

**Conclusion:** Delayed recognition by healthcare workers, higher weight, vital sign abnormalities, hepatomegaly, neurological symptoms, leukocytosis, neutrophilia, and lack of dextrose in intravenous solutions were associated with mortality in children with DF. These findings have implications for optimizing the diagnosis and management of severe pediatric dengue infection.

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

**1406. Comparison of Clinical Presentations and Burden of Respiratory Syncytial Virus in Infants Across Three Distinct Healthcare Settings**

Danielle A. Rankin, MPH, CIC<sup>1</sup>; Zaid Haddadin, MD<sup>1</sup>; Loren Lipworth, ScD<sup>2</sup>; Jon Fryzek, PhD, MPH<sup>3</sup>; Mina Suh, MPH, International Health<sup>3</sup>; Donald S. Shepard, PhD<sup>5</sup>; Rendie McHenry, MS<sup>1</sup>; Rebekkah Varjabedian, BS<sup>1</sup>; Kailee N. Fernandez, BS<sup>1</sup>; Christopher Rizzo, MD<sup>6</sup>; Christopher Nelson, PhD, Epidemiology<sup>6</sup>; Natasha B. Halasa, MD, MPH<sup>7</sup>; <sup>1</sup>Vanderbilt University Medical Center; Division of Pediatric Infectious Diseases, Nashville, Tennessee; <sup>2</sup>Division of Epidemiology - 104370, Nashville, Tennessee; <sup>3</sup>EpidStrategies, A Division of ToxStrategies, Inc., Rockville, MD; <sup>4</sup>Epidstrategies, Mission Viejo, California; <sup>5</sup>Brandeis University, Waltham, Massachusetts; <sup>6</sup>Sanofi, Swiftwater, Pennsylvania; <sup>7</sup>Vanderbilt University Medical Center, Nashville, Tennessee

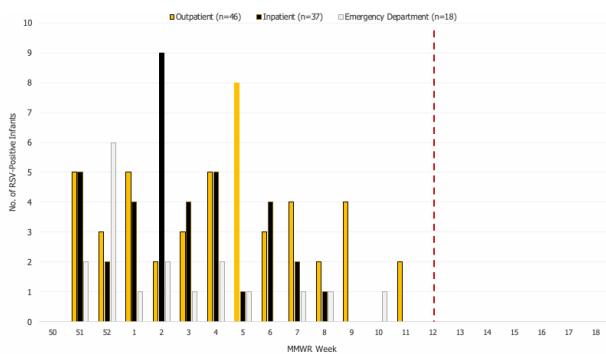
**Session:** P-64. Pediatric Viral Studies (natural history and therapeutic)

**Background.** Respiratory syncytial virus (RSV) accounts for the majority of lower respiratory tract illnesses in hospitalized infants. In the U.S., RSV hospitalizations are well characterized; yet, emergency department (ED) and outpatient (OP) visits are underrecognized. We evaluated the burden of RSV across three distinct healthcare settings during one respiratory season.

**Methods.** From 12/16/19-4/30/20, we conducted a prospective RSV surveillance study among Davidson County, TN infants under one year who presented to an inpatient (IP), ED, or one of four OP clinics with either fever or any upper respiratory (i.e., cough, earache, nasal congestion, rhinorrhea, sore throat) and/or lower respiratory [i.e., wheezing, crackles, rales, diminished breath sounds, shortness of breath (SOB)] symptoms. Demographic and illness history were collected during parental/guardian interviews, followed by medical chart abstraction. Nasal swabs were collected and tested for RSV using Luminex<sup>®</sup> NxTAG RPP. Due to the COVID-19 pandemic, on 3/16/20 enrollment at three of the four OP clinics ceased.

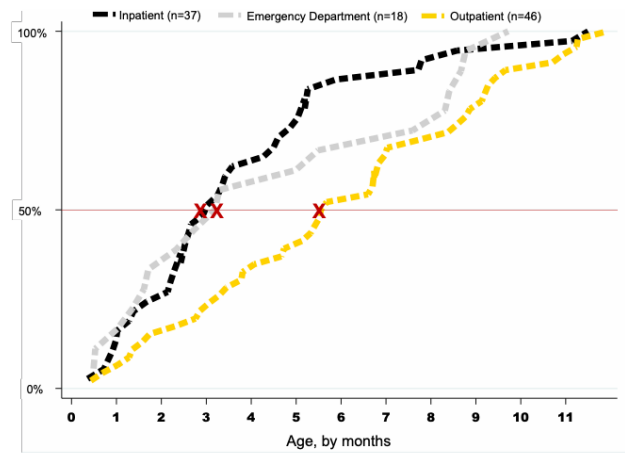
**Results.** A total of 627 infants were screened, of whom 473 (75%) were confirmed eligible, 364 (77%) enrolled, 361 (99%) were tested for RSV of which 101 (28%) were RSV+ (IP=37, ED=18, OP=46) (Figure 1). Compared to RSV-negative subjects, RSV+ subjects were younger (6.6 vs. 4.9 months, p< 0.001), 56% were male and 48% white. By setting, infants in the OP setting were older than those seen in the IP and ED [(p=0.002), Figure 2]. Compared to infants in the OP setting, hospitalized infants were more likely to present with SOB and rhonchi/rales, but less likely to have only upper respiratory symptoms (Figure 3) and be African American (p=0.046). Infants in the IP setting had a higher proportion of clinical RSV diagnostic testing (73%) compared to the ED (39%) and OP (28%) settings (p< 0.001).

Figure 1. Davidson County Infants with RSV by MMWR Week and Healthcare Setting (n=101)



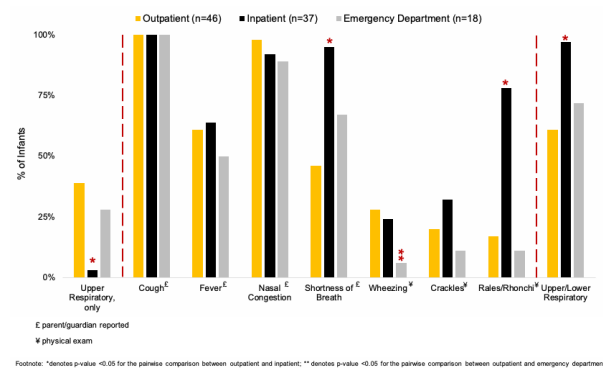
Footnote: Dashed line denotes the Morbidity and Mortality Weekly Report (MMWR) week in which study enrollment was halted in outpatient settings due to COVID-19.

Figure 2. Cumulative Enrollment of Davidson County Infants with RSV by Age in Months and Healthcare Setting (n=101)



Note: X denotes median age in each setting (Inpatient=3.0 months; Emergency Department=3.2 months; Outpatient=5.6 months)

Figure 3. Proportion of Davidson County Infants with RSV Showing each Clinical Symptom, by Healthcare Setting



Footnote: \*denotes p-value <0.05 for the pairwise comparison between outpatient and inpatient; \*\*denotes p-value <0.05 for the pairwise comparison between outpatient and emergency department

**Conclusion.** Two-thirds of RSV+ infants sought care from either an OP or ED setting, with nearly all hospitalized infants presenting with both upper and lower respiratory symptoms. The underutilization of diagnostic testing in the OP settings may underestimate the true burden of RSV. Future studies are essential to document the true prevalence of RSV in order to assess the need and impact of new interventions (e.g., immunizations, antivirals).

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**1407. Cytomegalovirus (CMV) infection in the first year of life in a cohort of infants in rural Guatemala**

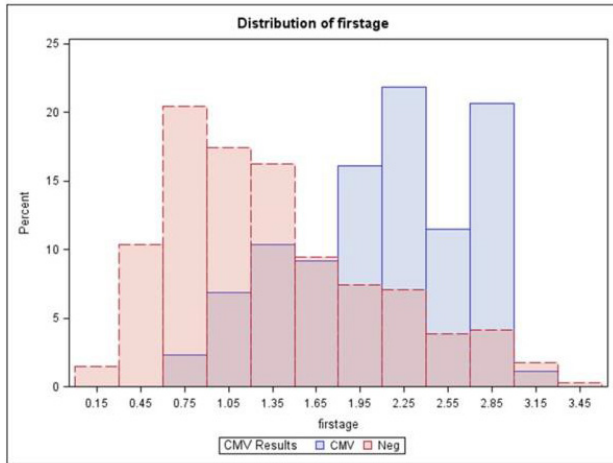
Flor M. Munoz, MD<sup>1</sup>; Molly Lamb, PhD<sup>2</sup>; Jesse Waggoner, MD<sup>3</sup>; Alejandra Paniagua-avila, MD<sup>4</sup>; Desiree Bauer, MSc<sup>2</sup>; Amy Connery, Psy.D. ABPP-CN<sup>5</sup>; Daniel Olson, M.D<sup>5</sup>; Muktha Natrajan, PhD, MPH<sup>6</sup>; Evan Anderson, M.D<sup>6</sup>; Mirella Calvimontes, M.

D<sup>4</sup>; Guillermo Bolanos, M.D<sup>4</sup>; Hana El Sahly, M.D<sup>1</sup>; Edwin J. Asturias, M.D<sup>5</sup>; <sup>1</sup>Baylor College of Medicine, Houston, TX; <sup>2</sup>Colorado School of Public Health, Aurora, Colorado; <sup>3</sup>Emory University, Atlanta, Georgia; <sup>4</sup>Fundacion para la Salud Integral de los Guatemaltecos, Guatemala City, Sacatepequez, Guatemala; <sup>5</sup>University of Colorado, Denver, CO; <sup>6</sup>Emory University Vaccine Center, Atlanta, Georgia

**Session:** P-64. Pediatric Viral Studies (natural history and therapeutic)

**Background.** Little is known about the epidemiology of Cytomegalovirus (CMV) infection in low resource countries. We evaluated the frequency and effects of post-natal CMV infection in infants from a prospective cohort study designed to assess the effects of post-natal Zika on neurodevelopment (ND) in rural Guatemala.

Infants with CMV infection (blue bars) were older compared CMV-negative (red bars) infants.



**Methods:** Infants were evaluated for CMV infection by PCR using urine samples collected at 0-3 months of age. ND testing was conducted by local psychologists using a culturally adapted Mullen Scales of Early Learning (MSEL). We explored associations between CMV infection and microcephaly, neurological, visual and hearing deficits, malnutrition and ND outcomes at 1 year of age.

**Results.** The infant cohort (N = 469) had a mean age at enrollment of 1.5 (SD 0.75) months; 47% were female and 71% were breastfeeding at 1 year. A total of 103 (22%) were CMV positive and the majority of these (97%) were > 4 weeks of age at testing. Infants > 4 weeks of age were more likely to be CMV positive (P < 0.0001) (Figure). Gender was not correlated with CMV positivity. Among children with head circumference (HC) measurements, microcephaly (HC < 2 SD) was present in 9/87 (10.3%) CMV positive and 35/338 (10.4%) CMV negative infants at 0-3 months of age (p = 0.99). Among 438 infants who underwent screening for hearing deficits and a complete ophthalmologic evaluation, none of the CMV positive children had abnormal vision or hearing. Abnormal neurological exams in the first year of life occurred in 50/100 (50%) CMV positive and 166/365 (45.5%) CMV negative infants (p = 0.56). There was no association between CMV infection at 0-3 months and MSEL overall or subdomain scores at 1 year (overall Relative risk (RR) 1.02, 95% CI 0.99-1.05, p=0.16). Malnutrition at 0-3 months (RR: 1.53, 95% CI 0.89-2.66, p = 0.13) and 1 year (RR: 1.10, 95% CI 0.77-1.58, p=0.59) was not associated with CMV infection at 0-3 months.

**Conclusion.** In a cohort of Guatemalan infants, postnatal CMV infection was common (22%) and more likely to occur after the neonatal period. There was no correlation between CMV infection and microcephaly at 0-3 months or at 1 year of age, nor with abnormal nutritional, neurologic, ophthalmologic, hearing or ND deficits at 1 year of age. This is the first epidemiologic report on CMV infection in early life in rural Guatemala.

**Disclosures.** Molly Lamb, PhD, BioFire (Grant/Research Support)

#### 1408. Enterovirus D68 RNA Visualized in the Anterior Horn of the Spinal Cord of a Pediatric Patient with Flaccid Paralysis

Matthew R. Vogt, MD, PhD<sup>1</sup>; Peter Wright, MD<sup>2</sup>; William Hickey, MD<sup>2</sup>; James E. Crowe, Jr, MD<sup>3</sup>; Kelli Boyd, DVM, PhD<sup>3</sup>; <sup>1</sup>UNC Chapel Hill School of Medicine, Nashville, Tennessee; <sup>2</sup>Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire; <sup>3</sup>Vanderbilt University Medical Center, Nashville, Tennessee

**Session:** P-64. Pediatric Viral Studies (natural history and therapeutic)

**Background.** Acute flaccid myelitis (AFM) is a polio-like paralyzing illness of children. AFM incidence is increasing during every other year outbreaks that occur in the United States simultaneously with outbreaks of enterovirus D68 (EV-D68) infection. Demonstrating that EV-D68 directly causes AFM has been challenging due to rare detection of the virus in the cerebrospinal fluid (CSF) of patients despite frequent detection at nonsterile sites. Murine studies have shown that EV-D68 can infect spinal cord anterior horn motor neurons and cause paralysis, similar to poliovirus. However, a key outstanding question is whether EV-D68 causes AFM in humans by direct viral pathogenesis or by indirect host immunopathogenesis.

**Methods.** We investigated the pathogenesis of AFM using tissues from a previously reported case of a 5-year-old boy who presented in fall 2008 with four days of progressive limb and voice weakness followed by incontinence, apnea, and death. He had a CSF pleocytosis of 2094/ $\mu$ L with EV-D68 identified in the CSF by sequencing of the VP1 gene. We designed probes for *in situ* hybridization (ISH) based on this sequence to stain formalin fixed paraffin embedded tissues from his autopsy. For immunohistochemistry (IHC) we used both commercial polyclonal anti-EV-D68 antibodies and our own human monoclonal antibodies that stain virus infected cells *in vitro*. Immunophenotyping was done by IHC.

**Results.** With ISH we identified EV-D68 RNA in the anterior horn of the patient's spinal cord, corresponding to the location of motor neuron cell bodies. This area was highly inflamed, with an infiltrate of lymphocytes and macrophages. Viral RNA was in low abundance, and we could not detect viral surface proteins by IHC. Neither RNA nor viral antigen was detected in the lungs, which had extensive inflammatory infiltrate.

**Conclusion.** Deaths in AFM patients are rare and often distant from initial presentation, but this patient died four days after onset of weakness, allowing us to directly demonstrate that EV-D68 can infect the human spinal cord. Low abundance of virus suggests the virus either reached the spinal cord prior to weakness onset or was cleared rapidly by the immune response. Therefore, both direct viral pathology and immune factors likely contribute to AFM disease in EV-D68 infection.

**Disclosures.** James E. Crowe, Jr, MD, IDBiologics (Board Member, Consultant, Grant/Research Support) Vanderbilt University (Other Financial or Material Support, Inventor on patent related to this abstract)

#### 1409. Genomic Variation Among Respiratory Syncytial Viruses

Christopher S. Anderson, PhD<sup>1</sup>; Yun Zhang, PhD<sup>2</sup>; Anthony Corbett, MS<sup>3</sup>; Chin-Yi Chu, MS<sup>3</sup>; Lu Wang, MS<sup>3</sup>; Xing Qiu, PhD<sup>3</sup>; Mathew McCall, PhD<sup>1</sup>; David Topham, PhD<sup>1</sup>; Tom Mariani, PhD<sup>1</sup>; Edward E. Walsh, MD<sup>1</sup>; Richard Scheuermann, PhD<sup>2</sup>; Mary T. Caserta, MD<sup>3</sup>; <sup>1</sup>University of Rochester, Rochester, New York; <sup>2</sup>J. Craig Venter Institute, La Jolla, California; <sup>3</sup>University of Rochester Medical Center, Rochester, NY

**Session:** P-64. Pediatric Viral Studies (natural history and therapeutic)

**Background.** Respiratory Syncytial Virus (RSV) can be easily classified into two subtypes (A and B) based on the nucleic acid sequence of their genome. Phylogenetic approaches have shown that within both subtypes separate lineages of viruses exist and new lineages continue to emerge. The role these genomic variations play in disease severity during RSV infection is largely unknown.

**Methods.** Next-generation viral RNA sequencing was performed on archived frozen nasal swabs of children infected with RSV in Rochester, NY between 1977-1998. Genomic variation was compared across year-of-isolation, age of host, and inpatient/outpatient status of host. Local RSV genomic variation was compared to variation of publicly available sequences isolated from hosts residing in other parts of the world.

**Results.** A and B subtypes demonstrated significant differences in the genetic sequence and primary-protein structure over time. G-protein was the most variable in both subtypes, but they differed in the number of unique genotypes detected. We found a significant association with disease severity (inpatient/outpatient status) and RSV phylogenetic topology, although the magnitude of the association differed by subtype. Variation in the primary protein structure of RSV viral proteins was also significantly associated with disease severity, but depended on which viral protein, and which subtype, was investigated. Lastly, local RSV genomic and protein-structure variation was similar to what was seen globally during this time period.

**Conclusion.** Overall, both subtypes demonstrated significant genetic change over time and these changes were associated with disease severity. These results suggest that the genetic variability of RSV may affect RSV disease in humans.

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#### 1410. Neonatal Herpes Simplex Virus (HSV) Infection: Is It the Only Pathogen?

Alvaro Dendi, n/a<sup>1</sup>; Ingrith Viviana Hoyos Garcia, MD<sup>2</sup>; Asuncion Mejias, MD, PhD, MSc<sup>3</sup>; Cory T. Hanlon, BS<sup>3</sup>; Pablo J. Sanchez, MD<sup>4</sup>; <sup>1</sup>University of the Republic, Uruguay, Montevideo, Montevideo, Uruguay; <sup>2</sup>Faculty of Medicine, Cali, Cauca, Colombia; <sup>3</sup>Nationwide Children's Hospital, Columbus, Ohio; <sup>4</sup>Nationwide Children's Hospital - The Ohio State University, Columbus, Ohio

**Session:** P-64. Pediatric Viral Studies (natural history and therapeutic)

**Background.** Neonatal HSV infection is associated with substantial morbidity and mortality. Therefore, prompt identification and treatment of infected neonates is paramount. At Nationwide Children's Hospital (NCH), Columbus, OH all neonates admitted in the first 2 weeks (up to 2010) and 4 weeks (since 2010) of age are evaluated for HSV infection in addition to routine bacterial and other viral infections. The frequency of co-infection with HSV and other potential pathogens is not fully known.

**Methods.** Retrospective review of the medical records of infants admitted to NCH with a diagnosis of neonatal HSV infection from 2001 to 2019. Patients less than 6 weeks of age were identified by review of the NCH Virology and Molecular Laboratory results for all positive HSV PCRs obtained from any body site as well as by discharge ICD-9 and ICD-10 codes for HSV infection. Medical records were reviewed for demographic, clinical, laboratory, outcome data, and maternal history of genital HSV lesions at or before delivery. Occurrence of positive bacterial and/or viral co-detection were identified. The data were managed using REDCap electronic data capture tools hosted at NCH.

**Results.** There were 93 infants with neonatal HSV infection (mean age, 9.5 days [IQR, 7-15]; 42%, HSV1; 53%, HSV-2). 32 infants had central nervous system infection