Children May Carry Coronavirus at High Levels, Study Finds

The research does not prove that infected children are contagious, but it should influence the debate about reopening schools, some experts said.

Coronavirus testing at a mobile clinic at the Walker Temple A.M.E. Church in south Los Angeles earlier this month. Mario Tama/Getty Images

By Apoorva Mandavilli

July 30, 2020

Leer en español

It has been a comforting refrain in the national conversation about reopening schools: Young children are mostly spared by the coronavirus and don't seem to spread it to others, at least not very often.

But on Thursday, a study introduced an unwelcome wrinkle into this smooth narrative.

Infected children have at least as much of the coronavirus in their noses and throats as infected adults, according to the research. Indeed, children younger than age 5 may host up to 100 times as much of the virus in the upper respiratory tract as adults, the authors found.

That measurement does not necessarily prove children are passing the virus to others. Still, the findings should influence the debate over

reopening schools, several experts said.

“The school situation is so complicated — there are many nuances beyond just the scientific one,” said Dr. Taylor Heald-Sargent, a pediatric infectious diseases expert at the Ann and Robert H. Lurie Children’s Hospital of Chicago, who led the study, published in JAMA Pediatrics.

“But one takeaway from this is that we can’t assume that just because kids aren’t getting sick, or very sick, that they don’t have the virus.”

The study is not without caveats: It was small, and did not specify the participants’ race or sex, or whether they had underlying conditions. The tests looked for viral RNA, genetic pieces of the coronavirus, rather than the live virus itself. (Its genetic material is RNA, not DNA.)

Still, experts were alarmed to learn that young children may carry significant amounts of the coronavirus.

“I’ve heard lots of people saying, ‘Well, kids aren’t susceptible, kids don’t get infected.’ And this clearly shows that’s not true,” said Stacey Schultz-Cherry, a virologist at St. Jude Children’s Research Hospital.

“I think this is an important, really important, first step in understanding the role that kids are playing in transmission.”

Jason Kindrachuk, a virologist at the University of Manitoba, said: “Now that we’re rolling into the end of July and looking at trying to open up schools the next month, this really needs to be considered.”

Latest Updates: Global Coronavirus Outbreak ›

Updated 2020-08-02T17:52:35.962Z

- The U.S. reels as July cases more than double the total of any other month.
- Top U.S. officials work to break an impasse over the federal jobless benefit.
- Its outbreak untamed, Melbourne goes into even greater

lockdown.

More live coverage: **Markets**

The standard diagnostic test amplifies the virus's genetic material in cycles, with the signal growing brighter each round. The more virus present in the swab initially, the fewer cycles needed for a clear result.

Dr. Heald-Sargent, who has a research interest in coronaviruses, began noticing that children's tests were coming back with low "cycle thresholds," or C.T.s, suggesting that their samples were teeming with the virus.

Intrigued, she called the hospital lab on a Sunday and asked to look back at test results for the past several weeks. "It wasn't even something we had set out to look for," she said.

She and her colleagues analyzed samples collected with nasopharyngeal swabs between March 23 and April 27 at drive-through testing sites in Chicago and from people who came to the hospital for any reason, including symptoms of Covid-19.

They looked at swabs taken from 145 people: 46 children younger than age 5; 51 children aged 5 to 17; and 48 adults aged 18 to 65. To forestall criticisms that really ill children would be expected to have a lot of the virus, the team excluded children who needed oxygen support. Most of the children in the study reported only a fever or cough, Dr. Heald-Sargent said.

To compare the groups fairly, the team included only children and adults who had mild to moderate symptoms and for whom they had information about when symptoms began. Dr. Heald-Sargent left out people who didn't have symptoms and who did not remember when they had started to feel ill, as well as those who had symptoms for more than a week before the testing.

The results confirmed Dr. Heald-Sargent's hunch: Older children and

adults had similar C.T.s, with a median of about 11 and ranging up to 17. But children younger than age 5 had significantly lower C.T.s of about 6.5. The upper limit of the range in these children was a C.T. of 12, however — still comparable to those of older children and adults.

“It definitely shows that kids do have levels of virus similar to and maybe even higher than adults,” Dr. Heald-Sargent said. “It wouldn’t be surprising if they were able to shed” the virus and spread it to others.

“One takeaway from this is that we can’t assume that just because kids aren’t getting sick, or very sick, that they don’t have the virus,” said one infectious disease expert. Tom Brenner/Reuters

The results are consistent with those from a German study of 47 infected children between the ages 1 and 11, which showed that children who did not have symptoms had viral loads as high as adults’, or higher. And a recent study from France found that asymptomatic children had C.T. values similar to those of children with symptoms.

C.T. values are a reasonable proxy for the amount of coronavirus present,

said Dr. Kindrachuk, who relied on this metric during the Ebola outbreaks in West Africa.

Still, he and others said that ideally researchers would grow infectious virus from samples, rather than test only for the virus's RNA.

"I suspect that it probably will translate into meaning that there is more actual virus there as well, but we can't say that without seeing the data," said Juliet Morrison, a virologist at the University of California, Riverside.

Some RNA viruses multiply quickly and are prone to genetic errors that render the virus incapable of infecting cells. Some RNA detected in children may represent these "defective" viruses: "We need to understand how much of that is actually infectious virus," Dr. Schultz-Cherry said.

(The researchers said they did not have access to the type of high-security lab required to grow infectious coronavirus, but other teams have cultivated virus from children's samples.)

The experts all emphasized that the findings at least indicate that children can be infected. Those who harbor a lot of virus may spread it to others in their households, or to teachers and other school staff members when

schools reopen.

Many school districts are planning to protect students and staff members by implementing physical distancing, cloth face coverings and hand hygiene. But it's unclear how well staff members and teachers can keep young children from getting too close to others, Dr. Kindrachuk said.

"Frankly, I just haven't seen a lot of discussion about how that aspect is going to be controlled," he said.

***[Like the Science Times page on Facebook.** | Sign up for the **Science Times newsletter.**]*

Observations from schools in several countries have suggested that, at least in places with mild outbreaks and preventive measures in place, children do not seem to spread the coronavirus to others efficiently.

Strong immune responses in children could limit both how much virus they can spread to others and for how long. The children's overall health, underlying conditions such as obesity or diabetes, and sex may also influence the ability to transmit the virus.

Some experts have suggested that children may transmit less virus because of their smaller lung capacity, height or other physical aspects.

Dr. Morrison dismissed those suggestions. The virus is shed from the upper respiratory tract, not the lungs, she noted.

"We are going to be reopening day care and elementary schools," she said. If these results hold up, "then yeah, I'd be worried."

Research Letter

July 30, 2020

Age-Related Differences in Nasopharyngeal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Levels in Patients With Mild to Moderate Coronavirus Disease 2019 (COVID-19)

Taylor Heald-Sargent, MD, PhD[1]; William J. Muller, MD, PhD[1,2]; Xiaotian Zheng, MD, PhD[1,2]; et al

Author Affiliations

JAMA Pediatr. Published online July 30, 2020. doi:10.1001/jamapediatrics.2020.3651

Children are susceptible to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) but generally present with mild symptoms compared with adults.[1] Children drive spread of respiratory and gastrointestinal illnesses in the population,[2] but data on children as sources of SARS-CoV-2 spread are sparse.

spread,[3] but school closures early in pandemic responses thwarted larger-scale investigations of schools as a source of community transmission. As public health systems look to reopen schools and day cares, understanding transmission potential in children will be important to guide public health measures. Here, we report that replication of SARS-CoV-2 in older children leads to similar levels of viral nucleic acid as adults, but significantly greater amounts of viral nucleic acid are detected in children younger than 5 years.

Methods

Between March 23 and April 27, 2020, we performed SARS-CoV-2 reverse transcriptase–polymerase chain reaction (PCR) on nasopharyngeal swabs collected at various inpatient, outpatient, emergency department, and drive-through testing sites at a pediatric tertiary medical center in Chicago, Illinois. The Ann & Robert H. Lurie Children's Hospital of Chicago Institutional Review Board provided an exemption and full waiver of HIPAA authorization and informed consent. A Clinical Laboratory Improvement Amendments–certified laboratory analyzed samples using a US Food and Drug Administration Emergency Use Authorization PCR assay (Abbot RealTime SARS-CoV-2 Assay performed on the m2000 RealTime System [Abbott Laboratories]). PCR amplification cycle threshold (CT) values were recorded, with lower values indicating higher amounts of viral nucleic acid.

This cohort included all individuals aged younger than 1 month to 65 years who tested positive for SARS-CoV-2. Patients with symptoms suggestive of a COVID-19–compatible illness and/or high-risk exposures were tested. We included the first sample tested for patients with multiple samples. Because patients with severe infection have lower CT values,[4] we excluded 7 children who required supplemental oxygen support. We also excluded 7 asymptomatic patients, 29 patients with unknown duration of symptoms, and 19 patients whose symptoms started more than 1 week prior to testing. Swabs were collected using a standard bilateral nasopharyngeal sampling procedure. Several controls, including samples with known copy numbers, were included in each PCR run. Median and interquartile ranges for each group were measured and compared using the nonparametric Wilcoxon rank sum test. Two-sided *P* values less than .05 were considered statistically significant. Analyses were performed using Stata/IC statistical software version 16.0 (StataCorp).

Results

Our final cohort included 145 patients with mild to moderate illness within 1 week of symptom onset. We compared 3 groups: young children younger than 5 years (n = 46), older children aged 5 to 17 years (n = 51), and adults aged 18 to 65 years (n = 48). We found similar median (interquartile range) CT values for older children (11.1 [6.3-15.7]) and adults (11.0 [6.9-17.5]). However, young children had significantly lower median (interquartile range) CT values (6.5 [4.8-12.0]), indicating that young children have equivalent or more viral nucleic acid in their upper respiratory tract compared with older children and adults (Figure). The observed differences in median CT values between young children and adults approximate a 10-fold to 100-fold greater amount of SARS-CoV-2 in the upper respiratory tract of young children. We performed a sensitivity analysis and observed a similar statistical difference between groups when including those with unknown symptom duration. Additionally, we identified only a very weak correlation between symptom duration and CT in the overall cohort (Spearman ρ = 0.22) and in each subgroup (young children, Spearman ρ = 0.20; older children, Spearman ρ = 0.19; and adults, Spearman ρ = 0.10).

Download

Figure. Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Reverse Transcriptase–Polymerase Chain Reaction (RT-PCR) Amplification Cycle Threshold (CT) Values From Nasopharyngeal Swabs Collected From Patients With Coronavirus Disease 2019

Children younger than 5 years had significantly lower CT values compared with children aged 5 to 17 years ($P = .02$) and adults 18 years and older ($P = .001$). CT values were similar between children aged 5 to 17 years and adults 18 years and older ($P = .34$). Midlines indicate the median, boxes indicate interquartile ranges, whiskers indicate the upper and lower adjacent values (within 1.5-fold the interquartile range), and isolated data points indicate outliers.

Discussion

Our analyses suggest children younger than 5 years with mild to moderate COVID-19 have high amounts of SARS-CoV-2 viral RNA in their nasopharynx compared with older children and adults. Our study is limited to detection of viral nucleic acid, rather than infectious virus, although SARS-CoV-2 pediatric studies reported a correlation between higher nucleic acid levels and the ability to culture infectious virus.[5] Thus, young children can potentially be important drivers of SARS-CoV-2 spread in the general population, as has been demonstrated with respiratory syncytial virus, where children with high viral loads are more likely to transmit.[6] Behavioral habits of young children and close quarters in school and day care settings raise concern for SARS-CoV-2 amplification in this population as public health restrictions are eased. In addition to public health implications, this population will be important for targeting immunization efforts as SARS-CoV-2 vaccines become available.

Article Information

Back to top

Accepted for Publication: May 31, 2020.

Corresponding Author: Taylor Heald-Sargent, MD, PhD, Division of Infectious Diseases, Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital, 225 E Chicago Ave, Box 20, Chicago, IL 60611 (thsargent@luriechildrens.org).

Published Online: July 30, 2020. doi:10.1001/jamapediatrics.2020.3651

Author Contributions: Drs Heald-Sargent and Kociolek had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Heald-Sargent, Muller, Kociolek.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Heald-Sargent, Muller, Kociolek.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Heald-Sargent, Kociolek.

Administrative, technical, or material support: All authors.

Study supervision: Muller, Patel, Kociolek.

Conflict of Interest Disclosures: Dr Muller has received grants from Ansun BioPharma, Astellas Pharma, AstraZeneca, Abbott Laboratories, Janssen Pharmaceuticals, Karius, Merck, Melinta Therapeutics, Roche, Tetraphase Pharmaceuticals, and Seqirus. Dr Patel has received grants from Aqua Pharmaceuticals. Dr Kociolek has received grants from Merck. No other disclosures were reported.

Funding/Support: Drs Heald-Sargent and Kociolek were supported by grants T32AI095207 and K23AI123525, respectively, from the National Institute of Allergy and Infectious Diseases.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

References

1. Lu X, Zhang L, Du H, et al; Chinese Pediatric Novel Coronavirus Study Team. SARS-CoV-2 infection in children. *N Engl J Med*. 2020;382(17):1663-1665. doi:10.1056/NEJMc2005073 PubMed | Google Scholar | Crossref
2. Paules C, Subbarao K. Influenza. *Lancet*. 2017;390(10095):697-708. doi:10.1016/S0140-6736(17)30129-0 PubMed | Google Scholar | Crossref
3. Cao Q, Chen YC, Chen CL, Chiu CH. SARS-CoV-2 infection in children: transmission dynamics and clinical characteristics. *J Formos Med Assoc*. 2020;119(3):670-673. doi:10.1016/j.jfma.2020.02.009 PubMed | Google Scholar | Crossref

4. Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. *Lancet Infect Dis*. 2020;20(6):656-657. doi:10.1016/S1473-3099(20)30232-2 PubMed | Google Scholar | Crossref

5. L'Huillier AG, Torriani G, Pigny F, Kaiser L, Eckerle I. Culture-competent SARS-CoV-2 in nasopharynx of symptomatic neonates, children, and adolescents. *Emerg Infect Dis*. 2020;26(10):26. PubMed | Google Scholar | Crossref

6. Moreira LP, Watanabe ASA, Camargo CN, Melchior TB, Granato C, Bellei N. Respiratory syncytial virus evaluation among asymptomatic and symptomatic subjects in a university hospital in Sao Paulo, Brazil, in the period of 2009-2013. *Influenza Other Respir Viruses*. 2018;12(3):326-330. doi:10.1111/irv.12518 PubMed | Google Scholar | Crossref

Comment

7 Comments for this article

EXPAND ALL

July 31, 2020

Age/CT relationship between 5-17 y.o.

S Eraly, MD, PhD |

Thank you and your group for your important contribution to our understanding of Covid-19 epidemiology! Recognizing that the analysis might be limited by the relatively small sample size, can you comment on the relationship between age and PCR amplification cycle threshold (CT) within the age range 5 to 17 y.o.?

It does not seem that the Age/CT relationship could be monotonic in this range, since one would in that case expect the median CT to be intermediate between those of younger children and adults. Is the lesser CT that would be expected for those at ...

READ MORE

July 31, 2020

How Was the Adult Population Chosen?

Marc Hainaut, MD, PhD | CHU Saint-Pierre, Université Libre de Bruxelles, Brussels, Belgium

Thank you for this contribution to our understanding of SARS-CoV-2 infection in children. Such data are really important even if we know the transmission of a communicable disease in a group does not depend solely on the number of viruses present in the secretions (especially when counted by PCR).

I understand the format of a « Research Letter » does not allow to put many details but the analyzed population remains unclear to me.

In the methods section it is written "all individuals aged younger than 1 month to 65 years who tested positive for SARS-CoV-2" were included. ...

READ MORE

July 31, 2020

Author Reply: Age vs PCR Amplification Cycle Threshold (CT)

Larry Kociolek, MD | Ann & Robert H. Lurie Children's Hospital of Chicago

Thank you for the comments. The sample size did not permit a robust analysis of CT by age for each pediatric age group, but we did assess age vs CT in the 5-17 year age group, and there was no relationship. R2 of that plot was 0.002. We chose to dichotomize our pediatric groups based on ages of school attendance.

Similar to the pediatric groups, all of the adults tested had symptoms for fewer than 7 days and none had severe disease. While the adult population in our study may not be generalizable, that does not ...

READ MORE

July 31, 2020

Pediatric Incidence Rates

Jason Bhardwaj, BSE, MBA | None

If the general incidence rate of mild to moderate disease is lower in the younger pediatric age cohort, is it possible that an alternate conclusion from the research is that greater viral levels are required to achieve the same severity of symptoms in the younger age cohort?

CONFLICT OF INTEREST: None Reported

August 1, 2020

Concerns

Aimee Renaud |

This research letter underemphasizes the fact that this analysis relies on not just a small sample but also one primarily obtained from a hospital setting as well as from mild to moderate patients with no additional weighting for the incredibly small incidence of this population within the under-10 population. This study has been interpreted as young people are more likely to carry higher viral load and that in no way is the outcome of this dataset. Please include additional data to quantify the actual population or caveat the limitations of this analysis.

CONFLICT OF INTEREST: None Reported

August 2, 2020

Quantitative Assay?

Mark Vieyra | University of Pennsylvania

The Abbot RealTime SARS-CoV-2 Assay that used in this paper says in its package insert that it is "intended for the qualitative detection of nucleic acid from SARS-CoV-2". I understand that one would expect the CT values to be lower with higher viral loads but the assay is not really designed to draw quantitative conclusions. I get that this is potentially interesting preliminary data but shouldn't this be confirmed with an assay that is designed to quantify viral RNA before we draw the conclusion that "young children can potentially be important drivers of SARS-CoV-2 spread in the general population"?

CONFLICT OF INTEREST: None Reported

August 2, 2020

qPCR Not Performed State of the Art

C X, PhD |

Your data seem plausible, however the qPCR data are not performed how they should.

- The Abbott test is only validated for qualitative purposes. A quantitative validation with a standard curve should have been included. Furthermore, this is a multiplex, which makes quantitation even harder. Cycle quantification values (Cqs) from different targets do influence each other.
- Getting quantitative data from such early PCR amplification cycle thresholds (Cts) is hard. Did you validate your linear range with a standard curve? I mean, at a Cq = 5 f.e. it gets really hard to correctly subtract your baseline. ...

READ MORE

See More About

Infectious Diseases | Otolaryngology | Pathology and Laboratory Medicine | Pediatrics | Public Health | Coronavirus (COVID19)

Coronavirus Resource Center

Others Also Liked

Practices to Foster Physician Presence and Connection With Patients in the Clinical Encounter

President Obama on US Health Care Reform

The State of US Health, 1990-2016

US Burden of Cardiovascular Disease, 1990-2016

Waste in the US Health Care System: Estimated Costs and Potential for Savings

BLOGS

AMA Style Insider

Subscriptions & Renewals

Email Subscriptions

Update Your Address

Contact Us

Frequently Asked Questions

JAMA CAREER CENTER

Physician Job Listings