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Letter

A public health antibody screening indicates a marked increase of SARS-CoV-2 exposure rate in children during the second wave

Markus Hippich,^{1,2} Philipp Sifft,¹ Jose Zapardiel-Gonzalo,¹ Merle M. Böhmer,^{3,4} Vito Lampasona,⁵ Ezio Bonifacio,^{6,7,11,*} and Anette-Gabriele Ziegler^{1,2,8,9,10,11,*}

The frequency of SARS-CoV-2 infections in preschool and school children is an important parameter for decisions regarding kindergarten and school openings and procedures. Evidence indicates that children have lower susceptibility to SARS-CoV-2 infection than adults, but data in children from the general population are relatively few.¹ We introduced a highly specific dual antibody testing strategy to monitor childhood SARS-CoV-2 antibody frequency in Bavaria, Germany through the Fr1da study.^{2,3} We reported a frequency of 0.87% during the first wave, which was 6-fold higher exposure than reported by PCR virus detection. Children tested in a multicenter, cross-sectional setting in southwest Germany recently reported a similar frequency during the first wave,⁴ and a previous study in Spain reported a frequency of <3% in children aged 1–9 years during the first wave.⁵ We have continued monitoring in Bavaria and have now tested 26,903 children aged 1–10 years from January 2020 to February 2021, including 22,183 children aged 1–5 years and 4,720 aged 6–10 years. Of those 15,523 were tested between January and August 2020 (first wave) and 11,380 between September 2020 and February 2021 (second wave). Kindergartens and day care centers re-opened in July 2020 and most remained open throughout the year until early December. Schools closed in March, re-opened from June to July and then September to mid-

December with an alternation of face-to-face teaching and homeschooling relative to the SARS-CoV-2 regional incidence.

An increase in SARS-CoV-2 antibody frequency was observed in children during the second wave (446 of 11,380; 3.92%, 95% confidence interval [CI], 3.57%–4.29%) as compared with that observed during the first wave (106 of 15,523; 0.68%, 95% CI 0.56%–0.82%, $p < 0.001$). Antibody frequencies increased in pre-school children from October 2020 and in school children from November 2020 and continued to rise in both age groups through February 2021, reaching 5.6% (95% CI, 4.7%–6.7%) and 8.4% (95% CI, 6.4%–10.9%) in pre-school and school children, respectively (Figures S1A and S1B). Antibody frequencies in 2021 were around 8-fold higher than those observed at the end of the first wave and remained 3- to 4-fold higher than the cumulative reported virus positive PCR frequencies in both pre-school ($p < 0.001$) and school children ($p < 0.001$). The five regions that bordered Austria or the Czech Republic had higher antibody frequencies (4.4%) than the two regions without a border to other countries (2.5%, $p < 0.001$). Both border countries had reported a high prevalence of virus infections. Antibody-positive children who were followed longitudinally ($n = 66$; median follow-up: 93 days; IQR 74–115 days) had increased titers of SARS-CoV-2-RBD antibodies over time (median

at first sample, versus last sample, RBD: 564.1 versus 854.6 units, $p = 0.001$) and 64 of 66 remained antibody positive. It is not expected that the increase is due to re-exposure, but rather the natural time course of antibody responses. Among the 446 children who were screened positive in the second wave, 413 (92.6%) completed questionnaires regarding symptoms. No symptoms were reported in a higher proportion of antibody-positive pre-school children (196 of 288; 68.0%) than antibody-positive school children (64 of 125; 51.2%; $p = 0.001$; Figure S1C).

Finally, the screening in the Fr1da study is done in the context of screening for pre-symptomatic type 1 diabetes defined by multiple islet autoantibodies.⁶ We observed multiple islet

¹Institute of Diabetes Research, Helmholtz Zentrum München, German Research Center for Environmental Health, Munich-Neuherberg, Germany

²German Center for Diabetes Research (DZD), Munich, Germany

³Bavarian Health and Food Safety Authority, Oberschleissheim, Germany

⁴Institute of Social Medicine and Health Systems Research, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany

⁵Diabetes Research Institute, IRCCS San Raffaele Scientific Institute, via Olgettina 60, Milano 20132, Italy

⁶Technische Universität Dresden, Center for Regenerative Therapies Dresden, Dresden, Germany

⁷Paul Langerhans Institute Dresden of the Helmholtz Center Munich at University Hospital Carl Gustav Carus and Faculty of Medicine, TU Dresden, Germany

⁸Forschergruppe Diabetes, Technical University Munich, at Klinikum rechts der Isar, Munich, Germany

⁹Forschergruppe Diabetes e.V. at Helmholtz Zentrum München, German Research Center for Environmental Health, Munich-Neuherberg, Germany

¹⁰Lead Contact

¹¹These authors contributed equally

*Correspondence: ezio.bonifacio@tu-dresden.de (E.B.), anette-g.ziegler@helmholtz-muenchen.de (A.-G.Z.)

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autoantibodies in 34 of 17,538 (0.19%, CI 0.13%–0.27%) children screened in 2019, 48 of 17,036 (0.28%, CI 0.21%–0.37%) screened in the first wave, and 26 of 12,281 (0.21%, CI 0.14%–0.31%) screened in the second wave. No cases of pre-symptomatic type 1 diabetes identified in the first and one case in the second wave also had SARS-CoV-2 antibodies, and there was no association between SARS-CoV-2 antibody positivity and islet autoantibody positivity ($p = 0.47$).

General childhood population surveillance of SARS-CoV-2 antibodies has shown a marked increase of SARS-CoV-2 exposure during the second wave as compared with the first infection wave. This increase was likely caused by a combination of events, including a generally higher virus exposure during fall and winter, by school openings, and by the introduction of new, more infectious, virus variants. By February 2021, virus sequencing in a sample of positive cases in the region estimated the frequency of virus variants (in particular, B.1.1.7) to be 65% in pre-school-age and 70% in school-age children with positive PCR. Our findings clearly demonstrate that both pre-school and school children are susceptible to SARS-CoV-2 infection and that the cumulative frequency of infection in children is substantial and higher than that reported in virus PCR-based surveillance. Some of this discrepancy is likely to be due to asymptomatic cases in childhood. Adequate measures to contain spread of virus within kindergartens and schools is, therefore, likely

to be necessary for controlling infection in the community.

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/10.1016/j.medj.2021.03.019>.

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AUTHOR CONTRIBUTIONS

M.H. and P.S. measured SARS-CoV-2 antibodies. M.H. and J.Z.-G. performed statistical analysis. J.Z.-G. established the database. V.L. provided antigen for the tests. M.M.B. provided data on health authority reported virus-positive cases and incidence in Bavaria. E.B. oversaw all antibody measurements. A.-G.Z. and E.B. were responsible for study design and data analyses. E.B., and A.-G.Z. drafted the manuscript. M.H. was involved in the interpretation

of the results and preparation of the manuscript. All authors read and approved the final version of the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing of interests.

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