Children and COVID-19

Advisory Committee to the NIH Director

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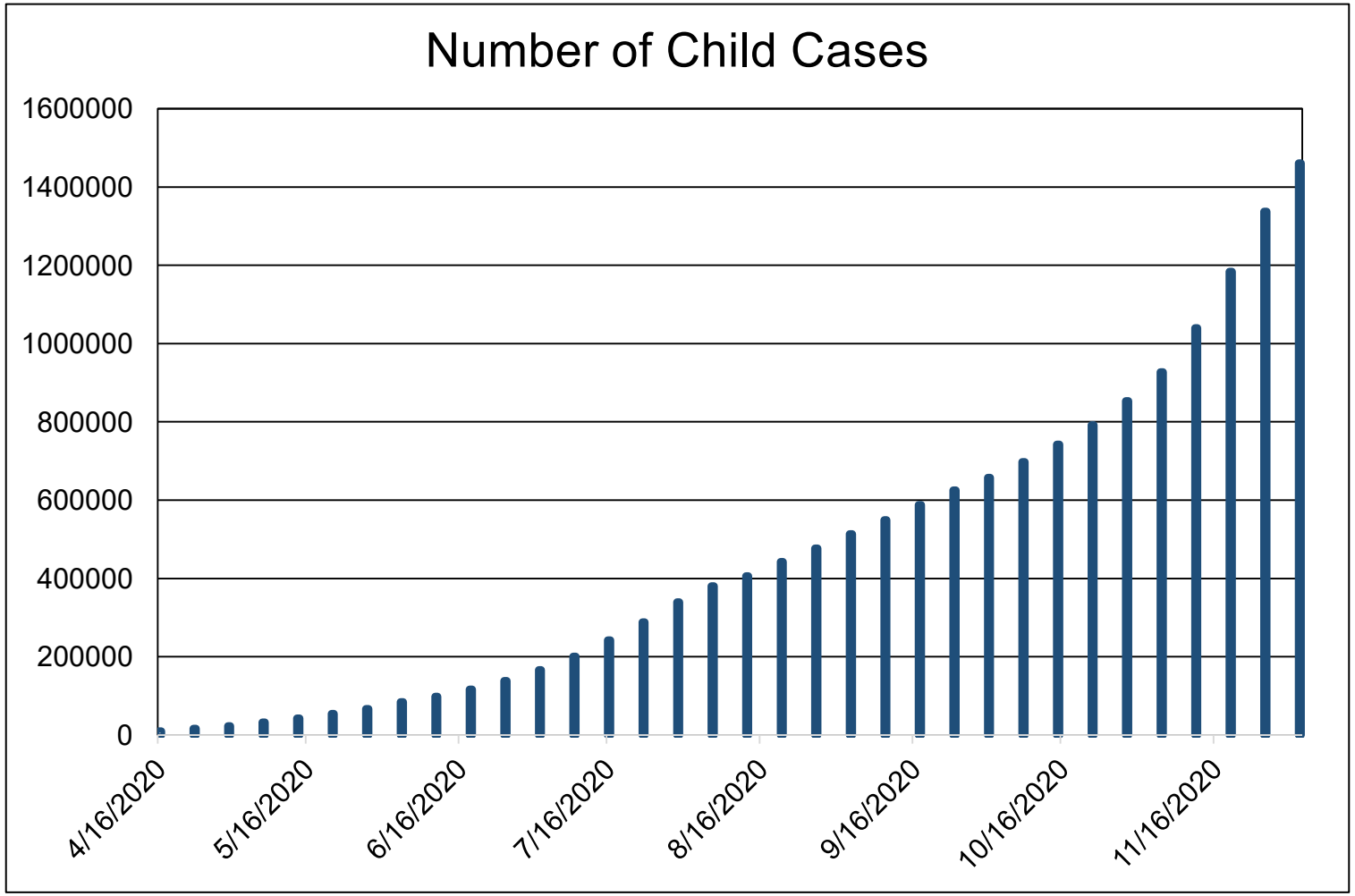
NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development


Children and
COVID-19

Cases of COVID-19 in Children are Increasing Rapidly

- Over past two weeks (11/26-12/3) there was a 23% increase in child COVID-19 cases
- More than 1.4 million children have been diagnosed with COVID-19
- Children represent 12% of all COVID-19 cases
- Data from AAP and CHA; 49 states, DC, NYC, PR, Guam



https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report

Talk Outline

- Children and COVID-19
- Multisystem Inflammatory Syndrome in Children (MIS-C)
- Long-Term Neurodevelopmental Effects
- Vaccines in Children
- Return to School
- Vertical Transmission
- Breast Milk and SARS-CoV-2 Transmission

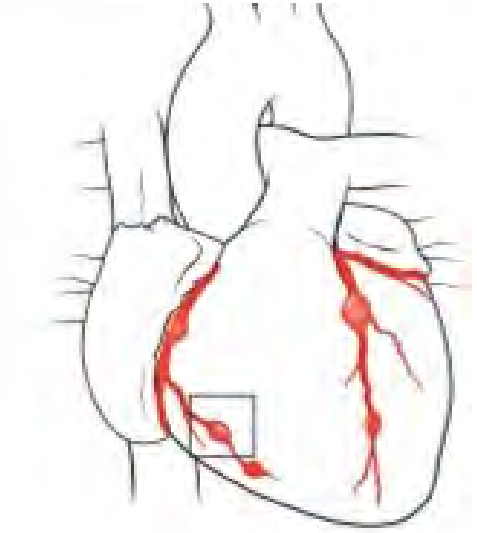
Research Goals for COVID-19 in Children

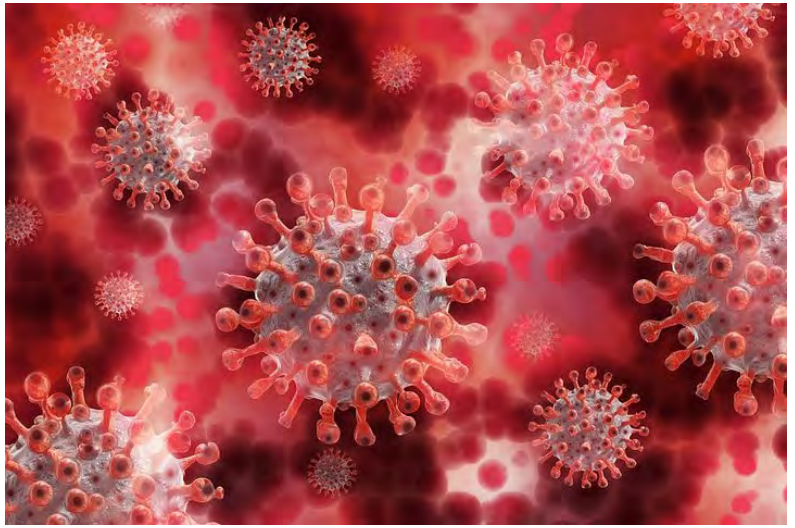
To Understand:

- **Range of clinical manifestations of SARS-CoV-2/COVID-19**
- **Etiology and clinical manifestations of MIS-C**
- **Variations in immune response underlying the wide range of clinical manifestations in children infected with SARS-CoV-2**
- **Determine the risk profiles for patients that develop**
  - **MIS-C**
  - **Severe post-acute sequelae of COVID-19**

Clinical Presentations of COVID-19 and MIS-C

- COVID-19 in children is typically mild and self limited, but they transmit the virus
- Around 1% of children who are positive for current or recent SARS-CoV-2 infection or COVID-19 exposure within prior 4 weeks develop MIS-C
- Symptoms of MIS-C:
  - Fever (≥38.0°C for ≥24 hours)
  - Laboratory evidence of inflammation
  - Clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
- Children become very ill quickly, requiring ICU admission, support of cardiovascular and respiratory systems and anti-inflammatory Rx, most recover after about a week

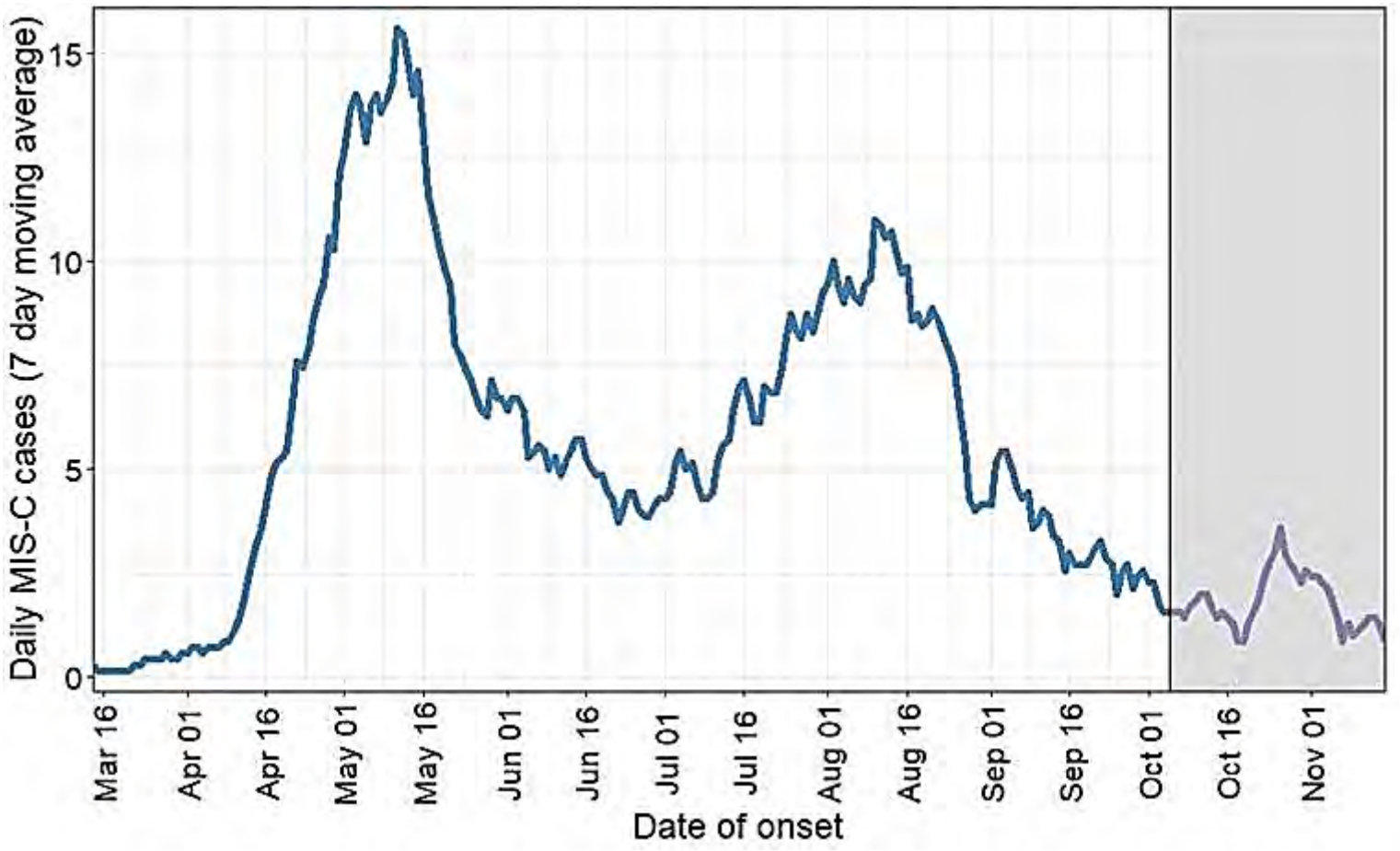




Multisystem Inflammatory Syndrome in Children (MIS-C)

As of December 4, 2020:

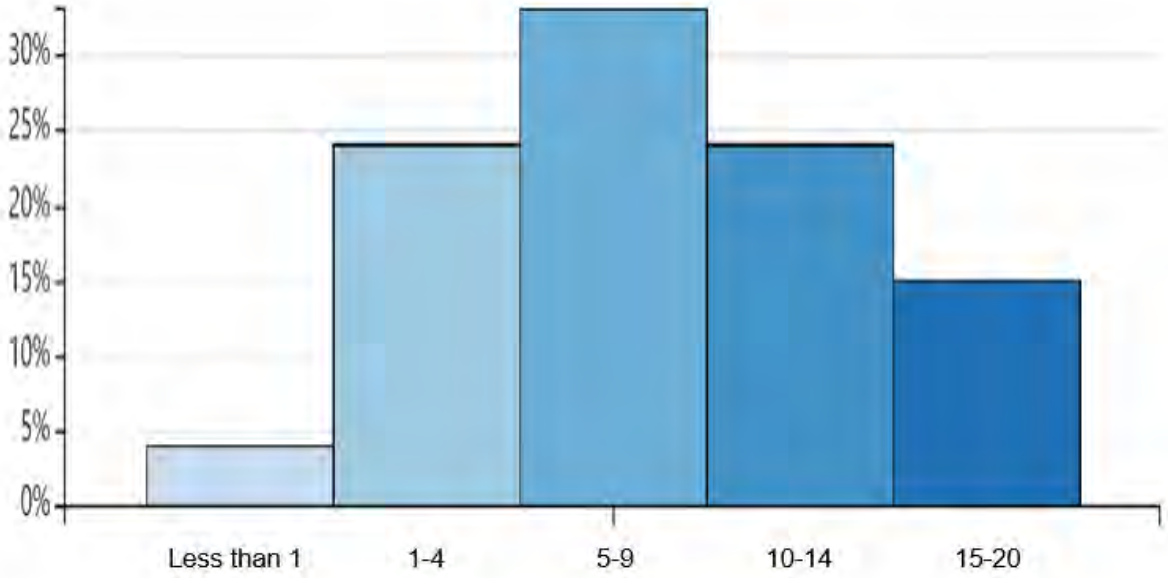
- 1,288 total confirmed cases
- 23 total deaths
- Data from 44 states, NYC and DC



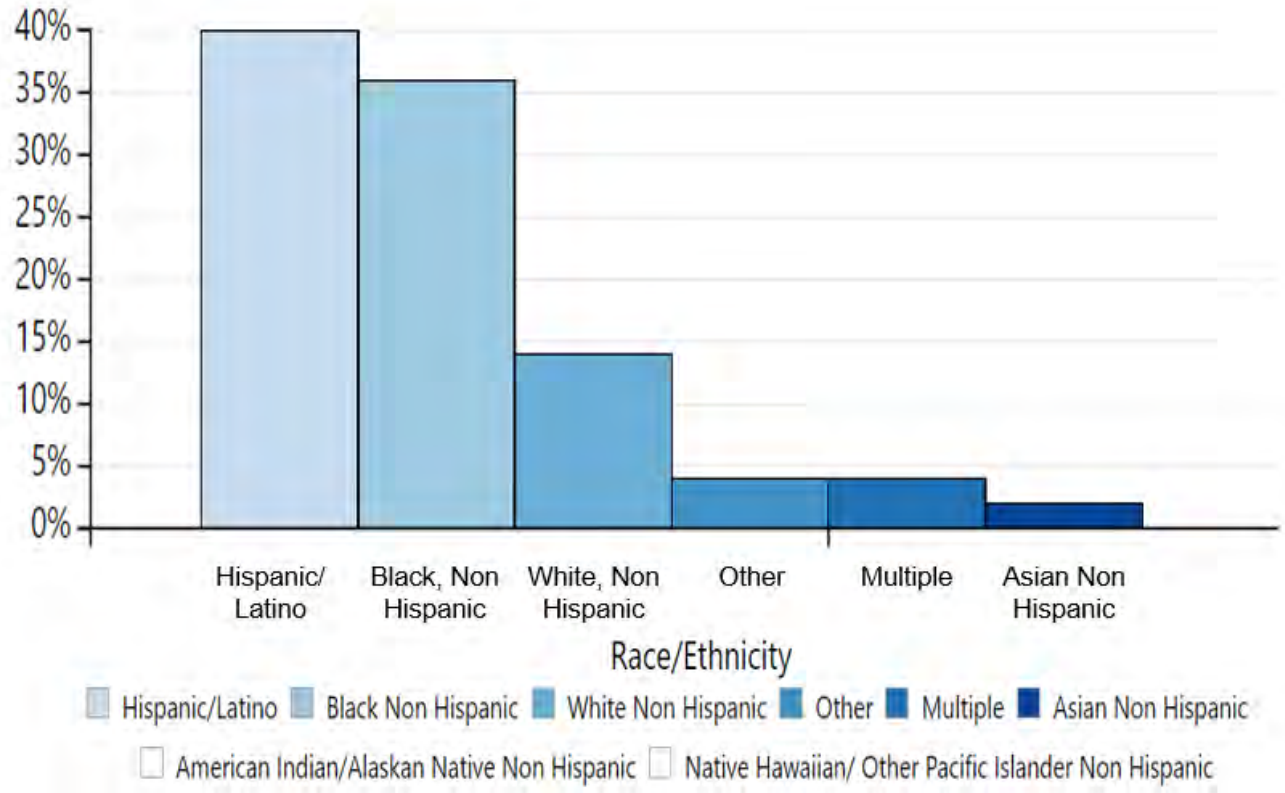
https://www.cdc.gov/mis-c/cases/index.html

MIS-C Demographics as of December 4, 2020

Cases by Age Group



Cases by Race & Ethnicity



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NIH: CARING for Children with COVID

Collaboration to Assess Risk and Identify loNG-term Outcomes for Children with COVID

- Leveraging networks from NICHD, NHLBI, NIAID to create a **centralized cohort** of children with COVID-19 and/or MIS-C
  - Capitalize on strengths of and existing relationships within each network: immune profiling (NIAID); cardiac effects (NHLBI); pharmacokinetics/pharmacodynamics (NICHD)
  - **Common data elements will be collected**
  - Clinical data, including WGS, will be shared and made **interoperable across data platforms**
  - Longitudinal protocols will follow children with MIS-C for five years
  - Current enrollment: 40 MIS-C patients across all networks (~40 sites to date)

CARING for Children with COVID Enrollment Sites

Active Sites

Sites pending activation

Predicting Viral-Associated Inflammatory Disease Severity in children with Laboratory Diagnostics and Artificial Intelligence (PreVAIL kIds)

RADxsm Radical (RADx-rad)
RADx-rad will support new, non-traditional approaches, including rapid detection devices and home-based testing technologies, that address current gaps in COVID-19 testing. The program will also support new or non-traditional applications of existing approaches to make them more usable, accessible, or accurate. These may lead to new ways to identify the current SARS-CoV-2 virus as well as potential future viruses.
Budget: $200 Million

- Develop novel, nontraditional approaches, testing strategies and technologies to ***understand the spectrum of pediatric SARS-CoV-2 illness, rapidly diagnose and characterize MIS-C associated with SARS-CoV-2,*** and ***predict the longitudinal risk of disease severity*** after exposure to and/or infection by SARS-CoV-2 to tailor management and optimize health outcomes
- Studies must include: Genetics, Omics & Other Biomarkers; Viral Dynamics & Immune Profiling Studies; Digital Health Platforms Leveraged for Children; Artificial Intelligence (AI) & Machine Learning
- Only the approaches, strategies and technologies that promise to lead to an accurate and reliable MIS-C prognostic algorithm to enhance the management and treatment of children will receive second phase of funding
- Awards pending in mid-December 2020

Long-Term Neurodevelopmental Effects

- **Increasing evidence of long-term neurological effects following SARS-CoV-2 infection in children**
  - Relevant to discussion and NIH research plans for post-acute sequelae
  - Important to include neurological measures in long-term follow-up studies
- **Neurodevelopmental effects on neonates following maternal SARS-CoV-2 infection are also unknown**
  - Administrative supplement (NIDA support) seeks to understand whether maternal infection with SARS-CoV-2 harms the developing brain or otherwise alters vulnerability to developmental and environmental adversities later in life
  - Imaging 50 infants born to mothers without infection and 50 infants born to mothers with confirmed SARS-CoV-2 infection
  - Follow-up assessments at 3 and 9 months; biospecimen collection included
  - Compared to existing ECHO cohort of ~1,500 infants born prior to Jan 1, 2020

Pediatric Vaccine Trials

- Increasing calls from multiple sectors to begin vaccine testing in children
  - Adolescent trials underway are not using NIH networks
- *Pfizer* is enrolling adolescents >12 in vaccine safety clinical trials
  - Enrollment targets 600 16 to 17-year-olds; 2000 12 to 15-year-olds
  - ClinicalTrials.gov Identifier: NCT04368728
- *Moderna* plans to enroll 3000 12-17 year-olds in the near future
  - ClinicalTrials.gov Identifier: NCT04649151
- A master protocol has been developed in consultation with NIAID for use in vaccine testing in children

Return to School

- Significant concerns regarding educational disparities for remote learning, long-term negative effects on neurodevelopment and social skills
- American Academy of Pediatrics has issued guidelines and advocates that all policy considerations should start with the goal of having students physically present in school
    - **Contingent on viral spread being under control in a given jurisdiction**
- For the most part, schools have not been drivers of community spread
- CDC updates guidance and checklists for safe return to school (https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/index.html)

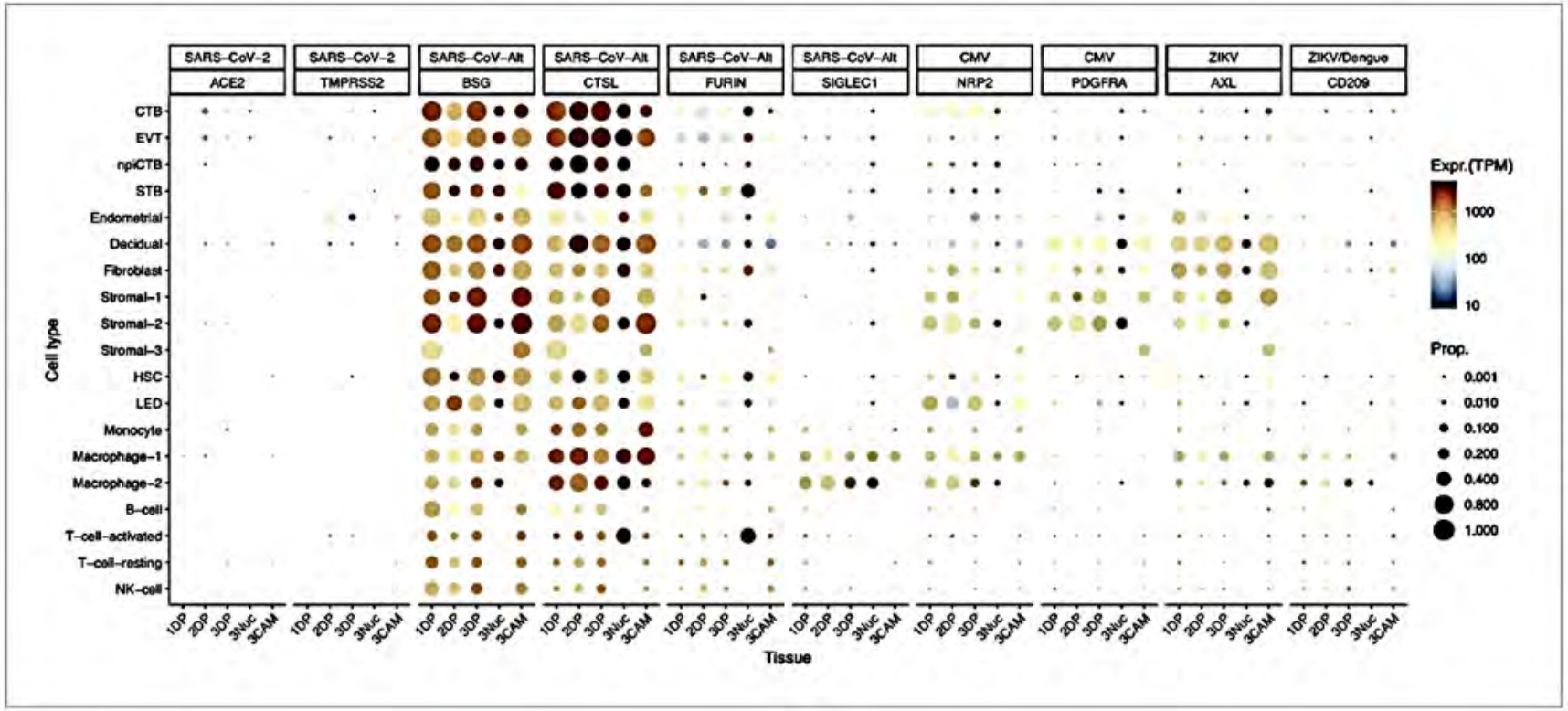
Viral Transmission: Placenta and Breast Milk

SARS-CoV2 and Vertical Transmission

- Research from the NICHD Intramural Perinatology Research Branch at Hutzel Hospital/Wayne State
- In their examination of single cell RNA sequencing of pregnant women infected with COVID-19 in their 3rd trimester investigators found that the placenta:
  - Lacks the mRNA required to manufacture the ACE2 receptor, the main cell surface receptor used by the SARS-CoV-2 virus to cause infection
  - Lacks the mRNA to make the serine protease TMPRSS2 that SARS-CoV-2 uses for cell entry
  - By contrast, receptors for Zika virus and cytomegalovirus that cause congenital infections are highly expressed in the placenta

https://elifesciences.org/articles/58716

SARS-CoV2 and Vertical Transmission



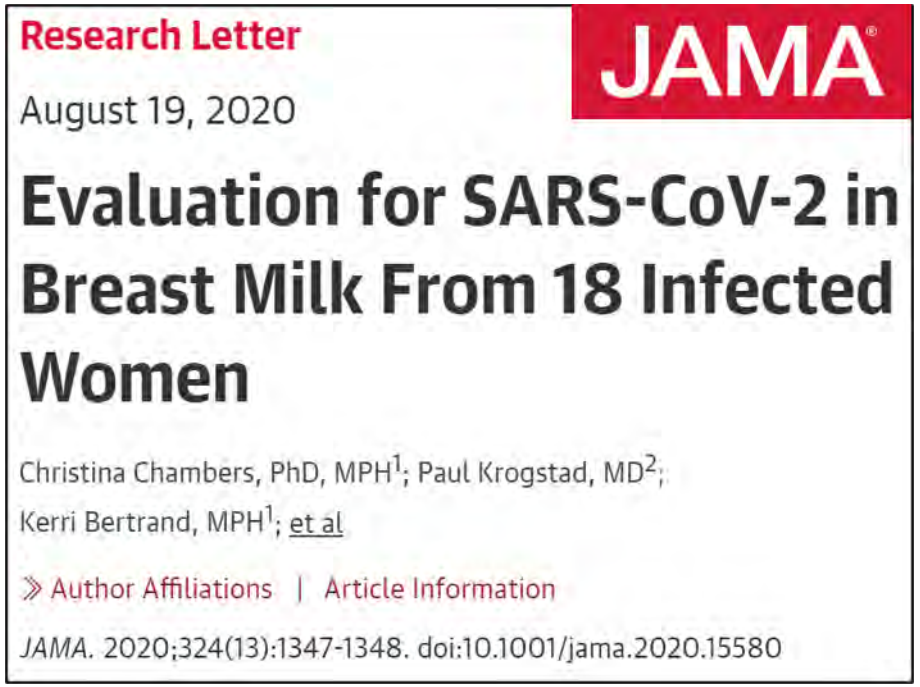
The receptor and enzyme are present in only miniscule amounts in the placenta, suggesting a **possible mechanism** for why SARS-CoV-2 has only rarely been found in fetuses or newborns of women infected with the virus

Rare but well documented cases of vertical transmission exist. These likely use alternate mechanisms, such as the transmembrane glycoprotein basigin (*BSG*) to enter cells

https://elifesciences.org/articles/58716

SARS-CoV-2 and Breast Milk

- Initial AAP recommendations advised COVID-19+ post-partum mothers not to breast feed
- Investigator-initiated work in an existing collaborative network supported by NICHD, NIAID and NIMH
- Study showed that replication-competent (active) virus is not transmitted to an uninfected infant via breast milk
- With proper hygiene, it is safe to breast feed
- Also found that human milk contains antibodies directed against SARS-CoV-2
- Might suggest the potential to use milk-derived antibodies for therapeutic use



Research Letter

JAMA

August 19, 2020

Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women

Christina Chambers, PhD, MPH[1]; Paul Krogstad, MD[2]; Kerri Bertrand, MPH[1]; et al

» Author Affiliations | Article Information

JAMA. 2020;324(13):1347-1348. doi:10.1001/jama.2020.15580

Thank You!