

# The acute management of paediatric coronavirus disease 2019 (COVID-19)

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**Keywords:** *Children; Coronavirus; COVID-19*

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection with a predominantly mild clinical disease trajectory in most children <sup>[1]-[6]</sup>. While clinical data available to date are based largely on the disease experience in China, Europe, and the United States, the paediatric literature on COVID-19 is still in its infancy and will undoubtedly evolve. Canadian guidelines have been developed, notably by the Public Health Agency of Canada <sup>[7]</sup>. This statement provides acute care guidance for community paediatricians working in both outpatient and inpatient settings.

## Clinical presentation

Most children presenting with fever and cough do not require hospital care. However, as with adults, infected children may not present with typical viral upper respiratory tract symptoms and can easily spread infection while remaining asymptomatic themselves <sup>[8]</sup>. As of mid-April, 2020, 11 published studies have described clinical features in 643 paediatric cases <sup>[3][4][9]-[17]</sup>. While 51 children (8%) were asymptomatic, the remaining 592 (92%) children presented with:

- Fever (n=335, 57%)
- Cough (n=322, 54%)
- Sore throat (n=169, 29%)
- Rhinorrhea (n=47, 8%)
- Diarrhea (n=68, 11%)
- Vomiting (n=56, 9%)

It is worth noting that asymptomatic rates are probably significantly higher, given that all these studies were based solely on cases presenting with clinical features.

One recent paper suggested that children younger than 5 years of age are more likely to experience severe COVID-19 symptoms than older children and should be promptly assessed <sup>[18]</sup>. Emerging data also appear to suggest that while infants with COVID-19 generally experience mild symptoms, they are at higher risk for severe disease than other paediatric age groups <sup>[17][18]</sup>. The Centers for Disease Control and Prevention (CDC) reported on U.S. cases for most of February and March, including 2,572 children with positive COVID-19 tests. They found that although symptomatic children experienced less fever, coughing, and shortness of breath compared

with adult patients, there were enough outlier cases of severe disease to raise concern. Of the 95 paediatric patients who were hospitalized, 59 (62%) were under 1 year of age, 5 (5%) were admitted to an intensive care unit (ICU), and 3 died (3%) [17]. Vigilant care of children with COVID-19 is warranted because severe morbidity and mortality can occur.

One study has suggested criteria for assessing the severity of paediatric COVID-19 cases which are adapted in Table 1 [2][3][10].

**Table 1. Definitions of clinical severity of COVID-19 in paediatric patients**

**Mild disease**

- Asymptomatic infection or upper respiratory tract symptoms (e.g., pharyngeal congestion, sore throat, or fever) for a short period (i.e., the WHO has specified less than 7 days)
- No oxygen support required
- No abnormal radiographs or evidence of sepsis

**Moderate disease**

- Symptoms such as fever, cough, fatigue, headache, vomiting, diarrhea, abdominal pain, myalgia, anosmia (loss of smell), or ageusia (loss of taste)
- Signs of increased work of breathing and an increased respiratory rate, but no hypoxemia (but no oxygen required)
- Pneumonia on chest x-ray (CXR)
- No evidence of sepsis

**Severe disease**

Features of respiratory distress or organ dysfunction, such as:

- Tachypnea (RR  $\geq$ 60 for infants <2 months; RR  $\geq$ 50 for infants 2 to 11 months; RR  $\geq$ 40 for children  $\geq$ 1 year of age)
- Hypoxemia (O<sub>2</sub> saturation <92%)
- Cardiovascular effects (e.g., myocardial injury)
- Central nervous system (CNS) effects (e.g., a decreased level of consciousness, depression, seizures, or coma)
- Gastrointestinal (GI) effects (e.g., dehydration, difficulty feeding, elevated liver enzymes)
- Coagulation dysfunction, rhabdomyolysis, or other vital organ dysfunction

**Critical illness**

Rapid disease progression *plus*:

- Respiratory failure requiring mechanical ventilation (acute respiratory distress syndrome (ARDS), persistent hypoxemia)
- Septic shock
- Organ failure requiring invasive monitoring and mechanical ventilation
  - Myocardial injury/heart failure
  - Liver injury/coagulation dysfunction
  - Kidney injury

*Information drawn from 2,3,10*

RR = respiratory rate

At present, and as with adults, a confirmed case of COVID-19 in children requires a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test for SARS-CoV-2, the virus causing the COVID-19 disease, based on nasopharyngeal or throat swab. A probable case of COVID-19 is any individual with symptoms consistent with COVID-19 who has been in contact with a known COVID-19 case.

## Screening

The early recognition of children at risk for infection with COVID-19 and their identification through testing and contact tracing are critical—and evolving—care steps. Individuals with severe illness need to be identified and provided with urgent supportive care. Appropriate management and safe, rapid referral to an appropriate ward or for consultation with a paediatric critical care specialist are of paramount importance<sup>[2]</sup>. Standardized and essential infection control precautions include hand hygiene, physical distancing, and the use of appropriate personal protective equipment (PPE).

## Protection guidelines

COVID-19 appears to spread directly and predominantly through droplet and contact transmission. Any health care provider (HCP) working with young patients who may have fever, respiratory, or GI symptoms must take all droplet and contact precautions, including wearing a mask, gown, and gloves, and eye protection, such as goggles or a face shield. Any patient with respiratory symptoms should also wear a mask, as should their accompanying caregiver. Community transmission is being reported in Canada, and because children infected with COVID-19 can be asymptomatic, HCPs should follow local or provincial/territorial protocols for mask-wearing while caring for patients who do not have respiratory or GI symptoms.

HCPs performing an aerosol-generating medical procedure (AGMP) for a young person with confirmed or suspected COVID-19 must wear an N95 respiratory mask, gown, gloves and eye protection (goggles or a face shield) to minimize risk of airborne transmission. The use of a protective barrier enclosure during intubation has been recommended by some practitioners<sup>[19]</sup>. For maximal protection, facial hair should be shaved to permit an optimal N95 fit test and avoid interfering with the respirator seal<sup>[20]</sup>. AGMPs should be performed in a negative pressure room with a closed door and limited access. The time needed for airborne micro-organisms to settle and to terminally clean after an AGMP will vary by room type and facility.

AGMPs include high-flow oxygen therapy (Optiflow or Airvo), non-invasive positive pressure ventilation (including bag-valve-mask ventilation), continuous positive airway pressure (CPAP), intubation and extubation, nasopharyngeal aspiration and suctioning, deep tracheal suctioning, and any aerosolized medical therapy. Obtaining a nasopharyngeal swab, chest compressions, and standard oxygen delivery via nasal cannula are not considered AGMPs.

The principles of patient and caregiver safety, PPE conservation, and social distancing are a challenge in the context of family-centred rounds. When caring for hospitalized patients with confirmed or suspected COVID-19, rounds should be conducted in a conference room or outside of patient rooms, while minimizing the number of direct participants. Entry to a patient's room should be limited to individuals required to perform a physical exam, and devices carried by HCPs, such as cell phones or laptops, should not be allowed in patient rooms. Dedicated stethoscopes are recommended, but when these are unavailable, personal stethoscopes must be cleaned between uses. To minimize interpersonal contacts, use technology to facilitate virtual communication among family and health team members.

## Diagnostic testing

At the present time, the question of whether to test for COVID-19 in an outpatient or emergency room setting depends on local or provincial/territorial guidance and the availability of testing kits and reagents. For any patient who tests positive for COVID-19 infection, notifying public health authorities is essential.

The primary testing modalities for COVID-19 include nasopharyngeal (NP) and throat swabs, with NP testing suggesting higher yield [21]. All patients admitted to hospital with fever, respiratory or GI symptoms, acute anosmia (loss of smell) or ageusia (loss of taste) should be tested for COVID-19.

Blood work, including investigations for sepsis, should be reserved for patients who require hospitalization and are clinically unwell. Depending on the clinical situation, testing may include complete blood count (CBC) and blood culture, electrolytes (including ionized calcium, magnesium, phosphate), glucose, renal function (BUN/CR), liver function tests (AST/ALT, bilirubin, LDH), troponin (if myocardial injury is of concern), coagulation screen (PT/PTT/INR/D-dimers, fibrinogen), blood gas, lactate, and inflammatory markers such as CRP, procalcitonin, and/or ferritin.

If there are cardiac concerns, consider a 12-lead electrocardiogram (ECG) and echocardiogram.

Viral co-infection can occur, and a positive result for another virus does not imply negative results for COVID-19. Testing for other viruses can be conducted depending on laboratory availability and infectious disease recommendations. Whenever possible, the same swab should be used to test for COVID-19 and influenza, RSV, and other viruses, to conserve swabs and limit patient discomfort.

Diagnostic imaging may include a chest radiograph or point-of-care ultrasound (if available) to rule out pneumonia, when clinically indicated (e.g., in cases of respiratory distress). In cases of severe disease, a chest computer tomography (CT) scan can help assess the extent of pulmonary disease, but may be challenging to perform in a dyspneic patient. CT imaging also increases radiation exposure. Decisions to perform imaging and blood work must weigh their clinical benefits against the risks of environmental exposure to, and equipment contamination by, COVID-19.

## Treatment

There is no evidence of any specific, established therapy being effective for treating children with COVID-19 at the present time, and consideration of specific therapeutic approaches in paediatric patients outside of clinical trial settings cannot be recommended. Most children infected with COVID-19 require symptomatic care.

Fever can be reduced by administering either:

- Acetaminophen (15 mg/kg q 4 h, as needed, up to 1 g/dose, to a maximum dose of 75 mg/kg/day or 4 g/day) orally, or
- Ibuprofen (10 mg/kg q 6 h, as needed, for children  $\geq 6$  months of age, to a maximum dose of 800 mg/dose) orally.

Some early concerns about ibuprofen use increasing risk for COVID-19 mortality and morbidity are not supported by evidence, and current therapeutic practice continues to be recommended [2][22].

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 [2]. NG tubes offer additional benefit as a route for nutritional support. However, when a poor or declining clinical status is evident, IV hydration is preferred over NG tube feeding. Avoid aggressive fluid management, which can impair alveolar oxygen exchange [2][23].

In cases of severe disease, additional pressure and ventilatory support may be required, including intubation [2]. To optimize first-pass success, intubation should be performed by the most experienced provider, with the fewest possible number of health care providers exposed in the room.

Antibiotics are not recommended to treat cases of COVID-19 without clinical suspicion of bacterial co-infection. Early studies in China found the rate of secondary bacterial infection to be low. However, when there is evidence for a secondary infection, appropriate antibiotics should be administered pre-emptively, without waiting for confirmatory test results.

- For sepsis, treat with an IV third-generation cephalosporin, such as cefotaxime (50 mg/kg/dose every 6 h, to a maximum 2 g/dose or 8 g/day), or IV ceftriaxone (75 mg/kg/dose every 12 to 24 h, to a maximum 4 g/day), with the addition of IV vancomycin (15

mg/kg/dose every 6 h, to a maximum 500 mg/dose) for severe disease.

- For pneumonia, first-line treatment for mild to moderately ill patients includes intravenous ampicillin (50 mg/kg/dose q 6 h, to maximum 3 g/dose), or oral amoxicillin (80 to 90 mg/kg/day, divided 2 to 3 times a day for 10 days, to a maximum 4 g/day).

When a paediatric patient has a confirmed IgE-mediated allergy or has experienced serious side effects from penicillin or cephalosporin use, consult an infectious disease specialist.

## Therapies not supported by evidence

- There is, as yet, no evidence that antiviral treatment improves COVID-19 outcomes in children. A number of trials looking at remdesivir, lopinavir/ritonavir (Kaletra), hydroxychloroquine (Plaquenil) are underway to evaluate these potential therapies for COVID-19.
- Corticosteroids have been used to treat adult patients with COVID-19, with no clear evidence of benefits or harm, and one study has suggested that corticosteroid use may increase viral replication (24). Treatment with steroids beyond established indications (e.g., asthma exacerbations or other chronic pathology) is not recommended.
- IV immunoglobulin (IVIG) has not yet been shown to be beneficial, and is not recommended.
- Studies of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers to treat COVID-19 have not shown clear benefit. One clinical trial evaluating losartan is ongoing, but its use to treat COVID-19 is not recommended. However, patients already taking these medications should continue to use them as prescribed.
- Studies on interleukin- (IL-) 6 receptor antagonists, such as tocilizumab, are underway to evaluate immune modulators as treatment for the cytokine release syndrome seen in some patients.

## Special considerations for COVID-19 infection treatment and management

### Vulnerable populations

Some paediatric populations should be considered at higher risk for severe COVID-19-related disease, even as evidence confirming this status is pending. These groups include infants, and children with a heart or lung disease (e.g., asthma, cystic fibrosis), or a neurological or neuromuscular condition, and children living with other chronic conditions such as diabetes mellitus, sickle cell disease, malignancies, and/or immunosuppressive conditions (e.g., post-organ transplant, chronic steroids), or those being ventilated at home [25].

### Treating children with acute asthma in the setting of COVID-19

Read this practice point, Paediatric asthma and COVID-19, for related guidance on managing asthma in community settings [26]. The risks of COVID-19 aerosolization associated with nebulized therapies are significant, such that medication delivery using a metered-dose inhaler (MDI) with an aerochamber and/or a dry powder inhaler (i.e., turbuhaler or diskus) is recommended over nebulization, whenever possible.

While the benefit of using steroids to minimize asthma symptoms must be weighed against the possible risk of increased viral replication with steroid use, acute asthma exacerbations should be treated with corticosteroids in accordance with current action plans [26].

For mild asthma exacerbations:

1. Use salbutamol (Ventolin) with an MDI and aerochamber, if needed.

For moderate asthma exacerbations:

1. Use salbutamol (Ventolin) and ipratropium bromide (Atrovent) x 3 by MDI and aerochamber, if needed.
2. Consider oral corticosteroids (dexamethasone, prednisone, or prednisolone).

For severe asthma:children

1. Use salbutamol (Ventolin) and ipratropium bromide (Atrovent) x 3 by MDI and aerochamber, if needed.
2. Use oral corticosteroids (dexamethasone, prednisone, or prednisolone) or IV corticosteroids (methylprednisolone or hydrocortisone), as needed.
3. Consider early use of IV magnesium sulfate (25 to 75 mg/kg, to a maximum 2500 mg/dose) with cardiorespiratory monitoring.
4. If a child's condition is not improving, consider nebulized salbutamol, optimally delivered in a negative pressure room and provided full PPE are available and all airborne precautions can be taken.
5. Consider IV salbutamol (Ventolin) with cardiorespiratory monitoring.

High-flow oxygen at any rate and non-invasive positive pressure ventilation are both considered AGMPs. Because young patients are already aerosolizing particles, nebulized salbutamol (Ventolin) could be considered. Until they test negative for COVID-19 or their condition improves to the point that AGMPs are not required, these patients should be cared for in a negative pressure room, if available, and all airborne precautions taken.

## Treating children with croup in the setting of COVID-19

For mild croup in older children and who are not distressed, consider avoiding corticosteroids.

For moderate to severe croup, administer oral corticosteroids (dexamethasone 0.6 mg/kg, to a maximum of 16 mg/dose).

For severe croup, nebulized epinephrine can be used, provided that full PPE are available and all airborne precautions can be taken.

Alternatives include an MDI for epinephrine and subcutaneous or intramuscular epinephrine.

An MDI for epinephrine delivery has been urgently approved by Health Canada, but the evidence is extremely limited for its use in croup. Equivalent dosing must be extrapolated from limited studies, with the current recommendations suggesting 2 puffs for infants under 1 year of age, and 4 puffs for older children. Repeat dosing for both age groups can be given every 15 minutes based on clinical assessment [27]-[29].

In settings where all airborne precautions cannot be taken, delivering epinephrine subcutaneously or intramuscularly may be considered, with dosing based on weight, as follows:

7.5 to 15 kg:	0.1 mg IM/SC
15 to 30 kg:	0.15 mg IM/SC
>30 kg:	0.3 mg IM/SC

## Post-discharge planning

The vast majority of children with mild COVID-19 infection are well enough to be discharged following outpatient evaluation. Instruct patients and families to self-isolate for at least 14 days from illness onset and for a minimum of 24 hours after symptoms resolve, as per local and/or provincial/territorial public health guidance. Warning signs and symptoms of COVID-19 infection should

be explained to parents, along with conditions that would lead to prompt re-examination.

For managing children with moderate COVID-19 symptoms, use clinical judgement regarding admission, observation, and intervention. Consider prompt referral for children with underlying risk factors or medical conditions.

Children with severe symptoms should be referred to a tertiary or regional centre for intensive care. Severe symptoms include RDS<sup>[18]</sup> and cytokine release syndrome<sup>[30]</sup>. The latter condition has been of particular concern in COVID-19-positive adults presenting with fever, elevated IL-6, and multi-organ failure<sup>[30]</sup>.

## Conclusion

In Canada, the burden of disease from COVID-19 in paediatric patients appears to be low at the present time. Many, perhaps most, children are either asymptomatic or have only mild upper respiratory or GI symptoms. Children with moderate symptoms should be carefully observed, and to optimize care, those with severe symptoms should be transferred to a regional or tertiary centre following critical care and infectious disease consultation.

Consideration should be given to health risks for HCPs, because children can present asymptotically or with mild symptoms only in any office or clinic setting. Be cautious when examining young patients, always using appropriate PPE and complying with all local or provincial/territorial public health guidelines.

Information on COVID-19 will be reviewed and updated in CPS documents as this pandemic and its literature evolve.

## Acknowledgements

This statement was reviewed by the Drug Therapy and Hazardous Substances and Infectious Diseases and Immunization Committees of the Canadian Paediatric Society. It has also been reviewed by the CPS Hospital Paediatrics and Paediatric Emergency Medicine Section Executives.

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**Last updated:** Apr 21, 2020