collected from neonates with CNS disease contained several unique amino acid variations in HSV proteins known to contribute to cell-to-cell spread and neurovirulence in mouse models.

Methods: To understand the relevance of these findings to neonatal CNS disease, we evaluated CNS disease- and SEM disease-associated neonatal HSV-2 isolates in neurologically-relevant *in vitro* and *in vivo* models.

Results: We found that HSV-2 isolates from neonates with CNS disease, as compared to those collected from neonates with SEM disease, displayed enhanced spread in human neuronally-differentiated SH-SY5Y or LUHMES cells and enhanced retrograde transport in rat neurons cultured in modified Campenot chambers. CNS disease-associated isolates also resulted in increased hind limb paralysis and zosteriform disease in a mouse flank scratch infection model, and increased death in a mouse direct intracerebral injection model of encephalitis. Notably, CNS disease and SEM disease-associated isolates resulted in equivalent outcomes following mouse intraperitoneal injection, suggesting similar systemic virulence.

Conclusion: These data suggest that virus-mediated differences in neuronal spread and transport may contribute to neurovirulence in neonatal HSV disease.

Disclosures: **All Authors**: No reported disclosures

174. Shotgun Metagenomics and Colonization by Antibiotic-resistant Bacteria in Pediatric Hematopoietic Stem Cell Transplant Recipients

Sarah M. Heston, MD[1]; Rebecca R. Young, MS, MS[2]; Mehreen Arshad, MD[3]; Kirsten Jenkins, BS[2]; Paul L. Martin, MD, PhD[2]; Doyle V. Ward, PhD[4]; Shakti Bhattarai, MS[5]; Vanni Bucci, PhD[5]; Patrick C. Seed, MD PhD[6]; Matthew S. Kelly, MD, MPH[2]; [1]Duke University, Durham, North Carolina; [2]Duke University Medical Center, Durham, North Carolina; [3]Northwestern University/Lurie Children's Hospital of Chicago, Chicago, Illinois; [4]University of Massachusetts Medical School, Worcester, Massachusetts; [5]University of Massachusetts, N.Dartmouth, Massachusetts; [6]Northwestern University Feinberg School of Medicine, Ann & Robert H. Lurie Children's Hospital, Stanley Manne Children's Research Institute, Chicago, Illinois

Session: O-33. Pediatric Infections and Immunology

Background: Bacteremia in hematopoietic stem cell transplant (HSCT) recipients most frequently arises from gut bacterial translocation and is associated with a higher mortality if the organism is antibiotic-resistant. We sought to determine the impact of prior antibiotic exposure on antibiotic resistance genes (ARGs) in the gut metagenomes of HSCT recipients to inform future infection prevention strategies.

Methods: We performed shotgun metagenomic sequencing of fecal samples collected during the transplant hospitalization from children (< 18 years of age) undergoing HSCT at Duke University between 2015 and 2018. Host-decontaminated sequencing reads were aligned to the Comprehensive Antibiotic Resistance Database. We used a negative binomial regression model to determine the impact of recent therapeutic antibiotic exposure on the number of ARGs prior to HSCT.

Results: Median age of the 77 children included in these analyses was 4.8 years, and 58% were male. Hematological malignancy was the transplant indication for 42% of children, and 87% of transplants were allogeneic. In the 654 longitudinal samples, we identified 926 unique ARGs, conferring resistance to 31 classes of antibiotics. The median number of ARGs per sample was 24 (interquartile range: 13, 49). The most common ARGs detected were dfrF (conferring resistance to trimethoprim), tetO (tetracyclines), and tetW (tetracyclines), each detected in >65% of samples. Of the 66 children with fecal samples collected prior to HSCT, 70% of children received therapeutic antibiotics in the 2 weeks prior to enrollment. Accounting for transplant indication, sex, and age, the incidence of ARGs was 47% higher in children who received recent therapeutic antibiotics (incidence rate ratio 1.47; 95% CI (1.03–2.13); p=0.04).

Conclusion: ARGs are commonly found in the gut metagenomes of pediatric HSCT recipients prior to HSCT and are associated with recent receipt of therapeutic antibiotics. Future directions for this dataset include determining the ability of ARGs in the metagenome to predict clinical outcomes, including mortality and infections. Understanding the colonization and acquisition of ARGs could inform infection prevention strategies and empiric therapies and lead to improved infectious outcomes in these high-risk patients.

Disclosures: **All Authors**: No reported disclosures

175. Randomized Double-blind Controlled Trial of Short vs. Standard Course Outpatient Therapy of Community Acquired Pneumonia in Children (SCOUT-CAP)

Derek Williams, MD, MPH[1]; C. Buddy Creech, MD, MPH[1]; Emmanuel B. Walter, MD, MPH[2]; Judith Martin, MD[3]; Jeffrey Gerber, MD, PhD[4]; Jason Newland, MD, MEd, FPIDS[5]; Lee Howard, RN, CCRC[6]; Meghan E. Hofto, MD, MPH[7]; Mary A. Staat, MD, MPH[8]; Randolph Oler, MS[9]; Thomas Conrad, PhD[9]; Bonifride Tuyishimire, PhD[9]; Melinda M. Pettigrew, PhD[10]; Vance G. Fowler, Jr., MD, MHS[11]; Henry Chambers, BA, MD[12]; Theoklis Zaoutis, MD, MSCE[4]; Scott R. Evans, PhD[13]; W. Charles Huskins, MD, MSc[14]; [1]Vanderbilt University Medical Center, Nashville, Tennessee; [2]Duke University School of Medicine, Durham, North Carolina [3]University of Pittsburgh, Pittsburgh, Pennsylvania; [4]Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; [5]Washington University, St. Louis, Missouri; [6]Arkansas Children's, Little Rock, Arkansas; [7]University of Alabama at Birmingham, Birmingham, Alabama; [8]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [9]Emmes Company, LLC, Rockville, Maryland; [10]Yale School of Public Health, New Haven, Connecticut; [11]Duke University, Durham, North Carolina; [12]UC San Francisco School of Medicine, San Francisco, California; [13]The George Washington University, Rockville, Maryland; [14]Mayo Clinic College of Medicine and Science, Rochester, Minnesota

DMID 14–0079 Study Group

Session: O-33. Pediatric Infections and Immunology

Background: Community-acquired pneumonia (CAP) in children is usually treated with 10 days of antibiotics. Shorter antibiotic courses may be beneficial if proven effective, with potentially fewer antibiotic adverse effects and decreased antibiotic exposure.

Methods: This randomized, double-blind, placebo-controlled superiority trial (NCT02891915) compared a strategy of short vs standard course ß-lactam therapy for outpatient CAP in children ages 6–71 months. Children demonstrating clinical improvement by day 3–5 of initial therapy were considered for enrollment. Enrolled children were randomized 1:1 to receive either 5 additional days of the originally prescribed antibiotic (standard) or matching placebo (short). The Desirability of Outcome Ranking (DOOR; PMID: 26113652) was the primary outcome, and was defined by classifying the global experience of children into an ordinal clinical response (OCR) that combined the response to CAP treatment and antibiotic adverse effects 11–15 days after the start of therapy. For those subjects with equivalent OCR, documented days of antibiotic administration was used to further rank the desirability of the outcome with the *a priori* assumption that shorter antibiotic exposure was more desirable. The OCR was a secondary outcome. The intention to treat population was used to estimate the probability of a more desirable outcome for the strategy of short vs. standard course therapy for both outcomes.

Results: 385 children were enrolled; 380 had complete data for analysis. Baseline characteristics were similar between the two strategies. In both strategies, > 90% of children had an adequate response to CAP treatment and most antibiotic adverse effects were minor (Table). In the OCR analysis, short course therapy had a 48% probability (95% CI: 42%-53%) of a more desirable outcome. In the DOOR analysis, short course therapy was superior to standard therapy with a 69% probability (95% CI: 63%-72%; p< 0.001) of a more desirable outcome.

Table: Ordinal Clinical Response (OCR) by Treatment Group

Rank	Adequate Response to CAP treatment[1]	Antibiotic Adverse Events[2]	Short Course (N=170) No. (%)	Standard Course (N=174) No. (%)
1 (Most Desirable)	Yes	None	97 (57)	107 (61)
2	Yes	Mild	47 (28)	42 (24)
3	Yes	Moderate	14 (8)	10 (6)
4	Yes	Severe	0	2 (1)
5	No	None or any grade	10 (6)	12 (7)
6	No, requiring clinic or ED encounter	None or any grade	2 (1)	1 (<1)
7	No, requiring hospitalization	None or any grade	0	0
8 (Least Desirable)	Death (any cause)	None or any grade	0	0

Abbreviation: ED, Emergency Department
[1]**Adequate response to CAP treatment** was defined as absence of all of the following: fever within preceding 48 hours AND elevated respiratory rate for age AND increased work of breathing AND development of persistent or worsening pneumonia, defined as receipt of a non-study antibiotic for pneumonia or treatment for a pneumonia-related complication with or without a subsequent clinic visit, emergency department encounter, or hospitalization.
[2]**Antibiotic adverse events** included fever (unrelated to pneumonia), changes in activity, headache, abdominal pain, vomiting, diarrhea, allergic reactions, stomatitis, and candidiasis, and were graded as mild (transient requiring minimal treatment or intervention and little impact on activities of daily living; moderate (often requires specific therapeutic intervention and/or interferes with activities of daily living but poses no significant risk of harm); and severe (significantly affects clinical status or interrupts activities of daily living and/or requires intensive therapeutic intervention).

Conclusion: Among children with CAP demonstrating initial clinical improvement with outpatient therapy, both strategies had a similar response to CAP treatment and antibiotic adverse effects, but short course therapy was superior in our *a priori* defined outcome that incorporated decreased antibiotic exposure.

Disclosures: **Emmanuel B. Walter, MD, MPH**, **Moderna** (Grant/Research Support)**Pfizer** (Grant/Research Support) **Jason Newland, MD, MEd, FPIDS**, **Merck** (Grant/Research Support)**Pfizer** (Other Financial or Material Support, Industry funded clinical trial) **Vance G. Fowler, Jr., MD, MHS**, **Achaogen** (Consultant)**Actavis** (Grant/Research Support)**Advanced Liquid Logics** (Grant/Research Support)**Affinergy** (Consultant, Research Grant or Support)**Affinium** (Consultant)**Allergan** (Grant/Research Support)**Ampliphi Biosciences** (Consultant)**Basilea** (Consultant, Research Grant or Support)**Bayer** (Consultant)**C3J** (Consultant)**Cerexa** (Consultant, Research Grant or Support)**Contrafect** (Consultant, Research Grant or Support)**Cubist** (Grant/Research Support)**Debiopharm** (Consultant)**Destiny** (Consultant)**Durata** (Consultant)**Forest** (Grant/Research Support)**Genentech** (Consultant, Research Grant or Support)**Integrated Biotherapeutics** (Consultant)**Janssen** (Consultant, Research Grant or Support)**Karius** (Grant/Research Support)**Locus** (Grant/Research Support)**Medical Biosurfaces** (Grant/Research Support)**Medicines Co.** (Consultant)**Medimmune** (Consultant, Research Grant or Support)**Merck** (Consultant, Research Grant or Support)**NIH** (Grant/Research Support)**Novadigm** (Consultant)**Novartis** (Consultant, Research Grant or Support)**Pfizer** (Grant/Research Support)**Regeneron** (Consultant, Research Grant or Support)**Tetraphase** (Consultant)**Theravance** (Consultant, Research Grant or Support)**Trius** (Consultant)**xBiotech** (Consultant) **W. Charles Huskins, MD, MSc**, **ADMA Biologics** (Consultant)**Pfizer, Inc** (Consultant)

176. Selected Impact of the 13-valent Pneumococcal Conjugate Vaccine (PCV13) on Invasive Pneumococcal Disease (IPD) at Eight Children's Hospitals in the United States. 2014–2019

Sheldon L. Kaplan, MD[1]; William J. Barson, MD[2]; Philana L. Lin, MD, MSc[3]; Jose R. Romero, MD[4]; John S. Bradley, MD[5]; Tina Q. Tan, MD[6]; Pia S. Pannaraj, MD, MPH[7]; Larry Givner, MD[8]; Kristina G. Hulten, PhD[1]; [1]Baylor College of Medicine, Houston, Texas; [2]Ohio State University College of Medicine and Public Health and