Evidence of Early Household Transmission of SARS-CoV-2 Involving a School-aged Child

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ABSTRACT

Introduction: Little is known about the role of school-aged children and household transmission at the start of the SARS-CoV-2 pandemic. To evaluate for SARS-CoV-2 in school-aged children and assess household transmission, we performed reverse transcription polymerase chain reaction on 670 archived specimens that were collected between September 1, 2019 and June 30, 2020 as part of a community-based study.

Case Presentation: A single SARS-CoV-2 case was detected in an 11-year-old girl on March 18, 2020, resulting in very low prevalence (0.15% [95% CI, 0.03–0.84]) in this population. This case was associated with SARS-CoV-2 detection in all other household members. Symptoms were reported as mild to moderate. Whole genome sequencing supported household transmission of near-identical viruses within the 19B clade.

Discussion: This case represents the earliest known household cluster of SARS-CoV2 in Wisconsin.

Conclusion: This case suggests that household transmission associated with school-aged children may have contributed to wide seeding across populations.

INTRODUCTION

The first laboratory detection of SARS-CoV-2 in Wisconsin was in a specimen collected on January 29, 2020, from a traveler returning to Madison (Dane County) from China.[1] By March 13, 2020, 334 adult and 2 pediatric cases had been reported to the Wisconsin Department of Health Services (Figure 1).

Although household transmission of SARS-CoV-2 was documented during April 2020 – September 2020 in Wisconsin,[2] early dynamics of SARS-CoV-2 transmission are unknown. We tested 670 archived specimens from school-aged children participating in a community-based influenza study (ORegon CHild Absenteeism due to Respiratory Disease Study [ORCHARDS], Oregon School District, Dane County), collected prior to and during the initial phase of the pandemic, to assess early transmission of SARS-CoV-2 in Wisconsin.

METHODS

ORCHARDS has enrolled students in kindergarten through12th grade for specimen and data collection at home since January 2015.[3] Parents of a child with an acute respiratory infection call the study telephone line to enroll; eligibility requires ≥2 symptoms (fever, cough, coryza, nasal congestion, sore throat) with onset ≤7 days. Families may participate in a transmission study requiring symptom recording and self-collected anterior nasal specimens on day 0 (day of study packet drop-off) and 7 days later (day 7). Families participating in ORCHARDS receive a $50 gift card. Self-collected specimens for ORCHARDS have high reliability.[4] This study was reviewed and approved by the University of Wisconsin Health Sciences Institutional Review Board.

All ORCHARDS specimens were assessed initially at the Wisconsin State Laboratory of Hygiene (WSLH) for influenza and other respiratory viruses via reverse transcription polymerase chain reaction (RT-PCR) multiplex testing,[5,6] but not SARS-

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CoV-2 due to limited testing and supply constraints at the time of collection. Aliquots of specimens were archived and frozen at –70°C at the WSLH. Archived specimens collected from students between September 1, 2019 and June 30, 2020 were tested for SARS-CoV-2 using RT-PCR,[7] with all testing completed on February 27, 2021. Whole genome sequencing was performed at the WSLH using the Illumina MiSeq platform.[8,9] Sequences were compared to 11 contemporaneous Wisconsin SARS-CoV-2 specimens.

RESULTS

One of 670 ORCHARDS specimens (0.15% [95% CI, 0.03–0.84]) was positive for SARS-CoV-2; this specimen was collected on March 18, 2020 (Table). Details of this child and the related household cluster are reported below.

Case Presentation – Child

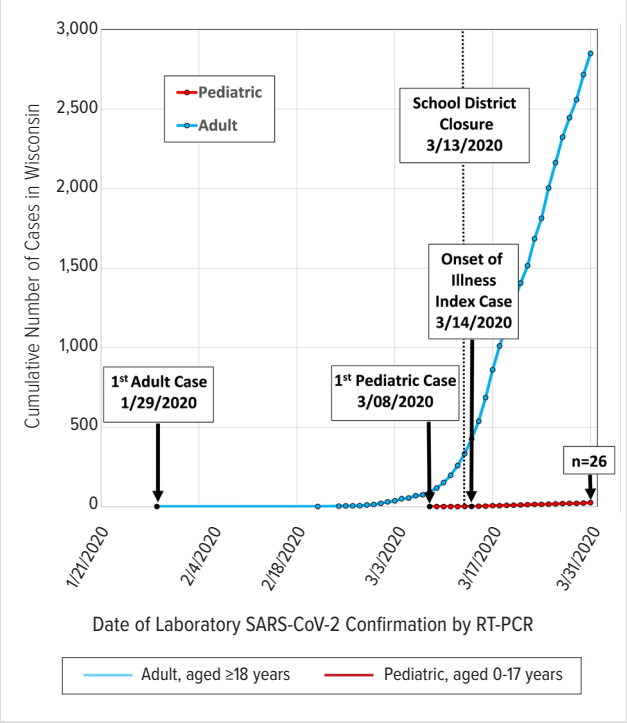
On March 17, 2020, the mother contacted ORCHARDS to report an influenza-like illness in her 11-year-old daughter. She was the only child in the household; the family reported no travel in the week prior to her illness onset on March 14, the day after the closure of her intermediate school (grades 5–6). Research staff provided a home study kit on March 18 (day 0). A moderate influenza-like illness with fever, cough, nasal discharge, fatigue, and headache was documented on day 0. By day 7 (March 25), her overall illness was rated as mild, with continuation of fever, cough, nasal discharge, fatigue, and nasal congestion. No medical visits occurred for this illness.

Case Presentation – Household Contacts

The 46-year-old mother reported onset of a moderate influenza-like illness on March 15 with symptoms of fever, chills, cough, fatigue, headache, and nasal congestion documented on day 0 (March 18). She did not seek medical care but missed 1 day of her work providing in-home daycare services. By day 7, her overall illness was rated as mild with continued cough, fatigue, headache, and nasal congestion. The 50-year-old father did not report any symptoms on day 0 (March 18). He then developed a mild illness with symptoms of fever, chills, nasal discharge, and muscle aches on March 23. He did not miss any time from his work outside the home and did not seek any medical care for this illness.

Following the modified ORCHARDS protocol, all household members self-collected anterior nasal specimens from both nostrils on days 0 and 7. The day 0 specimen from the ORCHARDS child was tested immediately after receipt and found to be negative for influenza and 14 additional respiratory viruses, not including SARS-CoV-2.[5,6] All other specimens were tested immediately for influenza and were negative. After detection of SARS-CoV-2 in the archived day 0 specimen of the ORCHARDS child, however, the remaining household speci-

Figure 1. Cumulative Number of Laboratory-Confirmed Adult and Pediatric SARS-CoV-2 Cases Reported to the Wisconsin Department of Health Services, January through March 2020



Dates of the first adult and pediatric cases, along with the day of symptom onset for the ORegon CHild Absenteeism due to Respiratory Disease Study (ORCHARDS) index case are shown. Cases confirmed by reverse transcription polymerase chain reaction (RT-PCR). The dotted line indicates timing of the Oregon School District closure. Case count data (2,850 cumulative adult cases and 26 pediatric cases by 3/31/2021) were provided by Wisconsin Department of Health Services.[1]

Table. Number of Specimens Collected and Specimens Positive for SARS-CoV-2 Per Study Period Between September 1, 2019, and June 30, 2020, From Students Participating in the ORegon CHild Absenteeism due to Respiratory Disease Study (ORCHARDS), Oregon School District, Dane County, Wisconsin

Specimen Collection Period	No. of Specimens Available	No. positive for SARS-CoV-2 (%)
September 2019	38	0 (0)
October 2019	38	0 (0)
November 2019	27	0 (0)
December 2019	63	0 (0)
January 2020	191	0 (0)
February 2020	237	0 (0)
Early-March 2020[a]	57	0 (0)
Late-March 2020[a]	18	1 (5.6)
April 2020	2	0 (0)
May 2020	2	0 (0)
June 2020	2	0 (0)
Total: September–June	**670**	**1 (0.15)**

[a]Early-March (until March 13, 2020) includes specimens collected following the standard ORCHARDS protocol and before school closure; late-March includes specimens collect after March 13, 2020 when Oregon School District schools were closed and the ORCHARDS protocol was modified.

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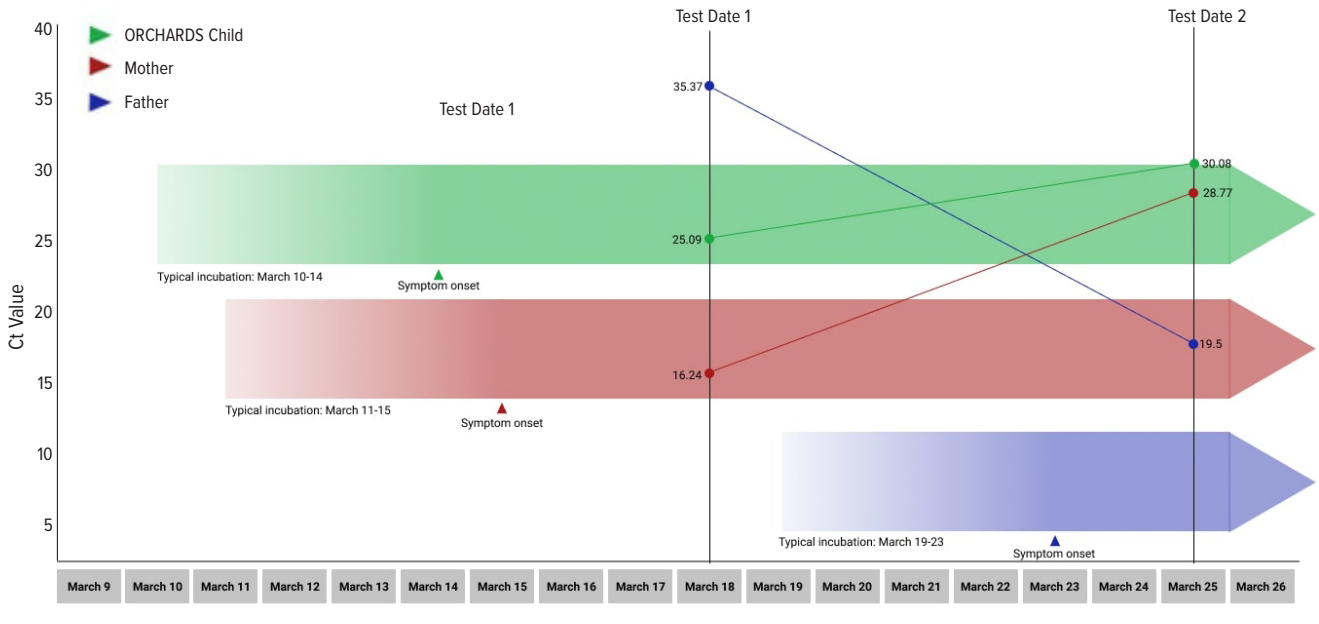
Figure 2. Time Course of SARS-CoV-2 Transmission Among Members of a Household in Wisconsin, March 2020



Abbreviation: ORCHARDS, ORegon CHild Absenteeism due to Respiratory Disease Study; Ct, cycle threshold.

Onset of symptoms for each household member is shown, along with the SARS-CoV-2 Ct values from reverse transcription polymerase chain reaction testing. Note that the manufacturer only provides instructions for interpreting Ct values as positive or negative for SARS-CoV-2 in a specimen. The hypothesized incubation period is provided for everyone.[10]

The GISAID accession numbers for these household members are EPI_ISL_803306, EPI_ISL_803327, EPI_ISL_803307, EPI_ISL_803638. The GISAID accession numbers of Wisconsin contemporaneous samples are 578531, 578455, 578445, 578454, 421325, 578380, 421328, 421329, 421324, 421331, and 417514.

mens (days 0 and 7) were then tested for SARS-CoV-2 at the WSLH using the TaqPath RT-PCR.

The days 0 and 7 specimens collected from each of the 3 household members were positive for SARS-CoV-2 (Figure 2). Specimens collected from the child and mother demonstrated increasing cycle threshold (Ct) values from day 0 to day 7, suggestive of decreasing viral loads.[10] The Ct value in RT-PCR is defined as the number of amplification cycles required for a signal to cross the threshold of detection. Specimens collected from the father demonstrated declining Ct values, suggestive of increasing viral load.

Whole genome sequencing performed by the WSLH on all specimens was not successful for 2 specimens (father day 0; child day 7) with Ct values > 30. Sequences for the remaining 4 specimens were aligned using Nextalign, visualized using Nextclade, and found to be near-identical (differing at 2 sites: nucleotide 942 in Spike and nucleotide 26.211 in ORF3a) and clustered with the 19B clade (Pango A.4 lineage).[11-13]

DISCUSSION

Low level of detection of SARS-CoV-2 in school-aged children is not surprising given the timeframe of specimen collection relative to low levels of this virus in Wisconsin,[1] eligibility criteria requiring acute respiratory infection, and closure of schools in the Oregon School District on March 13, 2020, and across the state no later than March 18, 2020. The sampling frame of ORCHARDS likely enhanced identification of uncommon events due to the longitudinal nature of this study, community recognition and trust, and the provision of an incentive for participation.

To our knowledge, this is the earliest detected household cluster of SARS-CoV2 in Wisconsin. Based upon onset, course of illness, and Ct values, the initial case was either the child or the mother. The child's exposures outside the home included public school classmates and friends. The mother's exposures outside of household members included the preschool children for whom she provided in-home care. The declining Ct values in the father likely represent within-home transmission from either his daughter or his wife.

Upon visual inspection of the Wisconsin-specific Nextstrain phylogentic tree (https://nextstrain.org/community/gagekmoreno/Wisconsin-SARS-CoV-2/ncov/wisconsin/2021-1-8), we found that 11 contemporaneous Wisconsin SARS-CoV-2 specimens were identical or near-identical to those of the family, consistent with limited local spread following a single introduction of a clade 19B virus. Given the known epidemiologic interactions among the family members, this cluster likely represents a single introduction followed by spread in the household. However, exposure through a shared outside source cannot be ruled out.

Furthermore, this cluster illustrates the potential role of unrec-

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ognized SARS-CoV-2 cases during the early pandemic in transmission outside of the home. The index child remained at home beginning March 14 because schools were closed in response to the pandemic. However, the mother, after taking a day off from work, resumed providing childcare to preschool children. The father—reporting only a mild illness despite a relatively low Ct value on day 7—continued to work outside of the home. We cannot determine whether there was onward spread from these individuals.

Finally, this cluster report underscores the importance of community-based surveillance programs and the banking of specimens for future evaluation. In this instance, a nationwide shortage of testing reagents precluded immediate testing. Had early results been available, they may have informed public health agencies on the frequency of mild COVID-19 infection and the high risk for household transmission. A handful of similar programs scatted across the state could provide real-time situation awareness of trends in respiratory pathogens.

CONCLUSIONS

In the early phases of the SARS-CoV-2 pandemic, unrecognized household transmission associated with school-aged children may have contributed to wide seeding across populations. Identification of this early household transmission cluster underscores the value of longitudinal, community-based, laboratory-supported surveillance that can be repurposed for public health response following emergence of a novel pathogen. Similar to the Seattle Flu Study,[14] we used specimens collected for a study of influenza and other respiratory viruses to examine early prevalence and transmission of SARS-CoV-2 in a low-risk population in Wisconsin. Hence, preestablished, community-based longitudinal research and surveillance platforms can act as a window on early transmission dynamics of newly emergent pathogens.

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