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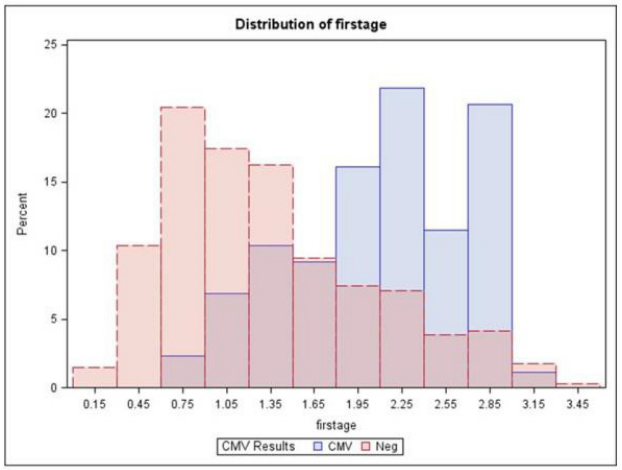
Session: P-64. Pediatric Viral Studies (natural history and therapeutic)

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

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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/μL 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

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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. Phylogenic 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.

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

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

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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