Recommendations for Antimicrobial Management of Pediatric Hospitalized Patients with COVID-19

See AHS Insite COVID-19 resources for current version.

Note: This is interim guidance and this document will be frequently updated as new information becomes available. As such, the most current web-based version of this document should preferentially be used.

This guideline has been developed by members of Pharmacy and Division of Pediatric Infectious Diseases in Calgary and Edmonton and with input from the provincial COVID-19 working group.

To date, there are no proven effective evidence-based therapeutic agents for the treatment of the novel coronavirus, SARS-CoV-2, and this is especially true with regards to treatment of special populations such as pediatrics or those with renal or liver dysfunction. **Supportive care remains the mainstay of therapy for infected individuals**. **The use of experimental treatments for patients with COVID-19 should ideally occur within the context of controlled clinical trials.** Post and pre exposure prophylaxis, preemptive therapy, and pre hospital therapy are outside the scope of this document. The recommendations outlined in this document do not indicate an endorsement of these agents, but is meant to support case-by-case basis decision making.

If the use of agents for COVID-19 outside of clinical trials is being considered, please consider the significant potential risks versus unverified benefits. As recommended by AHS Ethics, any off-label use of medication requires the prescriber's careful consideration of risk/benefit, consultation between experts and attending physician as needed, and documenting consent from the patient after discussion of the current state of evidence of benefit and harms.

We recommend consultation with Pediatric Infectious Diseases (ID):

- **if a patient is admitted to intensive care with presumed or confirmed COVID-19,**
- **if a COVID-19 patient is showing progression of illness,**
- **if Multisystem Inflammatory Syndrome in Children (MIS-C)is suspected in COVID-19 patients,**
- **or if ID consultation is judged beneficial or desired by primary clinical team**

Table 1: Classification of COVID-19 clinical illness in children (Dong et al, Qiu et al)

Mild Disease	Upper respiratory tract infection symptoms (e.g. nasal congestion, sore throat, and fever) for a short duration or asymptomatic infection May also include fatigue, myalgia, and gastrointestinal symptoms
Moderate Disease	Clinical and/or radiological signs of pneumonia Symptoms such as fever, cough, fatigue, headache, and myalgia No complications and manifestations related to severe conditions
Severe Disease	Moderate clinical features, PLUS manifestations that suggest disease progression: • Moderate to Severe Respiratory Distress • Severe Hypoxia • Dehydration, difficulty feeding, gastrointestinal dysfunction
Critical Illness	Rapid disease progression, plus any other condition(s): • Respiratory failure with need for mechanical ventilation (e.g. ARDS, persistent hypoxia despite non-invasive oxygen supplementation) • Decreased level of consciousness, depression, coma, convulsions • Myocardial injury • Elevated liver enzymes • Coagulation dysfunction, rhabdomyolysis, and any other manifestations suggesting injuries to vital organs

	• Septic shock • Other evidence of organ failure

Table 2: Suggested Investigations prior to considering investigational therapies for COVID-19 inpatients (Dong et al, Qiu et al, Lu et al)

1. Baseline labs (CBC & differential, AST, ALT, bilirubin, Cr, urea, CRP, blood cultures)
2. Specific investigations for hospitalized patients with COVID-19:
    - D-dimer; Fibrinogen, LDH (secondary infection and prognostic indicators), CK
    - CXR
    - ABG (selected patients)
    - Echocardiogram for critically ill patients
    - COVID-19 PCR testing and RVP (Nasopharyngeal swab)
    - Sputum or endotracheal aspirate if intubated (avoid bronchoscopy simply for specimen acquisition) for Gram stain and culture and Sars-Cov-2 PCR
    - If immunocompromised and clinically indicated, ET aspirate, bronchoscopy (if required) or induced sputum for PJP and Sars-Cov-2 PCR
3. In special circumstances, can consider:
    - For MIS-C presentations, please see special laboratory testing (link to MIS-C guideline)

Considerations for COVID-19 Management with Antiviral agents

- Consult your site administration or Infectious Disease Service to determine if enrollment into clinical trials is possible.
- Remdesivir is currently only available through a clinical trial, however to date (Dec 2020) there are no anti-viral clinical trials enrolling children in Alberta.

CRITERIA TO CONSIDER COVID-19 specific Anti-Therapeutics in Hospitalized Children*

Suspected or confirmed COVID-19 and severe or critical illness presentation

Patients with moderate COVID-19 presentation in presence of risk factors** that would put them at risk for severe disease

**Risk Factors: (Dong et al, 2020; Hong et al 2020; Wang et al, 2020)

- Age < 1 year of age
- Underlying conditions to be considered:
  - Immunocompromise***
  - Underlying comorbidities such as heart disease, lung disease, neurological disease, or diabetes mellitus***

*** These conditions have been identified indirectly by extrapolating from adult data and risk factors for severe disease in children with other human coronavirus infections.

Antiviral Therapeutic Considerations

These investigational treatments may be considered in laboratory-confirmed COVID-19 infection (or 'highly suspected' and expected delay of lab confirmation > 24 hours) requiring hospitalization due to severe illness (see criteria ABOVE). Clinical progression typically occurs between 5-7 days after symptom onset. Risk factors for disease progression in children are not clear, but at this point, the following may be considered: younger age (under 1 year), immunocompromise, and underlying comorbidities such as heart disease, lung disease, neurological disease, or diabetes mellitus.

Based on available information, the working group prioritizes the following options for clinicians' consideration (see the following for detailed rationale on current prioritization).

A. Neither experimental anti-viral agents or dexamethasone are recommended in cases **of mild or moderate COVID-19 pediatric illness in children.**

In severe illness with risk factors or **critically ill patients** requiring mechanical ventilation, possible treatment options include:

Dexamethasone*** (enteral or IV) 0.15 mg/kg once daily (max 6mg) for 10 days (or hospital discharge, whichever is sooner) may be considered

*** The safety and effectiveness of dexamethasone for pediatric COVID-19 treatment have not been sufficiently evaluated. As the RECOVERY trial only included a small number of pediatric patients, and mortality rates are low in pediatric COVID-19 patients, treatment with dexamethasone in this population should be considered on a case by case basis

Empiric Antimicrobial Therapy of Pneumonia in Hospitalized Suspect COVID-19 Pediatric Patients

Antibiotics are not recommended for all COVID-19 patients, but rather for severely ill patients or for suspicion of secondary bacterial process such as bacterial pneumonia. Therefore antibiotic therapy is recommended only for:

- empiric management of patients with pneumonia while COVID-19 is being confirmed and bacterial infection excluded, and
- initial management of potential bacterial superinfection.

COVID-19 clinical severity	Antibiotics recommended	Pediatric Dosages
Mild	No antibiotics recommended	N/A

Moderate	Amoxicillin or Ampicillin as tolerated PLUS consider Azithromycin****	Amoxicillin PO 45-90 mg/kg/day div TID Ampicillin IV 200-400 mg/kg/day div q6h Azithromycin IV/PO 10 mg/kg x 1, then 5 mg/kg/day q24h x 4 days
Severe	Ceftriaxone PLUS consider Azithromycin	Ceftriaxone IV 50-75 mg/kg/day given q24h Azithromycin dosage as above
Critical Illness	Ceftriaxone PLUS Azithromycin PLUS Consider Vancomycin	Ceftriaxone dosage as above Azithromycin dosage as above Vancomycin IV 15 mg/kg/dose q6h; adjust based on trough levels to target 10-20 mg/L

If symptoms clinically compatible with influenza and influenza RVP pending or positive, consider: Oseltamivir (Tamilflu®): ≤15 kg: 30 mg, >15 to 23 kg: 45 mg; >23 to 40 kg: 60 mg; >40 kg: 75 mg twice daily. Discontinue if influenza RVP negative.

**** Azithromycin use should be considered if the clinical and epidemiological presentation is in keeping with *M.pneumoniae* disease

Management of Possible Secondary Bacterial Infection/Ventilator Associated Pneumonia in Pediatric COVID-19 patients

Note: per Zhou et al, bacterial superinfection, which occurred in 29% of the reported Wuhan adult cohort, was defined as clinical symptoms or signs of pneumonia or bacteremia and a positive culture of a new pathogen obtained from lower respiratory tract specimens and/or blood culture.

Culture directed therapy is preferred; empiric therapy pending sputum/ET aspirate culture results:

Piperacillin-tazobactam 240-300 mg piperacillin/kg/day div q6-8h

OR

Meropenem 60 mg/kg/day div q 6-8h

REASSESS at 48-72 hours WITH VIRAL AND BACTERIAL LAB RESULTS

Additional Care

1. **Avoid** nebulized medications and do not do bronchoscopy for obtaining specimens alone (ET aspirate preferred) to reduce aerosolization risk.

2. If oxygen demand is increasing, **consider early referral for other forms of respiratory support** as patient outcomes may be superior and planned intubations are at a lower risk for infection transmission than emergent ones. (here insert link for critical care pathway already on insite)

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