# Evidence Search Service Results of your search request

## COVID Antibody Testing in Children

**ID of request:** 26962  
**Date of request:** 8th January, 2021  
**Date of completion:** 13th January, 2021

If you would like to request any articles or any further help, please contact:  Su Keill at [Su.keill@uhd.nhs.uk](mailto:Su.keill@uhd.nhs.uk)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: COVID Antibody Testing in Children. Su Keill. (13th January, 2021). POOLE, UK: East Dorset Library and Knowledge Service.

**Sources searched**  
BMJ (1)  
EMBASE (11)  
GOV.UK (3)  
Google (3)  
MEDLINE (24)  
MedRxiv (9)  
NY Times (2)  
Oxford University (1)  
University of Cambridge (1)

**Date range used** (5 years, 10 years): 2020 -   
**Limits used** (gender, article/study type, etc.): English language   
**Search terms and notes** (full search strategy for database searches below):

517 abstracts were checked on MedRxiv for any pre-prints, any papers included will have PP before the title. These papers will not have been peer-reviewed yet.

I will colour the remaining papers according to:

* PIMS-TS
* Kawasaki Disease
* MIS-C
* Antibody testing in children
* Antibody testing comparisons
* Vaccine Information

For more information about the resources please go to: <https://dorsetnhs.libguides.com>.

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## A. National and International Guidance

#### Medicines and Healthcare Products Regulatory Agency (MHRA)

**Information for Healthcare Professionals on Pfizer/BioNTech COVID-19 vaccine** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8137b4e5d0e6e095a84a9bd15794b3a2)

This medicinal product has been given authorisation for temporary supply by the UK Department of Health and Social Care and the Medicines & Healthcare products Regulatory Agency. It does not have a marketing authorisation, but this temporary authorisation grants permission for the medicine to be used for active immunization to prevent COVID-19 disease caused by SARS-CoV-2 virus in individuals aged 16 years of age and over.

**Information for Healthcare Professionals on COVID-19 Vaccine AstraZeneca** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=718eb37ef061a3c0c22417fe5512ab0d)

This medicinal product has been given authorisation for temporary supply by the UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency. It does not have a marketing authorisation, but this temporary authorisation grants permission for the medicine to be used for active immunisation of individuals aged 18 years and older for the prevention of coronavirus disease 2019 (COVID-19).

**Information for Healthcare Professionals on COVID-19 Vaccine Moderna** (2021)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bfdfe2b2e5727bc5a73c6bf020ed827e)

This medicinal product has been given authorisation for temporary supply by the UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency. It does not have a marketing authorisation, but this temporary authorisation grants permission for the medicine to be used for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus in individuals 18 years of age and older.

## B. Systematic Reviews

#### MedRxiv

**PP Safety, Tolerability, and Immunogenicity of COVID-19 Vaccines: A Systematic Review and Meta-Analysis** (0000)

Ping Yuan, Pu Ai, Yihan Liu, Zisheng Ai et al

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d0233279a0a24c539b6ccf53e059962c)

We aimed to summarize reliable medical evidence by the meta-analysis of all published clinical trials that investigated the safety, tolerability, and immunogenicity of vaccine candidates against coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The PubMed, Cochrane Library, EMBASE, and medRxiv databases were used to select the studies. 7094 articles were identified initially and 43 were retrieved for more detailed evaluation. 5 randomized, double-blind, placebo-controlled trials were selected. A total of 1604 subjects with either vaccines or placebo infections were included in the meta-analysis within the scope of these articles. According to the results, there is an increase in total adverse events for subjects with either low (95% CI: 1.90-4.29) or high (CI: 2.65-5.63) dose vaccination. The adverse effects of COVID-19 vaccine are mainly local ones including pain, itching, and redness, and no significant difference was identified in the systemic reactions. All adverse effects were transient and resolved within a few days. Moreover, the neutralizing and IgG antibody levels post different dose vaccinations were all significantly increased at day 14/21 (P = 0.0004 and P = 0.0003, respectively) and day 28/35 (P < 0.00001) in vaccine groups compared to placebo controls. Besides, the levels of neutralizing and IgG antibodies were also elevated significantly at from day 14 to 35, versus day 0 (All P < 0.001). In conclusion, our analysis suggests that the current COVID-19 vaccine candidates are safe, tolerated, and immunogenic, which provides important information for further development, evaluation, and clinical application of COVID-19 vaccine.

## C. Institutional Publications

#### New York Times

**How the Pfizer-BioNTech Vaccine Works** (2020)

Jonathan Corum and Carl Zimmer

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=9db6c37693cd245d442860a989d16edb)

Can only view one NY TImes article free per day. The German company BioNTech partnered with Pfizer to develop and test a coronavirus vaccine known as BNT162b2, the generic name tozinameran or the brand name Comirnaty. A clinical trial demonstrated that the vaccine has an efficacy rate of 95 percent in preventing Covid-19.

**How the Oxford-AstraZeneca Vaccine Works** (2021)

Jonathan Corum and Carl Zimmer

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=00dfcafb549deabcd498bae15e887843)

Can only view one NY TImes article free per day. The University of Oxford partnered with the British-Swedish company AstraZeneca to develop and test a coronavirus vaccine known as ChAdOx1 nCoV-19 or AZD1222. A clinical trial revealed the vaccine was 62 to 90 percent effective, depending on the initial dosage. Despite some uncertainty over trial results, Britain authorized the vaccine for emergency use in December, and India authorized a version of the vaccine called Covishield on Jan. 3.

**How Moderna’s Vaccine Works** (2021)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=3e6f98c746a1328eb4169efd4a259a7f)

Can only view one NY TImes article free per day. Moderna, a Massachusetts-based vaccine developer, partnered with the National Institutes of Health to develop and test a coronavirus vaccine known as mRNA-1273. A clinical trial demonstrated that the vaccine has an efficacy rate of 94.1 percent in preventing Covid-19.

#### Vaccine Knowledge Project

**COVID-19 vaccines** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b226cb92c12752f09692067b36912781)

COVID-19 is a disease caused by a new type of coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This virus was first detected in Wuhan, China, in December 2019 and has led to a Pandemic, announced by the World Health Organization on 11thMarch 2020. This page provides the following information: Key facts about COVID-19 vaccines Pfizer BioNTech vaccine Oxford AstraZeneca vaccine Who should have the vaccines? Safety and side effects Vaccine ingredients Nucleic acid and viral vector vaccines explained

#### phg Foundation

**RNA vaccines: an introduction** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=5961d82c8a544cbb86f769b9f0700d33)

RNA based vaccines, which are relatively quick and inexpensive to make and may be safer to use could herald more rapid control over the spread of infectious diseases, including COVID-19. This policy briefing summarises the essentials.

## D. Original Research

1. **Distinct antibody responses to SARS-CoV-2 in children and adults across the COVID-19 clinical spectrum**  
   Weisberg S.P. Nature Immunology 2021;22(1):25-31.

Clinical manifestations of COVID-19 caused by the new coronavirus SARS-CoV-2 are associated with age<sup>1,2</sup>. Adults develop respiratory symptoms, which can progress to acute respiratory distress syndrome (ARDS) in the most severe form, while children are largely spared from respiratory illness but can develop a life-threatening multisystem inflammatory syndrome (MIS-C)<sup>3-5</sup>. Here, we show distinct antibody responses in children and adults after SARS-CoV-2 infection. Adult COVID-19 cohorts had anti-spike (S) IgG, IgM and IgA antibodies, as well as anti-nucleocapsid (N) IgG antibody, while children with and without MIS-C had reduced breadth of anti-SARS-CoV-2-specific antibodies, predominantly generating IgG antibodies specific for the S protein but not the N protein. Moreover, children with and without MIS-C had reduced neutralizing activity as compared to both adult COVID-19 cohorts, indicating a reduced protective serological response. These results suggest a distinct infection course and immune response in children independent of whether they develop MIS-C, with implications for developing age-targeted strategies for testing and protecting the population.<br/>Copyright &#xa9; 2020, The Author(s), under exclusive licence to Springer Nature America, Inc.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=41f22401c28d9d38e450bc090e72eb67)

1. **Age-Related Differences in Immunological Responses to SARS-CoV-2.**  
   Wong Lydia Su Yin The journal of allergy and clinical immunology. In practice 2020;8(10):3251-3258.

There is a striking age-related disparity in the prevalence and severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-induced coronavirus disease 2019 infections, which might be explained by age-dependent immunological mechanisms. These include age-related physiological differences in immunological responses, cross-neutralizing antibodies, and differences in levels and binding affinity of angiotensin-converting enzyme 2, the SARS-CoV-2 target receptor; antibody-dependent enhancement in adults manifesting with an overexuberant systemic inflammation in response to infection; and the increased likelihood of comorbidities in adults and the elderly. Emerging immunological phenomena such as Pediatric Multi-System Inflammatory Disorder Temporally associated with SARS-CoV-2 or Multisystem Inflammatory Syndrome in Children are now being observed, though the underlying mechanisms are still unclear. Understanding the mechanisms through which pediatric patients are protected from severe novel coronaviruses infections will provide critical clues to the pathophysiology of coronavirus disease 2019 infection and inform future therapeutic and prophylactic interventions. Asymptomatic carriage in children may have major public health implications, which will have an impact on social and health care policies on screening and isolation practices, school reopening, and safe distancing requirements in the community.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=a7c19e5304002b6587a13cab57b02ebd)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=60113ec0007ef23e0692a8f60d3641cf)

1. **All that glisters is not COVID: Low prevalence of seroconversion against SARS-CoV-2 in a pediatric cohort of patients with chilblain-like lesions.**  
   Denina Marco Journal of the American Academy of Dermatology 2020;83(6):1751-1753.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=253919bbf89eb24b13909a3368c0d00b)

1. **Antibody Responses after Classroom Exposure to Teacher with Coronavirus Disease, March 2020.**  
   Brown Nicole E. Emerging infectious diseases 2020;26(9):No page numbers.

After returning from Europe to the United States, on March 1, 2020, a symptomatic teacher received positive test results for severe acute respiratory syndrome coronavirus 2. Of the 21 students exposed to the teacher in the classroom, serologic results suggested past infection for 2. Classroom contact may result in virus transmission.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b2ddc7e7fdeb3a6b6ada30d3392f40f8)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e3f4a68aa6102acedf5171f07c25b448)

1. **Are SARS-CoV-2 IgA antibodies in paediatric patients with chilblain-like lesions indicative of COVID-19 asymptomatic or paucisymptomatic infection?**  
   Diociaiuti A. Journal of the European Academy of Dermatology and Venereology 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=56661025ef6270c1884513fca64811ce)

1. **Can data from paediatric cohorts solve the COVID-19 puzzle?**  
   Do L.A.H. PLoS Pathogens 2020;16(9):No page numbers.

COVID-19, caused by SARS-CoV-2, is significantly more severe in adults than in children. The biological reasons for this difference remain to be elucidated. We have compared the most recent virological and immunological data related to COVID-19 between adults and children and contrasted this with earlier data from severe acute respiratory syndrome (SARS) caused by the related SARS-CoV-1 in 2003. Based on these available data, a number of hypotheses are proposed to explain the difference in COVID-19 clinical outcomes between adults and children. NF-kB may be a key factor that could explain the severe clinical manifestations of COVID-19 in adults as well as rare complications associated with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in paediatric COVID-19 patients.<br/>Copyright: &#xa9; 2020 Do et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1a950d96a2929e63470451f207fe7456)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=51f35af04a7f56d3b3b4f0facf51852a)

1. **Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2.**  
   Whittaker Elizabeth JAMA 2020;324(3):259-269.

ImportanceIn communities with high rates of coronavirus disease 2019, reports have emerged of children with an unusual syndrome of fever and inflammation.ObjectivesTo describe the clinical and laboratory characteristics of hospitalized children who met criteria for the pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (PIMS-TS) and compare these characteristics with other pediatric inflammatory disorders.Design, Setting, and ParticipantsCase series of 58 children from 8 hospitals in England admitted between March 23 and May 16, 2020, with persistent fever and laboratory evidence of inflammation meeting published definitions for PIMS-TS. The final date of follow-up was May 22, 2020. Clinical and laboratory characteristics were abstracted by medical record review, and were compared with clinical characteristics of patients with Kawasaki disease (KD) (n = 1132), KD shock syndrome (n = 45), and toxic shock syndrome (n = 37) who had been admitted to hospitals in Europe and the US from 2002 to 2019.ExposuresSigns and symptoms and laboratory and imaging findings of children who met definitional criteria for PIMS-TS from the UK, the US, and World Health Organization.Main Outcomes and MeasuresClinical, laboratory, and imaging characteristics of children meeting definitional criteria for PIMS-TS, and comparison with the characteristics of other pediatric inflammatory disorders.ResultsFifty-eight children (median age, 9 years [interquartile range {IQR}, 5.7-14]; 20 girls [34%]) were identified who met the criteria for PIMS-TS. Results from SARS-CoV-2 polymerase chain reaction tests were positive in 15 of 58 patients (26%) and SARS-CoV-2 IgG test results were positive in 40 of 46 (87%). In total, 45 of 58 patients (78%) had evidence of current or prior SARS-CoV-2 infection. All children presented with fever and nonspecific symptoms, including vomiting (26/58 [45%]), abdominal pain (31/58 [53%]), and diarrhea (30/58 [52%]). Rash was present in 30 of 58 (52%), and conjunctival injection in 26 of 58 (45%) cases. Laboratory evaluation was consistent with marked inflammation, for example, C-reactive protein (229 mg/L [IQR, 156-338], assessed in 58 of 58) and ferritin (610 μg/L [IQR, 359-1280], assessed in 53 of 58). Of the 58 children, 29 developed shock (with biochemical evidence of myocardial dysfunction) and required inotropic support and fluid resuscitation (including 23/29 [79%] who received mechanical ventilation); 13 met the American Heart Association definition of KD, and 23 had fever and inflammation without features of shock or KD. Eight patients (14%) developed coronary artery dilatation or aneurysm. Comparison of PIMS-TS with KD and with KD shock syndrome showed differences in clinical and laboratory features, including older age (median age, 9 years [IQR, 5.7-14] vs 2.7 years [IQR, 1.4-4.7] and 3.8 years [IQR, 0.2-18], respectively), and greater elevation of inflammatory markers such as C-reactive protein (median, 229 mg/L [IQR 156-338] vs 67 mg/L [IQR, 40-150 mg/L] and 193 mg/L [IQR, 83-237], respectively).Conclusions and RelevanceIn this case series of hospitalized children who met criteria for PIMS-TS, there was a wide spectrum of presenting signs and symptoms and disease severity, ranging from fever and inflammation to myocardial injury, shock, and development of coronary artery aneurysms. The comparison with patients with KD and KD shock syndrome provides insights into this syndrome, and suggests this disorder differs from other pediatric inflammatory entities.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b6e142950dea285a84faaf8d359f0efd)

1. **Clinical features and antibody responseof two pediatric patients presenting with new-onset acutemyeloid leukemia and concomitant severe COVID-19**  
   Patel P.A. Clinical Cancer Research 2020;26(18):No page numbers.

Objective: SARS-CoV-2 infection has led to a worldwide pandemic of COVID-19 (coronavirus disease 2019), placing individuals with pre-existing medical conditions at a higher risk for morbidity and mortality. Limited data inpediatric patients with malignancies suggest that severe COVID-19 illness is rare. The objective of this study was todescribe our experience of two adolescents who presented with new diagnoses of acute myeloid leukemia (AML)and concurrent COVID-19. <br/>Method(s): The clinical presentation, treatment, and serology of two patients who presented with AML andconcurrent SARS-CoV-2 infection were abstracted. Residual blood was tested for serial quantitative IgG by ELISA tothe SARS-CoV-2 spike protein receptor binding domain, which has high sensitivity and specificity to SARS-CoV-2.The study was approved by Children's Healthcare of Atlanta and Emory University IRBs. <br/>Result(s): Patient 1 was a 16-year-old Caucasian male with previously treated classical Hodgkin's lymphoma whopresented with fever, cough, hyperleukocytosis, and pulmonary infiltrates and was diagnosed with therapy-relatedAML (TR-AML). SARS-CoV-2 was detected by nasopharyngeal (NP) RT-PCR testing on admission. He receivedremdesivir for treatment of COVID-19 and modified induction therapy with cytarabine alone starting on hospital day(HD) 3. He demonstrated high SARS-CoV-2 IgG titer (1:1327.3) on HD 4 and cleared SARS-CoV-2 with a negativeNP RT-PCR on HD 14. He went on to receive additional myelosuppressive AML therapy on HD 26 with azacitidineand gemtuzamab ozogamicin. On HD 34, his IgG titer remains elevated (1:5621.4) and he is currently awaitingcount recovery. Patient 2 was a 19-year-old Hispanic, previously healthy male who presented with fever, cough, dyspnea, and hyperleukocytosis and was diagnosed with de novo AML (D-AML). He also tested positive for SARS-CoV-2 via NP RT-PCR on admission. He began standard induction therapy with cytarabine, etoposide, anddaunorubicin on HD 2. He developed hypoxemic respiratory failure on HD 4 and received COVID-19 directedtherapies of convalescent plasma, remdesivir, and tocilizumab. His serologic testing showed low SARS-CoV-2 IgGtiter (1:619.3) on HD 4 despite administration of convalescent plasma. His titers waned over the subsequent twoweeks and he continued to test positive for SARS-CoV-2 via NP RT-PCR on HD 21. He remains critically ill inmultiorgan failure with signs of neutrophil recovery on HD 25. <br/>Conclusion(s): COVID-19 can be severe in children with AML and make treatment decisions challenging. Clinicalpresentation, curative modalities (hematopoietic stem cell transplantation for TR-AML versus potentiallychemotherapy alone for D-AML), and concurrent COVID-19 were considered in determining induction therapy. Whiledifficult to draw definite conclusions from two patients, the differential serologic response in these patients seems tocorrelate with the intensity of therapy they received and may have contributed to the overall severity of their COVID-19.

1. **Clinical manifestations and pathogen characteristics in children admitted for suspected COVID-19**  
   Cai X. Frontiers of medicine 2020;:No page numbers.

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has spread around the world. However, approaches to distinguish COVID-19 from pneumonia caused by other pathogens have not yet been reported. We retrospectively analyzed the clinical data of 97 children with probable COVID-19. A total of 13 (13.4%) patients were confirmed positive for SARS-CoV-2 infection by nucleic acid RT-PCR testing, and 41 (42.3%) patients were found to be infected with other pathogens. Notably, no pathogen was detected in 43 (44.3%) patients. Among all patients, 25 (25.8%) had familial cluster exposure history, and 52 (53.6%) had one or more coexisting conditions. Fifteen (15.5%) patients were admitted or transferred to the PICU. In the 11 confirmed COVID-19 cases, 5 (45.5%) and 7 (63.6%) were positive for IgM and IgG against SARS-CoV-2, respectively. In 22 patients with suspected COVID-19, 1 (4.5%) was positive for IgG but negative for IgM. The most frequently detected pathogen was Mycoplasma pneumonia (29, 29.9%). One patient with confirmed COVID-19 died. Our results strongly indicated that the detection of asymptomatic COVID-19 or coexisting conditions must be strengthened in pediatric patients. These cases may be difficult to diagnose as COVID-19 unless etiologic analysis is conducted. A serologic test can be a useful adjunctive diagnostic tool in cases where SARS-CoV-2 infection is highly suspected but the nucleic acid test is negative.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6fd3abf3ccbb6c2b80ea0058917d4c8d)

1. **Comparison of commercial lateral flow immunoassays and ELISA for SARS-CoV-2 antibody detection**  
   Serrano M.M. Journal of Clinical Virology 2020;129:No page numbers.

Background: COVID-19 pandemic has spread worldwide since December 2019. Serological tests for SARS-CoV-2 antibody testing are needed for detection of current or past infections. A wide range of commercial tests is available. However, most of them need to be validated. Study design: The aim was to compare a commercial IgG and IgA ELISA (Euroimmun) with three lateral flow immunoassays (LFI): Hangzhou Alltest Biotech, Wuhan UNscience Biotechnology and Guangzhou Wondfo Biotech. Specificity was calculated with 62 available serum samples from 2018/19. The study included 152 sera from patients of which 109 were RT-PCR positive. Sensitivities for ELISA anti SARS-CoV-2 IgG and IgA were 81.5 % and 93.1 % and specificities 100 % and 80.6 %, respectively. LFI showed variable performances, overall results being better for Guangzhou Wondfo Biotech. <br/>Conclusion(s): Commercial serological tests are useful for detection of antibodies in patients with COVID-19. ELISA presented better results than LFI. The results allowed to incorporate the most sensitive LFI to the daily workflow, combining with ELISA. Careful validation is encouraged before clinical laboratories start using these tests.<br/>Copyright &#xa9; 2020 Elsevier B.V.

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1. **Coronavirus Infections in Children Including COVID-19: An Overview of the Epidemiology, Clinical Features, Diagnosis, Treatment and Prevention Options in Children.**  
   Zimmermann Petra The Pediatric infectious disease journal 2020;39(5):355-368.

Coronaviruses (CoVs) are a large family of enveloped, single-stranded, zoonotic RNA viruses. Four CoVs commonly circulate among humans: HCoV2-229E, -HKU1, -NL63 and -OC43. However, CoVs can rapidly mutate and recombine leading to novel CoVs that can spread from animals to humans. The novel CoVs severe acute respiratory syndrome coronavirus (SARS-CoV) emerged in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012. The 2019 novel coronavirus (SARS-CoV-2) is currently causing a severe outbreak of disease (termed COVID-19) in China and multiple other countries, threatening to cause a global pandemic. In humans, CoVs mostly cause respiratory and gastrointestinal symptoms. Clinical manifestations range from a common cold to more severe disease such as bronchitis, pneumonia, severe acute respiratory distress syndrome, multi-organ failure and even death. SARS-CoV, MERS-CoV and SARS-CoV-2 seem to less commonly affect children and to cause fewer symptoms and less severe disease in this age group compared with adults, and are associated with much lower case-fatality rates. Preliminary evidence suggests children are just as likely as adults to become infected with SARS-CoV-2 but are less likely to be symptomatic or develop severe symptoms. However, the importance of children in transmitting the virus remains uncertain. Children more often have gastrointestinal symptoms compared with adults. Most children with SARS-CoV present with fever, but this is not the case for the other novel CoVs. Many children affected by MERS-CoV are asymptomatic. The majority of children infected by novel CoVs have a documented household contact, often showing symptoms before them. In contrast, adults more often have a nosocomial exposure. In this review, we summarize epidemiologic, clinical and diagnostic findings, as well as treatment and prevention options for common circulating and novel CoVs infections in humans with a focus on infections in children.

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1. **COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study.**  
   Götzinger Florian The Lancet. Child & adolescent health 2020;4(9):653-661.

BACKGROUNDTo date, few data on paediatric COVID-19 have been published, and most reports originate from China. This study aimed to capture key data on children and adolescents with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection across Europe to inform physicians and health-care service planning during the ongoing pandemic.METHODSThis multicentre cohort study involved 82 participating health-care institutions across 25 European countries, using a well established research network-the Paediatric Tuberculosis Network European Trials Group (ptbnet)-that mainly comprises paediatric infectious diseases specialists and paediatric pulmonologists. We included all individuals aged 18 years or younger with confirmed SARS-CoV-2 infection, detected at any anatomical site by RT-PCR, between April 1 and April 24, 2020, during the initial peak of the European COVID-19 pandemic. We explored factors associated with need for intensive care unit (ICU) admission and initiation of drug treatment for COVID-19 using univariable analysis, and applied multivariable logistic regression with backwards stepwise analysis to further explore those factors significantly associated with ICU admission.FINDINGS582 individuals with PCR-confirmed SARS-CoV-2 infection were included, with a median age of 5·0 years (IQR 0·5-12·0) and a sex ratio of 1·15 males per female. 145 (25%) had pre-existing medical conditions. 363 (62%) individuals were admitted to hospital. 48 (8%) individuals required ICU admission, 25 (4%) mechanical ventilation (median duration 7 days, IQR 2-11, range 1-34), 19 (3%) inotropic support, and one (<1%) extracorporeal membrane oxygenation. Significant risk factors for requiring ICU admission in multivariable analyses were being younger than 1 month (odds ratio 5·06, 95% CI 1·72-14·87; p=0·0035), male sex (2·12, 1·06-4·21; p=0·033), pre-existing medical conditions (3·27, 1·67-6·42; p=0·0015), and presence of lower respiratory tract infection signs or symptoms at presentation (10·46, 5·16-21·23; p<0·0001). The most frequently used drug with antiviral activity was hydroxychloroquine (40 [7%] patients), followed by remdesivir (17 [3%] patients), lopinavir-ritonavir (six [1%] patients), and oseltamivir (three [1%] patients). Immunomodulatory medication used included corticosteroids (22 [4%] patients), intravenous immunoglobulin (seven [1%] patients), tocilizumab (four [1%] patients), anakinra (three [1%] patients), and siltuximab (one [<1%] patient). Four children died (case-fatality rate 0·69%, 95% CI 0·20-1·82); at study end, the remaining 578 were alive and only 25 (4%) were still symptomatic or requiring respiratory support.INTERPRETATIONCOVID-19 is generally a mild disease in children, including infants. However, a small proportion develop severe disease requiring ICU admission and prolonged ventilation, although fatal outcome is overall rare. The data also reflect the current uncertainties regarding specific treatment options, highlighting that additional data on antiviral and immunomodulatory drugs are urgently needed.FUNDINGptbnet is supported by Deutsche Gesellschaft für Internationale Zusammenarbeit.

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1. **COVID-19 in children: Heterogeneity within the disease and hypothetical pathogenesis**  
   Suratannon N. Asian Pacific Journal of Allergy and Immunology 2020;38(3):170-177.

The disease course of coronavirus disease 2019 (COVID-19) is usually mild and self-limiting in previously healthy children, but they may also develop severe disease. Severe COVID-19 infection is especially observed in very young children or those with underlying comorbidities. Moreover, a multisystem inflammatory syndrome that mimics the Kawasaki disease shock syndrome can develop in children that are genetically predisposed to displaying an overactive immune response to SARS-CoV-2 infection. In this review, we describe the clinical phenotypes of mild and severe COVID-19 and multisystem inflammatory syndrome in children (MIS-C). We also discuss the possible immuno-biological mechanisms that may be involved in the protection of children against COVID-19 and the development of multisystem inflammatory syndrome.<br/>Copyright &#xa9; 2020, Allergy and Immunology Society of Thailand. All rights reserved.

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1. **Differences of SARS-CoV-2 serological test performance between hospitalized and outpatient COVID-19 cases.**  
   Wolf Johannes Clinica chimica acta; international journal of clinical chemistry 2020;511:352-359.

BACKGROUNDSerological severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody assays differ in the target antigen specificity, e.g. of antibodies directed against the viral spike or the nucleocapsid protein, and in the spectrum of detected immunoglobulins. The aim of the study was to evaluate the performance of two different routinely used immunoassays in hospitalized and outpatient COVID-19 cases.METHODSThe test characteristics of commercially available spike1 protein-based serological assays (Euroimmun, EI-assays), determining IgA or IgG and nucleocapsid-based assays (Virotech, VT-assays) determining IgA, IgM or IgG were compared in 139 controls and 116 hospitalized and outpatient COVID-19 cases.RESULTSHospitalized COVID-19 patients (n = 51; 115 samples) showed significantly higher concentrations of antibodies against SARS-CoV-2 and differed from outpatient cases (n = 65) by higher age, higher disease severity scores and earlier follow up blood sampling. Sensitivity of the two IgG assays was comparable in hospitalized patients tested ≥ 14 days (EI-assay: 88%, CI95% 67.6-99.9; VT-assay: 96%, CI95% 77.7-99.8). In outpatient COVID-19 cases sensitivity was significantly lower in the VT-assay (86.2%, CI95% 74.8-93.1) compared with the EI-assay (98.5%, CI95% 90.6-99.9). Assays for IgA and IgM demonstrated a lack of specificity or sensitivity.CONCLUSIONSOur results indicate that SARS-CoV-2 serological assays may need to be optimized to produce reliable results in outpatient COVID-19 cases who are low or even asymptomatic. Assays for IgA and IgM have limited diagnostic performance and do not prove an additional value for population-based screening approaches.

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1. **Distinct clinical and immunological features of SARS-CoV-2-induced multisystem inflammatory syndrome in children.**  
   Lee Pui Y. The Journal of clinical investigation 2020;130(11):5942-5950.

BACKGROUNDPediatric SARS-CoV-2 infection can be complicated by a dangerous hyperinflammatory condition termed multisystem inflammatory syndrome in children (MIS-C). The clinical and immunologic spectrum of MIS-C and its relationship to other inflammatory conditions of childhood have not been studied in detail.METHODSWe retrospectively studied confirmed cases of MIS-C at our institution from March to June 2020. The clinical characteristics, laboratory studies, and treatment response were collected. Data were compared with historic cohorts of Kawasaki disease (KD) and macrophage activation syndrome (MAS).RESULTSTwenty-eight patients fulfilled the case definition of MIS-C. Median age at presentation was 9 years (range: 1 month to 17 years); 50% of patients had preexisting conditions. All patients had laboratory confirmation of SARS-CoV-2 infection. Seventeen patients (61%) required intensive care, including 7 patients (25%) who required inotrope support. Seven patients (25%) met criteria for complete or incomplete KD, and coronary abnormalities were found in 6 cases. Lymphopenia, thrombocytopenia, and elevation in inflammatory markers, D-dimer, B-type natriuretic peptide, IL-6, and IL-10 levels were common but not ubiquitous. Cytopenias distinguished MIS-C from KD and the degree of hyperferritinemia and pattern of cytokine production differed between MIS-C and MAS. Immunomodulatory therapy given to patients with MIS-C included intravenous immune globulin (IVIG) (71%), corticosteroids (61%), and anakinra (18%). Clinical and laboratory improvement were observed in all cases, including 6 cases that did not require immunomodulatory therapy. No mortality was recorded in this cohort.CONCLUSIONMIS-C encompasses a broad phenotypic spectrum with clinical and laboratory features distinct from KD and MAS.FUNDINGThis work was supported by the National Institutes of Health, National Institute of Arthritis and Musculoskeletal and Skin Diseases; the National Institute of Allergy and Infectious Diseases; Rheumatology Research Foundation Investigator Awards and Medical Education Award; Boston Children's Hospital Faculty Career Development Awards; the McCance Family Foundation; and the Samara Jan Turkel Center.

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1. **Dynamic surveillance of SARS-CoV-2 shedding and neutralizing antibody in children with COVID-19.**  
   Liu Pengcheng Emerging microbes & infections 2020;9(1):1254-1258.

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in China and quickly spread globally. In this study, we investigated the characteristics of viral shedding from different sites and the neutralizing antibody (NAb) response during the acute and convalescent phases of nine children with COVID-19. SARS-CoV-2 was detected in their nasopharyngeal swabs (9/9, 100%), stool samples (8/9, 89%), and oropharyngeal swabs (3/9, 33%) but was not detected in their serum and urine samples. The median duration of viral shedding detected in nasopharyngeal swabs, oropharyngeal swabs, and stools was 13, 4, and 43 days respectively, and the maximum duration of viral shedding detected from stools was 46 days after discharge. In children, nasopharyngeal swabs appear to be a more sensitive specimen type for the diagnosis of COVID-19 compared with oropharyngeal swabs. Three of eight patients produced NAbs in the acute phase, and NAbs were detected in all eight patients with convalescent sera. The results of this study provide valuable information for the diagnosis and surveillance of COVID-19 and development of SARS-CoV-2 vaccines for use in children.

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1. **Evaluation of Abbott anti-SARS-CoV-2 CMIA IgG and Euroimmun ELISA IgG/IgA assays in a clinical lab**  
   Manalac J. Clinica Chimica Acta 2020;510:687-690.

Background: We report our findings of test performance especially specificity of a fully automated Abbott Architect anti-SARS-CoV-2 CMIA IgG and Euroimmun anti-SARS-CoV-2 ELISA IgA/IgG in human plasma. <br/>Method(s): We used positive cohort of 97 samples from Covid-19 patients or healthcare workers, collected at late time points from symptom onsets. We also included another cohort of 215 samples as negative controls, 78 of which had positive serology test results of other infectious diseases or autoimmunity. Assay specificity was assessed by using a total of 847 anonymized samples which were collected before the Covid-19 pandemic from local patient populations seeking clinical care for rheumatoid diseases, thyroid cancer, and therapeutic drug monitoring. <br/>Result(s): Abbott IgG, Euroimmun IgG/IgA had high precision, demonstrated by both intra- and inter-day CVs of &lt;2%. There was no Abbott or Euroimmun IgG assay cross reactivity in the 78 samples with positive serology of non-SARS-CoV-2 infectious diseases and positive autoimmune antibodies. The Abbott IgG has specificity of 99.6%, while Euroimmun IgG and IgA were as high as 91.5% and 71.5%, respectively. <br/>Conclusion(s): Our evaluation confirmed high specificity of the Abbott IgG assay, while it was lower for Euroimmun IgG. Euroimmun IgA has suboptimal specificity which may limit its clinical use. Assay sensitivity was high for both Abbott and Euroimmun IgG assays.<br/>Copyright &#xa9; 2020 Elsevier B.V.

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1. **False-positive SARS-CoV-2 serology in 3 children with Kawasaki disease.**  
   To Kelvin Kw Diagnostic microbiology and infectious disease 2020;98(3):115141.

BACKGROUNDKawasaki disease (KD) is an acute febrile and eruptive disease with systemic vasculitis predominantly affecting young East Asian children. Recent reports showed that children with KD-like disease from KD low prevalence regions had positive SARS-CoV-2 serology despite a negative SARS-CoV-2 polymerase chain reaction (PCR) in respiratory samples.OBJECTIVESTo describe 3 pediatric Kawasaki Disease patients with false positive SARS-CoV-2 serology.STUDY DESIGNWe retrospectively recruited children with KD diagnosed during the COVID-19 outbreak in Hong Kong. Clinical characteristics and laboratory test results including SARS-CoV-2 PCR results were retrieved. We performed a microparticle-based immunoassay for the detection of IgG against nucleoprotein (NP) and spike protein receptor binding domain (RBD), and a microneutralization assay for the detection of neutralizing antibodies.RESULTSThree Chinese children with typical KD were identified. They had no epidemiological links with COVID-19 patients and tested negative for SARS-CoV-2 NPA PCR. They were treated with IVIG and aspirin, and were discharged without complications. Subsequently 2 of them were tested positive against anti-RBD and anti-NP antibodies and 1 was tested positive against anti- RBD antibodies. However, microneutralization assay showed that neutralizing antibodies were absent, suggesting a false-positive IgG result.CONCLUSIONDetection of neutralizing antibodies is recommended to confirm previous SARS-CoV-2 infection in IgG-positive but PCR-negative patients.

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1. **Immune responses to SARS-CoV-2 in three children of parents with symptomatic COVID-19.**  
   Tosif Shidan Nature communications 2020;11(1):5703.

Compared to adults, children with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have predominantly mild or asymptomatic infections, but the underlying immunological differences remain unclear. Here, we describe clinical features, virology, longitudinal cellular, and cytokine immune profile, SARS-CoV-2-specific serology and salivary antibody responses in a family of two parents with PCR-confirmed symptomatic SARS-CoV-2 infection and their three children, who tested repeatedly SARS-CoV-2 PCR negative. Cellular immune profiles and cytokine responses of all children are similar to their parents at all timepoints. All family members have salivary anti-SARS-CoV-2 antibodies detected, predominantly IgA, that coincide with symptom resolution in 3 of 4 symptomatic members. Plasma from both parents and one child have IgG antibody against the S1 protein and virus-neutralizing activity detected. Using a systems serology approach, we demonstrate higher levels of SARS-CoV-2-specific antibody features of these family members compared to healthy controls. These data indicate that children can mount an immune response to SARS-CoV-2 without virological confirmation of infection, raising the possibility that immunity in children can prevent the establishment of SARS-CoV-2 infection. Relying on routine virological and serological testing may not identify exposed children, with implications for epidemiological and clinical studies across the life-span.

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1. **Immune responses to SARS-CoV-2 infection in hospitalized pediatric and adult patients.**  
   Pierce Carl A. Science translational medicine 2020;12(564):No page numbers.

Children and youth infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have milder disease than do adults, and even among those with the recently described multisystem inflammatory syndrome, mortality is rare. The reasons for the differences in clinical manifestations are unknown but suggest that age-dependent factors may modulate the antiviral immune response. We compared cytokine, humoral, and cellular immune responses in pediatric (children and youth, age <24 years) (n = 65) and adult (n = 60) patients with coronavirus disease 2019 (COVID-19) at a metropolitan hospital system in New York City. The pediatric patients had a shorter length of stay, decreased requirement for mechanical ventilation, and lower mortality compared to adults. The serum concentrations of interleukin-17A (IL-17A) and interferon-γ (IFN-γ), but not tumor necrosis factor-α (TNF-α) or IL-6, were inversely related to age. Adults mounted a more robust T cell response to the viral spike protein compared to pediatric patients as evidenced by increased expression of CD25+ on CD4+ T cells and the frequency of IFN-γ+ CD4+ T cells. Moreover, serum neutralizing antibody titers and antibody-dependent cellular phagocytosis were higher in adults compared to pediatric patients with COVID-19. The neutralizing antibody titer correlated positively with age and negatively with IL-17A and IFN-γ serum concentrations. There were no differences in anti-spike protein antibody titers to other human coronaviruses. Together, these findings demonstrate that the poor outcome in hospitalized adults with COVID-19 compared to children may not be attributable to a failure to generate adaptive immune responses.

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1. **Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study.**  
   Davies Patrick The Lancet. Child & adolescent health 2020;4(9):669-677.

BACKGROUNDIn April, 2020, clinicians in the UK observed a cluster of children with unexplained inflammation requiring admission to paediatric intensive care units (PICUs). We aimed to describe the clinical characteristics, course, management, and outcomes of patients admitted to PICUs with this condition, which is now known as paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).METHODSWe did a multicentre observational study of children (aged <18 years), admitted to PICUs in the UK between April 1 and May 10, 2020, fulfilling the case definition of PIMS-TS published by the Royal College of Paediatrics and Child Health. We analysed routinely collected, de-identified data, including demographic details, presenting clinical features, underlying comorbidities, laboratory markers, echocardiographic findings, interventions, treatments, and outcomes; serology information was collected if available. PICU admission rates of PIMS-TS were compared with historical trends of PICU admissions for four similar inflammatory conditions (Kawasaki disease, toxic shock syndrome, haemophagocytic lymphohistiocytosis, and macrophage activation syndrome).FINDINGS78 cases of PIMS-TS were reported by 21 of 23 PICUs in the UK. Historical data for similar inflammatory conditions showed a mean of one (95% CI 0·85-1·22) admission per week, compared to an average of 14 admissions per week for PIMS-TS and a peak of 32 admissions per week during the study period. The median age of patients was 11 years (IQR 8-14). Male patients (52 [67%] of 78) and those from ethnic minority backgrounds (61 [78%] of 78) were over-represented. Fever (78 [100%] patients), shock (68 [87%]), abdominal pain (48 [62%]), vomiting (49 [63%]), and diarrhoea (50 [64%]) were common presenting features. Longitudinal data over the first 4 days of admission showed a serial reduction in C-reactive protein (from a median of 264 mg/L on day 1 to 96 mg/L on day 4), D-dimer (4030 μg/L to 1659 μg/L), and ferritin (1042 μg/L to 757 μg/L), whereas the lymphocyte count increased to more than 1·0 × 109 cells per L by day 3 and troponin increased over the 4 days (from a median of 157 ng/mL to 358 ng/mL). 36 (46%) of 78 patients were invasively ventilated and 65 (83%) needed vasoactive infusions; 57 (73%) received steroids, 59 (76%) received intravenous immunoglobulin, and 17 (22%) received biologic therapies. 28 (36%) had evidence of coronary artery abnormalities (18 aneurysms and ten echogenicity). Three children needed extracorporeal membrane oxygenation, and two children died.INTERPRETATIONDuring the study period, the rate of PICU admissions for PIMS-TS was at least 11-fold higher than historical trends for similar inflammatory conditions. Clinical presentations and treatments varied. Coronary artery aneurysms appear to be an important complication. Although immediate survival is high, the long-term outcomes of children with PIMS-TS are unknown.FUNDINGNone.

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1. **Is SARSCoV-2 nasopharyngeal swab still a gold standard in children?**  
   Marino Silvia Medical hypotheses 2020;144:110041.

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1. **Kinetics of Viral Clearance and Antibody Production Across Age Groups in Children with Severe Acute Respiratory Syndrome Coronavirus 2 Infection.**  
   Bahar Burak The Journal of pediatrics 2020;227:31.

OBJECTIVESTo improve understanding of transition from viral infection to viral clearance, and antibody response in pediatric patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.STUDY DESIGNThis retrospective analysis of children tested for SARS-CoV-2 by reverse transcription (RT) polymerase chain reaction (PCR) and immunoglobulin G antibody at a quaternary-care, free-standing pediatric hospital between March 13, 2020, and June 21, 2020, included 6369 patients who underwent PCR testing and 215 patients who underwent antibody testing. During the initial study period, testing focused primarily on symptomatic children; the later study period included asymptomatic patients who underwent testing as preadmission or preprocedural screening. We report the proportion of positive and negative tests, time to viral clearance, and time to seropositivity.RESULTSThe rate of positivity varied over time due to viral circulation in the community and transition from targeted testing of symptomatic patients to more universal screening of hospitalized patients. Median duration of viral shedding (RT-PCR positivity) was 19.5 days and time from RT-PCR positivity to negativity was 25 days. Of note, patients aged 6 through 15 years demonstrated a longer time of RT-PCR positivity to negativity, compared with patients aged 16 through 22 years (median 32 vs 18 days, P = .015). Median time to seropositivity, by chemiluminescent testing, from RT-PCR positivity was 18 days, whereas median time to reach adequate levels of neutralizing antibodies (defined as comparable with 160 titer by plaque reduction neutralization testing) was 36 days.CONCLUSIONSThe majority of patients demonstrated a prolonged period of viral shedding after infection with SARS CoV-2. It is unknown whether this correlates with persistent infectivity. Only 17 of 33 patients demonstrated adequate neutralizing antibodies during the time frame of specimen collection. It remains unknown whether immunoglobulin G antibody against spike structured proteins correlates with immunity, and how long antibodies and potential protection persist.

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1. **Low performance of rapid antigen detection test as frontline testing for COVID-19 diagnosis.**  
   Scohy Anaïs Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 2020;129:104455.

BACKGROUNDEnsuring accurate diagnosis is essential to limit the spread of SARS-CoV-2 and for the clinical management of COVID-19. Although real-time reverse transcription polymerase chain reaction (RT- qPCR) is the current recommended laboratory method to diagnose SARS-CoV-2 acute infection, several factors such as requirement of special equipment and skilled staff limit the use of these time-consuming molecular techniques. Recently, several easy to perform rapid antigen detection tests were developed and recommended in some countries as the first line of diagnostic.OBJECTIVESThe aim of this study was to evaluate the performances of the Coris COVID-19 Ag Respi-Strip test, a rapid immunochromatographic test for the detection of SARS-CoV-2 antigen, in comparison to RT-qPCR.RESULTS148 nasopharyngeal swabs were tested. Amongst the 106 positive RT-qPCR samples, 32 were detected by the rapid antigen test, given an overall sensitivity of 30.2%. All the samples detected positive with the antigen rapid test were also positive with RT-qPCR.CONCLUSIONSHigher viral loads are associated with better antigen detection rates. Unfortunately, the overall poor sensitivity of the COVID-19 Ag Respi-Strip does not allow using it alone as the frontline testing for COVID-19 diagnosis.

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1. **Mapping Systemic Inflammation and Antibody Responses in Multisystem Inflammatory Syndrome in Children (MIS-C).**  
   Gruber Conor N. Cell 2020;183(4):982.

Initially, children were thought to be spared from disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, a month into the epidemic, a novel multisystem inflammatory syndrome in children (MIS-C) emerged. Herein, we report on the immune profiles of nine MIS-C cases. All MIS-C patients had evidence of prior SARS-CoV-2 exposure, mounting an antibody response with intact neutralization capability. Cytokine profiling identified elevated signatures of inflammation (IL-18 and IL-6), lymphocytic and myeloid chemotaxis and activation (CCL3, CCL4, and CDCP1), and mucosal immune dysregulation (IL-17A, CCL20, and CCL28). Immunophenotyping of peripheral blood revealed reductions of non-classical monocytes, and subsets of NK and T lymphocytes, suggesting extravasation to affected tissues. Finally, profiling the autoantigen reactivity of MIS-C plasma revealed both known disease-associated autoantibodies (anti-La) and novel candidates that recognize endothelial, gastrointestinal, and immune-cell antigens. All patients were treated with anti-IL-6R antibody and/or IVIG, which led to rapid disease resolution.

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1. **Paediatric Inflammatory Multisystem Syndrome: Temporally Associated with SARS-CoV-2 (PIMS-TS): Cardiac Features, Management and Short-Term Outcomes at a UK Tertiary Paediatric Hospital.**  
   Ramcharan Tristan Pediatric cardiology 2020;41(7):1391-1401.

Children were relatively spared during COVID-19 pandemic. However, the recently reported hyperinflammatory syndrome with overlapping features of Kawasaki disease and toxic shock syndrome-"Paediatric Inflammatory Multisystem Syndrome-temporally associated with SARS-CoV-2" (PIMS-TS) has caused concern. We describe cardiac findings and short-term outcomes in children with PIMS-TS at a tertiary children's hospital. Single-center observational study of children with PIMS-TS from 10th April to 9th May 2020. Data on ECG and echocardiogram were retrospectively analyzed along with demographics, clinical features and blood parameters. Fifteen children with median age of 8.8 (IQR 6.4-11.2) years were included, all were from African/Afro-Caribbean, South Asian, Mixed or other minority ethnic groups. All showed raised inflammatory/cardiac markers (CRP, ferritin, Troponin I, CK and pro-BNP). Transient valve regurgitation was present in 10 patients (67%). Left Ventricular ejection fraction was reduced in 12 (80%), fractional shortening in 8 (53%) with resolution in all but 2. Fourteen (93%) had coronary artery abnormalities, with normalization in 6. ECG abnormalities were present in 9 (60%) which normalized in 6 by discharge. Ten (67%) needed inotropes and/or vasopressors. None needed extracorporeal life support. Improvement in cardiac biochemical markers was closely followed by improvement in ECG/echocardiogram. All patients were discharged alive and twelve (80%) have been reviewed since. Our entire cohort with PIMS-TS had cardiac involvement and this degree of involvement is significantly more than other published series and emphasizes the need for specialist cardiac review. We believe that our multi-disciplinary team approach was crucial for the good short-term outcomes.

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1. **Pediatric Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): Clinical Presentation, Infectivity, and Immune Responses.**  
   Yonker Lael M. The Journal of pediatrics 2020;227:45.

OBJECTIVESAs schools plan for re-opening, understanding the potential role children play in the coronavirus infectious disease 2019 (COVID-19) pandemic and the factors that drive severe illness in children is critical.STUDY DESIGNChildren ages 0-22 years with suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection presenting to urgent care clinics or being hospitalized for confirmed/suspected SARS-CoV-2 infection or multisystem inflammatory syndrome in children (MIS-C) at Massachusetts General Hospital were offered enrollment in the Massachusetts General Hospital Pediatric COVID-19 Biorepository. Enrolled children provided nasopharyngeal, oropharyngeal, and/or blood specimens. SARS-CoV-2 viral load, ACE2 RNA levels, and serology for SARS-CoV-2 were quantified.RESULTSA total of 192 children (mean age, 10.2 ± 7.0 years) were enrolled. Forty-nine children (26%) were diagnosed with acute SARS-CoV-2 infection; an additional 18 children (9%) met the criteria for MIS-C. Only 25 children (51%) with acute SARS-CoV-2 infection presented with fever; symptoms of SARS-CoV-2 infection, if present, were nonspecific. Nasopharyngeal viral load was highest in children in the first 2 days of symptoms, significantly higher than hospitalized adults with severe disease (P = .002). Age did not impact viral load, but younger children had lower angiotensin-converting enzyme 2 expression (P = .004). Immunoglobulin M (IgM) and Immunoglobulin G (IgG) to the receptor binding domain of the SARS-CoV-2 spike protein were increased in severe MIS-C (P < .001), with dysregulated humoral responses observed.CONCLUSIONSThis study reveals that children may be a potential source of contagion in the SARS-CoV-2 pandemic despite having milder disease or a lack of symptoms; immune dysregulation is implicated in severe postinfectious MIS-C.

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1. **Performance of six SARS-CoV-2 immunoassays in comparison with microneutralisation.**  
   Jääskeläinen A. J Journal of clinical virology : the official publication of the Pan American Society for Clinical Virology 2020;129:104512.

There is an urgent need for reliable high-throughput serological assays for the management of the ongoing COVID-19 pandemic. Preferably, the performance of serological tests for a novel virus should be determined with clinical specimens against a gold standard, i.e. virus neutralisation. We compared the performance of six commercial immunoassays for the detection of SARS-COV-2 IgG, IgA and IgM antibodies, including four automated assays [Abbott SARS-COV-2 IgG (CE marked), Diasorin Liaison® SARS-COV-2 S1/S2 IgG (research use only, RUO), and Euroimmun SARS-COV-2 IgG and IgA (CE marked)], and two rapid lateral flow (immunocromatographic) tests [Acro Biotech 2019-nCoV IgG/IgM (CE marked) and Xiamen Biotime Biotechnology SARS-COV-2 IgG/IgM (CE marked)] with a microneutralisation test (MNT). Two specimen panels from serum samples sent to Helsinki University Hospital Laboratory (HUSLAB) were compiled: the patient panel (N=70) included sera from PCR confirmed COVID-19 patients, and the negative panel (N=81) included sera sent for screening of autoimmune diseases and respiratory virus antibodies in 2018 and 2019. The MNT was carried out for all COVID-19 samples (70 serum samples, 62 individuals) and for 53 samples from the negative panel. Forty-one out of 62 COVID-19 patients showed neutralising antibodies.The specificity and sensitivity values of the commercial tests against MNT, respectively, were as follows: 95.1 %/80.5 % (Abbott Architect SARS-CoV-2 IgG), 94.9 %/43.8 % (Diasorin Liaison SARS-CoV-2 IgG; RUO), 68.3 %/87.8 % (Euroimmun SARS-CoV-2 IgA), 86.6 %/70.7 % (Euroimmun SARS-CoV-2 IgG), 74.4 %/56.1 % (Acro 2019-nCoV IgG), 69.5 %/46.3 % (Acro 2019-nCoV IgM), 97.5 %/71.9 % (Xiamen Biotime SARS-CoV-2 IgG), and 88.8 %/81.3 % (Xiamen Biotime SARS-CoV-2 IgM). This study shows variable performance values. Laboratories should carefully consider their testing process, such as a two-tier approach, in order to optimize the overall performance of SARS- CoV-2 serodiagnostics.

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1. **Prevalence of IgG against SARS-CoV-2 and evaluation of a rapid MEDsan IgG test in children seeking medical care**  
   Posfay-Barbe K.M. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2020;:No page numbers.

In a sample of 208 children seeking medical care, seropositivity rate of anti-SARS-CoV-2 IgG antibodies was 8.7%, suggesting a similar infection rate to that observed in adults, but &gt;100-fold the incidence of RT-PCR-confirmed pediatric cases. Compared to the gold-standard combined ELISA+immunofluorescence, the MEDsan IgG rapid diagnostic test performed accurately.<br/>Copyright &#xa9; The Author(s) 2020. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.

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1. **Quantitative SARS-CoV-2 Serology in Children With Multisystem Inflammatory Syndrome (MIS-C).**  
   Rostad Christina A. Pediatrics 2020;146(6):No page numbers.

OBJECTIVESWe aimed to measure severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serological responses in children hospitalized with multisystem inflammatory syndrome in children (MIS-C) compared with those with coronavirus disease 2019 (COVID-19), those with Kawasaki disease (KD), and hospitalized pediatric controls.METHODSFrom March 17, 2020, to May 26, 2020, we prospectively identified hospitalized children with MIS-C (n = 10), symptomatic COVID-19 (n = 10), and KD (n = 5) and hospitalized controls (n = 4) at Children's Healthcare of Atlanta. With institutional review board approval, we obtained prospective and residual blood samples from these children and measured SARS-CoV-2 spike receptor-binding domain (RBD) immunoglobulin M and immunoglobulin G (IgG), full-length spike IgG, and nucleocapsid protein antibodies using quantitative enzyme-linked immunosorbent assays and SARS-CoV-2 neutralizing antibodies using live-virus focus-reduction neutralization assays. We statistically compared the log-transformed antibody titers among groups and performed linear regression analyses.RESULTSAll children with MIS-C had high titers of SARS-CoV-2 RBD IgG antibodies, which correlated with full-length spike IgG antibodies (R 2 = 0.956; P < .001), nucleocapsid protein antibodies (R 2 = 0.846; P < .001), and neutralizing antibodies (R 2 = 0.667; P < .001). Children with MIS-C had significantly higher SARS-CoV-2 RBD IgG antibody titers (geometric mean titer 6800; 95% confidence interval 3495-13 231) than children with COVID-19 (geometric mean titer 626; 95% confidence interval 251-1563; P < .001), children with KD (geometric mean titer 124; 95% confidence interval 91-170; P < .001), and hospitalized controls (geometric mean titer 85; P < .001). All children with MIS-C also had detectable RBD immunoglobulin M antibodies, indicating recent SARS-CoV-2 infection. RBD IgG titers correlated with the erythrocyte sedimentation rate (R 2 = 0.512; P < .046) and with hospital (R 2 = 0.548; P = .014) and ICU lengths of stay (R 2 = 0.590; P = .010).CONCLUSIONSQuantitative SARS-CoV-2 serology may have a role in establishing the diagnosis of MIS-C, distinguishing it from similar clinical entities, and stratifying risk for adverse outcomes.

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1. **Risk factors for redetectable positivity in recovered COVID-19 children**  
   Peng D. Pediatric Pulmonology 2020;55(12):3602-3609.

Objective: To identify the risk factors for redetectable positivity (RP), and to provide a basis for prevention and control of coronavirus disease-2019 (COVID-19) in children. <br/>Method(s): A retrospective study was performed on all pediatric patients diagnosed with COVID-19. RP was defined as the positive result of real-time reverse transcriptase polymerase chain reaction (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) after symptom resolution and discharge. Children were defined as being less than 18 years old. <br/>Result(s): Fourteen out of 38 (36.8%) pediatric patients exhibited RP. Compared with the non-RP group (n = 24), the RP group (n = 14) had more family cluster infections, relatively higher white blood cell (WBC) count and longer plasma prothrombin time (PT), while age and gender were insignificant. T lymphocyte subclassification was observed at five-time points: the first test after admission, 2 weeks, and 1, 2, and 3 months after discharge. The RP group had a higher percentage and count of CD8+ T lymphocytes and lower CD4+/CD8+ ratio at 2 weeks, while a lower percentage and count of CD4+ T lymphocytes and lower CD4+/CD8+ ratio at 2 months. The positive rate of nasopharyngeal swabs by RT-PCR was higher during the onset, while that of anal swabs was higher during the recovery of COVID-19. <br/>Conclusion(s): Family cluster infection, higher WBC count, and longer PT are the early risk factors for RP in recovered COVID-19 children. The dynamic changes in number and ratio of CD4+ and CD8+ T lymphocytes may be involved in prolonged SARS-CoV-2 clearance. Nasopharyngeal swabs sampling during the onset and anal swabs sampling during the recovery may improve the positivity rate of RT-PCR.<br/>Copyright &#xa9; 2020 Wiley Periodicals LLC

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1. **SARS-CoV-2 antibody responses in children with MIS-C and mild and severe COVID-19**  
   Anderson E.M. Journal of the Pediatric Infectious Diseases Society 2020;:No page numbers.

SARS-CoV-2 antibody responses in children remain poorly characterized. Here, we show that pediatric patients with multisystem inflammatory syndrome in children (MIS-C) possess higher SARS-CoV-2 spike IgG titers compared to those with severe coronavirus disease 2019 (COVID-19), likely reflecting a longer time since onset of infection in MIS-C patients.<br/>Copyright &#xa9; The Author(s) 2020. Published by Oxford University Press on behalf of The Journal of the Pediatric Infectious Diseases Society. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

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1. **SARS-CoV-2 infections in children and young people.**  
   Felsenstein Susanna Clinical immunology (Orlando, Fla.) 2020;220:108588.

Though recent reports link SARS-CoV-2 infections with hyper-inflammatory states in children, most children experience no/mild symptoms, and hospitalization and mortality rates are low in the age group. As symptoms are usually mild and seroconversion occurs at low frequencies, it remains unclear whether children significantly contribute to community transmission. Several hypotheses try to explain age-related differences in disease presentation and severity. Possible reasons for milder presentations in children as compared to adults include frequent contact to seasonal coronaviruses, presence of cross-reactive antibodies, and/or co-clearance with other viruses. Increased expression of ACE2 in young people may facilitate virus infection, while limiting inflammation and reducing the risk of severe disease. Further potential factors include recent vaccinations and a more diverse memory T cell repertoire. This manuscript reviews age-related host factors that may protect children from COVID-19 and complications associated, and addresses the confusion around seropositivity and immunity.

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1. **SARS-CoV-2 infections with emphasis on pediatric patients: a narrative review.**  
   Yamamoto Lidia Revista do Instituto de Medicina Tropical de Sao Paulo 2020;62:e65.

This narrative review summarizes the main aspects underlying the new coronavirus SARS-CoV-2, its epidemiology, pathophysiology, pointing to differences of SARS-CoV-2 main receptors ACE2, in terms of expression and the amount of soluble ACE2 in the circulation of children, men and women, and also in those with risk factors such as the smokers and pregnant women or presenting with comorbidities (diabetes, obesity, hypertension and other cardiovascular diseases, renal and CNS pre-existing diseases). Clinical manifestations in adults and children were also described, emphasizing the particularities already seen in children, regarding signs, symptoms, viral excretion time and the involvement of all organs and systems. The COVID-19 in the pediatric population was divided into two sections: one dedicated to previously healthy children and adolescents with COVID-19, and the other to those who live with comorbidities and acquired COVID-19. A few paragraphs were reserved to the recently described severe multisystemic inflammatory syndrome associated with COVID-19 (MIS-C) that shares certain characteristics with Kawasaki disease. Some studies on the infection in pregnant and postpartum women, as well as neonates were shown. This review has also covered the laboratory diagnosis of COVID-19, passing through the imaging diagnosis made by the chest tomography revealing ground glass patching opacities, and results of non-specific exams such as the total blood with lymphopenia, the coagulation tests with increased prothrombin times, as well as marked increments of the D-dimer, troponin and proinflammatory cytokines. In the section devoted to the specific laboratory diagnosis of COVID-19, the most used RT-PCR protocols were described and some studies on the serological diagnosis with IgA, IgM and IgG detection were detailed, including the use of rapid immunochromatographic assays and discussing the ideal period after the onset of symptoms to perform each type of test. In the end, the management of pediatric patients with COVID-19 based mainly on supportive measures has been briefly commented.

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1. **Seroprevalence and immunity of SARS-CoV-2 infection in children and adolescents in schools in Switzerland: design for a longitudinal, school-based prospective cohort study**  
   Agne Ulyte International Journal of Public Health 2020;65:1549–1557.

Objectives This longitudinal cohort study aims to assess the extent and patterns of seroprevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in school-attending children, and their parents and school personnel. It will examine risk factors for infection, the relationship between seropositivity and symptoms, and temporal persistence of antibodies. Methods The study (Ciao Corona) will enroll a regionally representative, random sample of schools in the canton of Zurich, where 18% of the Swiss population live. Children aged 5–16 years, attending primary and secondary schools, and their parents and school personnel are invited. Venous blood and saliva samples are collected for serological testing in June/July 2020, in October/November 2020, and in March/April 2021. Bi-monthly questionnaires will cover SARS-CoV-2 symptoms and tests, health, preventive behavior, and lifestyle information. Hierarchical Bayesian logistic regression models will account for sensitivity and specificity of the serological tests in the analyses and complex sampling structure, i.e., clustering within classes and schools. Results and conclusions This unique school-based study will allow describing temporal trends of immunity, evaluate effects of preventive measures and will inform goal-oriented policy decisions during subsequent outbreaks.

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1. **Seroprevalence of SARS-CoV-2 antibodies in children: a prospective multicentre cohort study**   
   Waterfield T. Archives of Disease in Childhood 2020;:-.

Background Studies based on molecular testing of oral/nasal swabs underestimate SARS-CoV-2 infection due to issues with test sensitivity, test timing and selection bias. The objective of this study was to report the presence of SARS-CoV-2 antibodies, consistent with previous infection. Design This multicentre observational cohort study, conducted between 16 April to 3 July 2020 at 5 UK sites, recruited children of healthcare workers, aged 2–15 years. Participants provided blood samples for SARS-CoV-2 antibody testing and data were gathered regarding unwell contacts and symptoms. Results 1007 participants were enrolled, and 992 were included in the final analysis. The median age of participants was 10·1 years. There were 68 (6.9%) participants with positive SARS-CoV-2 antibody tests indicative of previous SARS-CoV-2 infection. Of these, 34/68 (50%) reported no symptoms prior to testing. The presence of antibodies and the mean antibody titre was not influenced by age. Following multivariable analysis four independent variables were identified as significantly associated with SARS-CoV-2 seropositivity: known infected household contact OR=10.9 (95% CI 6.1 to 19.6); fatigue OR=16.8 (95% CI 5.5 to 51.9); gastrointestinal symptoms OR=6.6 (95% CI 3.0 to 13.8); and changes in sense of smell or taste OR=10.0 (95% CI 2.4 to 11.4). Discussion Children demonstrated similar antibody titres in response to SARS-CoV-2 irrespective of age. Fatigue, gastrointestinal symptoms and changes in sense of smell or taste were the symptoms most strongly associated with SARS-CoV-2 antibody positivity.

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1. **The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19.**  
   Consiglio Camila Rosat Cell 2020;183(4):968.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is typically very mild and often asymptomatic in children. A complication is the rare multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19, presenting 4-6 weeks after infection as high fever, organ dysfunction, and strongly elevated markers of inflammation. The pathogenesis is unclear but has overlapping features with Kawasaki disease suggestive of vasculitis and a likely autoimmune etiology. We apply systems-level analyses of blood immune cells, cytokines, and autoantibodies in healthy children, children with Kawasaki disease enrolled prior to COVID-19, children infected with SARS-CoV-2, and children presenting with MIS-C. We find that the inflammatory response in MIS-C differs from the cytokine storm of severe acute COVID-19, shares several features with Kawasaki disease, but also differs from this condition with respect to T cell subsets, interleukin (IL)-17A, and biomarkers associated with arterial damage. Finally, autoantibody profiling suggests multiple autoantibodies that could be involved in the pathogenesis of MIS-C.

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1. **Viral targets for vaccines against COVID-19**  
   Lianpan Dai & George F. Gao Nature Reviews Immunology 2020;:-.

Vaccines are urgently needed to control the coronavirus disease 2019 (COVID-19) pandemic and to help the return to pre-pandemic normalcy. A great many vaccine candidates are being developed, several of which have completed late-stage clinical trials and are reporting positive results. In this Progress article, we discuss which viral elements are used in COVID-19 vaccine candidates, why they might act as good targets for the immune system and the implications for protective immunity.

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1. **What can we expect from first-generation COVID-19 vaccines?**  
   Malik Peiris and Gabriel M. Leung Lancet 2020;396(10261):1467-1469.

A first generation of COVID-19 vaccines is expected to gain approval as soon as the end of 2020 or early 2021. A popular assumption is that these vaccines will provide population immunity that can reduce transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and lead to a resumption of pre-COVID-19 “normalcy”. Given an initial reproduction number of around 2·2,1 which has since been revised to as high as about 4, and taking into account overdispersion of infections,2 perhaps about 25–50% of the population would have to be immune to the virus to achieve suppression of community transmission.

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1. **PP Antibody responses to SARS-CoV2 are distinct in children with MIS-C compared to adults with COVID-19**  
   Stuart P. Weisberg et al MedRxiv 0000;:-.

Clinical manifestations of COVID-19 caused by the novel coronavirus SARS-CoV-2 are associated with age. While children are largely spared from severe respiratory disease, they can present with a SARS-CoV-2-associated multisystem inflammatory syndrome (MIS-C) similar to Kawasaki's disease. Here, we show distinct antibody (Ab) responses in children with MIS-C compared to adults with severe COVID-19 causing acute respiratory distress syndrome (ARDS), and those who recovered from mild disease. There was a reduced breadth and specificity of anti-SARS-CoV-2-specific antibodies in MIS-C patients compared to the COVID patient groups; MIS-C predominantly generated IgG Abs specific for the Spike (S) protein but not for the nucleocapsid (N) protein, while both COVID-19 cohorts had anti-S IgG, IgM and IgA Abs, as well as anti-N IgG Abs. Moreover, MIS-C patients had reduced neutralizing activity compared to COVID-19 cohorts, indicating a reduced protective serological response. These results suggest a distinct infection course and immune response in children and adults who develop severe disease, with implications for optimizing treatments based on symptom and age.

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1. **PP Assessment of spread of SARS-CoV-2 by RT-PCR and concomitant serology in children in a region heavily affected by COVID-19 pandemic**  
   Robert Cohen MedRxiv 0000;:-.

Background. Several studies indicated that children seem to be less frequently infected with SARS-CoV-2 and potentially less contagious. To examine the spread of SARS-CoV-2 we combined both RT-PCR testing and serology in children in the most affected region in France, during the COVID-19 epidemic. Methods. From April 14, 2020 to May 12, 2020, we conducted a cross-sectional prospective, multicenter study. Healthy controls and pauci-symptomatic children from birth to age 15 years were enrolled by 27 ambulatory pediatricians. A nasopharyngeal swab was taken for detection of SARS-CoV-2 by RT-PCR and a microsample of blood for micro-method serology. Results. Among the 605 children, 322 (53.2%) were asymptomatic and 283 (46.8%) symptomatic. RT-PCR testing and serology were positive for 11 (1.8%) and 65 (10.7%) of all children, respectively. Only 3 children were RT-PCR-positive without any antibody response have been detected. The frequency of positivity on RT-PCR for SARS-CoV-2 was significantly higher in children with positive serology than those with a negative one (12.3% vs 0.6%, p<0.001). Contact with a person with proven COVID-19 increased the odds of positivity on RT-PCR (OR 7.8, 95% confidence interval [1.5; 40.7]) and serology (15.1 [6.6; 34.6]). Conclusion. In area heavily affected by COVID-19, after the peak of the first epidemic wave and during the lockdown, the rate of children with positive SARS-CoV-2 RT-PCR was very low (1.8%), but the rate of positive on serology was higher (10.7%). Most of PCR positive children had at the same time, positive serology suggesting a low risk of transmission.

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1. **PP Breath biomarkers of pediatric SARS-CoV-2 infection: a pilot study**  
   Amalia Z. MedRxiv 0000;:-.

COVID-19 control efforts have been hampered by transmission from pre-symptomatic individuals infected with SARS-CoV2. Prolonged asymptomatic respiratory viral shedding in children has been described and may be another important reservoir for ongoing transmission. The primary diagnostic approach to identify SARS-CoV2 infection relies on qPCR of specific viral sequences from respiratory samples, which is expensive, uncomfortable, relatively slow, and susceptible to false-negative results. A rapid non-invasive method to detect mild or asymptomatic infection would have a major impact on public health campaigns to control COVID-19. We hypothesize that candidate biomarkers characterize the exhaled breath of children with SARS-CoV2 infection. To test this hypothesis, we enrolled SARS-CoV-2-infected and -uninfected children admitted to a major pediatric academic medical center and analyzed their breath volatile composition. Targeted volatiles analysis revealed that six volatile organic compounds increased significantly in SARS-CoV-2-infected children. Three aldehydes (octanal, nonanal, and heptanal) drew special attention as candidate biomarkers, because viral infections have previously been shown to induce aldehyde production. Together, these biomarkers demonstrated 100% sensitivity and 66.6% specificity. Our work provides a solid framework upon which to build a future “breathalyzer” test for SARS-CoV-2 infection in children.

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1. **PP Clustering and longitudinal change in SARS-CoV-2 seroprevalence in school-children: prospective cohort study of 55 schools in Switzerland**  
   Agne Ulyte MedRxiv 0000;:-.

Background and aims The facilitating role of schools in SARS-CoV-2 infection spread is still debated and the potential of school closures to mitigate transmission unclear. In autumn 2020, Switzerland experienced one of the highest second waves of the SARS-CoV-2 pandemic in Europe while keeping schools open, thus offering a high-exposure environment to study SARS-CoV-2 infections in schools. The aim of this study was to examine longitudinal change in SARS-CoV-2 seroprevalence in children and the evolution of clustering within classes and schools from June to November, 2020, in a prospective cohort study of school children in the canton of Zurich, Switzerland. Methods Children from randomly selected schools and classes, stratified by district, were invited to participate in serological testing of SARS-CoV-2 in June-July and October-November 2020. Parents of children filled questionnaires on sociodemographic and health-related questions. 55 schools and 275 classes within them were enrolled, with 2603 children participating in the first, and 2552 in the second testing (age range 6-16 years). We evaluated longitudinal changes of seroprevalence in districts and investigated clustering of seropositive cases within classes and schools. Results Overall SARS-CoV-2 seroprevalence was 2.4% (95% CrI 1.4%-3.6%) in summer and 4.5% (95% CrI 3.2%-6.0%) in not previously seropositive children in late autumn, leading to estimated 7.8% (95% CrI 6.2%-9.5%) of ever seropositive children, without significant differences among lower, middle and upper school levels. Among the 2223 children with serology tested twice, 28 (40%) of previously seropositive were negative, and 109 (5%) previously negative became seropositive. Seroprevalence was not different between school levels or sexes, but varied across districts (1.7% to 15.0%). Between June-July and October-November 2020, the ratio of diagnosed to newly seropositive children was 1 to 8. At least one newly seropositive child was detected in 47 of 55 schools and 90 of 275 classes. Among 130 classes with high participation rate, 0, 1-2 or ≥3 seropositive children were present in 73 (56%), 50 (38%) and 7 (5%) classes, respectively. Class level explained slightly more variation of individual serological results (standard deviation of random effects (SD) 0.97) than school level (SD 0.61) in the multilevel logistic regression models. Symptoms were reported for 22% of seronegative and 29% of newly seropositive children since summer. Conclusions Under a regimen of open schools with some preventive measures in place since August, clustering of seropositive cases occurred in very few classes and not across entire schools despite a clear increase in seropositive children during a period of high transmission of SARS-CoV-2.

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1. **PP Seroprevalence of anti-SARS-CoV-2 IgG antibodies in children with household exposition to adults with COVID-19: preliminary findings**  
   Danilo Buonsenson et al MedRxiv 0000;:-.

Whether children are easily susceptible to SARS-CoV-2 infection is still a debated question and a currently a hot topic, particularly in view of important decisions on school opening. For this reason, we decide to describe preliminary data showing the prevalence of anti-SARS-CoV-2 IgG in children with known household exposure to SARS-CoV-2. Interestingly, our report shows that household transmission of SARS-CoV-2 is high in both adults and children, with similar rates of SARS-CoV-2 IgG in all age groups, including the younger children. A total of 44 out of 80 household contacts (55%) of index patients had anti SARS-CoV-2 IgG. In particular, 16 (59,26%) adult partners had IgG antibodies compared with 28 (52,83%) of pediatric contacts (P > 0.05). Among the pediatric population, children ≥ 5 years of age had similar probability of having SARS-CoV-2 IgG (21/39, 53.8%) compared with those < 5 years (7/14, 50%) (P > 0.05). Adult partners and children also had a probability of having SARS-CoV-2 IgG. Interestingly, 35.7% of children and 33.3% of adults with SARS-CoV-2 IgG were previously diagnosed as COVID-19 cases. Since this evidence of high rate of IgG in children exposed to SARS-CoV-2 has public health implication, with this comment we highlight the need of establishing appropriate guidelines for school opening and other social activities related to childhood.

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1. **PP The SARS-CoV-2 antibody landscape is lower in magnitude for structural proteins, diversified for accessory proteins and stable long-term in children**  
   Asmaa Hachim et al MedRxiv 0000;:-.

Background Children are less clinically affected by SARS-CoV-2 infection than adults with the majority of cases being mild or asymptomatic and the differences in infection outcomes are poorly understood. The kinetics, magnitude and landscape of the antibody response may impact the clinical severity and serological diagnosis of COVID-19. Thus, a comprehensive investigation of the antibody landscape in children and adults is needed. Methods We tested 254 plasma from 122 children with symptomatic and asymptomatic SARS-CoV-2 infections in Hong Kong up to 206 days post symptom onset, including 146 longitudinal samples from 58 children. Adult COVID-19 patients and pre-pandemic controls were included for comparison. We assessed antibodies to a 14-wide panel of SARS-CoV-2 structural and accessory proteins by Luciferase Immunoprecipitation System (LIPS). Findings Children have lower levels of Spike and Nucleocapsid antibodies than adults, and their cumulative humoral response is more expanded to accessory proteins (NSP1 and Open Reading Frames (ORFs)). Sensitive serology using the three N, ORF3b, ORF8 antibodies can discriminate COVID-19 in children. Principal component analysis revealed distinct serological signatures in children and the highest contribution to variance were responses to non-structural proteins ORF3b, NSP1, ORF7a and ORF8. Longitudinal sampling revealed maintenance or increase of antibodies for at least 6 months, except for ORF7b antibodies which showed decline. It was interesting to note that children have higher antibody responses towards known IFN antagonists: ORF3b, ORF6 and ORF7a. The diversified SARS-CoV-2 antibody response in children may be an important factor in driving control of SARS-CoV-2 infection.

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1. **PP Variation in SARS-CoV-2 seroprevalence in school-children across districts, schools and classes**  
   Agne Ulyte MedRxiv 0000;:-.

Importance: Understanding transmission and impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in school children is critical to implement appropriate mitigation measures. Objective: To determine the variation in SARS-CoV-2 seroprevalence in school children across districts, schools, grades, and classes, and the relationship of SARS-CoV-2 seroprevalence with self-reported symptoms. Design: Cross-sectional analysis of baseline measurements of a longitudinal cohort study (Ciao Corona) from June-July 2020. Setting: 55 randomly selected schools and classes stratified by district in the canton of Zurich, Switzerland (1.5 million inhabitants). Participants: Children, aged 6-16 years old, attending grades 1-2, 4-5 and 7-8. Exposure: Exposure to circulating SARS-CoV-2 between February and June 2020 including public lock-down and school closure (March 16-May 10, 2020). Main Outcomes and Measures: Variation in seroprevalence of SARS-CoV-2 in children across 12 cantonal districts, schools, and grades using a Luminex-based antibody test with four targets for each of IgG, IgA and IgM. Clustering of cases within classes. Analysis of associations of seropositivity and symptoms. Comparison of seroprevalence with a randomly selected adult population, based on Luminex-based IgG and IgA antibody test of Corona Immunitas. Results: In total, 55 schools and 2585 children were recruited (1337 girls, median age 11, age range 6-16 years). Overall seroprevalence was 2.8 % (95% CI 1.6-4.1%), ranging from 1.0% to 4.5% across districts. Seroprevalence was 3.8% (1.9-6.1%) in grades 1-2, 2.5% (1.1-4.2%) in grades 4-5, and 1.5% (0.5-3.0%) in grades 7-8. At least one case was present in 36/55 tested schools and in 43/128 classes with ≥50% participation rate and ≥5 children tested. 73% of children reported COVID-19 compatible symptoms since January 2020, but none were reported more frequently in seropositive compared to seronegative children. Seroprevalence of children was very similar to seroprevalence of randomly selected adults in the same region in June-July 2020, measured with the same Corona Immunitas test, combining IgG and IgA (3.1%, 95% CI 1.4-5.4%, versus 3.3%, 95% CI 1.4-5.5%). Conclusions and Relevance: Seroprevalence was inversely related to age and revealed a dark figure of around 90 when compared to 0.03% confirmed PCR+ cases in children in the same area by end of June. We did not find clustering of SARS-CoV-2 seropositive cases in schools so far, but the follow-up of this school-based study will shed more light on transmission within and outside schools.

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