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

Nationwide Children's Hospital, Columbus, Ohio; [3]UPMC Children's Hospital of PIttsburgh, Pittsburgh, Pennsylvania; [4]University of Arkansas for Medical Sciences and Arkansas Children's Hospital, Little Rock, Arkansas; [5]University of California San Diego/Rady Children's Hospital, San Diego, California; [6]Feinberg School of Medicine, Northwestern University, Chicago, Illinois; [7]Children's Hospital Los Angeles, Los Angeles, California; [8]Wake Forest School of Medicine, Winston-Salem, Oklahoma

US Pediatric Multicenter Pneumococcal Surveillance Study Group

Session: O-34. Pediatric Vaccines

Background: The 2011 IDSA/PIDS Clinical Practice Guidelines for the Management of Community-acquired Pneumonia (CAP) in Children Older than 3 months recommended empiric treatment with either ampicillin/penicillin or ceftriaxone based on PCV13 vaccine status and the local antibiotic susceptibilities of IPD isolates. No study has addressed differences in antibiotic susceptibilities for isolates from children with pneumococcal pneumonia (PP) based on PCV13 status.

Methods: Investigators from 8 US children's hospitals identified infants and children with IPD between 1/1/2014 and 12/31/2019. IPD was documented by positive cultures from a normally sterile site. PP diagnosis required an abnormal chest radiograph. Clinical data were recorded and isolates analyzed for serotype (ST) by the capsular swelling method and antimicrobial susceptibilities by standard methods. Administration of PCV7/13 was documented through the patient's medical records, health care provider or a vaccine registry. Fisher Exact was performed; $p < 0.05$ was significant.

Results: 690 IPD patients with isolates were available (0–18 y); 24% (166/690) of the isolates were PCV13 STs (ST3-75, ST19F-45, ST19A-36, ST7F-5, other STs-5). The most common non-PCV13 ST isolates were ST35B-60, ST23B-59, ST33F-47, ST22F-43, ST15C-35, ST23A-27, ST15B-26, ST10A-26, ST15A-23. Of non-PCV13 isolates, 41% (217/524) were among the 7 additional STs in PCV20. For children with PP (n=157), the distributions of penicillin (Table) (p=0.8) and ceftriaxone MICs were no different for isolates obtained from children regardless of prior PCV13 doses. Less than 7% of PP isolates were resistant to penicillin (MIC >2 µg/mL).

Table. Minimal inhibitory concentrations (MIC) of pneumococcal isolates related to the number of PCV13 doses each patient received prior to pneumococcal pneumonia (PP).

Penicillin MIC (µg/mL)	Number of PCV13 doses				
	0	**1**	**2**	**3**	**4**
≤ 0.125	26*	12	8	17	43
0.25–0.5	4	2	1	1	5
1	1	0	0	3	1
2	4	0	0	2	5
≥4	1	2	1	2	4

*Number of pneumococcal pneumonia patients/isolates. 145/157 patients had immunization and isolate susceptibility data available for analysis.

Conclusion: PCV13 status should not modify empiric antibiotics for children with suspected pneumococcal CAP. 41% of non-PCV13 IPD isolates were among the 7 additional PCV20 STs.

Disclosures: **Sheldon L. Kaplan, MD**, **Allergan** (Research Grant or Support)**Pfizer** (Grant/Research Support) **Tina Q. Tan, MD**, **Pfizer** (Grant/Research Support, Other Financial or Material Support, Chair, DMSB for PCV20 vaccine) **Pia S. Pannaraj, MD, MPH**, **AstraZeneca** (Grant/Research Support)**Pfizer** (Grant/Research Support)**Sanofi Pasteur** (Advisor or Review Panel member)

177. Safety of Measles and Pertussis-containing Vaccines in School-age Children Previously Diagnosed with Autism Spectrum Disorders

Ousseny Zerbo, PhD[1]; Sharareh Modaressi, MD, MPH[1]; Kristin Goddard, MPH[2]; Ned Lewis, MPH[3]; Bruce Fireman, MA[4]; Lisa Jackson, MD, MPH[5]; Stephanie Irving, MHS[6]; Matthew F. Daley, MD[7]; Darios Gethaun, MD, PhD, MPH[8]; Lei Qian, PhD[9]; James Donahue, DVM,PhD, MPH[10]; Nicola P. Klein, MD, PhD[11]; [1]Kaiser Permanente Vaccine Study Center, Oakland, California; [2]Kaiser Permanente, Oakland, California; [3]Kaiser Permanente Northern California, Oakland, California; [4]Kaiser Permanente Vaccine Study Center, Oakland, California, Oakland, California; [5]Kaiser Permanente Washington Health Research Institute, Seattle, Washington; [6]Kaiser Permanente Center for Health Research, Portland, Oregon; [7]Kaiser Permanente Colorado, Aurora, Colorado; [8]5Kaiser Permanente Department of Research and Evaluation, Pasadena, California, Pasadena, California; [9]Kaiser Permanente Southern California, Pasadena, California; [10]Marshfield Clinic Research Institute, Marshfield, Wisconsin, Marshfield, Wisconsin; [11]Kaiser Permanente Vaccine Study Center, Oakland, California, United States, Oakland, California

Session: O-34. Pediatric Vaccines

Background: Some parents, especially those of children with autism spectrum disorders (ASD), are uncertain about the safety of childhood immunization. We compared rates of fever, febrile seizure and emergency room (ER) visits following measles and pertussis-containing vaccines recommended between ages 4–6 years among children with and without ASD.

Risk of Fever, Febrile Seizure and ER Visits following Measles and Pertussis-containing Vaccine Among Children with and without Autism Spectrum Disorders Diagnosis.

Outcomes after immunization	Risk/control intervals (days)	Difference-in-difference analysis comparing children with vs. without ASD Ratio of rate ratio (95% CI)	Risk interval analysis among children with ASD (N = 14,947) Rate ratio (95% CI)	Risk interval analysis among children without ASD (N=1,650,041) Rate ratio (95% CI)
Risk following Measles-containing vaccines				
Fever[1]	7 - 10/14 - 28	1.07 (0.58 – 1.96)	1.22 (0.67 – 2.23)	1.14 (1.06 – 1.22)
Febrile seizure[2]	7 - 10/14 - 28	NE	NE	1.64 (1.05 – 2.55)
ER visits	4 - 10/14 - 28	1.11 (0.80 – 1.54)	1.13 (0.82 – 1.56)	1.02 (0.98 – 1.06)
Risk following Pertussis-containing vaccines				
Fever[1]	1 -3/14 - 28	1.16 (0.63 – 2.15)	1.38 (0.75 – 2.55)	1.19 (1.10 – 1.29)
Febrile seizure[2]	0 - 3/14 - 28	NE	NE	2.40 (1.58 – 3.52)
ER visits	0 – 3/14 - 28	0.87 (0.59 – 1.28)	1.11 (0.76 – 1.62)	1.27 (1.22 – 1.33)

[1] Fever diagnosed in outpatient settings
[2] Febrile seizure diagnosed in ER or inpatient settings
NE: Not estimated because cells counts were zero "0"

Methods: The study included children who were born between 1995–2012, aged 4–7 years at vaccination, and members of six integrated healthcare delivery systems within the Vaccine Safety Datalink. Children with ASD were defined based on receipt of two separate International Classification of Diseases (ICD)-9 or 10 codes. Outcomes (fever, febrile seizures, and ER visits) were identified in electronic health records. To minimize confounding by unmeasured factors related both to avoidance of vaccination and to outcomes of interest, we compared rates of each outcome between children with and without ASD, in risk and control intervals, by estimating the difference-in-differences on a log scale (i.e. the ratio of rate ratios) using logistic regressions. We also conducted risk interval analyses comparing rates of outcomes in risk intervals and control intervals within each group.

Results: The study included 14,947 children with ASD and 1,650,041 children without ASD. After measles or pertussis-containing vaccination, there were no differences in association between the two groups for fever or ER visits (Table). There were no febrile seizures identified among children with ASD. Within the ASD group, rates of fever, seizure or ER visits did not differ significantly between the risk and control intervals after vaccination. However, among the non-ASD group, measles and pertussis-containing vaccines were associated with higher rates of fever and seizure in risk intervals compared to controls intervals. Pertussis-containing vaccines were associated with increased risk of ER visits in risk interval compared to control interval (Table).

Conclusion: We found no difference in the risk of fever, and ER visits comparing children with autism to children without autism after measles or pertussis-containing vaccines. The study provides some reassurance that these vaccines are not less safe in children with ASD.

Disclosures: **Lei Qian, PhD**, **GlaxoSmithKlein** (Research Grant or Support) **Nicola P. Klein, MD, PhD**, **GSK group of companies** (Research Grant or Support)**Merck** (Grant/Research Support)**Pfizer** (Grant/Research Support)**Protein Science (now SP)** (Grant/Research Support)**Sanofi Pasteur** (Grant/Research Support)

178. Vaccine Effectiveness Against Influenza-associated Hospitalizations and Emergency Department (ED) Visits Among Children in the United States in the 2019–2020 Season

Angela P. Campbell, MD, MPH[1]; Constance E. Ogokeh, MPH[1]; Geoffrey A. Weinberg, MD[2]; Julie A. Boom, MD[3]; Janet A. Englund, MD[4]; John V. Williams, MD[5]; Natasha B. Halasa, MD, MPH[6]; Rangaraj Selvarangan, BVSc, PhD[7]; Mary A. Staat, MD, MPH[8]; Eileen J. Klein, MD, MPH[9]; Monica McNeal, MS[8]; Marian G. Michaels, MD, MPH[10]; Leila C. Sahni, PhD, MPH[11]; Laura S. Stewart, PhD[6]; Peter G. Szilagyi, MD, MPH[12]; Christopher J. Harrison, MD[13]; Robert Hickey, MD[14]; Barbara Pahud, MD, MPH[15]; Jennifer E. Schuster, MD[7]; Gina Weddle, DNP, RN, CPNP-AC/PC[7]; Mary Moffatt, MD[15]; Joana Y. Lively, MPH[1]; Brian Rha, MD, MSPH[1]; Manish Patel, MD[1]; [1]Centers for Disease Control and Prevention, Atlanta, Georgia; [2]University of Rochester, Rochester, New York; [3]Baylor College of Medicine and Texas Children's Hospital, Houston, Texas; [4]Seattle Children's Hospital/Univ. of Washington, Seattle, Washington; [5]University of Pittsburgh, Pittsburgh, Pennsylvania; [6]Vanderbilt University Medical Center, Nashville, Tennessee; [7]Children's Mercy Hospital, Kansas City, Missouri; [8]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [9]Seattle Children's Hospital, Seattle, Washington; [10]UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania; [11]Texas Children's Hospital, Houston, Texas; [12]University of California, Los Angeles, Los Angeles, California; [13]The Children's Mercy Hospital- Kansas City, Kansas City, Missouri; [14]Childrens Hospital of Pittsburgh, Pittsburgh, Pennsylvania; [15]The Children's Mercy Hospital, Kansas City, Missouri

Session: O-34. Pediatric Vaccines

Background: The 2019–20 influenza season was predominated by early onset B/Victoria viruses followed by A(H1N1)pdm09 virus circulation. Over 95% of circulating B/Victoria viruses were subclade V1A.3, different from the Northern Hemisphere