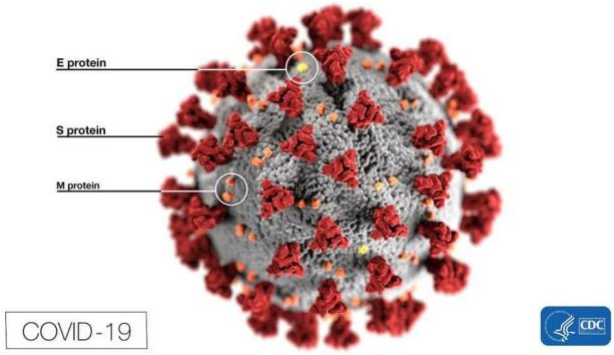
COVID-19 Primer for Pediatric EM Providers

Pediatric COVID-19 Literature Review | March 28, 2020 (Updates Highlighted)

Coronaviruses are a large group of viruses and one of the major causes of viral respiratory tract infections. There are **7 different coronaviruses**, including the novel coronavirus (SARS-CoV-2), which is the pathogen responsible for the **COVID-19 disease.**[1] Other types of coronaviruses include SARS-CoV (pathogen responsible for the Severe acute respiratory syndrome outbreak) and MERS-CoV (pathogen responsible for Middle East respiratory syndrome).[2]

It is suspected that coronaviruses initially evolved in bat populations and have been transferred to humans through intermediate mammalian hosts (such as Civets, Camels, and Pangolins).[3]



Studies performed on the other enveloped coronaviruses (SARS-CoV, MERS-CoV) found that they are **effectively inactivated with soap and water, or hand sanitizer** (>60% ethanol).[4-6]

Epidemiology

The COVID-19 pandemic was initially identified in December 2019 after a number of pneumonia cases were investigated in the city of Wuhan, in the Hubei province of China.[7] Data on the epidemiology of COVID-19 changes frequently as the pandemic progresses. However, some trends have emerged, including:

- A mortality rate between **3-4%,** with higher mortality in older age groups.
- A R_0 value similar to pandemic influenza. **R_0 represents the transmissibility of the virus.** In other words, for every 1 person with COVID-19, the R_0 represents how many others they would infect. Current estimated value for COVID-19 is **2.2-3.9**. (Measles: 12-15, seasonal influenza: 0.9-2.1)[6]

With regards to pediatric patients, Dong et al. (2020) reviewed the epidemiology of COVID-19 in Pediatric patients in China.[8] The authors identified 2143 pediatric patients with confirmed or suspected COVID-19. Of these cases, the median age was 7 years old. **112 pediatric patients (5.2%) were considered to have a severe presentation** (oxygen saturation <92%) and **13 patients (0.6%) were considered to have a critical presentation** (respiratory failure or multiorgan dysfunction). Critical presentations were more common in younger patients, with children **under 1 year of age representing 53.8% of all critical pediatric presentations**. Amongst the study population, there was 1 pediatric death (14-year-old, clinical details not reported).

The low SARS-CoV-2 case rate in pediatric patients has also been identified in other countries. For instance, based on a report from South Korea (which had an extensive SARS-CoV-2 testing strategy) detailing the first 7755 SARS-CoV-2 cases in the country, there were 480 cases in patients under 19 years of age (6.1%), with no deaths.[8]

Current evidence suggests that pediatric patients are as likely to become infected with COVID-19 as adult patients, but **less likely to become symptomatic or develop severe symptoms.**[10]

Incubation Period

Lauer et al. (2020) performed a pooled analysis of 181 confirmed COVID-19 cases in China.[11] For each of the 181 cases, the investigators recorded the time of possible exposure to SARS-CoV-2, any symptom onset, fever onset, and case detection. Based on this population, the authors found a **median incubation period of 5.1 days** (time to symptom onset). However, some patients did not become symptomatic until later from their exposure. Overall, **97.5% of patients became symptomatic within 11.5 days of exposure** (CI: 8.2 to 15.6 days).

Presentation

A recent systematic review was published on the clinical, laboratory and imaging features of COVID-19 that included all ages. Rodriguez-Morales et al. (2020) analyzed the data of 19 studies, which included a total of 2874 patients.[12] **Fever (88.7%), cough (57.6%), and dyspnea (45.6%) were the most common symptoms across all age groups**. Interestingly, fever was a less frequent symptom in children (43.9%). Less common symptoms included myalgias (11%), rhinorrhea (10%), and GI symptoms (3-10%). Of note, **only 44% of patients had fever at the time of presentation.**[7]

Laboratory findings include a decreased albumin (75.8%), elevated CRP (58.3%), lymphopenia (43.1%), and elevated LDH (57%). Chest x-ray findings were **predominantly bilateral consolidation (72.9%) and ground-glass opacification (68.5%).**

A smaller review of 171 children with confirmed SARS-CoV-2 infection who were treated at Wuhan Children's Hospital

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resulted in similar conclusions to the study by Rodriguez-Morales et al. (2020). **Cough (48.5%), pharyngeal erythema (46.2%), and fever (41.5%) were the most common symptoms throughout the course of illness.**[13] Interestingly, **15.8% of patients in this study were asymptomatic**, and diarrhea (9.4%), vomiting (6.4%), and nasal congestion (5.3%) were infrequent symptoms. The study identified an additional pediatric death that involved a 10-month old child who tested positive for SARS-CoV-2 who had a clinical course complicated by intussusception and multiorgan failure.

There has also been some early research into the effect of SARS-CoV-2 on the neonatal population, though the data is primarily from case series. Chen et al. (2020) performed a retrospective case review of 9 pregnant women who had COVID-19.[14] All women in the study underwent a caesarean section and there was **no evidence of vertical transmission of the virus** (none of the newborn children tested positive for SAR-CoV-2). In addition, there was **no evidence of SARS-CoV-2 in the amniotic fluid, newborn throat swabs, cord blood, or breastmilk samples**. However, in contrast to several additional case series,[15-17] Dong et al. (2020) reported a case of possible vertical transmission to a newborn from a mother with SARS-CoV-2.[18] The newborn was assessed immediately following a planned caesarean section and was found to have elevated IgM antibodies to SARS-CoV-2, but a negative nasopharyngeal swab for the virus. As IgM antibodies do not cross the placenta, the finding raises the possibility of in-utero inoculation.

Testing for SARS-CoV-2

The gold standard test for COVID-19 is a viral RT-PCR performed on nasopharyngeal swabs or aspirates. As there is currently no treatment for COVID-19, the intent of testing for SARS-CoV-2 is to effectively contain the virus amongst the population through self-isolation measures and to provide diagnostic clarity for unwell/admitted patients. As the test for COVID-19 is not a standardized investigation, test characteristics vary between institutions, with some reporting **the sensitivity between 66-80%.**[19] A false negative result can occur if the sample is improperly collected or collected too early in the course of illness. There is ongoing research into developing rapid, point-of-care testing for SARS-CoV-2, but many of these tests are still in early phases of study.[20]

Management of COVID-19

The management of COVID-19 is primarily supportive, but there is ongoing research investigating some potential therapies and vaccines.

Guidelines for the management of critically unwell patients vary depending on the institution and the age of the patient. While there are a number of guidelines for the management of critically ill adult COVID-19 patients,[21] **a provincial guideline for the management of critically unwell pediatric COVID-19 patients** has been released by the Provincial Critical Care Pediatric Communicable Disease Working Group.[22]

Pathogenic human coronaviruses (including SARS-CoV-2) bind to target cells through ACE-2 (angiotensin converting enzyme). A report by Fang et al. (2020) raised concerns about medications (including ibuprofen) that may upregulate the expression of ACE-2, potentially leading to worse outcomes in patients with COVID-19.[23] However, there is no robust evidence to support this theory at this time and the current position by the World Health Organization is that **they do not recommend against the use of ibuprofen.**

A number of medications have been identified as having a potential therapeutic effect against SARS-CoV-2 and a number of clinical trials are currently underway. While some of these studies identified in-vitro effects, a small observational study of **hydroxychloroquine (antimalarial) and azithromycin (antibiotic) demonstrated a higher rate of viral cure after 6 days of treatment in hospitalized patients with COVID-19.**[24] However, this study did not report patient-outcomes (such as mortality, time in ICU, etc.), so it is unclear of the actual clinical impact of this therapy at this time.

Currently, there is **no vaccine for SARS-CoV-2**. However, there are a number of ongoing clinical trials to identify an effective vaccine.

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