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COVID-19 in Children: Initial Characterization of the Pediatric Disease

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Abbreviations: ARDS: acute respiratory distress syndrome; COVID-19: coronavirus disease; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

The impact of the disease caused by the novel coronavirus, SARS-CoV-2,¹ COVID-19, has been widespread, with over 120,000 cases diagnosed in more than 100 countries since the virus was identified in January of 2020.² Preliminary data focused on severe respiratory manifestations, seen predominantly in adults, with scant initial data on the burden of COVID-19 in children.³ We therefore read with interest the findings of Dong and colleagues in this volume of *Pediatrics*, who reported a series of over 2000 children with suspected or confirmed COVID-19.⁴ The authors found that 13% of virologically-confirmed cases had asymptomatic infection, a rate that almost certainly understates the true rate of asymptomatic infection, since many asymptomatic children are unlikely to be tested. Among symptomatic children, 5% had dyspnea or hypoxemia (a substantially lower percentage than what has been reported for adults³) and 0.6% progressed to acute respiratory distress syndrome (ARDS) or multiorgan system dysfunction, a rate that is also lower than that seen in adults. Preschool-aged children and infants were more likely to have severe clinical manifestations than older children.

There are several salient points from this paper. First, while children are less likely to become severely ill than older adults, there are subpopulations of children with an increased risk for more significant illness. These are consistent with data on non-COVID-19 coronaviruses. One viral surveillance study in a pediatric intensive care unit in China reported that coronavirus was detected in more children with ARDS than human metapneumovirus.⁵ Another study in hospitalized Norwegian children detected coronaviruses in 10% of hospitalized children with respiratory tract infections.⁶ Younger age, underlying pulmonary pathology, and immunocompromising conditions have been associated with more severe outcomes with non-COVID-19 coronavirus infections in children.⁷

Second, the attributable risk for severe disease from COVID-19 in children is challenging to discern. Prior studies have shown that children from whom coronaviruses are detected from the respiratory tract can have viral co-infections in up to two-thirds of cases.⁶ In the study by Dong et al., testing for other viruses was not standardized, and two-thirds of cases were clinically diagnosed, not virologically confirmed. Furthermore, children without virologic confirmation were more likely to have severe disease than children from whom COVID-19 was detected, potentially because their symptoms were caused by other pathogens.

Third, children may play a major role in community-based viral transmission. Available data suggest that children may have more upper respiratory tract (including nasopharyngeal carriage), rather than lower respiratory tract involvement.⁴ There is also evidence of fecal shedding in the stool for several weeks after diagnosis,⁸ leading to concern about fecal-oral transmission of the virus, particularly for infants and children who are not toilet-trained, and for viral replication in the gastrointestinal tract.⁹ Prolonged shedding in nasal secretions and stool has substantial implications for community spread in daycare centers, schools, and in the home. Additionally, non-COVID-19 coronaviruses are detectable in respiratory secretions in a large percentage of healthy children,⁶ and the extent to which this is also seen in COVID-19 is unclear. Prolonged viral shedding in symptomatic individuals, combined with shedding in asymptomatic persons, would render contact tracing and other public health measures to mitigate spread less effective.

We have learned an amazing amount about COVID-19 in a short amount of time, with copious epidemiologic, virologic, and clinical data being published. The SARS-CoV-2 sequence, now published,¹⁰ was first posted to the bioRxiv preprint server a remarkable six weeks after the start

of epidemic, enabling the essential work of molecular epidemiology. The transmission of data has been surpassed only by the transmission of the virus itself. However, there is still much that we need to learn about the impact of this virus on children, as well as the impact of children on viral spread. While vertical transmission has not yet been reported,¹¹ many of the infants born to COVID-19-infected mothers were delivered surgically and quickly separated from their mothers. Many infectious diseases affect pregnant women more severely, and respiratory disease in pregnant women may result in poor fetal outcomes. Data on the basic reproductive number of the virus (the number of persons to whom an infected individual transmits the virus) have varied widely,^{12,13} and household studies can refine data we have on viral transmission and on viral shedding. Widespread availability of testing will allow for us to more accurately describe the spectrum of illness and may result in adjustment of the apparent morbidity and mortality rate as fewer ill individuals are diagnosed. While the focus on pandemics often is on the impact on the persons who utilize the highest resources or on the economically productive age groups, rigorously gauging the impact of COVID-19 on children will be important to accurately model the pandemic and to ensure that appropriate resources are allocated to children requiring care. Many infectious diseases affect children differently than adults and understanding those differences can yield important insights into disease pathogenesis, informing management and the development of therapeutics. This will likely be true for COVID-19, just as it was for older infectious diseases.

References

1. Gorbalenya AE, Baker SC, Baric RS, et al. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol.* 2020. doi: 10.1038/s41564-020-0695-z.
2. Johns Hopkins University Center for Systems Science and Engineering. Coronavirus COVID-19 global cases. Available online at: <https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>. Last accessed March 11, 2020.
3. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020; doi: 10.1001/jama.2020.1585.
4. Dong Y, Mo X, Hu, Y, et al. [Epidemiology of COVID-19 among children in China]. IN PRESS this issue *Pediatrics*.
5. Li YT, Liang Y, Ling YS, et al. The spectrum of viral pathogens in children with severe acute lower respiratory tract infection: a 3-year prospective study in the pediatric intensive care unit. *J Med Virol.* 2019;91(9): 1633-1642.
6. Heimdal I, Moe N, Kokstad S, et al. Human coronavirus in hospitalized children with respiratory tract infections: a 9-year population-based study from Norway. *J Infect Dis.* 2019;219(8):1198-1206.
7. Omigi C, Englund JA, Bradford MC, Qin X, Boeckh M, Waghmare A. Characteristics and outcomes of coronavirus infection in children: role of viral factors and an immunocompromised state. *J Pediatr Infect Dis Soc.* 2019;8(1):21-28.
8. Jiehao C, Jing X, Daojiong L, et al. A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clin Infect Dis.* 2020; doi: 10.1093/cid/ciaa198.
9. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterol.* 2020. doi: 10.1053/j.gastro.2020.02.055.
10. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020. doi: 10.1038/s41586-020-201207.
11. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet.* 2020;395(10226):809-815.
12. Jung SM, Akhmetzhanov AR, Hayashi K, et al. Real-time estimation of the risk of death from novel Coronavirus (COVID-19) infection: inference using exported cases. *J Clin Med.* 2020;9(2): doi: 10.3390/jcm9020523.
13. Hellewell J, Abbott S, Gimma A, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and controls. *Lancet Glob Health.* 2020; doi: 10.1016/S2214-109X(20)30074-7.

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