INTERIM GUIDELINES ON PULMONARY CARE IN PEDIATRIC COVID-19

September 30, 2020 Edition

Philippine Pediatric Society
Philippine Academy of Pediatric Pulmonologists

PAPP COVID TASK FORCE
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Chief Editors

Maria Theresa T. Policarpio, MD FPPS, FPAPP, FPSCCM, MMHA

Elma G. Dueñas, MD, DPPS, DPAPP MHM MBA

Contributors

Christian Allen L. Roxas, MD, DPPS, DPAPP, FPSCCM

Marichu J. De Chavez, DPPS, DPAPP

Sheila Almeda - Cirilos, MD DPPS, DPAPP

Joseph Dale R. Gutierrez, MD, FPPS, DPAPP

Yadnee V. Estrera MD, DPPS, DPAPP

Jerome V. Senen, MD, DPPS, DPAPP, FPSCCM

Elma G. Dueñas, MD, DPPS, DPAPP MHM MBA

Arnold Nicholas T. Lim, MD, DPPS, DPAPP, FPSCCM

Maria Cristina H. Lozada, MD, DPPS, DPAPP

Teresita P. Narciso, MD, FPPS, FPPS

Gerarda Ember R. Afable, MD, DPPS, DPAPP

Jonijohn R. Jimenez, MD, DPPS,DPAPP,FPSCCM,MHA

RAPID ADVICE ON THE PULMONARYCARE IN PEDIATRIC COVID-19

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 for pediatric patients with respiratory involvement is highlighted throughout the text. It is 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 ie., aerosolized procedures, proning in children, and airway therapies, performing special pulmonary procedures and disease management of asthma, childhood TB and Chronic Lung Disease in 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.

Maria Theresa T. Policarpio, MD FPPS, FPAPP, FPSCCM, MMHA
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 or at risk for severe acute respiratory infection (SARI) when infection with the COVID-19 virus is suspected.

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.

We searched the literature to identify relevant information, including existing guidelines and systematic reviews. 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://www.who.int/), CDC(Centers for Disease Control and Prevention, https://www.cdc.gov/) and DOH (Department of health, https://www.doh.gov.ph)

We identified relevant literature up to April 15,2020 for the first draft which was presented to the members of the Philippine Academy of Pediatric Pulmonologists (PAPP) last May 25,2020. Subsequent updates in the respiratory care management were added to address queries of evolving reports of clinical experiences reported in children until June 18,2020.

In this present update, a new search for pediatric COVID 19 specific updates on the respiratory management were done by the committee members until September 30, 2020. Discussions and meetings to evaluate relevance and need for the document update and revision were done. Local data collated form registry of Pediatric COVID 19 patients in PAPP affiliated institutions namely : Philippine General Hospital, St. Luke's Medical Center, Chong Hua Hospital, Makati Medical Center, Philippine Heart Center and the University of Santo Tomas Hospital was done and reported accordingly. The inclusion of the guidance recommendations from respective PAPP Task Force Committees in the Special Situations and Special Pulmonary Procedures deemed necessary were added to this update as a collective effort of the PAPP to provide respiratory care guidance to clinicians attending to children afflicted with the disease.

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

Because clinical information about the optimal management of COVID-19 is evolving quickly, this Guideline will be updated frequently as published data and other authoritative information becomes available. If there is a reason to believe one or more recommendations need updating, and plans should be made to start that process. In situation ie. new controversial areas, those in which new evidence has emerged or if there are concerns that one or more recommendations in a guideline may no longer be valid, the committee will make every effort to ensure to update the recommendations.

Disclaimer: 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. Due to the unavailability of reliable current sources on pediatric COVID-19 infection, the following evidence summaries are developed from the existing pool of available data obtained by the researchers, which were scrutinized further, and the final articles registered in this document were those that were warranted valid enough for citation (systematic reviews and meta-analyses were prioritized among other articles as they grant the most accurate findings). There is a need to conduct more systematic reviews of the available data with further specification on exposure and outcome variables which will be of great help in the determination of quality evidence for the consequent development of accurate clinical practice guidelines. Moreover, for the PECO questions which do not have scientific evidence yet, there should be at least observational studies done to answer these questions especially during this pandemic period.

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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

Joint Statement on Sleep Study from the following Societies:

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 disease burden and the demographic data of COVID-19 cases
- Local registry of Pediatric COVID19 from 5 Training Institutions under the Philippine Academy of Pediatric Pulmonologists (PAPP) are presented.
  These include the demographic data, clinical symptoms and presenting signs, imaging results of patients
- A new recommendation stating the Main Thoracic Findings in Children with MIS-C and COVID19 is included

Chapter 2

- Respiratory management Updates:
  - inclusion on the initial parameters for High Flow Nasal Cannula support
  - Revision of the PEEP setting recommendations for patients with Pediatric ARDS due to COVID19 based on new data
- The additional discussion on the potential use of proning among non-intubated children with Pediatric ARDS due to COVID19.

Chapter 3

- Inclusion of the Precautions in the limited use of nebulization during the COVID19 Pandemic

Chapter 4

- The new update on ending of isolation recommendation based on the new local and international guidelines. Home care after discharge is also discussed in this section
- Recommendation on mask use in children has been formulated for disease transmission control.
- Discussion on Mask use in Pediatric Care of COVID-19 patients

Chapter 5

- The Pediatric Pulmonary Care in Special Situations now include guidance for children with Asthma, Childhood TB and Chronic lung Disease during this pandemic and the necessary treatment guide for suspected and confirmed children with COVID19.

Chapter 6

- A new section for guidance in performing special procedures in respiratory care during the pandemic has been collated from the different PAPPCommittee groups on Pediatric Pre-operative Risk evaluation, Pulmonary Function Test, Bronchoscopy and Polysomnography (Sleep Study) as they give their respective recommendations for care in children during the COVID19 pandemic.

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RECOMMENDATIONS AT A GLANCE

I. Clinical Presentation of COVID-19

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.

II. Clinical Classification of COVID-19 Based on Severity of Pneumonia

Recommendation 2

Pneumonia in COVID-19 Children should be classified as non-severe or severe pneumonia.

III. Laboratory Examination

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.

Laboratory tests that may be requested:

1. Complete Blood Count
2. C Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR)
3. Procalcitonin

Laboratory tests that may be requested in severe cases:

1. Alanine Aminotransferase (ALT),
2. Aspartate aminotransferase (AST),
3. PT PTT
4. LDH
5. Creatinine,
6. Blood Urea Nitrogen (BUN), serum electrolytes
7. Creatinine kinase – MB (CK-MB)
8. D Dimer
9. Arterial Blood gases

IV. Chest Imaging in Pediatric COVID-19 Patient

A. Chest Radiography

Recommendation 4

Chest imaging should be requested

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

Recommendation 5

The following should be the structured reporting of CXR findings for pediatric COVID- 19 patients[10]

1. **Typical Findings Of Pediatric COVID-19**
   Bilateral distribution peripheral and/or subpleural GGOs and/or consolidation.
2. **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.
3. **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.
4. **Negative for Pediatric COVID-19**
   No CXR findings suggestive of pneumonia

V. Chest Computed Tomography

Recommendation 6

The following should be in the structured reporting for CT findings for pediatric COVID-19 patients[10]

1. **Typical findings of pediatric COVID-19**
   Bilateral, peripheral and/or subpleural GGOs and/or consolidation in lower lobe predominant pattern
2. **Indeterminate findings of pediatric COVID-19**
   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, or the “crazy paving” sign.
3. **Atypical findings of pediatric COVID-19**
   Unilateral segmental or lobar consolidation, central unilateral or bilateral GGOs and/or consolidation, discrete small nodules, lung cavitation, plural effusion, or lymphadenopathy.
4. **Negative for pediatric COVID-19**
   No Chest CT findings suggestive of suggestive of pneumonia in children

VI. 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 [101 103]

VII. Main Thoracic Findings in Children with MIS-C and COVID19

Recommendation 8

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.[157]

VIII. Respiratory Support for COVID-19 Patients

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

A. Precaution

Recommendation 9

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.[19]

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)

First line Approach

Recommendation 10

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%. [1]
   a. If patient continues to be hypoxemic, oxygen delivery via face mask with reservoir bag should be initiated
   b. 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.

Recommendation 11

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.

VIII. Airway Management and Tracheal Intubation Specific to COVID-19 Patient Group

A. Precaution

Recommendation 12

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

B. Intubation

Recommendation 13

We strongly recommend that intubation should not be further delayed if SpO2/FiO2 ratio < 221 in pediatric patients on bi-level NIV or CPAP and if there is no improvement in oxygenation (target SpO_2 92-97% and FiO_2) within 60 minutes.

Recommendation 14

The use of Bag Valve Mask (BVM) prior to intubation is not advised for suspected or confirmed COVID-19 patients due to its capacity to generate aerosols. However, if the bag/mask ventilation is necessary for pre-oxygenation, it is strongly recommended to follow safety measures to minimize aerosolization:

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.

Recommendation 15

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.

IX. Ventilator Management and Strategies

A. Lung Protective Strategies

Recommendation 16

The general principles of management of child with ARDS apply to a child with COVID-19 related ARDS. The lung protective strategies suggested are as follows:

- Low tidal volume (3-6ml/kg IBW) if poor respiratory compliance
  Low tidal volume (5-8ml/kg) if better preserved respiratory compliance
- 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[148)]
- Target plateau pressure <28cmH2O
- Permissive hypercapnia (pH >7.20)

B. Proning for Pediatric Covid-19 Patients

Recommendation 17

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

X. Airway Therapies and Respiratory Mechanics

Recommendation 18

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

Recommendation 19

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

Recommendation 20

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 should be avoided as much as possible. The Limited Indications of Nebulization Include:

1. Severe life-threatening respiratory distress,
2. Patients with compromised ventilation,
3. Uncooperative patients
4. Children with poor response to pMDI

Recommendation 21

It is strongly recommended that for suspected or confirmed COVID-19 children presenting with bronchospasm, *initial dose of salbutamol 2 puffs for children ≤ 5yo; 4 puffs children 6-11 yo and adolescent (100mcg/actuation)* delivered is strongly recommended.

If symptoms persist after initial bronchodilator: a further 2–6 puffs of salbutamol for <5 yo 4-10 puffs (>6 yo) may be repeated every 20 minutes until good clinical response is achieved.

Recommendation 22

In ventilator-supported children, clinicians should 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.

XI. AIRWAY CLEARANCE THERAPIES RATIONALE FOR USE FOR COVID-19

Recommendation 23 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

XII. DISCHARGE, ENDING ISOLATION & HOME CARE IN PEDIATRIC COVID-19

Recommendation 24

We strongly recommend that based on the latest DOH updated guidelines, symptomatic patients COVID-19 Patients (suspect/ probable/ confirmed) who have fulfilled completion of 14 days isolation, clinically recovered and no longer symptomatic can be discharged and tagged as recovered without RT-PCR or antibody testing and provided that there is a clearance from licensed physician.

Recommendation 25

We strongly recommend, home isolation should be discontinued based on the guidance for Symptom based-strategy with the following conditions: patient has completed 14 days quarantine OR patient has at least 3 days (72 hours) have passed since recovery (based on resolution of fever without use of antipyretics and improvement of respiratory symptoms) and has at least 10 days have passed since symptoms first appeared whichever is longer.

Use of Masks in Children

Recommendation 26

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. While older children (2 -11 years old) needing to be out from the home use these masks and face shields with adult supervision. Children above 12 years old follow mask use advise for adults. 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.[172,173]

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 doesn't compromise their breathing.[172, 174]

XIII. PULMONARY CARE IN SPECIAL SITUATIONS

Recommendation 27 CHILDHOOD ASTHMA The administration of existing medications for asthma controller medications should be continued for pediatric patients with asthma during the COVID-19 pandemic.

Recommendation 28 CHILDHOOD TUBERCULOSIS

1. Preventive measures should be observed by a patient with pediatric TB and the healthcare staff attending to them.
2. TB testing should continue during the COVID19 pandemic
3. In COVID-19 patients with Latent TB infection, TB preventive therapy (TPT) should be initiated and completed, with options on shorter rifampicin- containing preventive regimens.
4. Patients with Active TB disease coinfected with COVID-19, TB treatment should be continued.

Recommendation 29 CHRONIC LUNG DISEASES

Children with chronic lung conditions should continue to seek medical consults for regular follow-ups via remote consultation (telemedicine/ video conferencing) and should be given preventive vaccination like pneumococcal and influenza vaccines

XIV. PEDIATRIC PULMONARY SPECIAL PROCEDURES

Recommendation 30

PERFORMANCE OF BRONCHOSCOPY DURING THE COVID19 PANDEMIC

1. Contact precautions (face shield, mask, gown, and gloves) are the integral components of PPE strategy to prevent the transmission of this disease, and N-95 respirators or PAPRs represent additional precautions and must be worn by all health care workers.
2. Proper training on donning and doffing should be provided to health care workers. Proper personnel instruction on wearing PPE step-by-step should be made available at the changing area.
3. All patients undergoing bronchoscopy MUST undergo RT-PCR COVID swab test. The validity of the results should be 3 days.
4. Elective and non-emergent procedures may be deferred upon the discretion of the bronchoscopist and thoroughly discussed with the attending physician.
5. In emergency cases where the result of the RT-PCR COVID swab test is not known, the decision to proceed shall be upon the discretion of the bronchoscopist and the anesthetist. Nonetheless, a level 4 protection (PPE hazmat suits, N-95 respirators or PAPRs and face shield or eye googles) must be worn by all health care workers.
6. The number of health care workers assisting in the operating room/ bronchoscopy suite should be limited.
7. 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-CoV-2 RNA test from at least two consecutive nasopharyngeal swab specimens collected ≥ 24 h 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.

Recommendation 31

PEDIATRIC PREOPERATIVE EVALUATION IN CHILDREN PROCEDURE

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.
2. Pre-operative /pre-procedure screening will include clinical signs and symptoms of COVID-19 and significant exposure to COVID-19 (+) persons.
3. SARS-CoV2 PCR is the recommended screening test for asymptomatic patients scheduled for surgery/procedure.
4. 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
5. The use of antigen-detecting rapid diagnostic tests and the antibody testing for SARS-COV-2 are NOT recommended as pre-operative screening tools.

6. Radiographic imaging such as chest x-ray and/or chest CT scan is NOT recommended as a screening or diagnostic tool for COVID-19.
7. 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.

Recommendation 32 PERFORMING PULMONARY FUNCTION TEST PROCEDURES

Pulmonary Function Tests (PFT) 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 or 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.

Recommendation 33 PERFORMING POLYSOMNOGRAPHY PROCEDURE

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.

Chapter 1

1 Pediatric Burden of COVID-19

At present (September 29, 2020), we have over **33,249,563** cases around the world. **1,000,040 deaths** or 3% succumbed to the disease.[1] In the largest systemic review among children, done by Hoang et al, including 119 studies and a total of 7,780 COVID-19 positive children were included. Fifty six percent were males. Mean age was 8.9 years old. Most of the cases were asymptomatic and were only part of family clusters (75.6%). Many also had mild symptoms. Most of the symptoms are still respiratory (cough, rhinorrhea, chest pain or difficulty of breathing) and may or may not be accompanied by fever (Table 1). Other symptoms may include fatigue, myalgia and gastrointestinal symptoms. Children rarely progress to severe disease. Only 0.14% ~~or 11 patients~~ fulfilled the CDC criteria for Multisystem inflammatory syndrome in children (MIS-C).[2]

Table 1: Common symptoms of pediatric COVID – 19 patients[2]

Clinical Symptoms	# Patients	N(%)
Asymptomatic	2,367	456 (19.3)
Fever	2,445	1,446 (59.1)
Cough	2,445	1,367 (55.9)
Rhinorrhea, nasal congestion	2,445	488 (20.0)
Myalgia, fatigue	2,445	457 (18.7)
Sore throat	2,445	446 (18.2)
Shortness of breath, dyspnea	2,445	287 (11.7)
Abdominal pain, diarrhea	2,445	159 (6.5)
Vomiting, nausea	2,445	131 (5.4)
Headache, dizziness	2,445	104 (4.3)
Pharyngeal erythema	2,445	80 (3.3)
Decreased oral intake	2,445	42 (1.7)
Rash	2,445	6 (0.25)

Among the laboratories from this review, serum inflammatory markers, specifically D-dimer, procalcitonin, creatine kinase and interleukin-6, were consistently elevated. CBC was inconclusive and were mainly interpreted as inflammatory. Chest radiographs were mostly normal **(Table 2)**. 21% had patchy infiltrates. Only six percent had ground glass opacity. On the other hand, the most common chest CT scan finding was ground glass opacity at 32.9%. It is important to note that those who were probably requested for chest CT scan were the moderate to severe cases. It is also worth mentioning that 18.9% had normal chest CT scan. Consolidations were also noted.

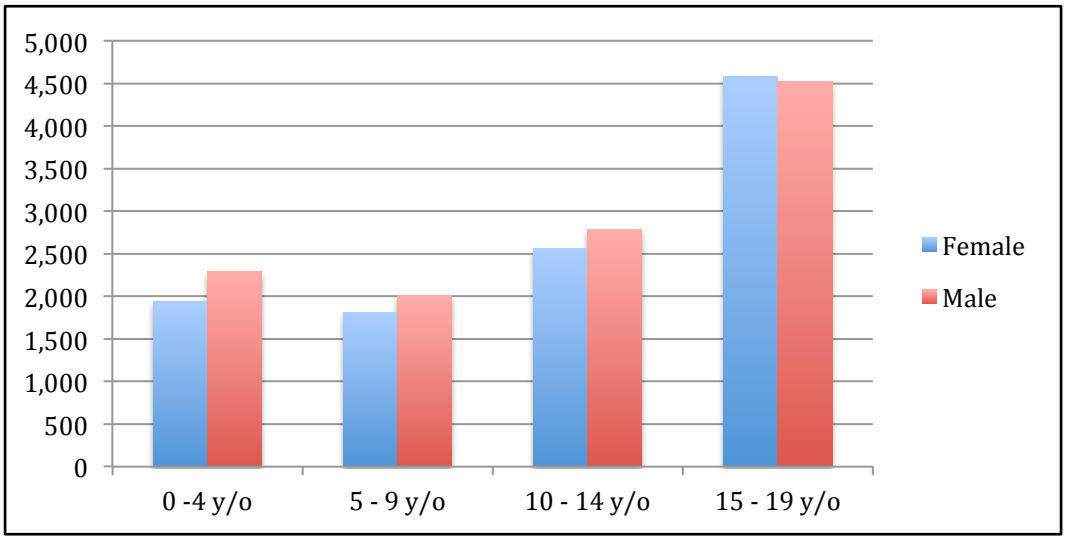
Table 2: Common radiographic findings in pediatric COVID – 19 [2]

	# Studies	# Patients	N(%)
Chest Xray Findings			
Normal	49	501	118 (23.6)
Patchy lesions	49	501	105 (21.0)
Ground-glass opacity	49	501	30 (6.0)
Consolidation	49	501	12 (2.4)
Computed Tomography (CT Findings)			
Normal	67	1,115	367 (32.9)
Patchy lesions	67	1,115	211 (18.9)
Ground-glass opacity	67	1,115	117 (10.5)
Consolidation	67	1,115	72 (6.5)

Local data[3]

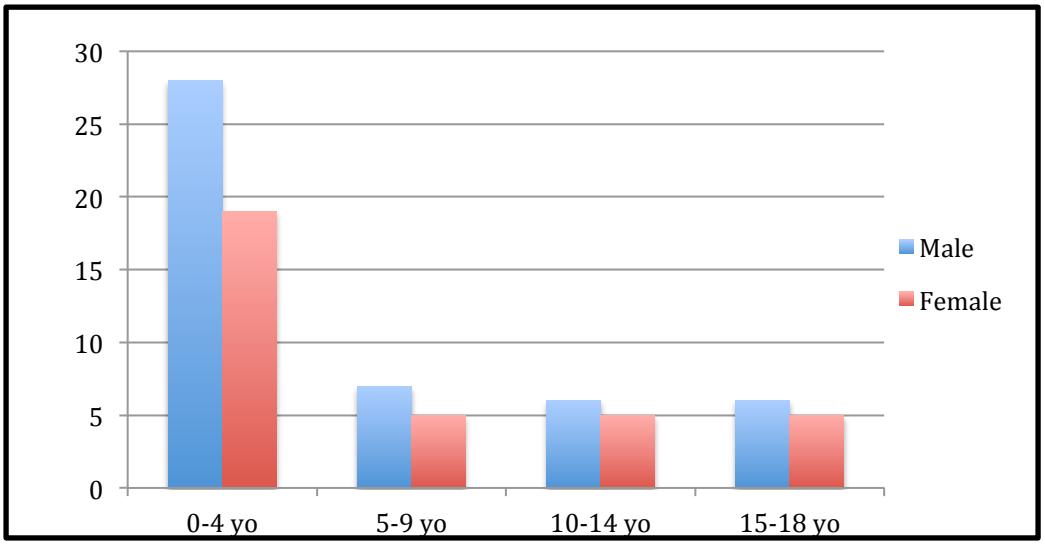
In our country, we have a total of 311,694[3]. Our death rate is 1.77%. Among who tested positive, 22,500 are children (Figure 1). That is 7.2% of the total diagnosed cases. In the Philippines, the percentage of affected children is steadily maintained at around six to seven percent of the total infected individuals. This mirrors the global percentage. There seemed to be no sexual predilection. Both males and females are equally affected. Among age groups, older children (15-19 y/o) are remarkably increased in number (40.5% of affected children) as compared to other age groups. However, many of them have mild symptoms or are asymptomatic. They usually do not require admission to a hospital. Infants to children ages 4 years old are the ones noted to have more frequent severe disease. They also have the greatest mortality at 1.3% as compared to 0.25% among other age groups.

Figure 1: Age distribution of national Pediatric COVID – 19 (as of September 30, 2020)[3]



Data of admitted pediatric COVID – 19 patients from the five training institutions of the Philippine Academy of Pediatric Pulmonologists, Inc. were collected. A total of 81 COVID -19 confirmed pediatric patients were documented. It is consistent with the national data that most moderate to severe infections that would require admission occurs with children at the 0-4 years old age group (58%) - see Figure 2).

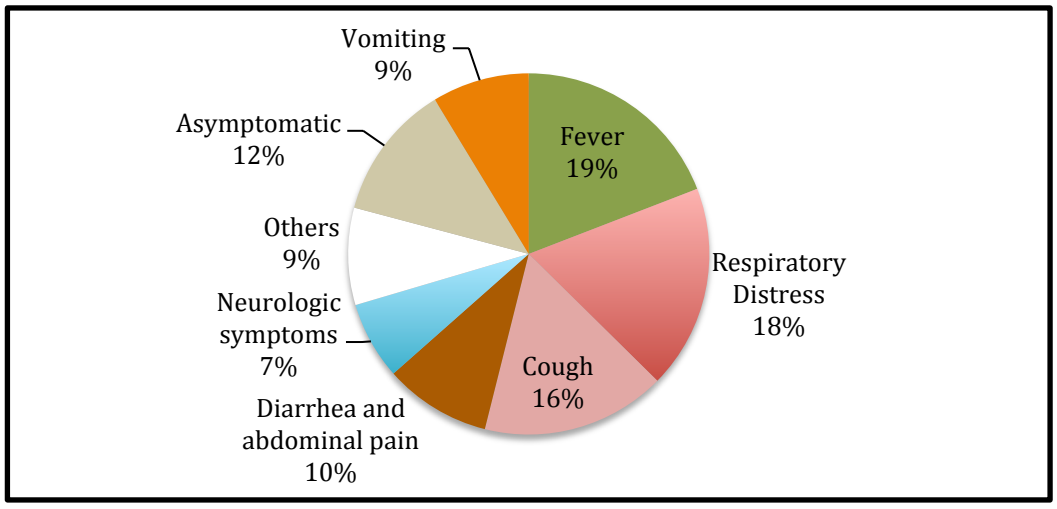
Figure 2: Age and Sex distribution of Pediatric COVID-19 Cases from PAPP Training Institutions



Clinical presentation and outcome

The most common clinical presentations were fever (19%), cough (16%) and respiratory distress (18% - see Figure 3). Gastrointestinal symptoms such as diarrhea and abdominal pain (10%) were also seen. Three patients (3.7%) were noted to have fulfilled the CDC MIS – C criteria. Eight deaths were reported. Five of them had congenital heart disease. One had cardiomyopathy. Fifty percent belonged to the 0-4 years age bracket.

Figure 3. Symptoms of COVID-19 patients in PAPP Training Institutions



Chest radiography
Chest imaging was not performed in all cases. Out of the 70 performed chest imaging, 32.4% were normal. 22.9% had infiltrates. 32.9% had some form of consolidation. A small number showed effusion and atelectasis. Ground glass opacities were the usual findings on the chest CT scan.

Clinical Features

1.1 Etiology, Pathogenesis, Incubation Period

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 last 2002 (SARS- CoV) and in Saudi Arabia last 2012 (MERS-CoV). Its genome has 82% similarity with SARS CoV hence designated the name SARS-CoV-2.[109]

The disease it caused 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.[246] Besides being highly contagious, it was apparent that the infection could be transmitted from 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.

Pathogenesis

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 on 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.[129] 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[129]

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.[12]

Based on data from the first cases in Wuhan and investigations conducted by the China CDC and local CDCs, 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.[12] 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[12.]

1.2 Mode of Transmission of COVID-19

Household or direct contact is the major transmission route for COVID-19 infection in children [4,14.] Having close contact with persons with a positive exposure history to COVID-19 pointed as another route for its infection in children [4,14.] There is no risk of vertical transmission of COVID-19 from infected pregnant mothers to their fetuses [4.]

According to the World Health Organization (WHO) report, SARS COV2 which spreads via oral and nasal droplets.[111] The WHO believes that further evidence is needed to assess the possibility of aerosol transmission. Some observations suggest that aerosol propagation is possible under the condition of long exposure to high concentrations of aerosols in a relatively closed environment[112.]

Children are unlikely to be the main drivers of COVID-19 infection. 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.[115] 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 show fever at all.[6 17]It is important for pediatric providers to 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 1. Signs and Symptoms

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).

Remarks

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)[4,14]. Other symptoms are variable when it comes to rate of occurrence. These may include shortness of breath, gastrointestinal symptoms, rhinorrhea and sore throat [4,14].

Physical examination may reveal tachypnea and tachycardia[14]. Auscultatory findings may reveal minimal rales or wheezing[5 14,]. 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[114]

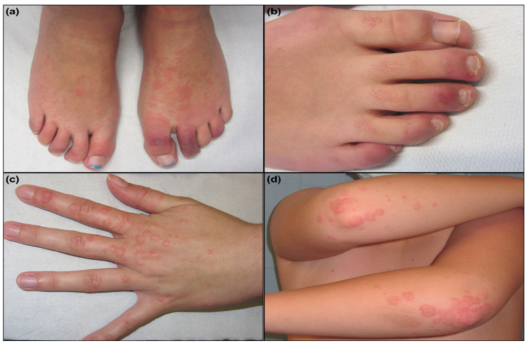


Figure 4.
Erythematous violaceous maculopapular rashes seen on fingers and elbows

Multisystem Inflammatory Syndrome in Children with COVID-19 (MIS-C)[196]

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 occurs.[116]

Many have evidence of cardiac inflammation, with or without coronary arterial dilation. Since those initial reports, the Royal College of Paediatrics and Child Health, the CDC, and the World Health Organization 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.

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 non-severe COVID-19, MIS-C children tend to have elevated Ferritin levels. 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.[116] 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 steroid are used. Outcome is generally good. Few cases of MIS-C patients who progress to pediatric ARDS were also reported.[117]

Table 2. CDC case definition of Multisystem Inflammatory Syndrome (MIS-C)[196]

All 4 criteria must be met:

3. Age <21 years

4. Clinical presentation consistent with MIS-C, including **all** of the following:

- Fever:
  - Documented fever >38.0°C (100.4°F) for ≥24 hours
    or
  - Report of subjective fever lasting ≥24 hours

1. Laboratory evidence of inflammation
   1. Including, but not limited to, **any** of the following:
      1. Elevated CRP
      2. Elevated ESR
      3. Elevated fibrinogen
      4. Elevated procalcitonin
      5. Elevated D-dimer
      6. Elevated ferritin
      7. Elevated LDH
      8. Elevated IL-6 level
      9. Neutrophilia
      10. Lymphocytopenia
      11. Hypoalbuminemia

- Multisystem involvement
  - **2 or more** organ systems involved:
    - Cardiovascular (eg, shock, elevated troponin, elevated BNP, abnormal echocardiogram, arrhythmia)
    - Respiratory (eg, pneumonia, ARDS, pulmonary embolism)
    - Renal (eg, AKI, renal failure)
    - Neurologic (eg, seizure, stroke, aseptic meningitis)
    - Hematologic (eg, coagulopathy)
    - Gastrointestinal (eg, abdominal pain, vomiting, diarrhea, elevated liver enzymes, ileus, gastrointestinal bleeding)
    - Dermatologic (eg, erythroderma, mucositis, other rash)
    - Severe illness requiring hospitalization

1. No alternative plausible diagnoses

- **Recent or current SARS-CoV-2 infection or exposure**

1. **Any** of the following:
   1. Positive SARS-CoV-2 RT-PCR
   2. Positive serology
   3. Positive antigen test
   4. COVID-19 exposure within the 4 weeks prior to the onset of symptoms

1.3.2 Spectrum of Illness Severity

For the severity of pediatric COVID-19 patients of the 2143 patients reported from China the Illness severity ranged from asymptomatic to critical.[98]

- Asymptomatic 4.4 %
- Mild 50.9 %
- Moderate 38.8 %
- Severe disease 5.2 %
- Critical disease 0.6%

In a systematic review and meta-analysis done included all age groups, from neonates to adolescents, majority of patients were categorized as having mild to moderate disease (98%).[4]

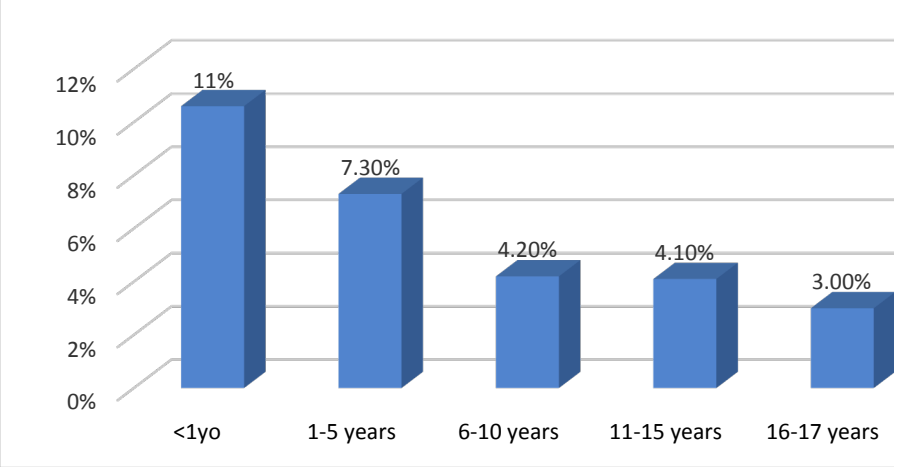


Figure 5.
Prevalence of Severe and Critical Disease in Children

The severity of illness by age showed that young children, particularly infants, were vulnerable and that half of the children with critical COVID-19 in this study were less than one year of age.[5.]

Severe disease is usually seen among infants or those with underlying conditions such as asthma, congenital heart disease or immunosuppression[14]. None of those who recovered from disease had permanent disability because of infection. Prognosis in children is generally good. Even if hospitalized, most will recover in two weeks.

Table 3. Theories on why children fare better than adults in SARS-CoV-2 infection[119,130]

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.[25] 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

1.3.3 Clinical Classification of Confirmed COVID-19

A. Clinical Classification of COVID-19 Based on Severity of Clinical features:

Table 4. Clinical Classification of COVID-19 Based on Severity of Clinical features: [5]

Asymptomatic	Symptomatic			
	Mild	**Moderate**	**Severe**	**Critical**
Absence of any clinical symptoms and signs chest imaging is normal RT-PCR (+)	Acute URTI fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. Congested pharynx No auscultatory abnormalities Other cases no fever, or only GI symptoms ie. as nausea, vomiting, abdominal pain and diarrhea.	Pneumonia fever, dry cough followed by productive cough, with fast breathing (according to age) some may have wheezing No hypoxemia CXR- pneumonia Chest CT shows lung lesions, which are subclinical	Early severe respiratory distress Fever, cough, +/- GI Sx dyspnea with central cyanosis Grunting, chest indrawing Oxygen saturation is < 90% at room air with other hypoxia manifestations Disease progresses in a week	Children can quickly progress to acute respiratory distress syndrome (ARDS) or respiratory failure, May also have shock, encephalopathy, myocardial injury or heart failure, Coagulation dysfunction, and acute kidney injury. Organ dysfunction can be life threatening.

C. Clinical Classification of COVID-19 Based on Severity of Pneumonia

Recommendation 2: Pneumonia in COVID-19 Children should be classified as non-severe or severe pneumonia
(Strong recommendation, Low-grade evidence)[6]

Pneumonia is considered a clinical syndrome associated with COVID-19 in children, with the following specifications [6]:

a. **Non-severe pneumonia** with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing: < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 in breaths/min) but no signs of severe pneumonia, including SpO2 ≥ 90% on room air (and no signs of severe pneumonia
b. **Severe pneumonia** presenting with cough or plus at least one of the following:
    1) Central cyanosis or SpO2 < 90%;
    2) Severe respiratory distress (e.g. grunting, very severe chest indrawing)
    3) Signs of pneumonia with a general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions.
    4) Fast breathing

SARS-COV2 is a pathogen causing a high prevalence of pneumonia in infected individuals. A study showed that the main clinical features of COVID-19 in children include pneumonia comprising about a fifth of the cases. Compared with children with H1N1 influenza, pediatric patients with COVID-19 had fewer upper respiratory symptoms but pneumonia was more frequent.[17]

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.

Although it is difficult to delineate each spectrum by signs and symptoms alone, it is still of paramount importance to differentiate them using other parameters because management will vary. A SARS Cov2 infected pediatric patient may have any of these disease spectrum but special emphasis would be made on ARDS as this is thought to be the central pathophysiologic mechanism of its progression to critical disease.

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.[151]

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 5 : Pediatric Acute Respiratory Distress Syndrome (PALICC Guidelines) [85]

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

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.[152]

While pediatric data are scarce, it is worth mentioning the findings related to adult COVID – 19. The ARDS Berlin criteria defined that for a patient to be diagnosed as having ARDS, the onset must be within 1 week of a known clinical insult or new or worsening respiratory symptoms. As the onset time of COVID-19-related ARDS was 8–12 days, it suggested that the 1-week onset limit defined by ARDS Berlin criteria did not apply to COVID-19-related ARDS.[132]

Lung compliance might also be relatively normal in some COVID-19-related ARDS patients who met ARDS Berlin criteria. This was obviously inconsistent with ARDS caused by other factors. In addition, the lung compliance was relatively high in some COVID-19-related ARDS patients, which was inconsistent with the severity of hypoxemia.[133]

Radiographic Findings in COVID –19 Pediatric ARDS

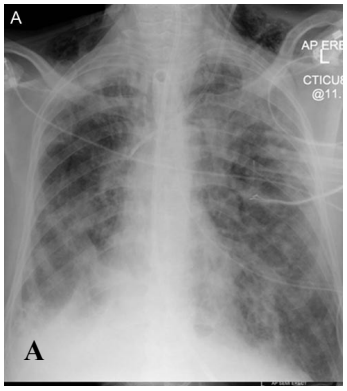
Based on the Berlin ARDS Definition, chest radiograph criterion include bilateral opacities consistent with pulmonary edema that are not fully explained by effusions, lobar/lung collapse, or nodules/masses on chest radiograph, there is also absence of cardiomegaly and septal lines.[134]

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. [156]

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 anterio-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.[135]

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.[136]

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.[13]



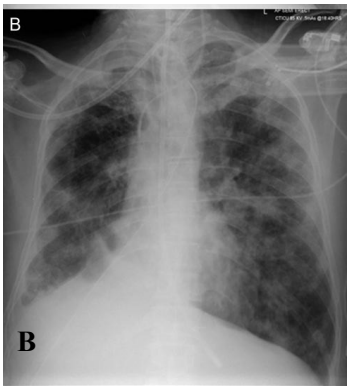


Figure. 5. A: Chest radiograph of patient with ARDS shows bilateral infiltrates. There is bilateral consolidation and a right pleural effusion. B: Chest radiograph of the same patient shows persistent bilateral infiltrates after 7 days[132]

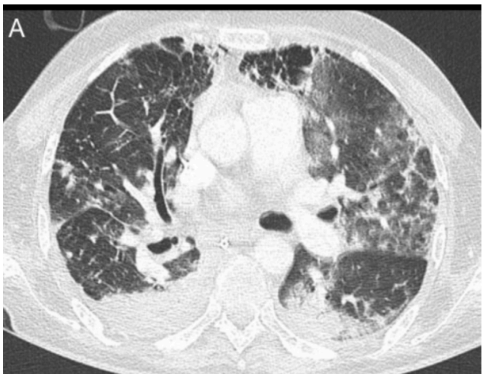


Figure 6 Computed tomogram shows bilateral dependent consolidation in a patient with ARDS, as well as ground-glass opacities in the non-dependent lung [133]

1.4 Case Definition

During the early part of COVID-19 pandemic the classification was changed. To guide transformation in database of terminologies comparison of old and new classification are tabulated below.

Table 6. Comparison of Old and New DOH Classification of COVID-19 Cases

OLD CLASSIFICATION	NEW CLASSIFICATION
Neither a Person under monitoring (PUM) or Person under Investigation	Non-COVID case
PUM	Not included in new classification
PUI (mild, severe, critical) who was not tested or awaiting test results	SUSPECT
PUI (mild, severe, critical) with inconclusive test results	PROBABLE
COVID Positive	CONFIRMED

Table 7. New DOH COVID-19 Case Definition Administrative Order No. 2020-0013

All Severe acute respiratory infection (SARI) cases with NO other etiology explaining the clinical presentation	**SUSPECT CASE**
Influenza-like illness (ILI) cases **with** any of the following: 1.) with no other etiology that fully explains the clinical presentation AND a history of travel to or residence in areas with reported local transmission of COVID-19 disease during the 14 days prior to symptom onset OR 2.) with contact to a confirmed or probable case of COVID-19 in two days prior to onset of illness of the probable/confirmed COVID-19 case until the time the probable/confirmed COVID-19 case became negative on repeat testing	
Individuals with fever or cough or shortness of breath or other respiratory signs or symptoms fulfilling **any one** of the following conditions: 1.) Aged 60 years and above 2.) With a comorbidity 3.) Assessed as having high-risk pregnancy 4.) Health worker	
Suspect case whom testing for COVID-19 is inconclusive	**PROBABLE CASE**
Suspect who tested positive for COVID-19 but whose test was not conducted in national or subnational reference laboratory or officially accredited laboratory for COVID-19 laboratory testing	
Any individual, irrespective of presence or absence of clinical signs and symptoms, who was laboratory confirmed for COVID-19 in a test conducted at the national reference laboratory, a subnational reference laboratory, and/or DOH-certified laboratory testing facility.	**CONFIRMED CASE**

Initially, the case definition classifies individuals as either Patients Under Investigation (PUI) or Persons under Monitoring (PUM). The evidence of local and community transmission necessitated a new classification with the aim of early detection and laboratory confirmation, especially among high risk and vulnerable population, to guide appropriate clinical management. [113]

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[120]. The average number of days before negative conversion in children is 12 days, usually 4 to 5 days after symptoms resolve[17]. RT PCR using blood sample can also be done and if positive may be indicative of viremia, hence severe disease[14 121]

2) **Serology**: Rapid antibody test using lateral flow immunoassay to detect IgM and IgG can also be used with an overall testing sensitivity of 88.66% and specificity of

90.63%[122]. We must take into account that IgM can only start to appear in 3 to 6 days from infection while IgG will appear after 8 days from infection. Therefore, if rapid antibody testing will be done, it should be requested at least 4 days from the onset of symptoms.[123] A false positive result may occur as the test is known to cross react with flu viruses. Even if patients have already recovered, these tests may remain positive as long as antibodies are present. Likewise, a false negative result can also be misleading especially if the patient has not mounted enough immune response when the assay was done.

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). [247]

The key is that the results of RT-PCR and IgM/IgG serological tests do not necessarily need to agree. A disagreement between the two tests, if any, can often be traced to the after-infection time points at which the tests were performed. RT-PCR testing may be appropriate for the detection of the SARS-CoV-2 virus during the acute phase, IgM/IgG is an appropriate test during the chronic phase. Since the exact time of infection is often unknown, combining RT-PCR and IgM/IgG testing can improve the accuracy of the COVID-19 diagnosis.

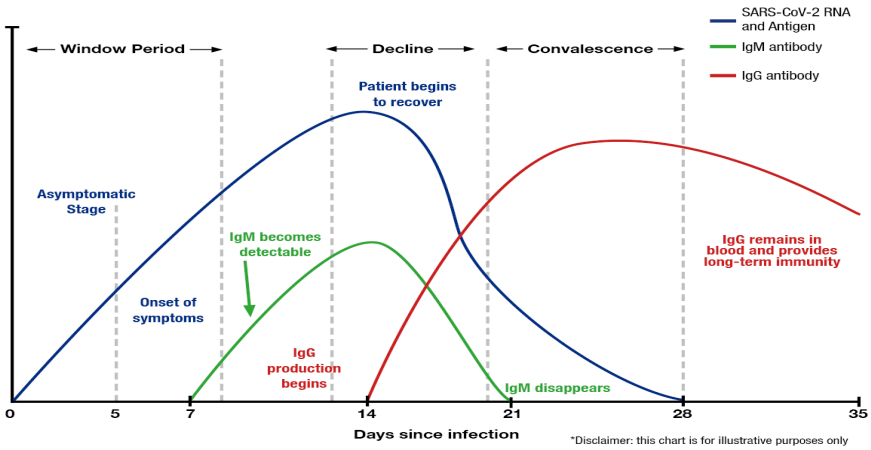


Figure 7 Variation of the Levels of SARS-CoV-2 RNA and Antigen, IgM and IgG after infection. [12]
http://www.diazyme.com/covid-19-antibody-tests

Techniques in doing RT PCR [106 107]

At present, Reverse Transcriptase Polymerase Chain Reaction (RT- PCR) of respiratory specimens for detection of SARS CoV 2 is the reference standard in confirming COVID – 19 infection. Detection of the virus is achieved by identifying the viral RNA through nucleic acid amplification, usually using a polymerase chain reaction. The most commonly tested sample types are swabs taken from the nasopharynx (more sensitive) and/or oropharynx. Swabs are then placed into a liquid to release viral RNA into the solution and subsequently amplified using reverse transcription-PCR.

Indications for nasal/oropharyngeal swab for RT-PCR for SAR CoV2 [247]

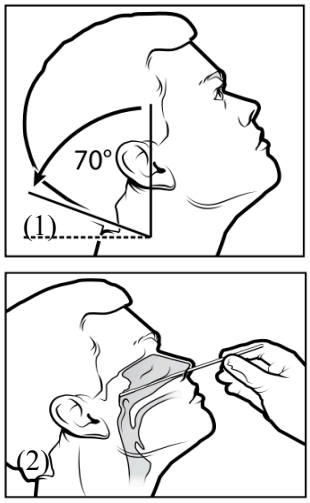
1. For symptomatic children
2. If the child has been in close contact, such as within 6 feet of a person with documented SARS-CoV-2 infection for at least 15 minutes even if asymptomatic
   Because of the potential for asymptomatic and pre-symptomatic transmission, it is important that contacts of individuals 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. It is important to realize that children can be infected and spread the virus but feel totally well and have no symptoms.

General Guidelines

Among most parts of the world, decisions about testing are left at the discretion of state and local health departments and/or individual clinicians but each test should be conducted in consultation with a healthcare provider. Specimens should be collected immediately once the decision to test is made regardless of the time of symptom onset.
A trained healthcare professional may collect from any of the following specimens:

1. **A Nasopharyngeal (NP) Specimen**
   Tilt the patient's head back 70^0 (1). Insert mini tip swab with a flexible shaft (wire or plastic) through the nostril parallel to the palate (not upwards) until resistance is encountered or the distance is equivalent to that from the ear to the nostril of the patient, indicating contact with the nasopharynx.
   Swab should reach depth equal to distance from nostrils to outer opening of the ear (2). Gently rub and roll the swab. Leave swab in place for several seconds to absorb secretions.

   Slowly remove swab while rotating it. Specimens can be collected from both sides using the same swab, but it is not necessary to collect specimens from both sides if the mini tip is saturated with fluid from the first collection. If a deviated septum or blockage create difficulty in obtaining the specimen from one nostril, use the same swab to obtain the specimen from the other nostril.



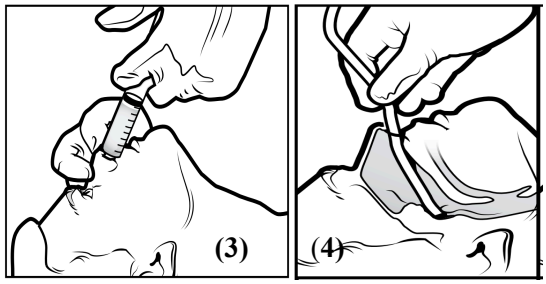
2. **An Oropharyngeal (OP) Specimen**
   Insert swab into the posterior pharynx and tonsillar areas. Rub swab over both tonsillar pillars and posterior oropharynx and avoid touching the tongue, teeth, and gums.

3. **A Nasal Mid-turbinate Swab or Deep Nasal Swab**
   This maybe self collected as long as supervised by a healthcare professional on site using a flocked tapered swab.

Tilt patient's head back 70 degrees. While gently rotating the swab, insert swab less than one inch (about 2 cm) into nostril (until resistance is met at the turbinates). Rotate the swab several times against nasal wall and repeat in other nostril using the same swab.

4. **An Anterior Nares (nasal swab) Specimen**
   This maybe self collected as long as supervised by a healthcare professional on site using a flocked or spun polyester swab. Insert the swab at least 1 cm (0.5 inch) inside the nostril (naris) and firmly sample the nasal membrane by rotating the swab and leaving in place for 10 to 15 seconds. Sample both nostrils with same swab.

5. **Nasopharyngeal Wash/Aspirate or Nasal Wash/Aspirate (NW) Specimen**
   Attach catheter to suction apparatus. Have the patient sit with head tilted slightly backward. Instill 1mL-1.5 mL of non-bacteriostatic saline (pH 7.0) into one nostril (3). Insert the tubing into the nostril parallel to the palate (not upwards). Catheter should reach depth equal to distance from nostrils to outer opening of ear (4). Begin gentle suction/aspiration and remove catheter while rotating it gently. Place specimen in a sterile viral transport media tube.



6. **Sputum**
   If patient can expectorate or has productive cough, sputum sample can be collected. However, induction of sputum to acquire a quality specimen is not recommended.
   Educate the patient about the difference between sputum and oral secretions (saliva). Have the patient rinse the mouth with water and then expectorate deep cough sputum directly into a sterile, leak-proof, screw-cap collection cup or sterile dry container.

7. **Bronchoalveolar Lavage, Tracheal Aspirate, Pleural Fluid, Lung Biopsy**
   Collect 2-3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container. These may be limited to patients presenting with more severe disease, including patients who are admitted to the hospital and/or intubated.

8. **Buccal swabs**
   Buccal swabs have low sensitivity in children.[150]

Storing

Once specimen is collected, swab/wash/aspirate should be placed immediately into a sterile transport tube containing 2-3mL of either viral transport medium (VTM), Amies transport medium, or sterile saline.

- Specimens should be placed into sterile viral transport media and immediately placed on refrigerant gel packs or at 4 degrees Celsius (refrigerator) for transport to the state public health laboratory.
- Keep specimens refrigerated (2-8 degrees Celsius, 26-46 degrees Fahrenheit) prior to shipping.

Collecting and Handling Specimens Safely

Healthcare professionals who will collect the specimen should maintain proper infection control and use recommended personal protective equipment, which includes an N95 or higher-level respirator (or facemask if a respirator is not available), eye protection, gloves, and a gown, when collecting specimens.

For providers who are handling specimens, but are not directly involved in collection (e.g. self-collection) and not working within 6 feet of the patient, gloves are recommended. They are also recommended to wear facemask or cloth face covering at all times while in the healthcare facility. PPE use can be minimized through patient self-collection while the healthcare provider maintains at least 6 feet of separation.

Bulk-packaged swabs may be used for sample collection; however, care must be exercised to avoid SARS-CoV-2 contamination of any of the swabs in the bulk-packaged container.

- Before engaging with patients and while wearing a clean set of protective gloves, distribute individual swabs from the bulk container into individual disposable plastic bags.
- If bulk-packaged swabs cannot be individually packaged:
    a. Use only fresh, clean gloves to retrieve a single new swab from the bulk container.
    b. Close the bulk swab container after each swab removal and leave it closed when not in use to avoid inadvertent contamination.
    c. Store opened packages in a closed, airtight container to minimize contamination.
    d. Keep all used swabs away from the bulk swab container to avoid contamination.
- As with all swabs, only grasp the swab by the distal end of the handle, using gloved hands only.

Use only synthetic fiber swabs with plastic or wire shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing. CDC is now recommending collecting only the NP swab, although OP swabs remain an acceptable specimen type. If both NP and OP swabs are collected, they should be combined in a single tube to maximize test sensitivity and limit use of testing resources. Proper labeling is a must and should include complete name, hospital number, type of specimen and date of collection.

Shipping:

If delivery will be delayed for more than 3-4 days, specimen should be frozen at -70 degrees Celsius (-94 degrees Fahrenheit). Ensure that the specimen will be received by the public health laboratory personnel during normal business hours. Specimens that can be delivered promptly to the laboratory can be stored and shipped at 2-8°C. When there is likely to be a delay in specimens reaching the laboratory, the use of viral transport medium is strongly recommended and specimens may be frozen to - 20°C or ideally -70°C and shipped on dry ice. It is important to avoid repeated freezing and thawing of specimens**.**

1.6 Laboratory Examination

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]

Laboratory tests that may be requested:

1. Complete Blood Count
2. C Reactive Protein (CRP),
3. Erythrocyte Sedimentation Rate (ESR)
4. Procalcitonin

Laboratory tests that may be requested in severe cases:

1. Alanine Aminotransferase (ALT)
2. Aspartate aminotransferase (AST)
3. PT PTT
4. LDH
5. Creatinine
6. Blood Urea Nitrgen (BUN)
7. Creatinine Kinase-MB (CK MB
8. D-Dimer
9. Arterial Blood Gases (ABG
10. Serum Ferritin

Rationale

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[14]. Leukopenia may also be seen in pediatric patients[14]. On the contrary to adult data, it was noted that there is increased leukocyte and neutrophil counts especially in patients with unfavorable COVID-19 progression[124]
Mild thrombocytopenia is commonly seen.

Inflammatory Markers: CRP, ESR may be elevated by as much as 30 to 100%[124]. Procalcitonin may be used to determine secondary bacterial infection which is common among severe cases[124]

Liver Function Tests: Alanine Aminotransferase (ALT), Aspartate aminotransferase (AST) Elevated liver enzymes (ALT, AST) are observed in up to 1/3rd patients and need to be monitored.

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

Lactate Dehydrogenase (LDH) may increase and is a predictive factor for early recognition of lung injury.

Serum Ferritin elevation indicates cytokine storm syndrome or organ damage.

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[17].

1.7 Chest Imaging in Pediatric COVID-19 Patient

1.7.1 Chest Radiography

Recommendation 4

- Chest Imaging should be requested
  1. 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
  2. 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 [10,20]

  (Strong Recommendation, Low grade evidence)

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.[10] 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.[20]

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

1. Bilateral distribution peripheral and/ or subpleural groundglass opacities (GGOs) and and “halo sign” or consolidation were the most common feature
2. Local or bilateral patchy shadowing
3. Viral pneumonia-like changes[4,14]

In a systematic review and meta-analysis done the most common radiographic features among 31% patchy consolidation and 48% of these patients were halo signs with ground

glass opacities. In 27% of the patients, there was no definite lung lesion.[4] 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. Viral pneumonia-like changes in 70.4% children undergoing chest imaging.[4,14]

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).[157]

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.[158]

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.[10]

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[10]

1. **Typical Findings Of Pediatric COVID-19**
   Bilateral distribution peripheral and/or subpleural GGOs and/or consolidation.
2. **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.
3. **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.
4. **Negative for Pediatric COVID-19**
   No CXR findings suggestive of pneumonia

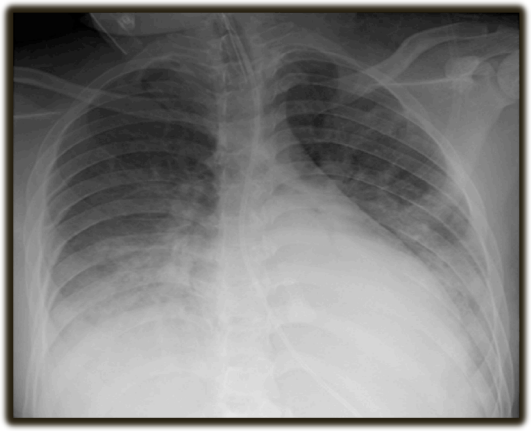
(Strong Recommendation, moderate-Grade Evidence

Table 7. Structured CXR Reporting for Pediatric COVID-19 patients

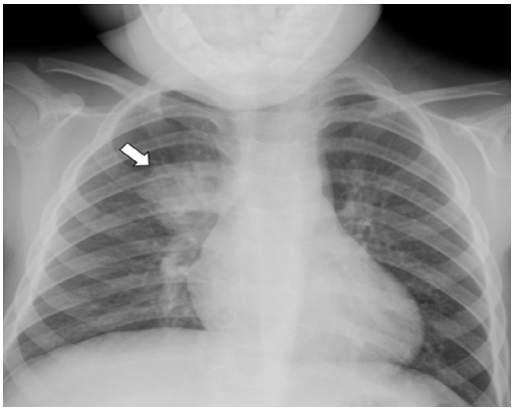
Classification	Rationale	CXR Finding(s)	Suggested Reporting Language
Typical	Commonly reported CXR findings of COVID-19 pneumonia in children	• Bilateral distribution peripheral and/or subpleural GGOs and/or consolidation	Imaging findings are commonly seen with COVID-19 pneumonia in children. Differential 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	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

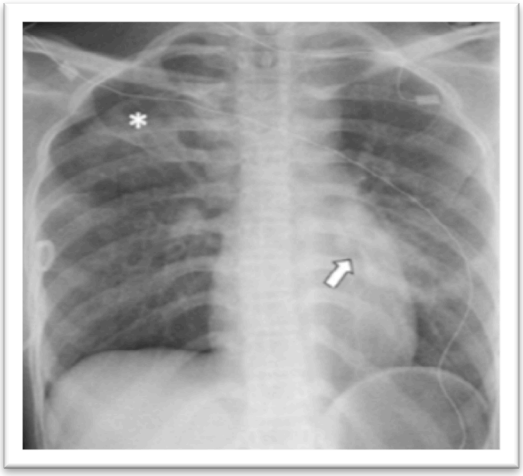
Chest Xray Images in Pediatric COVID-19[10]



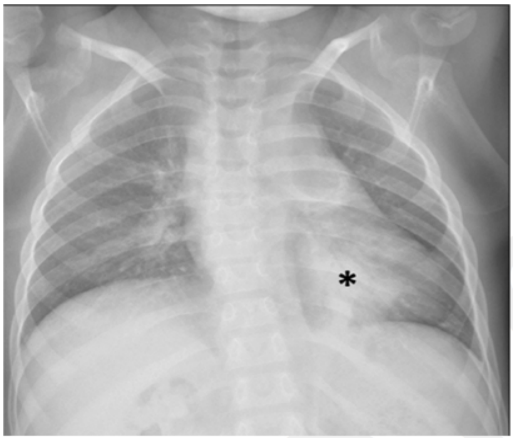
A. *A case of 16-year-old female with tuberous sclerosis and positive COVID-19 RT-PCR test. Chest radiograph shows bilateral lower lung zone-predominant consolidation(arrow) and ground-glass opacities, which is typical CXR findings of pediatric COVID-19 pneumonia.* [10]



B*. 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 infection.* [10]



C*. 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.* [10]



D*. 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. [10]

1.7.2 Chest Computed Tomography

Recommendation 6

The following shall be considered in the structured reporting for CT findings for pediatric COVID-19 patients[10]

- **Typical findings of pediatric COVID-19**
  Bilateral, peripheral and/or subpleural GGOs and/or consolidation in lower lobe predominant pattern
- **Indeterminate findings of pediatric COVID-19**
  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, or the "crazy paving" sign.
- **Atypical findings of pediatric COVID-19**
  Unilateral segmental or lobar consolidation, central unilateral or bilateral GGOs and/or consolidation, discrete small nodules, lung cavitation, plural effusion, or lymphadenopathy.
- **Negative for pediatric COVID-19**:No chest CT findings suggestive of suggestive of pneumonia in children
  (Strong Recommendation, Moderate-Grade Evidence)

Table 7 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).

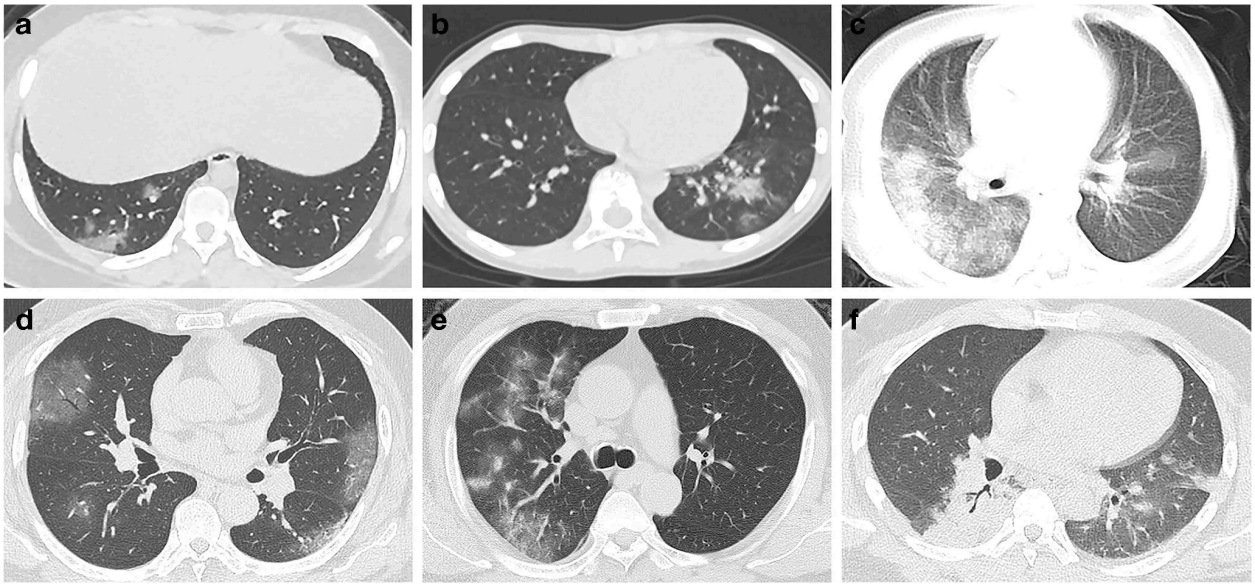


Fig 8a Chest CT imaging of coronavirus disease 2019 (COVID-19) pneumonia in children and adults. a Female, 14 years old. Chest CT showed scattered GGO in the inferior lobe of the right lung, located subpleural or extended from subpleural lesions. **b** Male, 10 years old. Chest CT showed consolidation 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.[127]

CT = Computed Tomography

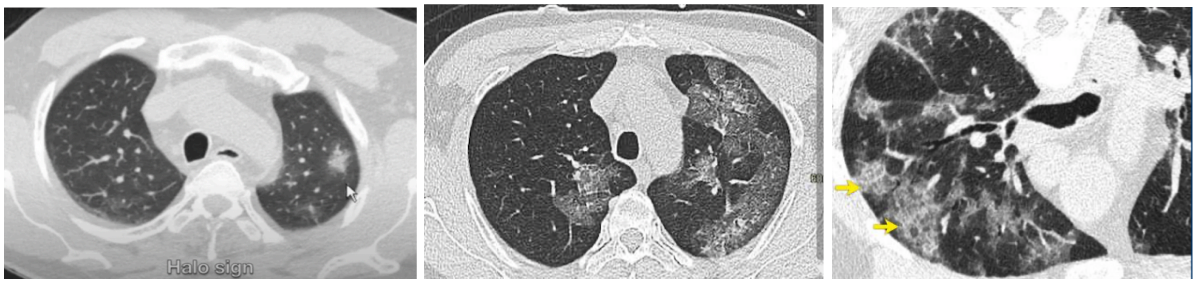


Fig 8.b A) Focal consolidation with a rim of surrounding ground glass opacity "halo sign" B) Bilateral ground-glass opacities c) Thickened interlobular and intralobular lines in combination with a ground glass pattern called "crazy paving"[127]

1.7.3 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 [125] [126]

(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-19patientsandshowedastrongcorrelationwithchestultrasound[30]

The well-known **Advantages of LUS** in terms of: [103]

1. Portability, Bedside Evaluation - It is a tool that could be used at bedside avoiding the need for transferring infected patients to 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:[99]

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.[102]

The lung ultrasound on patients with COVID-19 was performed using 12-zone method (table 8) The observational patterns occurred across a continuum from mild alveolar interstitial pattern to lung consolidation. The findings of lung ultrasound 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 8. CT and ultrasonographic features of COVID-19 pneumonia[99]

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[153]
Figure 9 series : Pediatric Ultrasound Findings

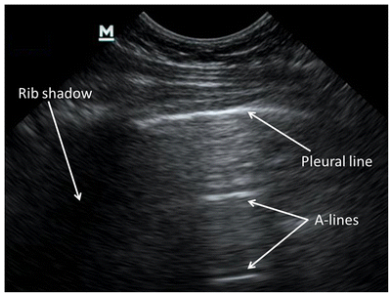


Figure 9A: **Normal Ultrasound in children :** note the A lines

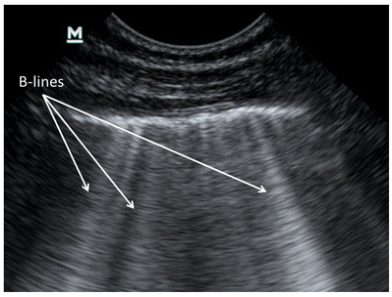


Figure 1B. **Pathologic Ultrasound**: note the B lines in a child with Pneumonia

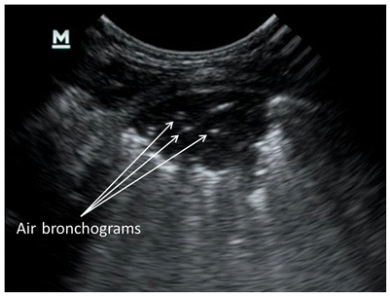
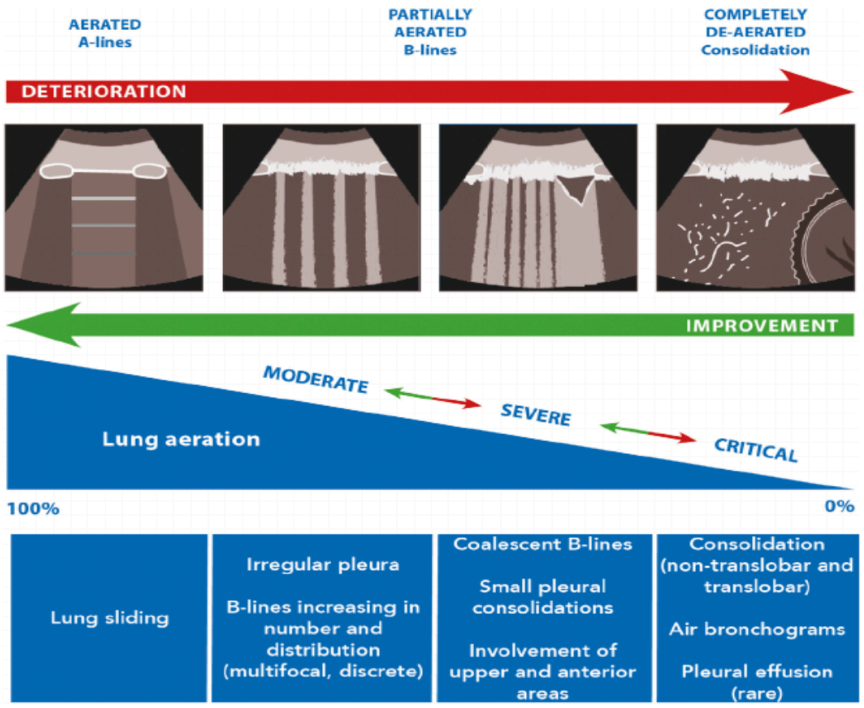


Figure 1.C : Pathologic Ultrasound: note the Air Bronchograms

Figure 10. Ultrasound guide for pediatric COVID-19[154]



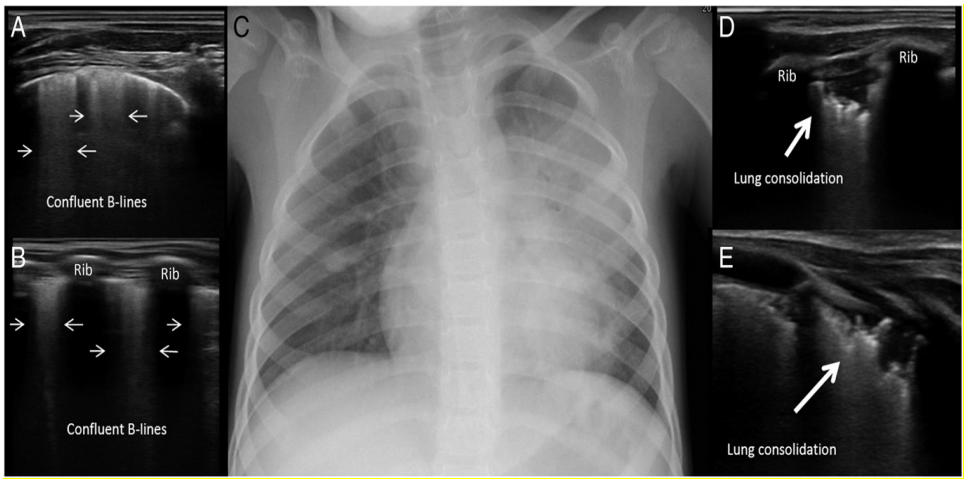


Fig 11- Chest Xray and Chest Ultrasound correlation *. See* ***A and B,*** *Multiple confluent B-lines (thin arrows).* ***C****, Chest radiography with left upper lobe consolidation and right central ground-glass opacities.* ***D*** *and* ***E,*** *A lung consolidation (thick arrows) at LUS.* [155]

1.7.4. Main Thoracic Findings in Children with MIS-C and COVID19[157]

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 come 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.[155]

RECOMMENDATION 8

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.[157]

(Weak recommendation, moderate grade evidence)

Table. 9. Differences in Imaging Findings between MIS-C Associated with COVID-19 and Typical COVID-19 in Children.[157]

	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.

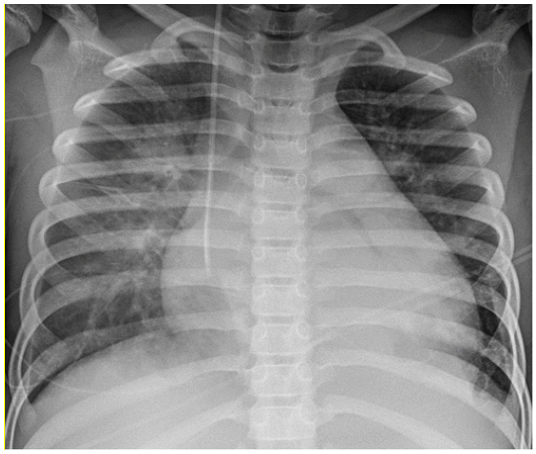


Figure 12a. *7-year-old male, with MIS-C associated with COVID-19, who presented with symptoms of fever, sore throat vomiting , abdominal pain, truncal rash, and hypotension. Frontal chest radiograph shows cardiomegaly, pulmonary edema, and small bilateral pleural effusions* [157] *Printed with Permission*

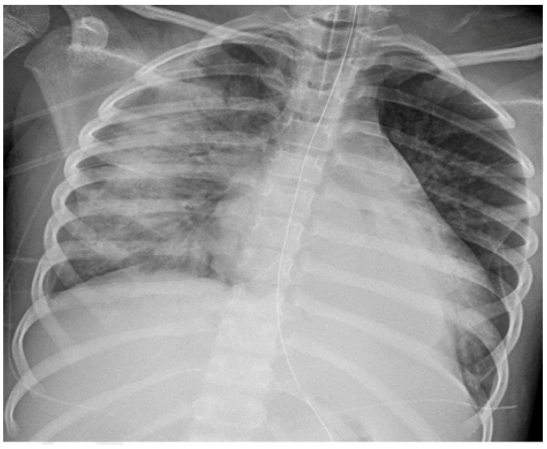


Figure 12b. *8-year-old female, who presented MIS-C associated with COVID-19, with fever, sore throat, vomiting, diarrhea, abdominal pain, back pain and fatigue. The patient ultimately progressed to develop hypoxic respiratory failure, hypotension, myocarditis, and acute kidney injury. Frontal chest radiograph shows an ARDS pattern with asymmetric, right greater than left, hazy opacities, and dense consolidative opacity in the left lung base, and cardiomegaly.*[157] *Printed with Permission.*

Chapter 2

2. RESPIRATORY SUPPORT FOR COVID-19 PATIENTS

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

A. Precaution

Recommendation 9

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.[19]

1. Preferably in an appropriate Airborne Infection Isolation Room (AIIR)
2. Use of a surgical mask over HFNC (figure 1) 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)

(Weak recommendation, low quality evidence)

B. First line Approach

Recommendation 10 [19.6 30 32]

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%.[26]
   a. If patient continues to be hypoxemic, oxygen delivery via face mask with reservoir bag should be initiated
   b. 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)

Remarks

The optimal respiratory support strategy for individuals with severe COVID-19 before invasive mechanical ventilation (IMV) is a subject of much debate. However, it has to be recognized that globally, there have been relatively few children admitted to critical care units with COVID-19. Therefore, most data and recommendations in the respiratory support of patients with COVID-19 are extrapolated from adult practice.

During resuscitation, 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.[149] 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.[32] 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% 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.[146] 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.[147] Initially, flow rates can be started at 1 to 2 L/kg/min. (*Refer to Table 10) 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.[32] The rationale is that a higher pressure level might be obtained when using CPAP/NIV.

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. Hence, surgical masks can reduce such spread.[138] [139] The Center for Disease Control and Prevention (CDC) 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 good children going out into the community. The recommendation of using surgical masks while on any respiratory support in this chapter is meant for children with hypoxemia, needing hospital admission, and is under oxygen supplementation and close clinical monitoring.

Table 10. 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

Recommendation 11

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.[19]

(Weak recommendation, low quality evidence)

Remarks:

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.[34]

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.[33]

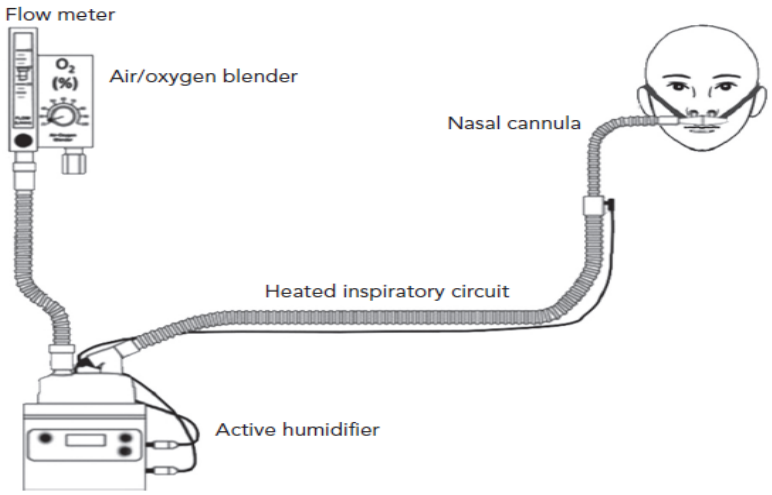


Figure13. High Flow Nasal Cannula (HFNC) Reprinted from: High Flow Nasal Cannula Oxygenation revisited in COVID-19. https://www.cfrjournal.com/journals/editions/cfr-volume-6-2020. Reprinted with permission.

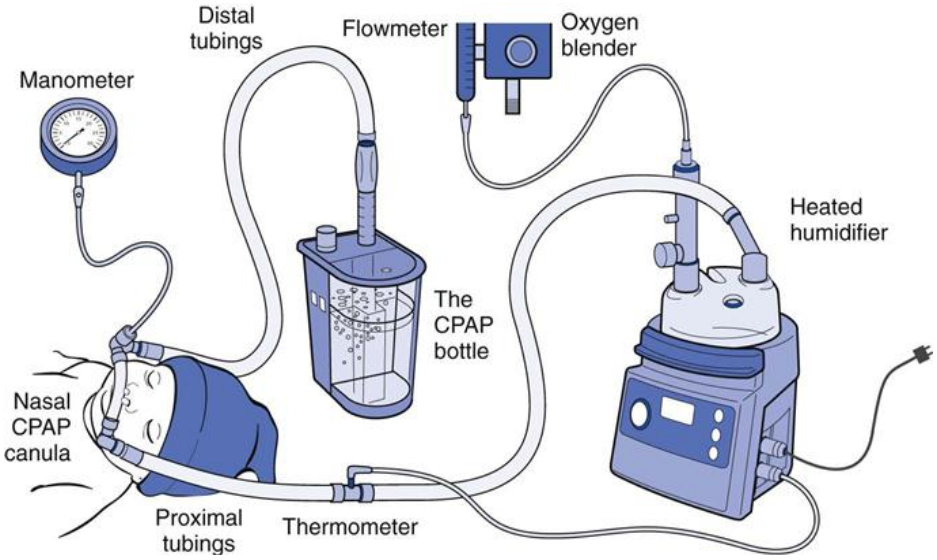


Figure 14. Diagram of Bubble CPAP delivery system. DiBlasi, R. M. (2016). Neonatal and Pediatric Mechanical Ventilation. In *Thoracic Key*. Retrieved from https://thoracickey.com/neonatal-and-pediatric-mechanical-ventilation/. Reprinted with permission.

2.2 Airway Management and Tracheal Intubation Specific To The COVID-19 Patient Group

A. Precaution

Recommendation 12

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[19]

(Strong recommendation, low quality evidence)

B. Indication for Intubation

Recommendation 13

We strongly recommend that intubation should not be further delayed if SpO2/FiO2 ratio < 221 in pediatric patients on bi-level NIV or CPAP and if there is no improvement in oxygenation (target SpO_2 92-97% and FiO_2) within 60 minutes.[32]

(Strong recommendation, Moderate quality evidence)

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 $\geq$ 97% to allow for valid measurement of the SpO2/FiO2 ratio and the OSI.

Recommendation 14

The use of Bag Valve Mask (BVM) prior to intubation is not advised for suspected or confirmed COVID-19 patients due to its capacity to generate aerosols. However, if the bag/mask ventilation is necessary for pre-oxygenation, It is strongly recommended to follow safety measures to minimize aerosolization: [19 32]

a. Two-Person technique/Two handed vice grip (figure 9), 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 quality evidence)

Optimize preoxygenation by placing 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. Aside from a clear drape, some centers also make use of an "aerosol box" (*figure 15*) to decrease aerosolization risks.[28] 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.[140]

Figure 15. Two-handed vice grip during BVM (right).
Reprinted 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 15

Rapid Sequence Intubation or rapid sequence induction and 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 peri-tubal leak and dissemination of secretions.[30]

(Strong recommendation, low grade evidence)

Children with ARDS may desaturate quickly during endotracheal intubation; hence, it is ideal for the most skilled and experienced person to perform it. This will also help to minimize the attempts. The use of video laryngoscopy is recommended over direct laryngoscopy.[30]

2.3 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 severity.[32]

Recommendation 16

The general principles of management of child with ARDS apply to a child with COVID-19 related ARDS. The lung protective strategies suggested are as follows: [6] [32]

a. Low tidal volume (3-6ml/kg IBW) if poor respiratory compliance Low tidal volume (5-8ml/kg) if better preserved respiratory compliance
b. Initial Positive End Expiratory Pressure (PEEP) of 8-10 cmH20 individualized for each patient's phase of ARDS and should be titrated when there is refractory hypoxemia (148)
c. Target plateau pressure <28cmH2O
d. Permissive hypercapnia (pH >7.20)

(Weak recommendation, low 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%.[32.] A lower level of plateau pressure (<28cmH2O) is targeted, and a lower target of pH is permitted (7.15–7.30). 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.[29]

The routine use of higher PEEP level is not advised, which varies from previous recommendations of PEEP use in ARDS. Individualized titration of PEEP in refractory hypoxemia is recommended a refractory hypoxemia defined paO2/FiO2 150; OI≥12; OSI ≥10 and FiO2 > 0.6 is present. The patient's hemodynamics must be monitored closely with increasing PEEP.[148]

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.

2.4. Prone Positioning For Mechanically Ventilated Confirmed Covid-19 Children

Recommendation 17: Prone positioning may be considered as part of treatment regimen for pediatric COVID-19 patients with moderate to severe ARDS

(Weak recommendation, low grade evidence). [32]

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-19.32 A review by Orloff, et al. on pediatric ARDS also reported that prone positioning might be considered as part of the treatment regimen for severe ARDS in children.[85] Both of these articles stated prone positioning as adjunctive therapy as part of the Pediatric Acute Lung Injury Consensus Collaborative (PALICC) guidelines. 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. However, the proning maneuver requires sufficient health care human resources and expertise for safety.6 The suggested indications and contraindications for proning in mechanically ventilated children with COVID-19 were adapted from previous studies and is stated in Table 11. Alternating supine and prone positioning in COVID-19 patients with ARDS reported favorable results with improvement in lung recruitability.[83] 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.[148]

At present, there are no local or international data on the use of awake proning in children with hypoxemia outside the neonatal intensive care. Most studies reviewed were on adults with RDS. In light of this lack of significant evidence, we cannot disagree with extrapolating the use of awake proning in children with hypoxemia and respiratory distress. Awake pronation is economical and can be done with minimal staff and with no equipment required. Furthermore, it appears to be a safe, inexpensive, and versatile strategy that can be leveraged across various healthcare systems.

A comprehensive Cochrane review, involving 24 studies among hospitalized infants and children with Acute Respiratory Distress Syndrome (ARDS). The outcome measures included were the following respiratory and oxygenation parameters: improvement in oxygen saturation, arterial oxygen, and oxygenation index.[82] Furthermore, there was also a statistically beneficial improvement in decreasing the respiratory rate in infants who underwent the prone positioning procedure.[84, 86]

There are no standard proning techniques for children with ARDS as different proning protocols were used in different trials. A team coordinated approach with pre-positioning

turning [108,101] and post positioning protocol have been described[101,105,108] An adapted list of preparation and prone positioning steps for proning among mechanically ventilated COVID-19 confirmed children below (*see Table 12)* 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.

Table 12. 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

The duration of proning practices varies between 12–18 hrs per day with the patient in the prone protocol. Prolonged prone positioning (>24 hrs) may be considered early in the disease trajectory. Improvements in the oxygenation were noted 2 hours after prone positioning in the study by Kornecki et al., but the reduction in Oxygenation Index was maintained among children with acute respiratory failure for a duration of until 12 hours.[105]

Prone positioning can be discontinued if PaO2/FiO2 ≥150; OI < 12; OSI < 10. 32 The clinical experience of the First Affiliated Hospital, China, reported that they ceased the proning procedure once the patient demonstrated improvement of the PaO2/FiO2 ratio to > 150.87. The assisted proning procedure may be considered safe for critically ill children with no serious adverse events noted. [82,105,]

Figure 16 Child 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*

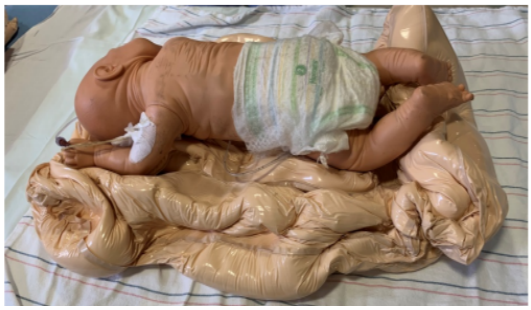


Figure 17 *Infant on Prone Position : Adapted with permission from Tracy Fulkerson,BSN RN CCRN*

Table 12. ***The* Preparation and 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 (infants/ 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 level of ETT 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 oronasal 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 patients head part, wipe oral secretions if any
18. Gently turn patient from PRONE to SUPINE while supporting the midtorso 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.

Chapter 3

3. AIRWAY THERAPIES AND RESPIRATORY MECHANICS

3.1 Aerosol and Delivery Devices

3.1.1 Aerosol Therapy Among Spontaneously Breathing Children

Supportive therapies are presently given to confirmed COVID-19 patients, which includes respiratory care especially for the critically ill. Children with COVID-19 often present with respiratory symptoms and those with signs and symptoms of bronchospasm will need deliver aerosol therapy to reverse this problem.

The common types of devices for aerosol therapy in the pediatric group include nebulizers, pressurized metered-dose inhaler (pMDI), dry powder inhaler (DPI) and Liquid metered-dose inhaler (LMDI). [16,36, 51]Much evidence was found on the equally efficacious function of nebulizers and pMDI when used to deliver bronchodilators and aerosolized steroids in children whether it be in the emergency department, inpatient and outpatient settings.[37-40]

However, nebulization alongside other Aerosol Generating Medical Procedures (AGMP) like HFNC, Noninvasive ventilation (BIPAP/CPAP) has been implicated for nosocomial transmission before and during the COVID-19 pandemic.[41-,46,138] In a review by Dhand and Li, these mentioned therapies have described the formed by an infected person, bringing these aerosols to traverse farther distances.[45] A study by Hui et al. reported dispersed virus laden aerosols in healthcare surfaces when using a jet nebulizer. They reported that the exhaled air leakage through a jet nebulizer's side vents can increase from 0.45 μ to 0.8 μ with worsening lung injury.[42] Ye et al. reported SARS-COV-2 contamination on hospital surfaces but did not test for airborne contamination.[54] While Van Doremalen et al. found SARS-CoV-2 in the air for 3 hours, suggesting airborne transmission[55]. A study by Fears et al. agrees with the latter report stating the virus remains in air for 16hours.[56] Thus, aerosol dispersion of possibly contaminated SARS-CoV-2 bioaerosols thru nebulization poses a health hazard during this pandemic.

Recommendation 18:

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)

Remarks

Evidence from recommendations as early as the start of the COVID-19 Pandemic until the present indicates the avoidance of nebulization and dry powder inhaler or metered-dose inhaler with spacer for spontaneously breathing patients.[8,45-52] The possible rationale for pMDI use recommendations is that it is enclosed with less risk of contamination of the internal component while needing no drug handling preparations [16] and the low emitted dose (100 µL/actuation) produces less aerosol mass with shorter treatment times.[47]

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[40]

  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.[51] *(Further discussion regarding the use of device techniques in Section 3.2.)*

Table 13. 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 spacer	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 [51,52]

Procedure of Pressured Metered Dose Inhaler with VHC

1. "Prime" the pMDI by releasing into the air or into the delivery chamber if it is new or has not been used for several days to provide adequate dose.
2. A single pMDI actuation should be delivered at a time, with the inhaler shaken in between. Multiple actuations into the spacer before inhalation may markedly reduce the amount of drug inhaled.
3. Static charge may accumulate on some delivery devices like plastic spacers, attracting drug particles and reducing lung delivery. This charge can be reduced by washing the spacer with detergent (without rinsing) and allowing it to air dry. Spacers made of anti-static materials or metals are less subject to this problem. If a patient or health care provider carries a new plastic spacer for emergency use, it should be regularly washed with detergent (e.g. monthly) to reduce static charge.[51]
4. Cleaning of pMDI delivery device is necessary according to the manufacturer's advice.

3.1.2 Aerosol Therapy Among Children on Non-Invasive Ventilation

Experts in aerosol therapy suggest 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.[46,48] Aerosol therapy is possible through HFNC with lower aerosol dispersion than ordinary open oxygen masks.[44] Berlinski included in vivo and in vitro studies in child lung models for NIV inhaled drug delivery via mesh nebulizers; indicating specific position placement of aerosol therapy device by nebulizer along the NIV circuit to improve aerosol delivery. Another option is to use a pMDI with a spacer adaptor attached to the ventilator circuit ,which should be actuated during inhalation however; this data is based on adult and in vitro studies[68] when delivered via a non-invasive ventilation circuit. The practitioner should strongly consider the device and interface at hand, availability of negative pressure rooms, and full PPE supply in each practice setting before initiating aerosol therapy.

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.
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, use in-line or closed system nebulization with filters by the mesh nebulizers attached to the ventilator circuit. [46,48,68] Should nebulization be done, keep the viral filter at the expiratory end of the single limb noninvasive , and ventilator limb to reduce secondhand aerosol exposure.
5) The procedure must be done in a negative pressure room with healthcare workers using PPE level 4 for AGMP, limiting one person in the said room with the patient during the procedure.

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

Recommendation 19.

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)

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.[47,52] The Australian Physiotherapy management of COVID-19 recommends (e.g., PariSprint with inline viral filter)[57] on precautions for aerosol generating medical procedures. 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 3.2B2.)*

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,clamp the ventilator tubings before tube detachment and aseptically adminiter the drug for aerosl treatment.
5. Proper personal protective equipment must be worn during the aerosol generating procedure in an Airborne Infection Isolation Room (AIIR).

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

Recommendation 20:
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[50]

1. Severe life-threatening respiratory distress,
2. Patients with compromised ventilation,
3. Uncooperative patients,
4. Children with poor response to pMDI

Aerosolization does not only occur during medical procedures; it also happens during ordinary breathing, coughing, and sneezing, where big droplets from dispelled secretions become aerosolized into smaller droplets until they dry up by evaporation.[47] However, procedures like nebulization and oxygen supplementation may cause admixture of sterile oxygen and clean aerosolized medication with the infected patient's breath contaminated with pathogens.

In the pre-COVID-19 era, nebulization by small volume nebulizers has been the easiest to use[16] as a form of aerosol medication delivery for patients. The aerosol produced is from the liquid medication transformed into a 1-5 μm sized aerosol particle range to allowing deposition to the lower airways.[16,44] However, nebulizers are under potential short-range aerosol transmission sources.[43] Notably, aerosol plumes are seen as "smoke leak "from the mask's exhalation vents during nebulizer use. Jet nebulizers (JN) have an open cup container design to be filled with medications used for treatment. 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. Contaminated aerosols are dispersed during the nebulization process,[47] this brings a risk where bystanders nearby could inhale the dispersed contaminated aerosols, including healthcare workers attending to the patient. On the other hand, vibrating mesh nebulizers (VMN) have the mesh to separate its medication from the patient's interface reducing contamination risks during exhalation. These nebulizer types also have low residual volume thereby decreasing pathogen growth if contaminated by handling.

Fugitive aerosols were emitted during nebulization with the non portable vibrating mesh nebulizers emitting lesser fugitive emissions than the jet nebulizers.[44] 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[42] A type of pneumatic jet nebulizer is the breath enhanced nebulizer which uses 2 one-way valves preventing aerosol leaks. Exhaled gas passes through an expiratory valve in the mouthpiece are found not to generate aerosol after inhalation.[16,138] However, contamination of the device may still occur due to its nebulizer cup design.

In a recent experimental study by Tang et al. ,they demonstrated the risk of using nebulizers without filters via face mask in a room even with the recommended 12 Air Changes/Hour(ACH)[88] A report on SARS-CoV2 states that its infectivity is maintained at a respirable particle size over short distances, in contrast to either betacoronavirus[56] and is found to be resilient in aerosol form.[55,56] Such findings should not be taken lightly. Our utmost intention to provide optimal care to patients but lower disease transmission to protect others, especially health workers, is more prudent during this pandemic.

If avoiding aerosol-generating procedures, nebulization is not possible, or the drug formulation necessitates the inhaled format of inhaled drugs is not in the pMDI or DPI, soft mist inhaler form, nebulization should be done under controlled conditions ensuring efforts to reduce risks of medical aerosol leaks, aerosol dispersion, and contamination of nearby surfaces from the procedure.

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

1. The procedure must be done in an airborne infection isolation room with negative ventilation with 6-12 air changes per hour or a portable HEPA unit can be placed in the room.[88] In cases of patients in cohort groups admitted in the COVID19 ward, they need to be moved to a negative pressure room for delivery of nebulization.
2. Incorporation of the liquid medication to the nebulization cup should be done aseptically. Have the patient wear a disposable surgical mask during the procedure and discard it after nebulization. In mechanically ventilated patients follow previously discussed precautions.
3. Single patient device use is recommended.
4. Place a filter on the exhalation part of a nebulizer (see Figure 18 & 19) to provide protection from infection and reduce secondhand aerosol breathing in hospitals and outpatient clinics.[16]
5. When performing aerosol generating procedures (AGPs) which include aerosolized treatment delivery by nebulization, the health care professional (HCP) should wear level 4 PPE (N95 or higher-level respirator such as disposable filtering facepiece respirators, and elastomeric respirators, eye protection, gloves and a gown).[8]
6. There should be only one patient in the room. For young children, limit to one person who will accompany the patient. The number of healthcare staff present during the procedure should be limited to only those essential for patient care and procedure support. 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.
7. Clean and disinfect the nebulizer equipment per manufacturer's advice and dispose the non reusable parts after each procedure.[58] Clean room surfaces promptly after each procedure as SARS-CoV2 are found in hospital objects and medical equipment and are viable within 3 hours.[55]

In local hospital settings, the procurement of pressurized metered-dose inhalers and respective interface and adaptor supplies must be prioritized. The pMDI with valve holding chamber or spacer is still the most feasible manner of delivery of bronchodilator

drugs. Then again, we cannot over emphasize, it is still best to minimize aerosol treatment among COVID-19 patients and may give aerosol therapy for children needing such only if with adherence to the stated precautions due to the current COVID-19 pandemic.

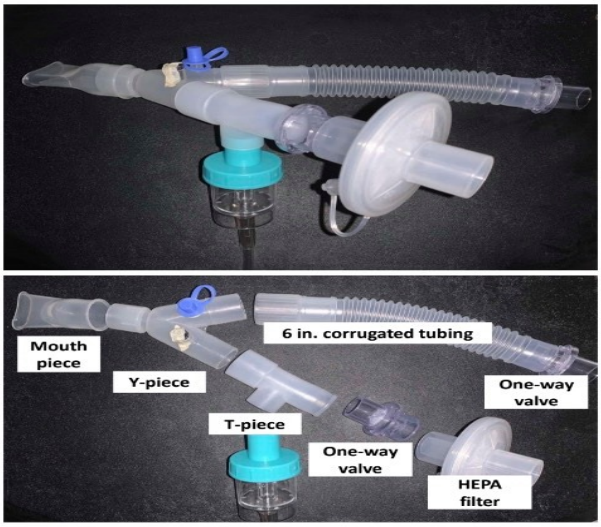
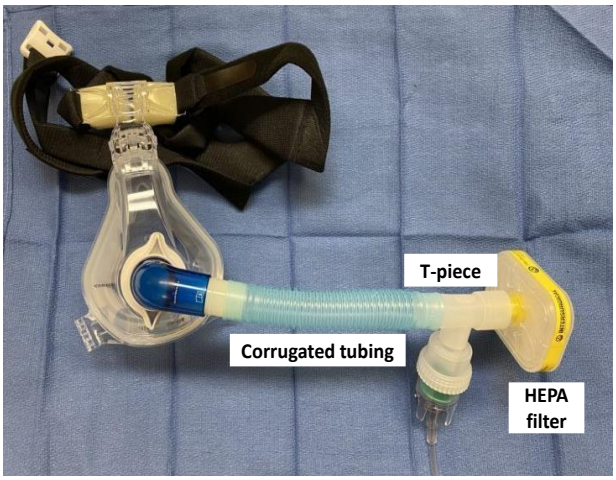


Figure 18. *Nebulizer attached with HEPA filter for a cooperative patient via a mouthpiece. This is a suggested set-up for COVID-19 patients and is an adjunct to the safety practice points during the limited use of nebulization as stated above.*



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

Figure 19. *HEPA filter in a single limb circuit for a patient with non-invasive ventilation via a face mask.*

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

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

Recommendation 21:

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)*[7, 51]

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.[38] 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). 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. [59]

The Global Initiative for Asthma 2020 recommends a dose of 2-6 puffs for children ≤ five years old and 4-10 puffs for children ≥ six years old.[51] Doses may be repeated every 20 minutes until a good clinical response is achieved based on the GINA guidelines.[51] 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.[38] 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.[66.67]

B. Pressurized metered dose inhaler (pMDI) Administration Techniques

B.1 Non – Intubated Children

Steps on how to use pMDI in Non-intubated children:

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.2. 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.[70] Drug losses within the ETT may be minimized by placing the aerosol generator at a distance from the ETT rather than attaching it directly.[71]

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.[70] 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.[9]

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.[72]

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.[63, 73] 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%.[74]

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°[9, 65, 75]

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

Recommendation 22:
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[9,18,69]

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 20*].

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.[69] 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. 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%).[69]

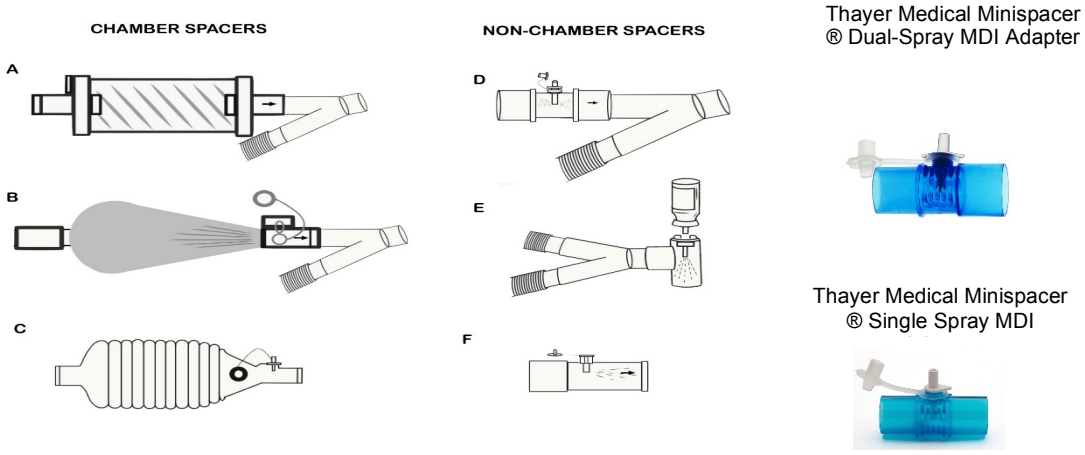


Figure 20. Different types of chamber/adapters used to connect the metered dose inhaler (MDI) canister to the ventilator circuit.
A, non-collapsible cylindrical chamber; **B**, aerosol cloud enhancer (ACE) spacer, with which the MDI flume is directed away from the patient; **C**, collapsible cylindrical 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.

Airway Clearance/ Respiratory Physiotherapy for COVID19 patients

Recommendation 23
For airway clearance procedures, we strongly recommend the following strategies among pediatric COVID-19 patients: Ensuring adequate oxygenation, appropriate inhalation therapy, keeping the respiratory tract unobstructed, appropriate reassessment of airway patency and non-invasive/invasive respiratory support and mechanical ventilation, and judicious use of fluids and vasoactive medications.

(*Strong recommendation, moderate grade evidence)*

The main objective of airway clearance is to facilitate clearance of respiratory secretions, inflammatory exudates, or aspirated material in infants and children.[78, 79]

Airway clearance or respiratory physiotherapy may be beneficial in the respiratory treatment and physical rehabilitation of patients with COVID-19, although a productive cough is a less common symptom, physiotherapy may be indicated if patients with COVID-19 present with airway secretions that they are unable to independently clear.

Thomas, et.al. highlighted key concepts in the principles of physiotherapy among patients with confirmed or suspected COVID-19. Respiratory 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:

a) Patients with copious airway secretions who may not be able to clear on their own,
b) High-risk patients with neuromuscular disorders and other co-morbid illnesses which result in increased mucus production or weak cough,
c) Mechanically ventilated patients with inadequate airway clearance,
d) Severe symptoms of pneumonia or with chest imaging findings showing consolidation[76]

Respiratory Physiotherapy techniques:

a) Positioning
b) Active cycle of breathing
c) Manual and/ or ventilator hyperinflation
d) Percussion and vibrations
e) Positive expiratory pressure therapy
f) Cough maneuvers
g) Airway suctioning

These are some examples of respiratory physiotherapy techniques that may be useful in aiding airway clearance for Covid-19 patients. However, the authors emphasized that because of aerosolization and exposure risks, these interventions should only be provided when clinically indicated.[57] Airway clearance procedures may be done only when needed and are not frequently required in COVID-19 patients.[77]

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.[57]

It is recommended 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. Furthermore, for personnel caring for critically ill patients with COVID19, it should be emphasized that they are adequately trained in proper use and donning and doffing of PPE.[57]

Chapter 4

DISCHARGE, ENDING ISOLATION and HOME CARE in PEDIATRIC COVID-19

4.1. Discharge from Hospital Among Symptomatic Children with COVID19

Recommendation 24:
We strongly recommend that based on the latest DOH updated guidelines, symptomatic patients COVID-19 patients (suspect/ probable/ confirmed) who have fulfilled completion of 14 days isolation, clinically recovered and no longer symptomatic can be discharged and tagged as recovered without RT-PCR or antibody testing and provided that there is a clearance from licensed physician.

(Strong recommendation, high grade evidence)

Based on the latest Department of Health of the Philippines (DOH) guidelines released last May 29, 2020 in the Memorandum No.2020-0258 on Expanded Testing for COVID-19, Symptomatic COVID-19 Patients (suspect/ probable/ confirmed) who have fulfilled completion of 14 days isolation, clinically recovered and are no longer symptomatic can be discharged and tagged as recovered without RT-PCR or antibody testing and provided that there is a clearance from licensed physician.[141]

The guidelines specify that for symptomatic patients, if there is no available RT-PCR, rapid antibody tests (RATs) may be used, however, “regardless of results, symptomatic patients must still be isolated for 14 days or until asymptomatic, whichever is longer.” [141]

If the symptomatic patient tested IgM negative on RAT, SARS-CoV2 RT-PCR testing must be obtained, and if the result of the RT-PCR is negative, the patient still has to complete the 14-day quarantine period; however, if the RT-PCR turns out to be positive, the patient is a confirmed COVID-19 patient and must be treated and isolated as such. In settings where RT-PCR testing is unavailable, the recommendation is to isolate the patient for 14 days until asymptomatic, whichever is longer.[141]

If the patient is symptomatic and IgM positive (probable COVID-19), RT-PCR testing must be done, and if positive, the patient is treated and isolated as COVID-19 patient. In case the RT-PCR is negative, the patient still has to complete the 14 day quarantine, or until asymptomatic, whichever is longer, and repeat RAT once without symptoms.[141] In cases wherein RT-PCR is not available, the patient must be isolated for 14 days or once without symptoms, whichever is longer, and repeat RATs is recommended once the patient is asymptomatic or at 14 days of quarantine, whichever is longer.

If on repeat RAT, the patient is IgG positive, the patient can be free from quarantine, while if IgM positive and IgG negative, the quarantine can be extended by 7-day increments and repeat testing. In case the patient still remains to be IgM positive but IgG positive for two consecutive repeat tests after the 14-day period, the patient may have a potential false positive result, and the patient may be referred to an infectious disease specialist for further evaluation and management.[141] The DOH, however, emphasizes that rapid antibody tests are not to be used for return-to-work decisions,[141] as these are not stand alone tests for the diagnosis of COVID-19.

Asymptomatic COVID-19 patient may be released from 14-day quarantine if he/ she remain asymptomatic for the whole 14-day quarantine period, even without RT-PCR or antibody testing. Furthermore, there is no need to repeat RT-PCR testing before discharge and tagging as recovery.[141]

Recommendation 25
We strongly recommend, that for ending home isolation, based on the updated CDC guidelines, home isolation may be discontinued if at least 10 days have passed since symptom onset **and** at least 24 hours have passed since resolution of fever without the use of fever-reducing medications **and** other COVID-19 symptoms have improved.

(Strong-recommendation, low-grade evidence)

4.2 ENDING QUARANTINE

Based on the latest DOH guideline as specified in the earlier recommendation, symptomatic COVID-19 patients who have recovered and are no longer symptomatic, completed 14 days of isolation can be discharged and labelled as recovered upon clearance by a medical doctor.[141] For asymptomatic patients, COVID-19 patients can end quarantine after 14 days if patients remains asymptomatic for the complete duration of the 14-day period.[141] Furthermore, the CDC recommends “14 days of quarantine after exposure **based on the time** it takes to develop illness if infected.”[142]

4.2.1. Ending Home Isolation/ Discontinuation of Isolation for Persons with COVID-19 Not in Healthcare Settings[142]

Based on the CDC guidance on ending home isolation updated as of July 3, 2020, there were several updated changes. Among these is the recommendation that a test-based strategy is no longer recommended to determine when to discontinue home isolation, except in certain circumstances. Furthermore, symptom-based criteria underwent modifications as follows: modified from *"at least 72 hours"* to *"at least 24 hours"* have passed since last fever without the use of fever-reducing medications and from *"improvement in respiratory symptoms"* to *"Improvement in symptoms"* to address expanding list of symptoms associated with COVID-19.[142] However, for patients with severe COVID-19 disease, duration of isolation for up to 20 days after symptom onset may be warranted, furthermore, consultation with infection control experts may be needed. Based on the updated CDC guidance, for COVID-19 patients who never develop symptoms, isolation and other precautions can be discontinued 10 days after the date of their first positive SARS-CoV2 RT-PCR test.[142]

4.2.2. Discontinuation of Transmission Based Precautions[143]

For the CDC guidance on Discontinuing Transmission-Based Precautions, updated in August 10, 2020, 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, (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 are 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-19 illness who are severely immunocompromised, the latest guidance from the CDC last August 10, 2020 stated 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]

4.2.3. Home Care Precautions

While caring for a COVID-19 patient at home, caregivers should 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]

It is advisable for the COVID-19 patient to have a separate bedroom and toilet/ bath and have patient stay in his or her own area away from other household members with a distance of at least 6 feet.[145] However, if this is not possible and the patient is in a shared space, good air flow must be ensured and windows maintained open to improve ventilation. Visitors over at the home of the patient must also be avoided.[144, 145] Aerosol generating procedures like nebulization should be avoided as advised earlier in this document. The pMDI use is advised for administering controller medications for children with chronic respiratory conditions such as bronchial asthma. Pediatric care and rehabilitation if needed should be continued post COVID-19 discharge. Current guidelines on discharge and isolation are evolving based on the recent available scientific evidence, knowledge and understanding of this novel disease, hence these recommendations may also change over time.

4.3 USE OF MASKS IN PEDIATRIC CARE

The Different Kinds of Masks

For the purposes of this report, three types available in the market will be discussed: Medical Masks, Respirators and Cloth Masks.

Medical masks

These are surgical or procedural masks that are affixed to the head with straps and is worn either around the ears, around the head or both. This device offers protection in two ways. First, by reducing the spread of respiratory droplets from the user towards other individuals and the surrounding environment.[159] Second, as general protection for both body fluid splashes and respiratory droplets up to 3 µg generated from sneezing or coughing.

Filtering Facepiece Respirators (FFR)

Filtering Facepiece Respirators (FFR), or respirators are inhalation protective devices and are able to filter 0.075 micrometer solid particles[160]. These are labelled based on their filtration properties and tested at national regulatory standards conditions. European labelled FFP2 can filter at least 94% solid NaCl particles and oil droplets and FFP3 has awhile filtration performance of 99%.[161] A fit testing is required to ensure tight fit around the user's face before using the respirator in the workplace. FFP2 equivalent models are N95 (US), P2 (Australia and New Zealand), DS (Japan), Korea 1st class (Korea) and K95 (China).

It is best to wear a respirator without expiratory valve when both respiratory protection and source control need to be achieved. The use of FFP2 masks with an expiratory valve are not indicated as protective for COVID-19. In community settings, these may even lead the user to spread the virus to others. However, if only respirator with exhalation valve is available, cover the exhalation valve with a surgical or procedure mask that does not interfere with the respirator fit.[160, 163-165]

Guidance on mask use in Pediatric care are described as follows:

1. According to the World Health Organization,[159] all healthcare workers including community health workers who work in clinical areas should continuously wear a medical mask during the entire shift apart from mealtimes and drinking. This guidance should be implemented together with frequent hand hygiene and social distancing in crowded and shared areas like dressing rooms and the cafeteria. It is also of importance to wear the mask continuously in high risk areas such as triage area, out-patient department, emergency room, COVID-19 unit (provided the patient is wearing a medical mask), cancer, hematologic and transplant units, long term care and residential facilities.
2. In the case of COVID-19 intensive and semi-intensive care units where aerosol generating procedures (AGP) are performed, the healthcare worker should wear a respirator (N95, FFP2 or FFP3 standard or its equivalent) continuously during the entire shift. Targeted use of respirators only when doing high risk procedures is not effective.[159,160,166]
3. Targeted continuous medical mask use may result to potential self-inoculation due to the following reasons: if one's mask is not replaced when wet, soiled or damaged, if the mask is manipulated with contaminated hands and if the mask is lowered around the neck during interposed break periods. Moreover, continuous use of the mask has a potential risk of droplet transfer and splash to the eyes if not worn with eye shields, distancing[159,164,166]. Finally, healthcare workers may be contaminated by improper removal of the facemask or respirator. Filtering facepiece respirators should be removed after the removal of other components of PPE and just before removing the gloves. Regular training on donning and doffing in the presence of a partner will decrease risk of contracting COVID-19.[159,160]
4. In cases where there is a shortage of FFRs, decontamination of used respirators may be needed. Ultraviolet germicidal irradiation, vaporous hydrogen peroxide and moist heat methods may preserve the filtering performance of FFR. The use of autoclave, 160 degrees dry heat, 70% isopropyl alcohol, microwave irradiation, bleach, soap and water are not recommended because they could affect the filtering performance.[167,168]

Non-Medical Masks

Non-medical (also referred to as fabric) masks are considered as neither medical device nor personal protective equipment. It has a potential benefit for source control in areas with known or suspected widespread transmission with limited resources to implement physical distancing, contact tracing, appropriate testing, isolation and care for suspected or confirmed COVID-19 cases and settings with high population density like in the urban poor areas and where adequate social distancing cannot be achieved (e.g. airplanes, trains, bus and jeepneys).[14, 15, 159, 169, 170, 171]

4.3.1. Use of Masks in Children

Recommendation 26

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. While older children (2 -11 years old) needing to be out from the home use these masks and face shields with adult supervision. Children above 12 years old follow mask use advise for adults. 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.[172,173]
   (Strong recommendations, moderate grade evidence)
2. 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.[172,174]
   (Strong recommendations, low to moderate-grade evidence)

Remarks

The benefits of wearing masks in children for COVID-19 control has been subject to queries as young children lack the developmental ability to tolerate its use, keep the safety measures involved to prevent transmission with mask use and may cause risks of suffocation. The use of masks and face shields in young children warrant adult supervision and other resources to prevent transmission.

There World Health Organization and Centers for Disease Control are presently the international recommending bodies stating an actual ages of children who will and will not use masks in the community. The recommendations from the CDC (COVID-19 and Children) which states that cloth face coverings **should not** be placed on well children at a younger age bracket of less than 2 years old because of the danger of suffocation.[173]

A summary of the WHO released guidance last August 21, 2020, for the use of masks among children in the context of COVID-19 in the different age strata are as follows:

1. Children 0 to 5 years of age should not wear masks for source control
2. Children 6 to 11 years of age, a risk-based approach should be applied to the decision to use of a mask.

3. Children and adolescents 12 years or older should follow the WHO guidance for mask use in adults and/or the national mask guidelines for adults.
4. Children of any age with developmental disorders, disabilities or other specific health conditions that might interfere with mask wearing, the use of masks should not be mandatory and should be assessed on a case by case basis by the child's educator and/or medical provider.

The authors would wish to adopt the American Academy of Pediatrics (AAP) and the Centers for Disease Control (CDC) recommendations in age limits on masks use, whereby children ages 2years and less should not be wearing any face coverings when needing to be in the community. 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.[248] Cultural considerations in Filipino families include the participation of extended family members from different households when a child is brought to the community for limited religious and social practices. In Chapter 2, we stated that the use of surgical masks while on any respiratory support among admitted children with suspected or confirmed COVID-19 is meant for children with hypoxemia, needing hospital admission and required oxygen supplementation with close clinical monitoring.

The World Health Organization (WHO) states that children should not be wearing face coverings during play or doing exercise like running, jumping, or playing on the playground to not to compromise their breathing.[174] Sweat produced during exercise can make the mask wet more quickly making it difficult to breath and promote bacteria growth.

It is imperative to encourage all other important public health measures to family members caring for the children: [174]

- maintaining physical distancing of at least a 1-meter
- limiting the number of playing children
- reminding children of the need to have clean hands while providing access to hand hygiene facilities

Vigorous exercise in a confined space may contribute to the transmission of COVID-19 and should be limited.[173] When physical distancing is not possible, and the exercise is nonvigorous, a cloth face mask should be worn. 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).[175,248] 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.[175] Parental and sports coaching staff guidance are essential during these activities as well.

Chapter 5

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

5.1. ASTHMA IN CHILDREN DURING THE COVID-19 PANDEMIC

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

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 (Appendix A.1)*
7. Routine spirometry testing is not advisable to decrease the risk of viral transmission.

Recommendation 27
The administration of existing medications for asthma controller medications should be continued for pediatric patients with asthma during the COVID-19 pandemic.

(Strong recommendations, Low grade evidence)

5.1.1 Use of Inhaled Corticosteroids as Asthma Controller Medication

Remarks
Reports of pediatric patients with COVID19 globally[89,90,91,92] did not describe asthma as a noted risk for acquiring COVID-19 as of data collection for this report. Although among American children who tested positive for SARS-CoV2, a growing number of reported pediatric COVID confirmed cases from the United States, 345 pediatric cases with information on underlying conditions, 80 cases (23%) had at least one underlying condition was found. The most common underlying conditions were chronic lung disease (including asthma).[26]
Guideline based managements on the use of inhaled steroids help to minimize risk of an

asthma exacerbation and are not affected when one is infected with the SARS-CoV2 virus.[49,51,93] Stopping them may worsen asthma control and thereby increase the risk for complications of COVID-19 leading to associated need for interaction with the health care system. Beyond the direct risk of the infection itself, there is also a risk of experiencing an asthma exacerbation triggered by coronavirus infection.[93] It is worthwhile to note that viral infections are primary causes of wheezing in children less than 5 years old[51] and among older individuals as overwhelming evidence demonstrate the association of asthma exacerbations with viral infections in the community.[94]

5.1.2. USE OF SYSTEMIC CORTICOSTEROIDS DURING ACUTE EXACERBATIONS

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.[93]

The GINA 2020 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.[51]

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.

5.2. 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.[176] 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.[177] 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%).[178] 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).[179,180]

Recommendation 28

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. 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)

4. In patients with active TB disease coinfected with COVID-19, TB treatment should be continued.
   (Strong recommendations, low-moderate grade evidence)

5.2.1. Actions to be taken by person with TB during COVID-19 pandemic.[181, 182]

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.

5.2.2. Actions to be taken by staff working in TB laboratories, healthcare facilities and community healthcare workers during COVID-19 pandemic.[181, 182]

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.

5.2.3. TB Testing must continue during COVID-19 pandemic.[181]

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.[181] 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.[183]

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.[184, 185-188]

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 Xpert Ultra assay as the initial test to the diagnosis of pulmonary TB and drug-resistant TB which replace smear microscopy and culture.[189]

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 2 year 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.

<u>Diagnostic tests for bacteriological confirmation of TB in children and adolescents with presumptive TB</u>***

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.

<u>Pulmonary TB</u> 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.[189]
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.[189]

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.[189]

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).*[189]

5.2.4. 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.[181, 190]

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%.[191] Forum of International Respiratory Societies (FIRS) strongly advocates TB prevention as an essential step towards ending TB.[192]

5 Recommended TB Preventive treatment options

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

TB Preventive treatment for PLHIV

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

MDR-TB Preventive treatment

1. Six months of daily levofloxacin

* Strong recommendation, moderate to high certainty in the estimates of effect.
** Conditional recommendation, low to moderate certainty in the estimates of effect.
*** 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 1A : 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.*[193]

Table 1B : 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.* [190]

Table 1C : Levofloxacin-containing TB Preventive Treatment*

	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.* [190]

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.[190]

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.[190]

5.2.5. In patients with active TB disease coinfected 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 2: Current Recommendation on TB treatment Regimens in Children[193]

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 positive pulmonary TB; Severe forms of EPTB other than TB meningitis and osteoarticular TB	2RHZE	4RH
TB meningitis; Osteoarticular TB	2RHZE	10RHR
R-Rifampicin; H-Isoniazid; Z-Pyrazinamide; E- Ethambutol		

Table 3: Current recommendation on TB treatment regimens for drug-susceptible TB in adolescents [193]

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 4: Recommendation on daily TB treatment in FDC for young children[193]

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 Copyright 2020 Department of Health[193]

5.2.6. 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.

5.3. PATIENTS WITH CHRONIC LUNG DISEASES OR DISEASES WITH PROMINENT RESPIRATORY COMPONENT AND THE COVID-19 PANDEMIc

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.[197] Underlying medical conditions associated with increased risk of severe disease were based on adult data, however, protective strategies have been applied across all ages.[200]

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.[98, 211]

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]

Recommendation 29

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)

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.[210] 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.[198]
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.[198]
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.[198]

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.[205] 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.[200]

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.[210] 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.[20]

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.[206]
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.[198]
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.[198]

Chapter 6

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

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

By the PAPP Task Force in Pediatric Bronchoscopy

RECOMMENDATION 30

1. Contact precautions (face shield, mask, gown, and gloves) are the integral components of PPE strategy to prevent the transmission of this disease, and N-95 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-CoV-2 RNA test from at least two consecutive nasopharyngeal swab specimens collected ≥ 24 h 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)*

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.

6.2. INTERIM PRE-OPERATIVE / PRE-PROCEDURAL GUIDLEINES DURING THE COVID 19 PANDEMIC

By the PAPP Committee on Pre-Operative Evaluation

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

4) 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)

5) 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)

6) 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)

7) 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)

Remarks

Patients who are infected with the virus have been reported to have a higher perioperative morbidity and mortality when undergoing surgical procdures.[217] Patients who are scheduled for surgery, endoscopy[216] and other procedures should always be assumed to be potential carriers of the virus throughout the duration of their hospital stay, even if they pass the pre-assessment triage including normal temperature, no history of exposure or travel, and no respiratory symptoms.

Asymptomatic patients may have the potential of transmitting the virus.[195] Viral transmission may occur up to three days before patients become symptomatic.[218] 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. Significant exposure is exposure to contacts who are confirmed positive for COVID-19 for the past 14 days or history of travel to or residence in an area with local transmission. [221]

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-CoV2 is detection of SARS-CoV2 RNA by reverse transcription polymerase chain reaction (RT-PCR) testing. The reported sensitivity of SARS-CoV2 testing is approximately 70% to 90%, meaning that up to 30% of infected patients will be reported as free of the virus.[222] Clinicians must be mindful that a negative test does not negate the possibility that an individual is infected. Patients should undergo SARS-CoV-2 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. After the patient is tested negative for COVID-19, the patient should remain self-isolated or on home quarantine until the procedure date.

For urgent and elective surgeries, the following are recommended:

- If the patient travelled to a country/locality with sustained community transmission, delay the surgery for 14 days following return, even if asymptomatic. 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.
- If the patient presents with influenza-like illness or unexplained cough at the time of the procedure, defer the surgery until they have recovered. NOTE: Classification and examples of cases of surgery as emergent, urgent and elective is found in the Philippine Society of Pediatric Surgeons Interim Guidelines for Pedi

6.3. RECOMMENDATIONS FOR PEDIATRIC PULMONARY FUNCTION TESTING DURING THE COVID19 PANDEMIC

By the PAPP Committee on Pulmonary Function Testing

Recommendation 32

Pulmonary Function Tests (PFT) 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.

3. 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 SarsCoV2 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 preoperative 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.

B. 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. This timeline is based on the WHO discharge criteria for COVID-19.

C. 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.

D. 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.

E. 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 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.

F. <u>The Conduct of the Pulmonary Function Test</u>

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 chall

6.4. 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 32 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. *(See Algorithm in Appendix B. 1 & 2)*

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.

B. **Modified Enhanced Community Quarantine (MECQ)**

Same recommendations as Enhanced Community Quarantine (ECQ)

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.

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

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