Alliance Member Webinar

featuring

Diana W. Bianchi, MD

November 9, 2021
Today’s Guest

Diana W. Bianchi, MD
Director, Eunice Kennedy Shriver National Institute of Child Health and Human Development
The Importance of Research for Keeping Kids in School and Pregnant Women Healthy During the COVID-19 Pandemic

Diana W. Bianchi, M.D.
November 9, 2021
Mission Statement
The NICHD leads research and training to understand human development, improve reproductive health, enhance the lives of children and adolescents, and optimize abilities for all.
Talk Outline

Research to Address the Impact of SARS-CoV-2 Infection on

Children

- MIS-C
- PreVAIL klds
- The “summer of delta”
- Return to School
  - Test to Stay in school

Women of Reproductive Age

- GRAVID
- Vaccines
  - Pregnant Women
  - Lactating Women
- Menstruation
Multi-system Inflammatory Syndrome in Children (MIS-C) April 2020

Children are falling ill with perplexing inflammatory syndrome thought to be linked to covid-19

Number of cases remains small, but officials are on high alert because of severity

Young adults are also affected by Kawasaki-like disease linked to coronavirus, doctors say

For Parents: Multisystem Inflammatory Syndrome in Children (MIS–C) associated with COVID–19

Boston Children's Hospital to lead nationwide study on COVID-19 in children

CDC-funded study will seek factors that increase vulnerability to the novel coronavirus
Daily MIS-C and COVID-19 Cases in Children 2020-2021

5,526 confirmed cases
48 total deaths

https://www.cdc.gov/mis/cases/index.html
## NIH Rapid Acceleration of Diagnostics (RADx)℠

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<thead>
<tr>
<th>Project</th>
<th>Description</th>
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<td><strong>RADx Tech</strong></td>
<td>Highly competitive, rapid three-phase challenge to identify the best candidates for at-home or point-of-care tests for COVID-19</td>
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<td><strong>RADx-Advanced Testing Program (RADx-ATP)</strong></td>
<td>Rapid scale-up of advanced POC technologies to accelerate and enhance and validate throughput – and support of ultra-high throughput machines and facilities</td>
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<td><strong>RADx-Radical (RADx-rad)</strong></td>
<td>Develop and advance novel, non-traditional approaches or new applications of existing approaches for testing</td>
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<td><strong>RADx-Underserved Populations (RADx-UP)</strong></td>
<td>Interlinked community-engaged projects focused on implementation strategies to enable and enhance testing of COVID-19 in underserved and/or vulnerable populations</td>
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RADx\textsuperscript{SM}-rad Supported Study: Predicting Viral-Associated Inflammatory disease severity in children with Laboratory diagnostics and artificial Intelligence (PreVAIL klds)

**Goal:** Develop translational tools 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

- Genetics; Omics; Other biomarkers
- Viral Dynamics and Immune Profiling Studies
- Digital Health Platforms Leveraged for Children
- Artificial Intelligence
Predicting Viral-Associated Inflammatory disease severity in children with Laboratory diagnostics and artificial Intelligence

- 8 Teams w/ multi-disciplinary expertise to address Program aims
- Access to diverse patient populations in > 75 sites across 30 US States
- International collaborations in UK, Canada, Asia, & S. America
- Enrolling >16,000 children with substantial racial and ethnic diversity
- Leveraging established biorepositories
- The studies include both prospective and retrospective enrollments
PreVAIL klds Prospective Enrollments – Ahead of Target

Prospective Enrollment Summary

Enrolled Participants

Legend

Baseline Clinical Phenotypes

Prospective Enrollment Breakdown (Actuals)

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
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<tr>
<td>Control</td>
<td>78</td>
</tr>
<tr>
<td>Febrile Controls</td>
<td>92</td>
</tr>
<tr>
<td>Kawasaki Disease</td>
<td>380</td>
</tr>
<tr>
<td>Severe</td>
<td>1,123</td>
</tr>
<tr>
<td>Non-Severe</td>
<td>258</td>
</tr>
<tr>
<td>MIS-C</td>
<td>528</td>
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<tr>
<td>Total Enrollment</td>
<td>2459</td>
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PreVAIL kIds Progress To Date

• In addition to prospective cohort, five awards have enrolled 21,651 patients retrospectively across all clinical phenotypes, from mild to severe COVID-19 and MIS-C

• Early results have identified:
  • Potential signatures of 4 genes that predict severe disease
  • Certain cytokines in saliva that may predict disease severity
  • Effects of intravenous immunoglobulin treatment for MIS-C
    • Works by reducing activated IL-1β+ neutrophils
  • Four projects have initiated discussions with company partners for commercialization support
Successful multi-PI PreVAIL kIds Collaboration

CLOCK (Collaborative Long-term study of Outcomes of COVID-19 in Kids)

MPIs: Kleinman, Annapragada, Chiu, Manlhiot, Salazar & Sethuraman

RECOVER is Powered by Collaboration
Children and COVID-19: the summer of delta

Week ending 10/28/2021
Return to School Phases I and II
OTA-21-004 and OTA-21-007

Awards: ~$33M awarded in April 2021 (Phase I)
        ~$25M awarded in June & July 2021 (Phase II)

Overview

- Provide evidence for effectiveness, sustainability and scalability of COVID-19 testing approaches and mitigation strategies in school settings
- Generate information to understand social, behavioral and ethical implications of implementation of COVID-19 testing within identified communities
- 16 sites across 13 states
- Range of settings including public, charter, tribal, early education, and special education schools

- Initial focus was on children and adolescents below the age eligible for vaccination via Emergency Use Authorization (age 16 for Phase I; age 12 for Phase II) and all school personnel
- Advance methods to integrate testing in return to or maintenance of in-person instruction (“Test to stay”)
- Preliminary results in NC showed increased access to testing and decreased days in quarantine
- Both surveillance and post-exposure testing are important
NIH RADx℠-Underserved Populations: Return to School

Lessons Learned from Testing in Schools

Direct **communication with parents** is far more effective than email for increasing enrollment in testing.

**Strong relationships** with school nurses and other medical **consultants** vital for testing results dissemination. **Engagement with communities** about the who, what, when, and where of testing ensures families receive accurate information.

Framing COVID-19 testing as a school **safety measure** with other mitigation strategies increases participation in research. **Trusted school champions** are instrumental in recruiting staff and students for testing.

With mitigation strategies in place, including testing, **in-school transmission has been low.**
Gestational research assessments for covid-19 (GRAVID)

- Medical records analysis of up to 24,500 women who gave birth at a clinical center within NICHD’s Maternal-Fetal Medicine Units Networks to examine maternal and neonatal outcomes for pregnant women with and without SARS-CoV-2 infection.

- Early results analyzing data from 1,200 SARS-CoV-2+ pregnant women showed that pregnant women with severe symptoms of COVID-19 had a higher risk of complications during and after pregnancy.
  
  - Those with severe symptoms were at higher risk for cesarean delivery, postpartum hemorrhage, hypertensive disorders of pregnancy, and preterm birth.

12 Centers; 39 individual hospital sites

Lack of Inclusion in Research Complicates Decisions Regarding Vaccination for Pregnant and Lactating People

- Pregnancy increases risk of hospitalization, need for ICU care, and medical ventilation with COVID-19

- Prevention is key

- At start of pandemic, evidence for the utility, safety, and effectiveness of the available vaccines in pregnancy was unknown

- Implementing PRGLAC recommendations could have improved the situation faced by pregnant and lactating women

[Viewpoint](https://jamanetwork.com/journals/jama/fullarticle/2776540)
Some Suggestions from our Viewpoint Article

• Pregnant people are no longer considered as a vulnerable population

• It is not too early to begin preparing now for the next epidemic or pandemic

• If animal studies and initial Phase I safety data are reassuring, make a plan for inclusion of pregnant people

• Create registries (e.g., CDC’s V-Safe), use existing networks, share data and biospecimens

• Liability risks to pharma can be mitigated by programs such as the Countermeasures Injury Compensation Program  [www.hrsa.gov/cicp](http://www.hrsa.gov/cicp)
  • Provides benefits to pregnant and non-pregnant people who are injured by products designed to treat or prevent public health threats
Benefits of Vaccination for Pregnant and Lactating People

- **mRNA COVID-19 vaccines induce comparable immune responses** in pregnant and lactating people and nonpregnant controls
  - Vaccines generate higher antibody titers than natural SARS-CoV-2 infection during pregnancy
  - Early data (from Israel) suggest mRNA vaccination during pregnancy reduces infection risk

- After vaccination, some **antibodies cross the placenta and protect the infant**
  - Current research is investigating
    - How long the protection lasts
    - Whether maternal antibodies can pass to the infant via breastmilk

- Pregnant and lactating people are **relatively less protected after the first dose** of the vaccines compared to nonpregnant people
  - After the second dose, both pregnant and nonpregnant people had similar antibody levels
  - **Extremely important for pregnant and lactating people to receive two doses**

COVID-19 Vaccination and Menstruation

• This topic generated interest from social media and traditional journalism

• NICHD awarded $1.6 million in one-year supplemental grants to five institutions to explore links between COVID-19 vaccination and menstrual changes

• The new awards will help to provide evidence as to whether menstrual changes are linked to vaccination, how long the changes last and determine underlying mechanisms

Washington Post, September 7, 2021
Do Vaccines Disrupt the Menstrual Cycle? Biological Plausibility

- Menstruation itself is an inflammatory process with the recruitment of natural killer cells, macrophages, mast cells, neutrophils, dendritic cells, and T cells playing roles in the breakdown and regeneration of the functional endometrium each cycle.

- The ACE-2 receptor, the target of the spike protein of SARS-CoV-2 in a range of biologic tissues, is expressed in the uterus and is thought play a functional role.

- There are also functional roles for immune cells at the level of the ovaries (folliculogenesis, ovulation, and corpus luteum regression) and potential crosstalk of signaling even at the neuroendocrine level.
Keep up with NICHD and COVID

- https://www.nichd.nih.gov/research/supported/COVID
Questions?
Join us next time!

Tuesday, November 16, 2021, 1:30 p.m. ET

Bill Novelli
Professor and Founder Business for Impact Center McDonough School of Business Georgetown University

Matthew Myers
President and CEO Campaign for Tobacco-Free Kids

Georges C. Benjamin, MD
Executive Director American Public Health Association
Public Health Thank You Day

Monday, November 22

Learn more:
www.publichealththankyouday.org