Center for Childhood Infections & Vaccines

June 2022 Volume 9, Issue 1

CCIV Grand Rounds

Donna Farber, PhD, from Columbia University College of Physicians and Surgeons, visited Emory in April for CCIV's Pediatric Grand Rounds. Her talk, "Tissue-mediated development of adaptive immunity in humans," occurred on April 20th, 2022. The event was the first Pediatric Grand Rounds to use a hybrid format since the start of the pandemic, with Dr. Farber also visiting with CCIV faculty and trainees throughout the day.

Dr. Farber is the George H. Humphreys Professor of Surgical Sciences, Professor of Microbiology and Immunology, and Division Chief of Surgical Sciences at Columbia University. She is also a fellow with the American Association for the Advancement of Science.

Dr. Farber's research program focuses on immunological memory and memory T-cells as essential mediators of

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Grand Rounds Cont.,

protective immunity. Currently, Dr. Farber's lab is using total transcriptome profiling and bioinformatics approaches to study the mechanisms for how memory T-cells become targeted to and maintained in the lung.

As part of the NIH-funded "Human Immunology Project Consortium," Dr. Farber's work involves immunologists, molecular biologists, and computational biologists across five institutions to study human adaptive and innate lymphocyte compartmentalization and maintenance in tissues throughout the lifespan. This research is facilitated by rapid access to tissues from organ donors when they cannot be used for clinical purposes. Dr. Farber also has ongoing studies on infant immunity and memory T-cells in relation to vaccines. These studies are looking at how protective responses can be established in babies who are most susceptible to infection & immune pathologies.

Dr. Farber's Grand Rounds in April explored the ways the COVID-19 pandemic afforded scientists with the opportunity to study immunity to a novel pathogen in both adults and children at the same time. A highlight of her talk included her discussion of tissue resident memory in children. Dr. Farber highlighted the ways in which children handle some respiratory illnesses much more efficiently than adults, and offered potential reasons based on her lab's studies of T and B-cell immunity.

Dr. Farber's visit to Emory and Children's was a great success, and we are grateful to her for making the trip. Both the Grand Rounds talk and lunch with trainees had among the highest attendance at similar CCIV events to date! §

Resources

CCIV and Children's Publication Citation

Remember to cite CCIV and Children's Healthcare of Atlanta in your publications. This is vital to ensure recognition of our work by both Emory and Children's. This requirement applies to all center members, whether lab-based or non-lab based. Children's has been a significant supporter of the research operations that make all of our work possible and should be acknowledged.

The proper affiliation citation is: Center for Childhood Infections and Vaccines (CCIV) of Children's Healthcare of Atlanta and Emory University Department of Pediatrics, Atlanta, GA USA.

Want your web profile updated?

Do you have a profile on our website you want to update? Fill out this form to do so.

Did you notice our new logo? We'll continue rolling out our new look all year!

Social Media: @EmoryCHOA_CCIV

Center Director

Ann Chahroudi, MD, PhD

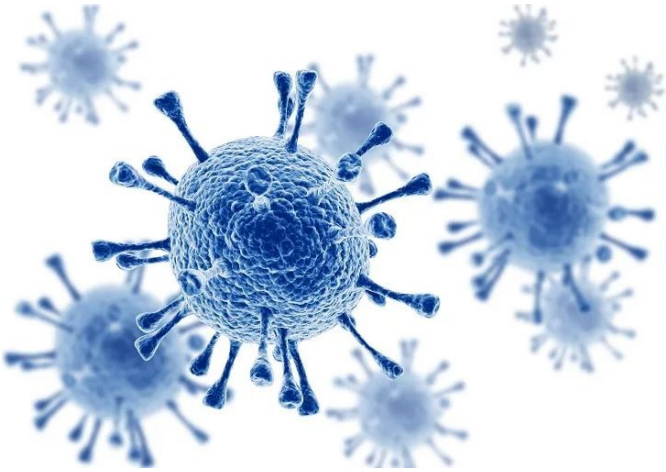
ann.m.chahroudi@emory.edu

Program Manager

Megan Vallowe, PhD

megan.vallowe@emory.edu

Improving care for adolescents living with HIV



According to the CDC, half of all new STIs in the United States occur in adolescents and young adults (AYAs) between ages 15-24. AYAs living with HIV are at a higher risk of additional STIs.

Despite nation-wide recommendations for people living with HIV to have annual STI screenings, such screenings frequently do not occur. This is especially true for extragenital sites, despite accounting for a significant number of new STI infections, such as gonorrhea and chlamydia. Additionally, very few AYAs self-report exposure, leading to even higher inadequate screening levels.

A study led by Andres Camacho-Gonzalez and published in the *Pediatric Infectious Disease Journal* in April, looked at incidence and reinfection rates of STIs among AYAs living with HIV in Atlanta. The retrospective chart review found that the study population had disproportionately high first and recurrent incidence rates of STIs, specifically gonorrhea and chlamydia. The most frequent presentation of these two STIs in the study was asymptomatic extragenital infection. Since only 28% of ID physicians providing HIV care in the US report routinely conducting extragenital STI testing, most of those infections would likely have been missed.

The study also found that health care providers do not necessarily perform routine sexual risk assessments—fewer than half of AYAs in the study reported having one in the last year—and also over rely on self-reporting to determine whether to perform annual STI screenings.

Given their findings, Camacho-Gonzalez and his team recommend increasing the number of STI screenings, and that such screenings must include all three anatomic infection sites, regardless of self-reported exposures. Increasing the number of STI screenings is crucial given that HIV and STI co-infection has been associated with lower CD4 T-cell counts and higher HIV viral loads in addition to increased HIV and STI transmission rates.

Another common concern for AYAs living with HIV is their transition time from pediatric to adult care. Unfortunately, the best time and preparation strategy for making this transition is still unknown. The clinical guidelines that do exist also focus on age-based transitions to adult care rather than an individual's readiness to transition. As a result, AYAs' transition from pediatric to adult care typically have poor retention in care and viral suppression.

To begin addressing this issue, Brian Zanoni and his team created a transition readiness score for adolescents with perinatally-acquired

HIV as they move from pediatric to adult care. The results of their study were published in April in *AIDS and Behavior*. They found that adolescents on first-line ART, with documented HIV status disclosure, and a higher rating on the HIV Adolescent Readiness to Transition Scale had much higher odds of viral suppression after transition to adult care.

The team hopes that the transition readiness scale can help identify adolescents ready to move to adult care and to identify intervention areas for those with lower readiness scores.

Zanoni is continuing his work to improve transitions to adult care for AYA's living with perinatally-acquired HIV through a clinical trial in South Africa. That protocol was published in the *Journal of Medical Internet Research*. The trial, which began enrolling participants in 2021, will test the effectiveness a new mobile-phone based intervention called the Interactive Transition Support for Adolescents Living with HIV using Social Media (InTSHA).

InTSHA uses encrypted group chats via WhatsApp to foster peer support and communication between adolescents, caregivers, and health care providers. The app builds on existing support programs as well as the Social-ecological Model of Adolescent and Young Adult Readiness for Transition (SMART).

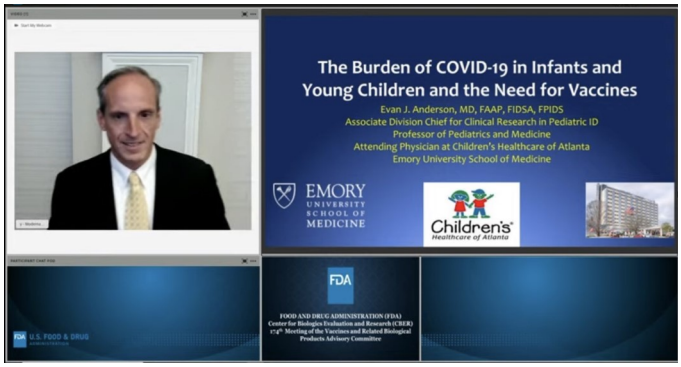
Currently, the study has enrolled nearly 80 participants from 15-19 years of age living in South Africa. If successful, Zanoni hopes to progress InTSHA to a larger randomized controlled trial from both urban and rural populations. He recently submitted an R01 which was scored and is being considered for funding. The R01 will evaluate the use of in-person vs mHealth support during transition to adult care. §

Awards & Accomplishments

Ann Chahroudi, MD, PhD, was elected as a member of the American Society for Clinical Investigation.

Andi Shane, MD, received the 1998 Society Award, given to a physician for passionate dedication to pediatrics, leadership, and philanthropic support of Children's mission.

Jairo Fonseca, MD, incoming ID fellow, was recently selected for the Pediatric Scientist Development Program.

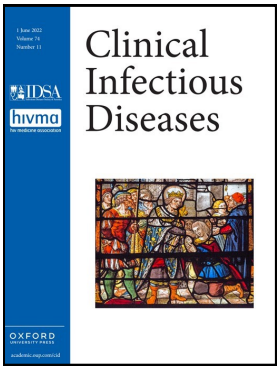


Evan Anderson, MD, FPIDS, presented to the FDA's 174th Meeting of the Vaccines and Related Biological Products Advisory Committee.

Pratik Patel, MD, ID fellow, received a 2022 Warshaw Award to support his research on bloodstream infections and stem cell transplants.

Improving Influenza Vaccines

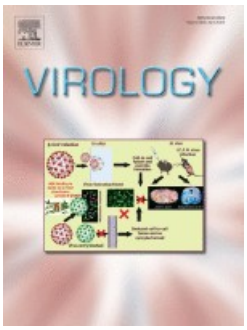
Influenza leads to 290,000 - 600,000 deaths each year globally (WHO). In the United States since the 2010-2011 season, there have been an average of 36,000 deaths and 430,000 hospitalizations each year (CDC). As such, describing the burden of influenza disease in children and refining vaccines remain critical parts of combating this deadly virus. A number of CCIV investigators are continually involved in these efforts.



A team led by CCIV Investigators, Satoshi Kamidani and Evan Anderson, recently published findings in *Clinical Infectious Diseases* on influenza hospitalization rates among different pediatric age groups. Their cross-sectional study identified hospitalized children under 18 with influenza from 2010-2019.

Over the course of nine flu seasons, adjusted influenza-associated hospitalization rates in children ranged from 10 to 375 per 100,000 persons each season, with the highest hospitalization rates among infants under 6 months. Additionally, the use of antiviral treatment during this time significantly increased from 56% to 85%. Influenza vaccination coverage among hospitalized children over time was suboptimal (33-44%) and consistently lower than the national average of US influenza vaccination rates in each season (51-63%).

While hospitalization and death rates were greatest among younger children in this population group, those who were older had a higher risk of severe outcomes among hospitalized children. The study found that hospitalized children 13 years and older had higher chances of developing pneumonia, ICU admission, mechanical ventilation, and death.



Another CCIV-led research team, which included Xuemin Chen, Christina Rostad, Larry Anderson, and Evan Anderson, published their findings in *Virology* on influenza antibody-dependent cellular cytotoxicity (ADCC) antibodies and their associations with protection from disease.

Multiple antibodies have been associated with protection from influenza. For instance, influenza ADCC antibodies have shown protection against disease and cross-protective potential among influenza strains. As such, the study team sought to learn if ADCC antibodies also contribute to year-to-year differences in vaccine effectiveness. Through the development of ADCC antibody assays, the team was able to learn more about these antibodies' contributions to vaccine immunogenicity.

Of the 70 participants in a 2014-2015 study of influenza vaccination, all had ADCC antibodies prior to vaccination. This was not surprising given the likelihood of multiple exposures to influenza infections and vaccines throughout participants' lives. However, the team also found a modest boost in ADCC concentration levels after vaccination, suggesting a relationship between vaccination and ADCC antibodies.

Quite unexpectedly, the team found significant differences between ADCC antibody concentrations among vaccine and circulating strain proteins, with higher antibody titers observed against vaccine strains. This finding suggests that differences in ADCC antibody concentrations between vaccine and circulating strain immune responses may contribute to vaccine effectiveness. This potential connection, the team recommends, is an avenue for further research to improve available influenza vaccines. §

Junior Faculty Spotlight: Manish Sharma

Manish Sharma, PhD, joined the Division of Infectious Diseases in the Department of Pediatrics at Emory University School of Medicine in 2021. Over the past year, Sharma's research on the HIV-1 virus focused on cell entry sites, as well as novel labeling of HIV-1 viral particles and real time imaging.

Prior to joining Emory's Pediatric ID Division, Sharma studied Japanese encephalitis virus (JEV) pathogenesis, specifically its effect on children as JEV has a 30-50% mortality rate. JEV motivated Sharma to learn more about neuroscience and neurotropic viruses, which took him to the Neuroscience Department at Scripps Research, Florida where he began studying Huntington Disease.

While at Scripps, Sharma was part of a team that first demonstrated the Rhes protein was responsible for tunneling nanotubes between two cells. These nanotubes subsequently transported the Huntington disease protein (mHTT) from one neuron to another.

Sharma and his colleagues at Scripps published their findings in the *Journal of Cell Biology*. They also proposed a potential mechanism for how Rhes-mediated neuron to neuron propagation of mHTT can cause further damage to different parts of the brain. The team's further studies showed that mHTT spreading was further diminished in Rhes-deleted mouse brains, indicating that the Rhes protein is a physiological mediator of mHTT transport *in vivo*. This study was recently published in *Science Advances*.

Similar to this Rhes protein, HIV-1 also promotes tunneling nanotubes and transmits from one cell to another. This spreads the infection and depletes immune cells. However, the mechanism by which this occurs is not clear.

Emory's strengths, especially in Pediatric Infectious Diseases and HIV-1 research, along with our cutting-edge resources and Sharma's commitment to return to working on issues in child health, drew him here. Currently, Sharma has two projects: one on a novel approach to pinpointing HIV-1 fusion and one on cell-to-cell transmission of HIV-1 via tunneling nanotubes in macrophages and CD4+ T-cells.

HIV-1 fusion sites within cells remain controversial. There is evidence both for HIV-1 fusion directly with the cell plasma membrane and for productive entry through endocytosis. Sharma's future plan is to combine single virus tracking with a novel triple-labeling strategy intended to pinpoint HIV-1 entry site(s) in cells.

Using this method, HIV-1 pseudoviruses will be co-labeled with (i) a lipophilic dye (DiD) that discriminates between virus fusion with the plasma membrane and endosomes, (ii) ecliptic pHluorin, an extraviral pH sensor that is quenched in mildly acidic environment, and (iii) HIV-1 Gag-imCherry that labels the viral core.

Through triple-labelling, Sharma plans to explore the HIV-1 transmission in host cells, especially in primary macrophages and T-cells for direct visualization of HIV-1 entry and fusion in the cells. §

Collaboration Corner

Meet our new affiliate members!

M.G. Finn, PhD, is Professor in the School of Chemistry & Biochemistry & the School of Biological Sciences at Georgia Tech. Finn's current interests include the use of virus-like particles as molecular & catalytic building blocks for vaccine development. His group's efforts in vaccine development focus on anti-glycan & anti -peptide immune response, lymph node targeting, adjuvant delivery, and bacterial & trypanosomal pathogens.

Erica L. Johnson, PhD, is an Immunologist and Associate Professor of Microbiology, Biochemistry & Immunology and Obstetrics & Gynecology at Morehouse School of Medicine (MSM). Johnson's current research goals are to (1) define the dynamics of innate immune signaling in macrophages at the maternal-fetal interface and their control of HIV, HCMV, and ZIKV during pregnancy; (2) determine the mechanisms by which HCMV exposure promotes in utero HIV transmission; and (3) elucidate the impact of maternal infection and/or inflammation on the developing fetal immune system.

Steven Crooke, PhD, is the Vaccine Immunology Team Lead for the Centers for Disease Control. His research currently focuses on developing novel diagnostic assays to support vaccine-preventable disease surveillance, the implementation of reverse genetics systems and systems biology to better understand viral vaccine immune responses, and the design and evaluation of novel vaccine candidates.

Chris LaRock, PhD, is an Assistant Professor in the Department of Microbiology & Immunology in the Emory School of Medicine. His research examines immune defenses against bacterial infection, specifically Streptococcus pyogenes, for which there is no current vaccine.

Interested in collaborating with our new affiliate members?

Contact megan.vallowe@emory.edu to connect.

Upcoming Events

CCIV 6th Annual Symposium & Research Retreat

Our 6th Annual Symposium will take place this November. We hope the symposium will be in person this year & to combine the event with a research retreat for CCIV members. More info to come!

CCIV Weekly Seminars

CCIV Monday Seminars will resume this fall, starting **August 22nd**. Weekly seminars are held every Monday from 1-2 PM. This fall will feature external or faculty speakers at least once a month, in addition to trainees and alumni!