing as close to the time of the procedure as possible and preferably done 48 hours prior to the procedure. The Philippine Society of Pediatric Surgeons recommends the surgery be done within 3-7 days when the sample has been obtained, allowing for a delay in turnaround-time of the laboratory results[236]

After the patient is tested negative for COVID-19, the patient should remain self-isolated or on home quarantine until the procedure date.[240] In local areas, where there is limitation in RT -PCR testing facilities, resumption of elective surgeries is recommended to be delayed until the testing capacity of the country or institution can cater to preoperative testing of patients. [240]

Antibody testing does NOT have a role in pre-operative screening and risk stratification. Antibodies develop in the second week of symptoms and not all patients who are infected with SARS-CoV-2 develop detectable antibodies.[241] The use of antigen-detecting rapid diagnostic tests is NOT recommended for clinical diagnosis. [241]

Radiographic imaging such as chest x-ray and/or chest CT scan is NOT recommended as a screening or diagnostic tool for COVID-19. In congruence with our previous statement on pre-operative evaluation[242,] chest radiograph is NOT a routine test and should be determined by patient indication and procedural needs.

Timing of Surgery

We adopt the recommendations from the Philippine College of Surgeons and Philippine Society of Pediatric Surgeons[236,237] as follows:

- **Emergent surgeries** shall be done even without RT-PCR results.
  (All patients should be swabbed on admission.)

- For **urgent and elective surgeries**, the following are recommended:

  1. If the patient travelled to a country/locality with sustained community transmission, delay the surgery for 14 days following return, even if asymptomatic.

  2. If the patient has been in direct contact with a confirmed COVID-19 positive patient, delay the surgery for 14 days following last contact, even if asymptomatic.

  3. If the patient presents with influenza-like illness or unexplained cough at the time of the procedure, defer the surgery until they have recovered.

  4. For patients who had recent COVID-19 infection[243]:

     a) Four weeks for an asymptomatic patient or recovery from only mild, non-respiratory symptoms.
     b) Six weeks for a symptomatic patient (e.g., cough, dyspnea) who did not require hospitalization.
     c) Eight to 10 weeks for a symptomatic patient who is diabetic, immunocompromised, or hospitalized.
     d) Twelve weeks for a patient who was admitted to an intensive care unit due to COVID-19 infection.

These timelines should not be considered definitive; each patient's preoperative risk assessment should be individualized, factoring in surgical intensity, patient comorbidities, and the benefit/risk ratio of further delaying surgery.

7.3 RECOMMENDATIONS FOR PEDIATRIC PULMONARY FUNCTION TESTING DURING THE COVID19 PANDEMIC

By the PAPP Committee on Pulmonary Function Testing

Recommendation 34 PULMONARY FUNCTION TEST (PFT)

Pulmonary Function Tests in children during the COVID-19 pandemic is vital for the management of children with respiratory conditions. The tests must be performed with the following measures to reduce the risk of SARS-CoV2 transmission:

1. Routine PFT should not be performed. The PFTs should be limited to those patients for whom the results would be essential for making immediate treatment decisions.

2. A PFT Laboratory waiting area must be established for the purpose of triage and screening of patients, caregivers, and laboratory staff.

3. The PFT laboratory must ensure the use of Personal Protective Equipment (PPE) for patients, caregivers, and laboratory staff.

4. The testing environment and equipment must have optimal cleaning and disinfection as provided by the institutional infection control standards.

5. PFT Procedures:

- Tidal breathing test must be performed first before any ventilation maneuvers.
- A single-patient use pressurized metered-dose inhaler (pMDI) via a spacer should be the preferred device for the administration of Salbutamol in children.
- Methacholine challenge tests and aerosol treatments must be avoided.

(Strong recommendations, moderate-high grade evidence)

Remarks

The conduct of Pulmonary Function Tests (PFT) in children during the COVID-19 pandemic requires measures. to reduce the risk of SARS-CoV2 transmission while providing results that would be vital in the management of children with respiratory conditions. PFTs pose a significant risk of disease transmission because these are inherently droplet or aerosol-generating procedures. Based on the current available evidence, the following recommendations will minimize the risk of viral transmission when performing lung function studies in children.

A. Scheduling and Prioritization of Patients

1. The decision on whether or not to conduct the PFT should be carefully weighed against the
   potential risk for Sars-CoV2 transmission.
2. Routine PFT should not be performed. PFTs should be limited to patients for whom the test results
   would be essential for making immediate treatment decisions such as patients undergoing pre-
   operative evaluation for surgery and patients undergoing surveillance during chemotherapy.
3. There should be no walk-in patients. All patients referred for PFT should be pre-screened,
   preferably by a Pediatric Pulmonologist, before getting an appointment for the test.
4. Impulse oscillometry and fractional exhaled nitric oxide measurement, which do not require forced maneuvers and reduce the potential for coughing and droplet formation, may also be considered as a possible alternative to PFT for the diagnosis and assessment of patients with asthma.

C. COVID-19 Screening of Patients, Caregivers, and Staff

1. Symptoms and exposure screening for COVID-19 must be done for patients, accompanying persons, and PFT laboratory staff before a scheduled PFT is performed. An online consultation is also recommended prior to a scheduled PFT for the purpose of screening for any signs and symptoms of respiratory disease.
2. COVID-19 RT-PCR testing must first be done before the PFT. The RT-PCR test must be done 3-7 days before the PFT since COVID-19 test results may have delayed release.

a. In cases where the patient gets a negative COVID-19 RT-PCR test, the patient and the accompanying companion should remain self-isolated or on home quarantine until the day that the PFT is scheduled.
b. In cases where the patient tests positive for COVID-19, the PFT must not be scheduled and the patient must not be allowed into the PFT laboratory.
c. The PFT should be postponed until at least 3 weeks after the resolution of symptoms and/or two negative COVID-19 PCR tests performed at 24-hour interval.
d. This timeline is based on the WHO discharge criteria for COVID-19.

D. PFT Laboratory Waiting Area Arrangements

1. Patients are advised to arrive at the PFT laboratory within 15 minutes prior to their scheduled appointment to avoid queuing in a waiting area and to minimize exposure with other patients.
2. Waiting rooms must be rearranged so that there is at least a 1-meter distance between seats to conform to guidelines for physical distancing.
3. The patient and accompanying person will be asked to use a hand sanitizer and wear masks when at the PFT laboratory. The patient and the accompanying person should be wearing an N95 mask or its equivalent and a face shield.

E. Personal Protective Equipment (PPE) inside the PFT laboratory

1. The use of Personal Protective Equipment (PPE) inside the PFT laboratory is aimed at limiting aerosolized droplet acquisition for staff, patient and caregiver during the lung testing procedures.
2. Technicians must wear an N95 mask, face shield, and gloves inside the pulmonary laboratory.
3. If any tests require aerosolization of any medication, the technician should wear complete PPE: gown, gloves, face shield, and an N95 respirator, a powered air purifying respirator, or both.

F. Optimal Testing Environment and Equipment

1. Negative pressure rooms or HEPA filtration systems with UV germicidal lamps are recommended. Air purification or ultraviolet and ozone decontamination systems should be applied according to the indications of the hospital for rooms where aerosol-generating procedures are performed.

a. When the use of negative pressure rooms, HEPA filtration and UV light are not available in the testing environment, pulmonary function testing may still resume, provided PPE, time-between patients and cleaning precautions are followed to protect patients and staff from viral transmission.
    b. Patients should be tested one at a time in designated enclosed testing rooms. Testing room door should remain closed for the duration of test.

2. The interval time between each procedure should be enough to avoid aggregation and allow for disinfection of the exterior surfaces of the spirometer (and plethysmography cabin) and air quality generation.
3. Disposable materials (filters, mouthpiece, nose clips, flow sensors) should be discarded after a single patient use.
4. Disposable inline filters must be used during PFT, and cleaning and disinfection procedures for environment and equipment in PFT laboratories should be consistently performed.
5. Aside from the standard cleaning and change of filter of the testing equipment, other measures for disinfection such as wiping down of equipment, seats, and Plexiglass separators with disinfectant wipes are recommended.
6. The staff must maintain current recommendations for cleaning equipment. Use manufacturer and/or institutional infection control committee recommendations for equipment sanitation.

G. The Conduct of the Pulmonary Function Test

1. It is recommended that the tidal breathing test be performed first before any ventilation maneuvers in order to avoid changing the static volumes (FRC, RV) and bronchial caliber (VEMS, respiratory mechanics, resistance). This may minimize potential risks of contamination by micrometrical particles exhaled during forced exhalation.
2. A pressurized metered-dose inhaler (pMDI) via a spacer should be considered as the preferred device for the administration of salbutamol in children. The use of nebulizers should be avoided. Spacers should not be shared among patients.
3. Exposure to aerosolized particles may be reduced by avoiding methacholine challenge.

7.4. GUIDELINES FOR SLEEP STUDY DURING THE COVID-19 PANDEMIC

This is an excerpt of the Joint Statement released last May 28,2020 by the

a. *Philippine Society of Sleep Medicine (PSSM)*
b. *Philippine Neurological Association (PNA)*
c. *Philippine College of Chest Physicians (PCCP)*
d. *Philippine Academy of Pediatric Pulmonology (PAPP)*
e. *Philippine Academy of Sleep Surgery (PASS) of the Philippine Society of Otolaryngology – Head and Neck Surgery (PSO-HNS)*

Recommendation 35 POLYSOMNOGRAPHY (SLEEP STUDY)

In performing Sleep Studies, the necessary the necessary triage and screening of consultations prior to the set schedule of the test strict infection control measures are imposed upon the patient, sleep technologist and the sleep center as a facility to prevent transmission of SARS-CoV-2. The quarantine level status set by the Philippine Interagency Task Force for Emerging Infectious Disease (IATF- EID) should guide the sleep laboratory on its operation.

(Strong recommendations, moderate to high grade evidence)

Remarks

The quarantine level set by the Philippine Interagency Task Force for Emerging Infectious Disease (IATF- EID) should guide the sleep laboratory on its operation.

A. Enhanced Community Quarantine (ECQ)

1. Only diagnostic sleep studies may be performed.
2. If positive airway pressure (PAP) titration is necessary for urgent cases, the patient should have a negative SARS-CoV-2 RT-PCR test and had practiced self-quarantine for at least a week prior to the study PAP titration should be performed in a negative pressure room.
3. If a negative pressure room is not available, the room should be fitted with a High Efficiency Particular Air or High Efficiency Particulate Air (HEPA) filter at the very least.
   a. An air change per hour (ACH) rate of >12 is recommended. The hospital engineering department should be contacted to provide ACH information in the event that a portable HEPA filter unit is necessary to augment the existing fixed heating, ventilation, and air-conditioning (HVAC) system for air cleaning.[88]
4. Sleep technicians must wear level 3 PPE which consist of cap, goggles/ face shield, N95 respirator, gloves, shoe covers and surgical gown.
5. Defer sleep studies for children, pregnant, and elderly patients, unless there is an urgent medical reason.

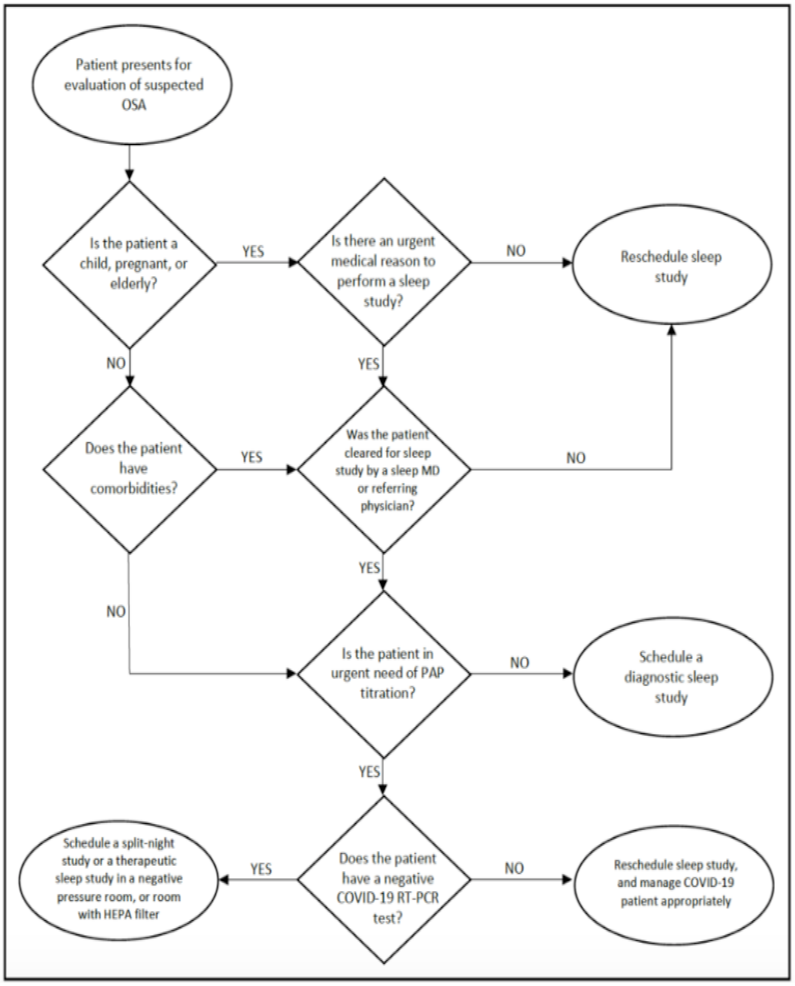
6. Patients with co-morbidities (e.g. hypertension, diabetes, obesity, etc.) should be cleared by the sleep doctor or referring physician prior to the sleep study.
7. Do not operate PAP devices in a clinic setting.

A. Modified Enhanced Community Quarantine (MECQ)

Same recommendations as Enhanced Community Quarantine (ECQ)

Figure 22. **ALGORITHM IN PERFORMING POLYSOMNOGRAPHY (SLEEP STUDY) DURING THE COVD19 PANDEMIC**

Figure 1: Decision tree for polysomnography (PSG) during Enhanced Community Quarantine (ECQ) & Modified Enhanced Community Quarantine (MECQ).



C. General Community Quarantine (GCQ)

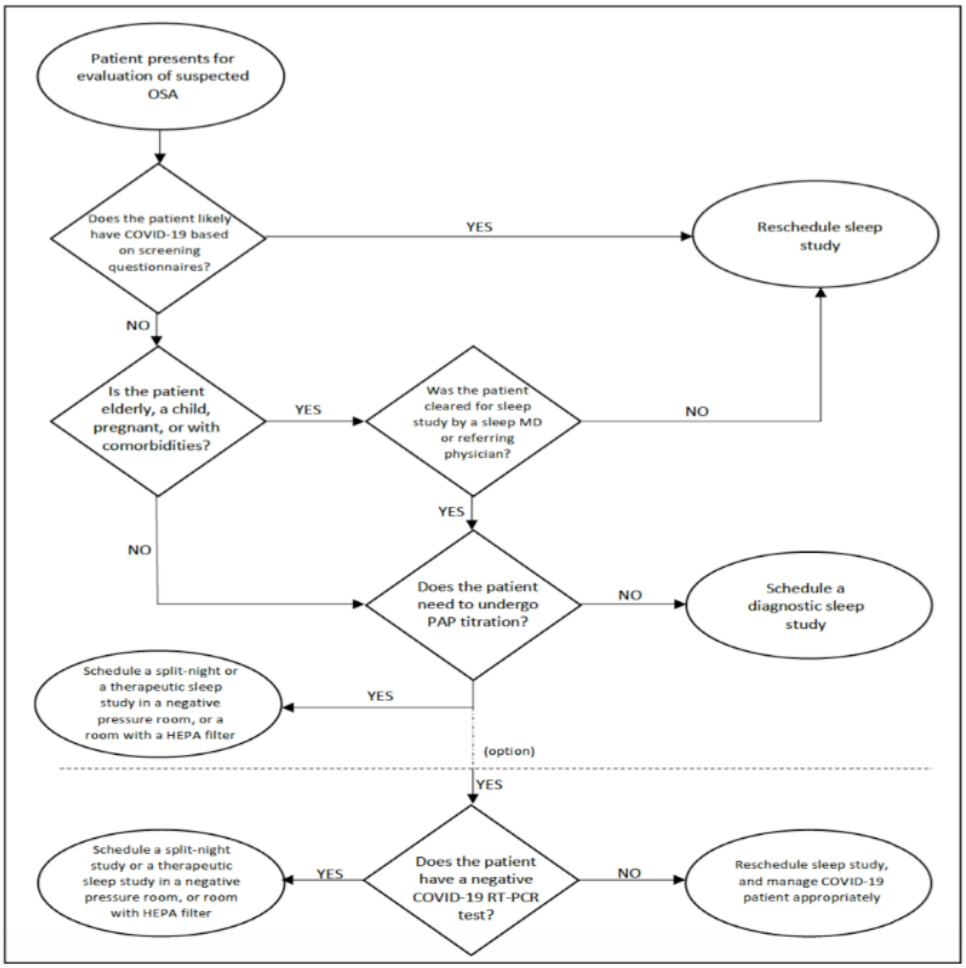
1. COVID-19 status of patient may be determined using appropriate screening questionnaires prior to scheduling and re-evaluation on the day of the sleep study.
2. PAP titration may be done based on the clinical judgment of the sleep physician. It should be performed in a negative pressure room. If a negative pressure room is not available, the room should be fitted with a HEPA filter at the very least.

a. An air change per hour (ACH) rate of >12 is recommended. The hospital engineering department should be contacted to provide ACH information in the event that a portable HEPA filter unit is necessary to augment the existing fixed heating, ventilation, and air-conditioning (HVAC) system for air cleaning.[88]

3. Sleep technician should wear level 3 PPE during a PAP titration.
4. A level 3 PPE must consist of cap, goggles/face shield, N95 respirator, gloves, shoe covers and surgical gown.
5. Children, pregnant, elderly, patient with co-morbidities (e.g. diabetes mellitus, hypertension) shall be scheduled based on the clinical judgment of the sleep doctor or referring physician.
6. A COVID-19 RT-PCR test could be requested based on the clinical judgment of the sleep doctor prior to a titration or split-night study.
7. Do not operate PAP devices in a clinic setting without appropriate PPE.

Figure 23. **ALGORITHM IN PERFORMING POLYSOMNOGRAPHY (SLEEP STUDY) DURING THE COVD19 PANDEMIC**

Figure 2: Decision tree for polysomnography (PSG) during General Community Quarantine (GCQ)



D. Normal Conditions – same recommendations as GCQ until further notice

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APPENDICES

APPENDIX A. Infection Prevention & Control Recommendations for Health Workers

- Determine the appropriate PPE they would need when caring for the patient and follow the recommendations for droplet and contact precautions.
- Patient must be placed in a room with good ventilation.
- For caregivers and patient >2 years old: face mask only, unless the patient is to perform aerosol-generating procedure at home (nebulization) for which the caregiver would need to don level 4 PPE.
- If heating, ventilation and air-conditioning (HVAC) systems are used, they should be regularly inspected, maintained, and cleaned.
- For mechanical systems, increase the percentage of outdoor air, using economizer modes of HVAC operations and potentially as high as 100%
- Use of fans for air circulation should be avoided if possible unless it is in a single occupancy room when there are no other individuals present. If the use of fans is unavoidable, increase outdoor air exchange by opening windows and minimize air blowing from one person directly to another.
- Limit the number of household members present during any visits and request that they maintain a distance of at least 1 meter (m) from the health worker.
- When providing care or working within 1m of the patient request that the patient (more than 2 years old) wear a medical mask.
- Perform hand hygiene after any type of contact with the patient or his/her immediate environment.
- When washing hands with soap and water, use disposable paper towels to dry hands. If paper towels are not available, use clean cloth towels and replace them frequently
- Provide instructions to caregivers and household members on how to clean and disinfect the home, as well as on the safe and correct use and storage of cleaning materials and disinfectants.
- Clean and disinfect any reusable equipment used in the care of the patient before using on another patient according to standard precautions and established protocols.
- Remove PPE and perform hand hygiene before leaving the home and discard disposable PPE. Clean and disinfect reusable items (i.e. eye protection) or store reusable items for decontamination later according to established protocols.
- Do not reuse single use PPE.
- Dispose of waste generated from providing care to the patient as infectious waste in strong bags or safety boxes as appropriate, close completely and remove from the home.

APPENDIX B. Infection Prevention & Care Advice for Caregivers Providing Care to COVID-19 Patients at Home

- Limit the patient's movement around the house and minimize shared space. Ensure that shared spaces (e.g. kitchen, bathroom) are well ventilated.
- Household members should avoid entering the room where the patient is located or, if that is not possible, maintain a distance of at least 1m from the patient.
- Assign one caregiver who is in good health and has no underlying chronic conditions.
- Visitors should not be allowed in the home until the patient has completely recovered and has been released from isolation.
- Perform proper hand hygiene before and after preparing food, before eating, after using the toilet, and whenever hands look dirty.
- If hands are not visibly soiled, an alcohol-based hand rub can be used. For visibly soiled hands, always use soap and water.
- A medical mask should be provided to the patient more than 2 years old, worn as much as possible by the patient and changed daily and whenever wet or dirty from secretions. Individuals who should practice rigorous respiratory hygiene; that is, coughing or sneezing into a bent elbow or tissue and then immediately disposing of the tissue followed by hand hygiene.
- Materials used to cover the mouth and nose should be discarded or cleaned appropriately after use (e.g. wash handkerchiefs, using regular soap or detergent and water).
- Caregivers should wear a medical mask that covers their mouth and nose when they are in the same room as the patient. Masks should not be touched or handled during use. If the mask gets wet or dirty from secretions, it must be replaced immediately with a new clean, dry mask. Remove the mask using the appropriate technique, which is to untie it, rather than touching the front of the mask, to discard it immediately after use and then to perform hand hygiene.
- Avoid direct contact with the patient's body fluids, particularly oral or respiratory secretions, and stool. Use disposable gloves and a mask when providing oral or respiratory care, and when handling stool, urine and other waste. Perform hand hygiene before putting on the mask and gloves and after removing gloves and the mask.
- Do not reuse disposable medical masks or gloves.
- Gloves and protective clothing (e.g. plastic aprons) should be used when cleaning surfaces or handling clothing or linen soiled with body fluids. Depending on the context, wear either utility or single-use gloves.
- Clean and disinfect surfaces that are frequently touched in the room where the patient is being cared for, such as bedside tables, bedframes, and other bedroom furniture at least once daily. Clean and disinfect bathroom and toilet surfaces at least once daily. Regular household soap or detergent should be used first for cleaning, and

then, after rinsing, regular household disinfectant containing 0.1% sodium hypochlorite (i.e. equivalent to 1000 ppm) should be applied by wiping surfaces.

- Use dedicated linen and eating utensils for the patient; these items should be cleaned with soap and water after use and may be re-used instead of being discarded.
- Place contaminated linen in a laundry bag. Do not shake soiled laundry and avoid contaminated materials coming into contact with skin and clothes.
- Clean the patient's clothes, bed linen, and bath and hand towels using regular laundry soap and water.
- After use, utility gloves should be cleaned with soap and water and decontaminated with 0.1% sodium hypochlorite solution. Single-use gloves (e.g. nitrile or latex) should be discarded after each use. Perform hand hygiene before putting on and after removing gloves.
- Waste generated at home while caring for a COVID-19 patient during the recovery period should be packed in strong bags and closed completely before disposal and eventual collection by municipal waste services. If such a service does not exist, waste may be buried. Burning is the least preferred option, as it is bad for human health and the environment.
- Avoid other types of exposure to contaminated items from the patient's immediate environment (e.g. do not share toothbrushes, cigarettes, cutlery, crockery, towels, washcloths or bed linen).