

# Pediatric Ambulatory Guidance for COVID-19

There is a great deal of information being published at a rapid pace which is difficult to keep up with. The following is aimed as an introduction regarding clinical features and treatment related to pediatric COVID-19 in the ambulatory setting. There will be ongoing additions and modifications based on your questions and as the science evolves. These principles are based on a variety of published cohort studies and guidelines from leading national societies.

## **Clinical features of Pediatric COVID-19 (SARS -CoV2)**

In the United States, approximately 2% of confirmed cases of COVID-19 are among persons aged <18 years. Median age was 11 years (range 0-17) and about 23% of pediatric cases had at least one underlying condition. In general, pediatric patients have a good prognosis and recover within 1 to 2 weeks after disease onset.

The clinical spectrum of COVID-19 in pediatric patients ranges from mild disease with non-specific symptoms of acute respiratory illness to respiratory failure, septic shock and a potentially severe condition known as multisystem inflammatory syndrome in children (MIS-C). Though the incidence of asymptomatic infection with COVID-19 is thought to be common, the true prevalence of asymptomatic SARS-CoV-2 infection is not well-understood because asymptomatic children are not tested routinely.

Children of all ages appear to be susceptible to infection by SARS-CoV-2 and so far, the majority of COVID-19 cases in children are mild. Though more investigation and systematic surveillance of the role of children in this pandemic needs to be done, SARS-CoV-2 infects children of all ages, and despite the high proportion of mild or asymptomatic infections, it would be naive not to consider them as transmitters. Therefore, consideration must be given to the potential role children play in transmission to others at high risk for severe disease and complications from COVID-19.

Although infrequent, hospitalization rates appear to be highest among children younger than 1 year of age and in those with underlying conditions

|        |                            |      |        |
|--------|----------------------------|------|--------|
| Author | COVID Standardization Team |      |        |
| Date   | 5/20/2020                  | Time | 2 p.m. |

(e.g., chronic lung disease including asthma, cardiovascular disease, and immunosuppression). Some patients develop worsening of illness during the second week of symptoms.

The incubation period following exposure is typically 4-5 days but may be as long as 14 days. While specific data on the incubation period for COVID-19 in the pediatric population are limited, it is thought to extend to 14 days, similar to that of adult patients with COVID-19.

Frequent signs and symptoms of infection:

| <b><u>Symptom</u></b> | <b><u>Reported Incidence<br/>In Pediatrics</u></b> | <b><u>Reported Incidence<br/>In Adults</u></b> |
|-----------------------|--|--|
| Fever                 | 41.5 - 56%   | 77-98%   |
| Cough                 | 48.5 - 54%   | 48-82%   |
| Myalgia or fatigue    | 23%  | 11-52%   |
| Shortness of breath   | 13%  | 3-31%  |
| Headache              | 28%  |  |
| Sore Throat           | 24%  |  |
| Diarrhea              | 13%  |  |
| Nausea/Vomiting       | 11%  |  |
| Runny Nose            | 7%   |  |
| Abdominal Pain        | 6%   |  |

Overall, fewer children than adults experience fever, cough or shortness of breath. Fever may be subjective or documented. Other non-specific symptoms such as myalgias, headache and sore throat are common. GI symptoms such as diarrhea and nausea/vomiting have been reported up to 24 % of the time and may precede other URI type symptoms. There are reports however of isolated GI symptoms. Anosmia and loss of taste have been suggested in case reports and if occurring in the absence of other known causes such as allergic rhinitis or sinusitis should prompt consideration of COVID-19 infection.

- Asymptomatic incidence (no clinical signs or symptoms with normal chest imaging) around 4%
- Mild (mild symptoms, including fever, fatigue, myalgia, cough) illness around 51%
- Moderate illness (pneumonia with symptoms or subclinical disease with abnormal chest imaging) around 39%
- Severe illness (dyspnea, central cyanosis, hypoxia) around 5%
- Critical illness (acute respiratory distress syndrome [ARDS], respiratory failure, shock, or multi-organ dysfunction) around 0.6%
- Cutaneous Involvement in 12.5% of patients with spontaneous resolution in 10 days
  - "COVID toes (acro-Ischemia)" - pernio-like lesions largely in asymptomatic children and adolescents

### **Multisystem Inflammatory Syndrome in Children (MIS-C)**

A rare, but potentially very serious inflammatory condition in children has recently been linked to COVID-19 and requires vigilance on the part of providers who care for children and adolescents. The presentation may fulfill all or part of the criteria for Kawasaki disease, presents more often in children over the age of 5 years and cases reported the most common symptoms as GI symptoms, conjunctivitis,odynophagia and conjunctivitis. Patients thought to have this condition or possibly meeting criteria require prompt identification and transfer of care to a site in which providers are able to comfortably provide pediatric intensive care, if needed.

The CDC recently released case definition for MIS-C:

- An individual under 21 years presenting with fever, laboratory evidence of inflammation and evidence of clinically severe illness requiring hospitalization with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **and**
- No alternative plausible diagnoses; **and**
- Positive for current or recent SARS-CoV-2 infection by reverse-transcriptase polymerase chain reaction, serology or antigen test; or COVID-19 exposure within the four weeks prior to the onset of symptoms.

The CDC noted the fever should be at least 38 degrees Celsius for at least 24 hours or a subjective fever lasting 24 hours. Evidence of inflammation could include but is

not limited to an elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase, or interleukin 6, elevated neutrophils, reduced lymphocytes and low albumin.

### **Admission Criteria for patients with COVID-19**

The decision to manage a pediatric patient with mild to moderate COVID-19 in the outpatient or inpatient setting should be decided on a case-by-case basis. Pediatric healthcare providers should consider the patient's clinical presentation, requirement for supportive care, underlying conditions, and the ability for parents or guardians to care for the child at home. Additionally, as the primary mode of transmission to children currently has been within the household, consideration for health status and underlying health conditions of the parents or guardians and potential household exposures due to care of other dependent children may need to be considered.

Most patients with COVID-19 will not require hospitalization and can be managed with supportive care and measures in place for careful monitoring.

Progression of symptoms are concerning signs that require further evaluation for acute management and/or hospitalization. Disposition will be determined on a case by case basis between the parent or guardian and health care team.

### **Diagnostic Testing**

Test results may take up to 5 days to come back.

### **Risk of Disease based on Age and Co-morbidities**

Among individuals < 18 years with COVID-19, an estimated 5.7% were reported to be hospitalized, with 0.58%–2.0% admitted to an ICU setting. Children aged <1 year accounted for the highest percentage (15%–62%) of hospitalization among pediatric patients with COVID-19. The percentage of patients hospitalized among those aged 1–17 years was lower, estimated at 4.1%–14%, with little variation among age groups

Among the pediatric cases for which information on both hospitalization status and underlying medical conditions was available, 77% of hospitalized patients, including all patients admitted to an ICU, had one or more underlying medical condition; among patients who were not hospitalized, 12% patients had underlying conditions.

Based upon available information to date, those at high-risk for severe illness from COVID-19 include:

- Infants < 1 year
- Children exposed to or Adolescents who are smoking tobacco or vaping
- People living in congregate settings such as shelters, correctional facilities, Behavioral Health facilities or long-term care facilities
- Other high-risk conditions could include:
  - People with chronic lung disease, including asthma
  - People with Chronic Kidney Disease, including those on dialysis
  - People who have hypertension, cardiovascular disease, serious heart conditions (e.g., congenital heart defects)
  - People with diabetes
  - People who are on immunosuppressive therapy
  - People who are immunocompromised including cancer treatment
  - People with HIV
  - Obesity
  - Transplant patients
  - Children with medical complexity
- People who are pregnant should be monitored since they are known to be at risk with severe viral illness, however, to date data on COVID-19 has not shown increased risk

### **Specific Treatment Considerations for COVID-19 patients in the Ambulatory setting**

- Treatment is supportive for non-hospitalized patients with COVID-19
- There are no recommended pharmacological treatments for COVID-19 patients in the ambulatory setting at this time. There is not discussion of treatment for hospitalized pediatric patients in this document.
- Parents or guardians may seek specific treatments (including prophylaxis) such as hydroxychloroquine, chloroquine, or combination of those with azithromycin. At this point these treatments should be

avoided for ambulatory patients given the lack of evidence for efficacy AND potential drug supply limitations for those more ill in the community.

➤ **Investigational over-the-counter and Alternative Medications**

ChristianaCare does not endorse the use of these supplements or medications for treatment of COVID-19. For Informational use only.

➤ **Self-issued prophylaxis** – Physicians should not be writing medications (including hydroxychloroquine or azithromycin) for self or family prophylaxis.

➤ **Hemodialysis (HD) considerations:**

- **Patients and family members** – Educate on proper hand hygiene, undergo screening for respiratory illness / body temperature, use of a medical mask /surgical mask, limit accompanying persons.
- **Healthcare Practitioner / Staff** - proper hand hygiene, screened for respiratory illness / body temperature, use of personal protective equipment (effective mask, cap, gown, goggles/face shield, gloves).

➤ **Peritoneal dialysis (PD) consideration**

- **Home environment** - Air out the room in which PD is being performed twice daily for 30 minutes, to avoid convective airflow when connecting catheter to tubing, close windows and air-conditioned vents, properly clean floors and surfaces
- **Patients and family members** – proper hand hygiene, use of a medical mask /surgical mask, continue with isolation, disinfect PD effluent (500 mg/L chlorine-containing solution for 1 h and poured into the toilet).

➤ **Maintenance Medications:**

- All patients should remain on their regularly prescribed medications. Optimal control of chronic disease is critical and despite published opinion pieces or news articles there is no evidence to support stopping inhaled or systemic steroids, immunosuppressive medications, biologic agents, or ACEi/ARB therapy to lessen the risk of developing COVID-19 infection.

- Patients chronically on agents to control their cardiovascular disease such as aspirin and ACEi/ARB should be continued on these agents unless their clinical status dictates otherwise.
  - At this time, there is no evidence that children with hypertension, cardiovascular disease, or chronic kidney disease who are taking ACE inhibitors or ARBs, are at increased risk of SARS-CoV-2 infection or more severe COVID-19. Given the proven benefits of these medications in all patients, and the unique circumstances that make these agents particularly beneficial for youth with these chronic conditions, many scientific societies affirming the continued use of ACE inhibitors and ARBs in accordance with current guidelines.
- Patients that are chronically on immunosuppressive medications, biologic agents, systemic steroids, or chemotherapeutic medications should have the continuation of these medications addressed with the prescribing physician in the setting of an infection.
- **Steroids:** Oral steroids should be avoided as a treatment option specifically for COVID-19 pediatric patients in the ambulatory setting. These may be considered for alternative diagnosis such as exacerbations of chronic lung disease. Inhaled steroids can be continued.
- **Osetamivir:** Osetamivir is not effective for COVID-19.
- **Acetaminophen vs. NSAIDs:** Acetaminophen should be used for fever control. There is a hypothetical link between NSAID use and aggravation of COVID-19 symptoms, but this is not supported by the FDA as of March 19, 2020.
- **MDI and Nebulizer Treatment:**
  - Nebulized formulations of medications carry a higher risk of aerosolization of particles. *If possible, patients should utilize MDI's for acute management of symptoms even if the medication is expired.*
  - For patients who require nebulized formulations of medications (due to lack of efficacy or availability of MDI's) for ongoing control, the parents or guardians should be advised to use them in an

isolated section of the home, preferably a garage or patio, and minimize exposure to other family members to that location. Aerosol droplets may remain in circulation for 2-3 hours.

- Nebulized formulations in a healthcare setting should be administered only in an isolated setting with clear procedures regarding specialized PPE utilization for high risk aerosolization.
- **CPAP:** Patients on CPAP with COVID-19 infection should discuss options with you and their Sleep Medicine physician. When using CPAP, separate from other family members.
- Breastfeeding is still recommended, although care should be taken to prevent the transmission of virus from mother to baby through proper hygiene. <https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/maternal-or-infant-illnesses/covid-19-and-breastfeeding.html>
- Masks should not be worn by children younger than 2 years old or by individuals who are unable to remove the mask by themselves or are unconscious.

## **References**

1. CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children — United States, February 12–April 2, 2020. MMWR Morbidity and Mortality Weekly Report. ePub: 6 April 2020. DOI: <http://dx.doi.org/10.15585/mmwr.mm6914e4externalexternal.icon>.
2. CDC Coronavirus Disease 2019 (COVID-19) Cases, Data, & Surveillance. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases. Accessed May 16, 2020. [https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html?CDC\\_AA\\_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-in-us.html](https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-in-us.html)
3. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA
4. Dong Y, Mo X, Hu Y, et al. Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. Pediatrics
5. Cai J, Xu J, Lin D, et al. A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. Clin Infect Dis
6. Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang ZJ. Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China. JAMA
7. Su L, Ma X, Yu H, et al. The different clinical characteristics of corona virus disease cases between children and their families in China – the character of children with COVID-19. Emerging Microbes and Infection 2020; 9(1): 707-13.

8. Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and Outcomes of Children with Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. *JAMA Pediatr*. Published online May 11, 2020. doi:10.1001/jamapediatrics.2020.1948
9. South, AM, Brady, TM & Flynn, JT. ACE2, COVID-19, and ACE Inhibitor and ARB Use during the Pandemic: The Pediatric Perspective. *Hypertension* (May 2020). <https://doi.org/10.1161/HYPERTENSIONAHA.120.15291>
10. CDC. Coronavirus Disease 2019 (COVID-19). Accessed on April 22, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>.
11. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *NEJM*. 2020;382:929-936.
12. [https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-patients-use-non-steroidal-anti-inflammatory-drugs-nsaids-covid-19?utm\\_campaign=FDA%20advises%20patients%20on%20use%20of%20NSAIDs%20for%20COVID-19&utm\\_medium=email&utm\\_source=Eloqua](https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-patients-use-non-steroidal-anti-inflammatory-drugs-nsaids-covid-19?utm_campaign=FDA%20advises%20patients%20on%20use%20of%20NSAIDs%20for%20COVID-19&utm_medium=email&utm_source=Eloqua)
13. ASHP Document – Assessment of evidence for COVID-19-Related Treatments. <https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/ASHP-COVID-19-Evidence-Table.ashx?la=en&hash=B414CC64FD64E1AE8CA47AD753BA744EDF4FFB8C>. Accessed on March 23, 2020.
14. McCreary E and Pogue JM. COVID-19 treatment: a review of early and emerging therapies. *Open Forum Infectious Diseases*. March 2020. Accessed ahead of print.
15. Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19). CDC Health Alert Network CDCHAN-00432; May 14, 2020. <https://emergency.cdc.gov/han/2020/han00432.asp>
16. Royal College of Paediatrics and Child Health Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19, <https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf>
17. Riphagen S, Gomez X, Gonzales-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet*. 2020. Advance online publication, doi: 10.1016/S0140-6736(20)31094 [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31094-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31094-1/fulltext)
18. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, Bonanomi E, D'Anitga L. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet*. 2020. Advance online publication, doi: 10.1016/S0140-6736(20)31129-6 [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31103-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31103-X/fulltext)
19. L'Huillier AG, Torriani G, Pigny F, Kaiser L, Eckerle I. Shedding of infectious SARS-CoV-2 in symptomatic neonates, children and adolescents. medRxiv. 2020:2020.04.27.20076778.
20. Jones TC, Mühlemann B, Veith T, Zuchowski M, Hofmann J, Stein A, et al. An analysis of SARS-CoV-2 viral load by patient age. 2020. Available from: [https://zoonosen.charite.de/fileadmin/user\\_upload/microsites/m\\_cc05/virologie-ccm/dateien\\_upload/Weitere\\_Dateien/analysis-of-SARS-CoV-2-viral-load-by-patient-age.pdf](https://zoonosen.charite.de/fileadmin/user_upload/microsites/m_cc05/virologie-ccm/dateien_upload/Weitere_Dateien/analysis-of-SARS-CoV-2-viral-load-by-patient-age.pdf).