

COVID-19 in Children: Looking Forward, Not Back

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In the fall of 2020, some of the fiercest debates waged in both academic and public arenas concern the relative ability of children to acquire and transmit severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19): rightfully so, because there are enormous implications for children, parents, and schools. To date, much of the data have come from studies of COVID-19 within household clusters early during the pandemic. In this issue of *Pediatrics*, Laws et al¹ add to this body of literature with a secondary analysis of a previously reported household contact study.² They describe infection rates, transmission dynamics, and symptom profiles in a cohort of US children with household SARS-CoV-2 exposure between March and May 2020 in Milwaukee, Wisconsin, and Salt Lake City, Utah.¹

The authors found that secondary infection rates in household contacts were similar in children (19 of 68 contacts; 28%) and adults (36 of 120 contacts; 30%). Having an infected parent was associated with a marked increase in risk for secondary infection in a child. Possible child-to-adult or child-to-child transmission was observed in 2 of 10 and 1 of 6 households, respectively, with potential for such events. Infected children generally had mild symptoms and were less likely than adults to report lower respiratory tract symptoms or loss of taste or smell. With their findings, the researchers provide additional confirmation that the overwhelming

majority of children with SARS-CoV-2 infection develop mild symptoms^{3,4} but question whether children are less susceptible to infection or less likely to transmit SARS-CoV-2. Limitations of the study include convenience sampling and a relatively small sample size because only 33 households analyzed included children.

Household contact tracing studies similar to that conducted by Laws et al¹ arguably provide the best evidence regarding pediatric susceptibility to SARS-CoV-2, in which the intensity of exposure between household contacts is higher and more consistent than in nonhousehold settings. Although not universal,⁵ the preponderance of data from numerous countries continues to support the notion that children are less susceptible to infection than adults.⁶⁻¹³ The results of recent meta-analyses suggest that overall susceptibility in children is approximately one-half of that of adults, with the greatest effect seen in younger children.^{14,15} In this study, younger children had lower rates of infection: the odds ratio for infection in 5- to 12-year-olds compared with 13- to 18-year-olds was 0.36 (95% confidence interval: 0.13-1.05).¹ Notably, in virtually all previous studies, researchers have relied on reverse transcription polymerase chain reaction to detect infection and, often, only test symptomatic contacts. That 4 pediatric infections in this study could only be detected by antibody seroconversion suggests that reverse transcription polymerase chain reaction-based case detection

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(symptoms-based or otherwise) in children may underestimate the true infection prevalence.

At the population level as well, children continue to be underrepresented among SARS-CoV-2 infections. In numerous large-scale studies, researchers have indicated that children, particularly children <10 years old, have much lower rates of infection than adults do.^{16–19} In the United States, however, between August 27 and September 10, pediatric SARS-CoV-2 infections increased from 9.5% to 10% of all infections, reflecting a months-long summer trend in which regions experienced severe outbreaks and physical distancing recommendations were relaxed or ignored as testing capacity increased.²⁰ Although concerning, children <18 years old represent 22.3% of the US population,²¹ and this increase has been driven primarily by infections in older children.

The role of children in the transmission of SARS-CoV-2 is similarly problematic. In this study, the researchers found that 20% and 17% of households had potential child-to-adult transmission and child-to-child transmission, respectively, but numbers are too small to draw definitive conclusions. Despite some reports of likely onward household transmission from infected children,^{22,23} in most studies, researchers suggest that children appear less likely to transmit, compared with adults, or present as index cases in household clusters.^{7,13,19,24–26} In a study from South Korea, researchers generated considerable alarm when they reported that children 10 to 19 years old appeared as likely as adults to transmit infection to household contacts.²⁷ However, in a subsequent, more detailed, analysis of 107 pediatric index cases and their household contacts, researchers found definitive evidence of only 1 instance of onward transmission from

a teenager, giving a household secondary attack rate of 0.5%.²⁸

A significant limitation of household cluster data is that most were generated during school closures, when opportunities for nonhousehold exposure to SARS-CoV-2 among children were scarce. Newer data-reporting experiences in summer camps, child care settings, and schools (both preclosure and postreopening) are helping to fill this gap. Importantly, in areas with low prevalence rates and appropriate mitigation policies, children occasionally become infected, but there have been no significant outbreaks. For example, in schools or child care programs in Ireland, Australia, France, Singapore, Germany, and Rhode Island, no to little facility-based transmission of SARS-CoV-2 by children was reported, despite the presence of infected children.^{29–34} However, in areas with widespread community transmission or less strict mitigation procedures, large outbreaks have occurred.^{35–38} Consistently, these outbreaks reveal that infected adults are typically responsible for introducing the virus into these settings, questionable testing strategies enable outbreak initiation, and inconsistent use of masks or cloth facial coverings makes containment of the virus challenging.

So, where does this leave us now? First, children clearly are capable of acquiring and transmitting SARS-CoV-2. Second, the preponderance of current data still indicates that children have reduced susceptibility and infectivity compared with adults, although this requires further monitoring because increased testing capacity and relaxation of community mitigation may continue to diminish the magnitude of these differences, which were so stark early during lockdown periods. Third, the importance of mitigation measures, especially the use of masks, including

among children, is now incontrovertible.³⁹

Moving forward, there remains a critical need for more high-quality pediatric SARS-CoV-2 research. Studies in children are often limited by small sample sizes and binning into convenient age cohorts that belie important differences in biology and behavior. The starkest example is to group all children <18 years old as a single-aged cohort, when there is ample evidence that younger children and older teenagers represent completely different patient populations in the context of SARS-CoV-2. For example, in the same region of France, higher rates of potential school-based transmissions were apparent in high schools, compared with primary schools.^{38,40} A major step forward in pediatric SARS-CoV-2 research would be the universal establishment of reasonable age strata to enable more appropriately powered and comparable studies. Elucidating the mechanisms responsible for differences in symptomatology, susceptibility, and infectivity between adults and children will remain important. However, at this point, we also need to shift our focus toward the interventions most important for minimizing the transmission of SARS-CoV-2 to and from children, understanding the pathogenesis of multisystem inflammatory syndrome in children, and advocating for appropriate pediatric clinical trials for SARS-CoV-2 vaccine candidates.

As SARS-CoV-2 continues its inexorable march through susceptible populations, we must remember that there is no setting on Earth guaranteed to be safe from SARS-CoV-2. With that sobering recognition, we must work to fulfill the medical, academic, social, and emotional needs of children, despite knowing that providing such care cannot ever be completely free of infectious disease risk. As has been shown in the US and around the world, with appropriate

mitigation strategies, we can successfully minimize (although not eliminate) the risk of COVID-19. We fear that one day, we will look back on this terrible pandemic and recognize the extent to which we have failed our children, by being more afraid of their infection and transmission risks than of the prospect of letting them down precisely when they needed us most.

ABBREVIATIONS

COVID-19: coronavirus disease 2019

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

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