A Clinical Pathway for Hospitalized Pediatric Patients With Initial SARS-CoV-2 Infection

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ABSTRACT

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread quickly across the globe, creating unique and pressing challenges for today’s physicians. Although this virus disproportionately affects adults, initial SARS-CoV-2 infection can present a significant disease burden for the pediatric population. A review of the literature yields descriptive studies in pediatric patients; however, no evidence-based or evidence-informed guidelines for the diagnosis and treatment of the hospitalized pediatric patient have been published in peer-reviewed journals. The authors, working at a quaternary care children’s hospital in the national epicenter of the SARS-CoV-2 pandemic, found an urgent need to create a unified, multidisciplinary, evidence-informed set of guidelines for the diagnosis and management of coronavirus disease 2019 in children. In this article, the authors describe our institutional practices for the hospitalized pediatric patient with confirmed or suspected initial SARS-CoV-2 infection. The authors anticipate that developing evidence-informed and institution-specific guidelines will lead to improvements in care quality, efficiency, and consistency; minimization of staff risk of exposure to SARS-CoV-2; and increased provider comfort in caring for pediatric patients with SARS-CoV-2 infection.
FIGURE 1  Emergency department (ED) and inpatient SARS-CoV-2 pathway. CBC/diff, complete blood cell count with differential; CDC, Centers for Disease Control and Prevention; CMP, comprehensive metabolic panel; CPK, creatinine phosphokinase; DVT, deep vein thrombosis; HEPA, high-efficiency particulate air; ID, infectious disease; IL-1, interleukin 1; LDH, lactate dehydrogenase; PE, pulmonary embolus; PTT, partial thromboplastin time; PT/INR, prothrombin time and international normalized ratio; SpO₂, pulse oxygen saturation.
### 1. Isolation Procedures

- All patients
  - Droplet and contact precautions: surgical mask, eye protection, gown, and gloves

- Patients undergoing AGPTs (4)
  - Droplet and contact precautions: surgical mask, eye protection, gown, and gloves
  - Airborne precautions: N95 respirator
  - AIIR

### 2. Discharge

- Telehealth follow-up for patients with suspected SARS-CoV-2 infection is preferred when available and clinically appropriate
- Counsel all close household contacts to wash their hands before and after contact with the patient and to sterilize toys and tableware frequently
- Because guidelines for at-home isolation and quarantine discontinuation are rapidly evolving, provide families with latest CDC instructions and encourage them to review with their primary care provider during (Telehealth) follow-up
- For patients residing at long-term care facilities, discuss with facility to determine safety of discharge, including the ability of the facility to isolate and quarantine patients

### 3. Risk Stratification

- **Low risk**
  - Asymptomatic patients with incidentally noted SARS-CoV-2 infection

- **Moderate risk**
  - Neither low risk nor high risk

- **High risk (any of the following)**
  - Oxygen saturation by pulse oximetry reads < 90% in room air (excluding certain patients with cyanotic heart disease)
  - Chronic respiratory support needs (eg, NIPPV, tracheostomy care) with acute respiratory distress
  - Underlying chronic lung disease
  - History of moderate or severe asthma
  - Known tobacco use, including vaping or smoking
  - Hemodynamically significant heart disease
  - Hypertension
  - Diabetes mellitus (type 1 or 2)
  - Obesity
  - Vasculitis
  - Chronic kidney disease
  - Immunosuppression (eg, chronic autoimmune disease, primary immune disease, organ transplant recipient, hematologic malignancy)
  - Significant potential for clinical decompensation

### 4. AGPTs

- Open suctioning (not in-line suctioning)
- Nebulized treatments
- High-flow nasal cannula
- NIPPV
- Sputum induction
- Endotracheal intubation
- Nasotracheal intubation
- Cardiopulmonary resuscitation
- Bag-valve mask ventilation
- Existence of a tracheostomy

Note: Metered-dose inhaler treatments and nasogastric intubation are not considered AGPTs. The literature is divided on whether low-flow nasal cannula, face mask oxygen, and nasopharyngeal swabbing for SARS-CoV-2 PCR testing are AGPTs.

**FIGURE 1** Continued.
As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection continues to spread across the globe, the prompt response from the medical community has been impressive. Scientists have collected and analyzed data, shared insights and recommendations, and created ever-evolving sets of clinical practice guidelines.1,2 As SARS-CoV-2 disproportionately affects adults, both in absolute case count and in illness severity,3 the majority of available scientific literature thus far has been focused on diagnosis and treatment in the adult patient population. However, we are increasingly recognizing that SARS-CoV-2 infection also presents a significant disease burden in the pediatric population and that certain pediatric patients are at risk for severe disease.4-6 To our knowledge, no evidence-based or evidence-informed guidelines for the diagnosis and treatment of the hospitalized pediatric patient have been published in peer-reviewed journals.7,8 Recently, there has been a proposed link between SARS-CoV-2 infection and pediatric multisystem inflammatory syndrome potentially associated with coronavirus disease 2019 (COVID-19).9 We will not be addressing this hyperinflammatory condition in this article, but rather, we will be focusing solely on hospitalized pediatric patients presenting with initial SARS-CoV-2 infection. The authors work at a quaternary care children’s hospital in New York City, the current national epicenter of the COVID-19 crisis. With many hospitals in the region diverting pediatric patients to our institution to accommodate their surges in adult admissions, we have cared for a comparatively large number of pediatric patients with initial SARS-CoV-2 infection in the inpatient setting, >100 at the time of this writing. Our institution therefore faced an urgent need for pediatric-specific guidelines for the diagnosis and management of these patients.

In collaboration with pediatric infectious disease, pediatric emergency medicine, and pediatric critical care medicine colleagues, we have reviewed the relevant literature on COVID-19 in pediatrics and adults to create guidelines for the diagnosis and management of the hospitalized pediatric patient with confirmed or suspected initial SARS-CoV-2 infection at our institution. In addition, we detail how available data have informed our approach, which will allow others to create guidelines tailored to their own institution-specific practices that continue to be evidence informed.

**ISOLATION**

The primary mode of transmission for SARS-CoV-2 is currently understood to be via respiratory droplets and contact with respiratory secretions or fomites.1 Therefore, for all pediatric patients with suspected or confirmed SARS-CoV-2 infection, droplet and contact precautions are required for all staff entering the patient room. This includes a surgical mask, eye protection, gown, and gloves.
The extent of airborne transmission in SARS-CoV-2 spread remains a topic of debate. However, evidence continues to strongly suggest that the risk of airborne transmission is clinically significant during aerosol-generating procedures and therapies (AGPTs). In an effort to balance the personal protective equipment conservation with patient and health care worker safety, we follow the national trend to require airborne precautions only for patients undergoing AGPTs. These include open suctioning (not in-line suctioning), nebulized treatments, high-flow nasal cannula, noninvasive positive pressure ventilation (NIPPV), sputum induction, endotracheal intubation, nasotracheal intubation, cardiopulmonary resuscitation, bag-valve mask ventilation, and the existence of a tracheostomy. Of note, metered-dose inhaler treatments and nebulized treatments require airborne precautions and AirR placement in addition to droplet and contact precautions.
precise con
stage of transport (Fig 1). That isolation measures are in place at each hospital should be coordinated to ensure well. All patient movement within the institution performs nasopharyngeal PCR testing using the cobas Roche SARS-CoV-2 polymerase chain reaction (PCR) test has become available at our institution was able to convert several pressure AIIRs through the installation of high-efficiency particulate air filters in precise configurations. This may represent a feasible option for other institutions as well. All patient movement within the hospital should be coordinated to ensure that isolation measures are in place at each stage of transport (Fig 1).

TESTING

Hospital-based testing guidelines for SARS-CoV-2 infection have evolved repeatedly because of the changing availability of testing materials. At this time, our institution performs nasopharyngeal PCR testing using the cobas Roche SARS-CoV-2 test on all patients who require hospitalization for any reason (regardless of clinical suspicion of SARS-CoV-2 infection) because asymptomatic infection and transmission is common. For institutions where universal testing of all admitted patients is not feasible, we suggest targeted testing, focusing on symptomatic individuals as well as those for whom test results could impact clinical care. Examples of asymptomatic patients who may benefit from testing include patients listed for a bone marrow transplant, patients on immunosuppressing medications, patients living in residential facilities, and patients anticipated to receive AGPTs. At the time of writing, standard respiratory viral panel PCR testing has been restricted at our hospital to prioritize SARS-CoV-2 testing resources. For institutions that have not restricted standard respiratory viral panel PCR testing, it is important to note that a positive finding on a standard respiratory viral panel does not rule out SARS-CoV-2 coinfection because coinfection with multiple respiratory viruses is common in children. Additionally, at our institution, cerebrospinal fluid PCR testing has been performed in select patients with neurologic symptoms, and stool PCR testing has been performed in patients in whom gastrointestinal symptoms are prominent. These tests are done on a case-by-case basis and in discussion with subspecialty consultants for research purposes and only if the specimen in question had already been obtained for other reasons. Recently, SARS-CoV-2 testing on lower respiratory tract specimens, including sputum, bronchoalveolar lavage, and tracheal aspirate specimens, by using the Altona Diagnostics SARS-CoV-2 qualitative real-time PCR test has become available at our institution. Lower respiratory tract testing may be indicated for patients for whom there is a high clinical suspicion for COVID-19, for patients who have at least 1 negative SARS-CoV-2 nasopharyngeal swab result, and for patients who have existing access to the lower respiratory tract via an endotracheal tube or a tracheostomy. It may also be indicated to allow for discontinuation of isolation precautions in patients with an endotracheal tube or a tracheostomy.

RISK STRATIFICATION

Current literature from the adult population suggests that patients with certain underlying illnesses are at higher risk of serious disease if infected with SARS-CoV-2. These underlying illnesses include hypertension, cardiovascular disease, diabetes mellitus, obesity, pulmonary disease, chronic kidney disease, malignancy, and immunosuppression. In addition, the adult literature reveals that patients with cough, dyspnea, early and significant hypoxemia, lymphopenia with or without neutrophilia, and higher fever are more likely to require intensive care and have higher morbidity and mortality. Because much remains unknown regarding pediatric SARS-CoV-2 infection, our institution conservatively uses host risk factors and respiratory signs to identify which children may be at high risk for more serious disease. In the absence of published peer-reviewed data on risk stratification in pediatric patients with SARS-CoV-2 infection, our institution uses clinically informed criteria for risk stratification. We identify pediatric patients as high risk if they are infected with SARS-CoV-2 and meet any of the following risk criteria: oxygen saturation by pulse oximetry reads <90% in room air (excluding certain patients with cyanotic heart disease); chronic respiratory support needs (eg, NIPPV, tracheostomy care) with acute respiratory distress; underlying chronic lung disease; history of moderate or severe asthma; known tobacco use, including vaping or smoking; hemodynamically significant heart disease; hypertension; diabetes mellitus (type 1 or 2); obesity; vasculitis; chronic kidney disease; and immunosuppression (eg, chronic autoimmune disease, primary immune disease, organ transplant recipient, hematologic malignancy).

INITIAL WORKUP FOR THE SARS-COV-2–POSITIVE HOSPITALIZED PEDIATRIC PATIENT

There are limited data to guide which studies should be performed routinely on pediatric patients admitted with SARS-CoV-2 infection. In the pediatric population, the laboratory abnormalities most commonly cited include elevated procalcitonin levels, elevated C-reactive protein (CRP) levels, and lymphopenia. In adults, lymphopenia with or without neutrophilia has been noted to correlate with disease severity. A number of adult studies have also revealed that more severe disease is associated with elevations in the following: ferritin, high-sensitivity troponin, creatinine, D-dimer, lactate dehydrogenase, interleukin 1, interleukin 2, interleukin 6 (IL-6), and interleukin 10 levels; prothrombin time and international normalized ratio; partial thromboplastin time; creatine phosphokinase (CPK) levels; and liver function tests. This suggests that these tests may have a role in risk stratification and clinical monitoring.
Our workup for pediatric patients with SARS-CoV-2 infection is therefore primarily based on extrapolation from the adult literature with additional guidance from expert consensus at our institution. We send the following studies on all SARS-CoV-2–positive children within 24 hours of hospital admission: complete blood cell count with differential, comprehensive metabolic panel, CRP, procalcitonin, CKP, ferritin, and D-dimer. We do not routinely send blood and respiratory cultures unless there is a clinical suspicion for bacterial coinfection. For high-risk patients, we consider obtaining lactate dehydrogenase levels, prothrombin time and international normalized ratio, partial thromboplastin time, high-sensitivity troponin levels, and the cytokine panel (eg, interleukin 1, IL-6), HIV 1 and 2 antibody and antigen testing and hepatitis B serologies are obtained on all patients for whom immune-modulating therapy or potentially hepatotoxic therapy is being considered.

We recommend additional imaging studies only as clinically indicated. If a chest radiograph is obtained, a portable anterior and posterior view is likely sufficient in most clinical scenarios. If available and if clinically appropriate, bedside imaging is encouraged at our institution to minimize patient transport within the hospital.

**INPATIENT MONITORING AND MANAGEMENT**

**Vital Sign Monitoring**

Vital sign frequency is based on clinical assessment, and our institution also aims to minimize frequency to reduce unnecessary staff exposure to SARS-CoV-2. All patients with hypoxemia, supplemental oxygen requirement, and/or chronic respiratory support needs (eg, NIPPV, tracheostomy care) are placed on continuous pulse oximetry, if available, because our experience has included patients who rapidly and unexpectedly decompensated.

**Respiratory**

Hypoxemia has been identified as an early warning sign of impending respiratory failure among adult patients with SARS-CoV-2 infection. All hospitalized patients require an assessment of chronic respiratory support needs, a bag-valve mask to be kept at the bedside, and a discussion of the need for endotracheal intubation supplies to be kept at the bedside. We titrate supplemental oxygen to achieve a goal oxygen saturation by pulse oximetry of \( \geq 92\% \) (excluding certain patients with cyanotic heart disease). Any degree of hypoxemia or dyspnea is closely monitored because greater hypoxemia and earlier dyspnea in adults have been important early identifiers of SARS-CoV-2 pneumonia and predictors of future respiratory decompensation.

At our institution, we routinely use NIPPV on the inpatient medical-surgical unit for patients with escalating respiratory distress. However, because we have experienced some cases of rapid and unexpected respiratory decompensation in pediatric patients with COVID-19, we call the rapid response team for any patient with worsening respiratory distress or requiring oxygen supplementation \( >4 \text{ L/minute} \). At this time, we avoid initiation of NIPPV and high-flow nasal cannula, as clinically appropriate, while patients are on the inpatient medical-surgical unit, deferring escalation of support until ICU transfer.

It is important to avoid all nebulized treatments if possible, including albuterol and normal or hypertonic saline, because these are considered aerosol generating. We recommend metered-dose inhalers when bronchodilators are indicated, if available and clinically appropriate. If nebulized treatments are required, airborne precautions and AIIR placement is necessary in addition to droplet and contact precautions.

**Cardiovascular**

A baseline electrocardiogram is routinely obtained, and the use of QTc-prolonging medications (eg, ondansetron) is limited in our institution. This practice was developed when hydroxychloroquine and/or azithromycin treatment was more common. We anticipate that this practice may change as these experimental therapies are less frequently used. If hydroxychloroquine and/or azithromycin are started, QTc should then be monitored. In patients with persistent tachycardia, we test for N-terminal pro-brain natriuretic peptide, high-sensitivity troponin, and CKP levels, and we perform an echocardiogram to evaluate for myocarditis, pericarditis, and pericardial effusions.

**Hematology**

In the adult literature, acute COVID-19 infection can lead to systemic coagulation activation and thrombotic complications, for which the pathophysiology is not yet fully understood. Some evidence suggests that anticoagulation therapy may decrease mortality in severe COVID-19 infections. In addition, the International Society on Thrombosis and Hemostasis released interim guidelines suggesting consideration of prophylaxis doses of low–molecular-weight heparin in all hospitalized patients (including those not critically ill) with acute COVID-19 if no contraindications are present.

The extent to which adults’ risk of COVID-19–related coagulopathy translates to the pediatric population is unclear; and the data on coagulopathy in pediatric patients with COVID-19 are sparse. It is therefore prudent to exercise clinical judgment when deciding on anticoagulation regimens in pediatric patients with SARS-CoV-2 infection. At our institution, chemoprophylaxis is recommended by hematology in nearly all patients with COVID-19 infection aged \( \geq 12 \) years and weighing \( \geq 30 \text{ kg} \), unless clinically contraindicated. For patients <12 years old or weighing <30 kg, there was no universal recommendation or standardized practice for chemoprophylaxis. If deep vein thrombosis or pulmonary embolus is identified in any patient, treatment-dose anticoagulation is initiated in consultation with hematology.

**Fluids, Electrolytes, Nutrition, Gastrointestinal**

A goal fluid balance of net neutral to net negative is favored at our institution to prevent pulmonary edema. For non–high-risk patients, a regular diet is initiated as tolerated. For high-risk patients who are...
deemed at risk for respiratory decompensation, we prefer nil per os for the first 24 hours of hospitalization. Intravenous fluids should be provided, as clinically indicated, to maintain the goal fluid balance noted above. We use isotonic fluids containing dextrose unless otherwise clinically contraindicated. We strictly monitor input and output on each patient because acute kidney injury has been described in the adult literature.27,34,35

Infectious Disease
In non–high-risk patients, supportive care only is recommended. A dedicated COVID-19 pediatric infectious disease team consults on every SARS-CoV-2-positive patient admitted to the hospital and makes recommendations regarding the initiation of experimental therapies. For high-risk patients, we consider remdesivir if the patient is eligible for a clinical trial or if the patient meets criteria for compassionate use. For institutions without the ability to offer high-risk patients experimental therapies through clinical trials, it may be helpful to consult nearby institutions conducting such trials to determine the appropriateness of transfer.

Because current guidelines do not recommend limiting systemic steroid use,36 we do not avoid systemic steroids in our patients with COVID-19. However, systemic steroids are used on a case-by-case basis in patients when there is suspicion for significant cytokine release or if they are otherwise indicated for an underlying condition (e.g., status asthmaticus, adrenal insufficiency). Immune modulators, such as IL-6 receptor antagonists, are also considered in high-risk patients with suspicion for significant cytokine release.

As with adults, at this time there is insufficient evidence to recommend other experimental agents in pediatric patients, such as lopinavir and ritonavir, hydroxychloroquine, and azithromycin.39,37

Laboratory Monitoring
If there is clinical and/or laboratory evidence of significant cytokine release (e.g., high fever, tachycardia, elevated inflammatory markers), trending CRP, procalcitonin, ferritin, and D-dimer levels may be helpful to monitor for disease progression.

Adult patients with COVID-19 sometimes manifest hepatitis,34 pancreatitis,36 acute kidney injury,27,34,35,48 and/or risk for deep vein thrombosis or pulmonary embolus.31–33,41,42 We consider trending studies related to these adult complications on a case-by-case basis in our hospitalized pediatric patients.

Care Coordination
When feasible, daily comanagement rounds with subspecialists are favored to maximize care coordination and consolidate health care worker exposure to the patient. Telehealth is used, as able and clinically appropriate, to minimize providers’ contact with patients (and other providers).

DISCHARGE
Telehealth follow-up for patients with suspected or confirmed SARS-CoV-2 infection is preferred when available and clinically appropriate. It is important to counsel families that all close household contacts should wash their hands before and after contact with the patient and to sterilize toys and tableware frequently. Because guidelines for at-home isolation and quarantine discontinuation are rapidly evolving, we provide families with the latest instructions available from the Center for Disease Control and Prevention and encourage them to review with their primary care provider during (Telehealth) follow-up.41–46 For patients residing at long-term care facilities, it is important to discuss with the facility to determine the safety of discharge, including the ability of the facility to isolate and quarantine patients.

NEWBORN CONSIDERATIONS
The American Academy of Pediatrics (AAP) has issued recent guidance on caring for newborns delivered by mothers infected with SARS-CoV-2.47 This guidance includes the recommendation to bathe newborns immediately as a means of prevention of vertical transmission. Our review of the literature has not revealed compelling evidence supporting the vertical transmission of SARS-CoV-2.5,48 Given the established benefits of delayed bathing in newborns (including preventing hypothermia, allowing skin-to-skin contact, and promoting breastfeeding) the practice of routine immediate bathing has not been adopted at our institution.

For SARS-CoV-2–positive mothers, AAP guidelines currently recommend separating the infant and mother immediately after delivery.47 If a family does not wish to follow this recommendation for separation, the AAP recommends encouraging 6 ft of distance at all times between the mother and newborn unless the mother is breastfeeding or providing direct care. The use of surgical masks and meticulous breast and hand hygiene is recommended.67 To date, none of the mothers in our newborn nursery have elected to be separated from their newborns. In cases in which mothers are too ill to care for their newborns, the infants are transferred to a separate room and placed in an isolette with a temperature probe. These rooms have large windows to allow for frequent assessments by staff without entering. Routine vital signs and nursing care are performed as usual.

The AAP recommends performing nasopharyngeal SARS-CoV-2 PCR testing on all newborns born to mothers with COVID-19 at 24 hours of life and again at 48 hours of life. Because of limited testing resources and lack of clear evidence that early testing would alter our management of these newborns, we perform routine testing only once during the newborn’s hospitalization. Our newborn hospitals endeavor to ensure that plans for follow-up care with a pediatric provider (via phone, Telehealth, or office visit) are arranged before discharge.

Of note, childbirth and neonatal resuscitation are considered to be aerosol generating. It is therefore important for the birthing partner and all hospital staff in attendance to use appropriate personal protective equipment for droplet, contact, and airborne precautions.48

CONCLUSIONS
COVID-19 remains a disease that affects adults with greater frequency and severity than children. However, with the ongoing
spread of SARS-CoV-2, the pediatric population has been increasingly impacted. Whereas most pediatric patients recover with supportive care at home, a subset of patients require inpatient hospitalization, including critical care. It therefore remains imperative that institutions devote attention to the development of standardized diagnostic and therapeutic guidelines for hospitalized pediatric patients.

In this article, we present a single-center guide to care for hospitalized pediatric patients with suspected or confirmed initial SARS-CoV-2 infection. Anecdotally, we have noted improvements in care quality and efficiency after implementation of this protocol. In addition to minimizing staff exposure to SARS-CoV-2, we have noted enhanced interdisciplinary communication, improvements in provider satisfaction with consistency and quality of care, and improved provider comfort in caring for patients with this novel disease. We therefore share our approach in hopes that others will be able to more efficiently and effectively create their own evidence-informed, institution-specific guidelines and see similar positive outcomes. Because new information regarding SARS-CoV-2 is rapidly emerging, it remains imperative that pediatric providers continue to stay abreast of the current literature, focusing on high-quality studies and reports that will best guide evidence-informed care.

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