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health authorities, political leaders, and institutions. It is important that policy makers maintain the public's trust through use of evidence-based interventions and fully transparent, fact-based communication.

We declare no competing interests.

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- 1 WHO. Pneumonia of unknown cause—China. <https://www.who.int/csr/don/05-january-2020-pneumonia-of-unknown-cause-china/en/> (accessed March 5, 2020).
- 2 Cohen J, Kupferschmidt K. Labs scramble to produce new coronavirus diagnostics. *Science* 2020; **367**: 727.
- 3 Koo JR, Cook AR, Park M, et al. Interventions to mitigate early spread of COVID-19 in Singapore: a modelling study. *Lancet Infect Dis* 2020; published online March 23. [https://doi.org/10.1016/S1473-3099\(20\)30162-6](https://doi.org/10.1016/S1473-3099(20)30162-6).
- 4 Tan CC. SARS in Singapore—key lessons from an epidemic. *Ann Acad Med Singapore* 2006; **35**: 345–49.
- 5 Kupferschmidt K, Cohen J. China's aggressive measures have slowed the coronavirus. They may not work in other countries. March 2, 2020. <https://www.sciencemag.org/news/2020/03/china-s-aggressive-measures-have-slowed-coronavirus-they-may-not-work-other-countries> (accessed March 9, 2020).
- 6 Kupferschmidt K, Cohen J. Can China's COVID-19 strategy work elsewhere? March 6, 2020. <https://science.sciencemag.org/content/367/6482/1061?rss%253D1> (accessed March 11, 2020).
- 7 Chao DL, Halloran ME, Obenchain VJ, Longini IM. FluTE, a publicly available stochastic influenza epidemic simulation model. *PLoS Comput Biol* 2010; **6**: e1000656.
- 8 Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in Shenzhen, China: analysis of 391 cases and 1286 of their close contacts. *medRxiv* 2020; published online March 4. DOI:10.1101/2020.03.03.20028423 (preprint).
- 9 Gonsalves GS, Kapczynski A, Ko AI, et al. Achieving a fair and effective COVID-19 response: an open letter to Vice-President Mike Pence, and other federal, state, and local leaders from public health and legal experts in the United States. <https://docs.google.com/document/d/1NVOSECOEp8deYnmJfOouKtRHcNcbmNrk7dW752dzMeE/edit> (accessed March 5, 2020).
- 10 Kass NE. An ethics framework for public health. *Am J Pub Heal* 2001; **91**: 1776–82.

## COVID-19 in children: the link in the transmission chain

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), emerged from Wuhan, Hubei province, China, in late 2019 and has now reached pandemic status.<sup>1</sup> Coronaviruses typically cause mild upper respiratory tract infections;<sup>2</sup> however, SARS-CoV-2,<sup>3</sup> severe acute respiratory syndrome coronavirus (SARS-CoV),<sup>4</sup> and Middle East respiratory syndrome coronavirus (MERS-CoV)<sup>5</sup> have all been associated with severe illness and death. Common symptoms reported in adults with COVID-19 are fever, dry cough, and fatigue; severe cases have been associated with dyspnoea and bilateral ground-glass opacities on chest CT.<sup>3</sup> In China, the SARS-CoV-2 reproductive number is estimated at 2.<sup>6</sup> The combined case-fatality rate is 2% in China,<sup>7</sup> and the risk of death is increased significantly in older people (approximately 15%).<sup>7</sup> It is noteworthy that infants and children have not been featured prominently in COVID-19 case statistics. An analysis from China has shown that children younger than 10 years account for only 1% of COVID-19 cases,<sup>7</sup> similar to the proportion for SARS-CoV and MERS-CoV epidemics.<sup>4,5</sup>

Infants and young children are typically at high risk for admission to hospital after respiratory tract infection with viruses such as respiratory syncytial virus and influenza virus.<sup>8</sup> Immaturity of the respiratory

tract and immune system is thought to contribute to severe viral respiratory disease in this age group.<sup>8</sup> Therefore, the absence of paediatric patients with COVID-19 has perplexed clinicians, epidemiologists, and scientists. Case definitions and management strategies for children are absent because of the limited number of paediatric patients with COVID-19. In *The Lancet Infectious Diseases*, Haiyan Qiu and colleagues<sup>9</sup> have shed light on this under-represented population with a clinical report of 36 paediatric patients (aged 1–16 years) with PCR-confirmed COVID-19. Their analyses have important implications for clinical management of younger people with SARS-CoV-2 infection and social distancing policies to prevent virus transmission.

The patients in this study<sup>9</sup> were being treated at three hospitals located in Zhejiang province, China, which is 900 km from Wuhan. The children accounted for roughly 5% of total patients with COVID-19. Patients were stratified by disease severity and were assessed in hospital (mean duration of hospitalisation, 14 [SD 3] days) for secondary bacterial and fungal infection, sepsis, immune responses, and organ dysfunction (lung, liver, heart, and kidney). All children underwent CT examination for diagnosis of pneumonia.



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Ten (28%) patients were asymptomatic latent cases identified because either an adult family member had the infection or they had been exposed to the epidemic area.<sup>9</sup> Contact tracing was also used to identify paediatric infections during the SARS-CoV and MERS-CoV epidemics.<sup>4,5</sup> None of the children developed severe illness or died, similar to findings of SARS-CoV paediatric cases in 2002–03.<sup>4</sup> The most commonly reported clinical finding in children with COVID-19 was pneumonia (19 [53%]); fever, dry cough, or both were the next most frequent symptoms. All children with COVID-19 were aggressively treated, which was also standard for children with SARS-CoV infection.<sup>4</sup> Treatment for COVID-19 consisted of aerosolised interferon alfa in all children, lopinavir-ritonavir syrup twice a day for 14 days in 14 (39%), and supplemental oxygen for six (17%). Paediatric patients were discharged after two negative SARS-CoV-2 PCRs.

Qiu and colleagues have done a very important preliminary study defining the clinical picture for children infected with SARS-CoV-2, which will be valued globally. Although this work will assist with case identification, management, and social policy guidance, much more information is needed to establish the optimum management regimen. Specifically, the data showed that paediatric patients with COVID-19 had mild or asymptomatic disease accompanied by pneumonia in about half the cases.<sup>9</sup> It is unclear which children should be targeted for antiviral and immunomodulatory treatment, particularly in view of the high proportion of asymptomatic infected contacts. Together, these results could suggest that children have specific mechanisms regulating the interaction between the immune system and respiratory machinery, which could be contributing to milder disease. Possibly, lung infiltrates have a protective role during paediatric SARS-CoV-2 infection, similar to lymphocytes participating in inducible bronchus-associated lymphoid structure development after respiratory insult.<sup>10</sup> Correlation between chest radiography and CT findings might give additional insight into the clinical importance, if any, of the CT findings. In view of the substantial radiation exposure associated with CT, if children are only experiencing

mild disease, routine use of CT might not be warranted and needs further assessment for the management of paediatric cases.

The most important finding to come from the present analysis is the clear evidence that children are susceptible to SARS-CoV-2 infection, but frequently do not have notable disease, raising the possibility that children could be facilitators of viral transmission. If children are important in viral transmission and amplification, social and public health policies (eg, avoiding interaction with elderly people) could be established to slow transmission and protect vulnerable populations. There is an urgent need to for further investigation of the role children have in the chain of transmission.

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- Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): situation summary. March 15, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/summary.html> (accessed March 17, 2020).
- Varghese L, Zachariah P, Vargas C, et al. Epidemiology and clinical features of human coronaviruses in the pediatric population. *J Pediatric Infect Dis Soc* 2018; **7**: 151–58.
- Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun* 2020; published online Feb 26. DOI:10.1016/j.jaut.2020.102433.
- Denison MR. Severe acute respiratory syndrome coronavirus pathogenesis, disease and vaccines: an update. *Pediatr Infect Dis J* 2004; **23**: S207–14.
- Al-Tawfiq JA, Kattan RF, Memish ZA. Middle East respiratory syndrome coronavirus disease is rare in children: an update from Saudi Arabia. *World J Clin Pediatr* 2016; **5**: 391–96.
- Zhao S, Lin Q, Ran J, et al. The basic reproduction number of novel coronavirus (2019-nCoV) estimation based on exponential growth in the early outbreak in China from 2019 to 2020: a reply to Dhungana. *Int J Infect Dis* 2020; published online Feb 20. DOI:10.1016/j.ijid.2020.02.025.
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; published online Feb 24. DOI:10.1001/jama.2020.2648.
- Hong L, Luo Y. Respiratory viral infections in infants: causes, clinical symptoms, virology, and immunology. *Clin Microbiol Rev* 2010; **23**: 74–98.
- Qiu H, Wu J, Liang H, Yunling L, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis* 2020; published online March 25. [https://doi.org/10.1016/S1473-3099\(20\)30198-5](https://doi.org/10.1016/S1473-3099(20)30198-5).
- Rangel-Moreno J, Hartson L, Navarro C, Gaxiola M, Selman M, Randall TD. Inducible bronchus-associated lymphoid tissue (iBALT) in patients with pulmonary complications of rheumatoid arthritis. *J Clin Invest* 2006; **116**: 3183–94.