Management of children with acute novel coronavirus 2019 disease (COVID-19) admitted to IWK Health: Fourth Interim guidance

Developed by:
Division of Infectious Diseases
Department of Pediatrics
IWK Health Centre
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Preamble

The purpose of this guideline is to provide recommendations for assessment and management of pediatric patients with acute COVID-19. This guidance does not apply to children with confirmed or suspected multisystem inflammatory syndrome temporally associated with SARS-CoV-2 infection. More guidance can be found here: Multidisciplinary Guidance Regarding the Use of Immunomodulatory Therapies for Acute Coronavirus Disease 2019 in Pediatric Patients
and IWK Guidance MIS-C

These recommendations are based on a literature review of targeted therapies for COVID-19, review of other pediatric guidelines, and discussion with infectious disease specialists and infectious disease pharmacists across Canada. They reflect the consensus of the Division of Infectious Diseases at the IWK, with input from the Departments of Emergency Medicine and Critical Care, and Divisions of General Pediatrics, Immunology, Rheumatology, Hematology, and Cardiology.

Recommendations

Most children with COVID-19 require only supportive care.

Fever can be managed by administering either acetaminophen or ibuprofen. Early concerns about ibuprofen use increasing risk for COVID-19 morbidity and mortality are not supported by evidence.

Supportive care includes oxygen therapy with or without airway management, and nasogastric (NG) or intravenous (IV) hydration when a child is unable to tolerate oral fluids. NG tubes offer an additional benefit as a route for nutritional support. However, when poor or declining clinical status is evident, IV hydration is preferred over NG tube feeding. The aim for fluid rehydration is euvolemia. Replace any fluid losses, provide normal maintenance IV hydration if euvolemic, and avoid aggressive fluid management, which can impair alveolar oxygen exchange.

In cases of severe disease, additional pressure and ventilatory support may be required, including non-invasive or invasive mechanical ventilation. To optimize first-pass success, intubation should be performed by the most experienced provider, with the fewest number of HCPs in the room to minimize potential for infection.

See Table 1 for recommended approach to investigations and non-pharmacological management of pediatric patients hospitalized with COVID-19. Further guidance is available from the Canadian Paediatric Society.

Corticosteroids

- Dexamethasone can be considered for moderate, severe and critical COVID-19 cases requiring oxygen. The suggested dose of dexamethasone is 0.15 mg/kg, IV or PO, to a maximum of 6 mg once daily for up to 10 days or until discharge. Consultation with an infectious disease or paediatric critical care physician is recommended.
- Though randomized controlled trials in adults suggest that dexamethasone reduces mortality in patients with severe COVID-19, there are currently limited data on the benefits and risks of dexamethasone in children with severe disease who require supplemental oxygen or mechanical ventilation.
- Given the breadth of immunosuppression associated with glucocorticoid use in this setting and the risk for impairing antiviral immunity, caution is warranted, especially when early after onset of COVID-19 symptoms (within 5 days).

Remdesivir

- Remdesivir, a nucleotide analog prodrug that inhibits viral RNA polymerases, has been authorized in Canada to treat severe symptoms of COVID-19 in children >12 years old and weighing at least 40 kg, who have pneumonia and require supplemental oxygen.
- There are limited published data on the safety or effectiveness of remdesivir in children, while clinical trials in adults suggest only modest clinical benefit in those requiring oxygen who do not require mechanical ventilation and WHO no longer recommends its use as of November 2020.
- Remdesivir may also be considered for children with moderate disease who are at high risk for developing more severe illness. The dose for children >40 kg is 200 mg on day 1, then 100 mg on days 2 to 5, with continuation for an additional 5 days if there is no clinical improvement. While the evidence for the use of this medication in children is limited, remdesivir has been used in children of all ages, including neonates, and can be considered on a case-by-case basis in consultation with paediatric infectious disease experts**.**

Antibiotic treatment

- Antibiotics should only be considered in patients with evidence or suspicion of secondary bacterial infection. Antibiotics have no effect against the SARS-CoV-2 virus and concomitant bacterial pathogens at presentation have not been widely described.
- Azithromycin is **not** recommended for treatment of COVID-19.
- In patients with suspected secondary bacterial pneumonia, IV ampicillin or po amoxicillin is appropriate first-line empiric antibiotic therapy.
- In severely or critically ill patients with suspected sepsis, IV ceftriaxone is recommended.

Biologic immunomodulators

- Biologic immunomodulators *may be considered* in patients with severe to critical disease within 14 days of onset who despite optimal steroid therapy for 24-48 hours, are demonstrating increasing oxygen or ventilatory requirements or have features of hyperinflammation suggesting Cytokine Release Syndrome (CRS) or related syndromes (e.g., CRP >75mg/L, elevated ferritin > 500 ng/mL, persistent fever or other evidence of CRS). This should be done in consultation with Immunology and Rheumatology.

- More guidance can be found here: Multidisciplinary Guidance Regarding the Use of Immunomodulatory Therapies for Acute Coronavirus Disease 2019 in Pediatric Patients.
  And here: IDSA Guidelines on the Treatment and Management of Patients with COVID-19
- The decision to modify existing biologic regimens in patients with underlying chronic inflammatory or autoimmune conditions should be made in consultation with the prescribing subspecialist and must take into account the risk of flare of the underlying auto-inflammatory condition or macrophage activation syndrome.

Monoclonal Antibodies

- Monoclonal antibodies designed specifically to block infectivity of SARS-CoV-2
- The safety and efficacy (effectiveness) of sotrovimab or the combination of casirivimab and imdevimab have not been directly assessed in pediatric patients (<18 years of age) in clinical trials. Evidence from randomized trials and observational studies in adult patients suggest that outpatient monoclonal antibody therapy soon after diagnosis reduces the need for hospitalization. However, the benefits and risks in children are uncertain**.**
- Sotrovimab is approved under an Interim Order for children and youth 12 years of age and older with mild-to-moderate COVID-19.
- Bamlanivimab is **not recommended** for use.
- Casirivimab and Imdevimab (REGEN-COV) is not effective against the Omicron variant and is not recommended for use at this time.
- It is recommended that monoclonal antibodies only be given to patients at high risk of being hospitalized or dying due to COVID-19. They are not authorized to be used in patients who are hospitalized or require oxygen therapy due to COVID 19. Their use should be in accordance with criteria set out by NSH
- Please refer to clinical order set for "Anti-SARS-CoV-2 Monoclonal Antibody Therapy for COVID-19: IWKMOANCO"

Monoclonal Antibody Quick Link Resources

Nirmatrelvir/Ritonavir (Paxlovid)

- Health Canada has authorized the combination of two medications, nirmatrelvir and ritonavir, taken together to treat adults ≥18 years of age with non-severe COVID-19.
- **Health Canada did not authorize use for < 18 years of age at this time**

Paxlovid Eligibility Criteria NSH
Paxlovid Medication Summary NSH
Paxlovid Patient Information

Investigational COVID-19 therapies

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- Use of off-label or experimental therapies for children with COVID-19 outside of approved, randomized, controlled clinical trials ***is not recommended*.**
- **Hydroxychloroquine is *not recommended***
- **Lopinavir-ritonavir is *not recommended***

Table 1. Investigation and management of pediatric patients hospitalized with COVID-19 by disease severity. *

Disease severity	Investigations	Management
Mild disease • Symptoms of acute respiratory tract and/or mild lower respiratory tract infection; fatigue, myalgia, GI symptoms • Mild to no increased work of breathing • No O_2 requirement	• No routine investigations if being managed at outpatient • If admitting to hospital due to presence of risk factor for disease severity, consider work-up as for moderate disease	• Supportive care as Outpatient
Moderate disease • Increase RR, increased work of breathing • Requires no more than low flow supplemental oxygen to maintain SpO_2 ≥90%	• Consider NP swab for influenza PCR if not done • CBC + differential, lytes, Cr, ALT, CRP (see clinical order set)† • Consider blood culture if febrile • Consider Chest X-Ray or lung ultrasound (if available) for suspicion of pneumonia • In consultation with ID and Rheumatology consider additional investigations as for severe disease (see below) if concern for disease progression based on clinical status or initial labs	• Admit to Pandemic Response Unit • **See Clinical Order Set**: Orders for Confirmed Acute COVID-19 Pediatric Patients • **Initiate dexamethasone** • **Consider ID consult** • Consider Rheumatology consult • **Consider PICU consult** if rapidly progressing disease • Low flow supplemental O_2 to keep SpO_2 90-95% • Supportive care

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Severe disease • Moderate or severe work of breathing or significant hypoxia warranting non-invasive ventilation (i.e., more than low flow supplemental O_2)	• Swab for influenza PCR if not done • Consider extended respiratory panel (requires NP swab) • **Labs as per moderate disease** (clinical order set) **PLUS**: Urea, AST, GGT, albumin, bilirubin, Lactate, LDH, ferritin, ESR, triglycerides, INR, PTT, fibrinogen, D-dimer† • Blood culture if febrile • Chest X-ray or lung ultrasound • Consider ECG due to risk of myocarditis • Consider lymphocyte subsets and other immunologic work-up in consultation with Immunology‡	• Admit to PRU • **See Clinical Order Set**: Orders for Confirmed Acute COVID-19 Pediatric Patients • **Initiate dexamethasone** • **ID consult** • **Consider PICU consult** if no early response to HFNC or escalating requirements • Consider Rheumatology consult • Consider Immunology consult • Consider Respirology consult • Consider Hematology consult • Consider Cardiology consult • Empiric ceftriaxone IV pending cultures if secondary bacterial sepsis suspected • Supportive care as per PRU/PICU
Critical disease • Respiratory failure, acute respiratory distress syndrome • Shock • Multi-organ failure including myocardial dysfunction, AKI, coagulation dysfunction	• Recommendations as per severe disease to be enacted at discretion of PICU	• Admission / transfer to PICU • Recommendations as per severe disease to be enacted at discretion of PICU

*Adapted from guidelines developed by the World Health Organization, Pediatric Infectious Diseases Society, Division of Infectious Diseases, Hospital for Sick Children, and PHAC Clinical management of patients with COVID-19: Second interim guidance.
†Recommended to monitor for early signs of disease progression and end-organ dysfunction
‡To evaluate for signs of cytokine storm and/or inborn error of immunity