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Session: 184. Late Breaker Oral Abstract Session 2
Friday, October 4, 2019: 2:45 PM

Background. Since 2014 there have been global biennial outbreaks of acute flaccid myelitis (AFM), a rare but severe "polio-like" illness of as yet-unknown etiology primarily affecting children. Enteroviruses (EVs),, especially EV-D68 and EV-A71, have been implicated in association with AFM cases, but proving causality has been difficult as EVs are rarely isolated from cerebrospinal fluid. In addition, early identification of EV-associated AFM is challenging given that the diagnosis is reliant on potentially subjective clinical and radiological criteria with no specific biomarkers described to date.

Methods. We leveraged existing and newly generated data from a clinical CSF metagenomic assay for pathogen identification at University of California, San Francisco (UCSF) to interrogate the host response at the transcriptome level by RNA sequencing (RNA-Seq). These transcriptome RNA-Seq data were used to create statistical classification models to discriminate among viral infections that have been linked to AFM, including EV-D68, EV-A71, West Nile virus, and Powassan virus. The dynamic range of CSF cellularity (0 to $>10^6$ cells/mL), resulting in varying trancriptome coverage, as well as technical variation across samples required the development and validation of novel normalization techniques. In total, we analyzed ~50 CSF samples split into independent training and test sets.

Results. We were able to demonstrate a distinct signature of AFM that was able to predict the virus associated with AFM in blinded test samples with >80% accuracy. The key transcriptional features that best discriminated EV-A71 from EV-D68-associated AFM involved protein targeting, viral transcription, viral gene expression, and translation initiation pathways.

Conclusion. Here we demonstrate a novel approach to diagnosis of AFM that relies on host transcriptional biomarkers from cerebrospinal fluid. In the future, this method might allow earlier diagnosis of AFM to drive appropriate therapies and vaccines and predict patient outcomes, as well as guide research studies on the pathophysiology of EV-associated AFM.

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

LB15. Measles Outbreak in New York State (NYS) Outside of New York City, 2018–2019

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Session: 294. Late Breaker Oral Abstract Session 2
Saturday, October 5, 2019: 1:45 PM

Background. The United States is experiencing one of the largest and longest measles outbreaks since elimination was declared in 2000 and is at risk of losing this status. Most cases occurring in NYS were reported in undervaccinated communities.

Methods. We included all confirmed NYS measles cases (excluding NYC) from outbreak counties from October 1, 2018 to July 25, 2019. We used the CSTE measles case definition requiring an acute febrile rash illness and either laboratory confirmation or direct epidemiologic linkage to a lab-confirmed case. For each case, demographic and clinical characteristics were obtained. A medical record review was completed for those reported to have an encounter at a hospital, emergency department, or urgent care center.

Results. There were 371 cases of measles reported, including 11 internationally imported cases. Most occurred in Rockland county (n = 283); followed by Orange (n = 55), Westchester (n = 18), Sullivan (n = 14) and Greene (n = 1) (Figures 1 and 2). The median age was 5.5 years; 79% of all cases occurred among children younger than 18 years of age (Figure 3). Most cases (79%) had not received any doses of measles vaccine. Of the 371 cases, 263 (71%) were children who had received 0 doses of measles, mumps, rubella vaccine (MMR), 218 (83%) of whom were over 1 year of age (Table 1). There have been no deaths or documented cases of encephalitis. Twenty-eight (8%) patients were diagnosed with pneumonia and 25 (7%) patients were hospitalized. Among 17 hospitalized children, 5 (29%) were admitted to the intensive care unit (ICU) (ages 1 day to 7 years). There were two preterm births at 34 and 25 weeks gestation to women with measles while pregnant. During October 1, 2018–July 31, 2019, providers in outbreak counties vaccinated 72,465 individuals with MMR, a 46% increase from the same period the year prior.

Conclusion. Unvaccinated children were identified as the largest group affected and experienced severe complications; nearly 30% of hospitalized children were admitted to an ICU. These data support the critical need for continued education and outreach on the risks of measles and the value of vaccination to prevent continued circulation in undervaccinated communities and potential further cases of severe disease.

Figure 1. Map of Measles Cases in the New York State outside of New York City, 2018-2019

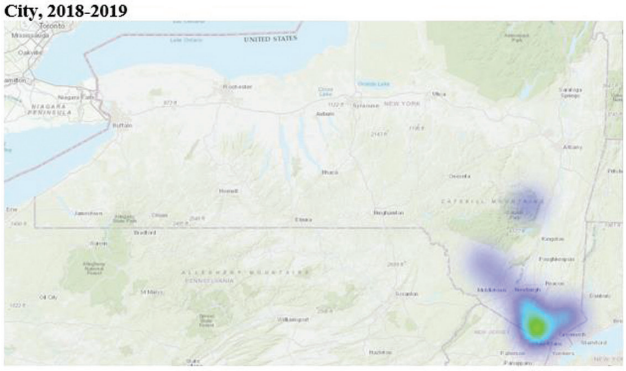

Figure 2: New York State (excluding New York City) Measles Cases by Week and County (by rash onset date), 2018-2019

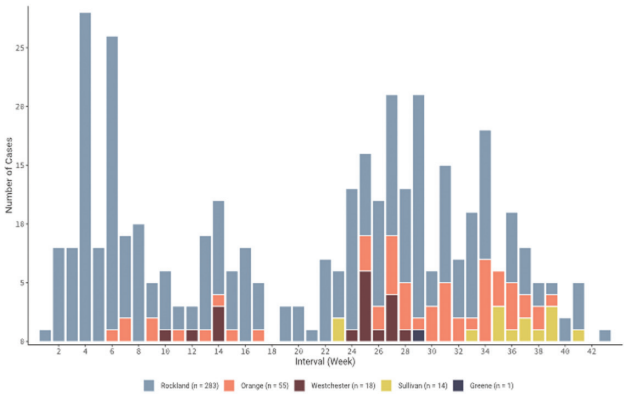

Figure 3: Age Distribution of Confirmed Measles Cases in New York State (excluding New York City), 2018-2019

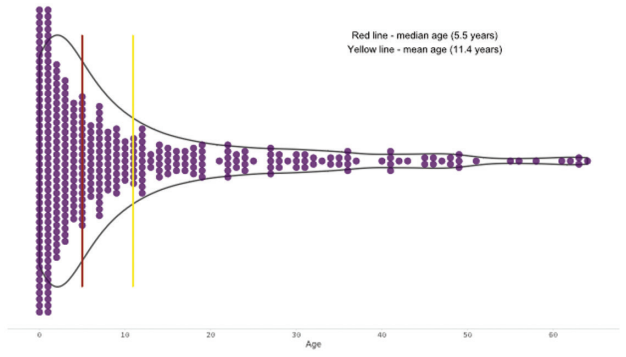

Table 1: Measles Vaccination Status by Age Group in New York State (excluding New York City), 2018-2019

Age Group	# MMR Doses				Total
	0	1	2	Unknown	
< 6 Months	17	0	0	0	**17 (4.6%)**
6 - 11 Months	28	3	0	0	**31 (8.4%)**
1-4 Years	108	13	2	1	**124 (33.4%)**
5-17 Years	110	1	3	6	**120 (32.3%)**
18+ Years	31	3	7	38	**79 (21.3%)**
Total	**294 (79.2%)**	**20 (5.4%)**	**12 (3.2%)**	**45 (12.1%)**	**371**

Disclosures. Kirsten St. George, MAppSc, PhD, Akonni Biosystems (Other Financial or Material Support), ThermoFisher (Grant/Research Support), Zeptometrix (Other Financial or Material Support, royalty generating collaborative agreement); others, no disclosures reported..

LB16. The Role of Adults in the Measles Outbreak in New York State Outside of New York City, 2018–2019

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Session: 294. Late Breaker Oral Abstract Session 2
Saturday, October 5, 2019: 1:55 PM

Background. The United States is experiencing the largest measles outbreak since elimination was declared in 2000, with the majority of cases in NYS reported in undervaccinated communities. The objective of this evaluation was to describe adult measles cases in the NYS measles outbreak outside of New York City (NYC).

Methods. We included all confirmed cases aged ≥18 years in NYS residents (excluding NYC) during October 1, 2018–July 25, 2019 that met the CSTE measles case definition. We defined measles cases attributable to adults as the sum of measles cases among adults and children who contracted disease directly from adults.

Results. Among 371 confirmed measles cases, the median age was 5.5 years (range: 1 day to 64 years); 79 (21%) were in adults, 4 (5%) of whom were born before 1957 (3 unvaccinated and 1 with unknown vaccine status). Among the 75 cases born during or after 1957, 65 (87%) were unvaccinated or had unknown vaccine status, while 3 had one dose and 7 had 2 doses of measles vaccine. Notably, 5 of 11 internationally imported measles cases were adults, and all were unvaccinated or had unknown vaccine status. During the first month of the outbreak, 26 of the 51 (51%) cases were attributable to adults; of the 26, 15 (58%) were in adults and 11 (42%) were in children who acquired infection from adults (Figure 3).

Conclusion. The majority of measles cases occurred in unvaccinated children emphasizing the importance of ongoing and focused efforts on pediatric vaccination. However, measles cases in unvaccinated adults played an important role in both importations and disease transmission early in the outbreak. These data strongly support current recommendations of 1 dose of measles, mumps, rubella vaccine (MMR) for most adults and 2 doses of MMR for adults traveling internationally and at high-risk such as those in outbreak areas, as determined by local/state public health.

Figure 1: Age of Confirmed Measles Cases by Measles Vaccination Status in New York State (excluding New York City), 2018-2019

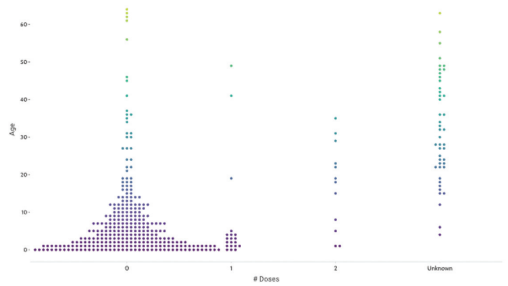


Figure 2: Age of Confirmed Measles Cases by Rash Onset Date Over Time, New York State (excluding New York City), 2018-2019

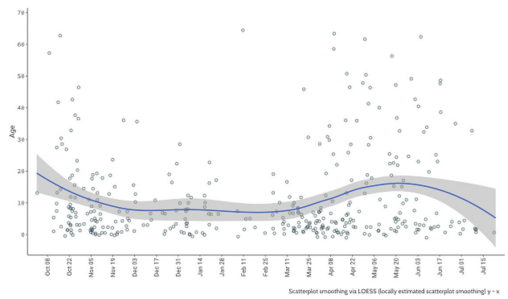
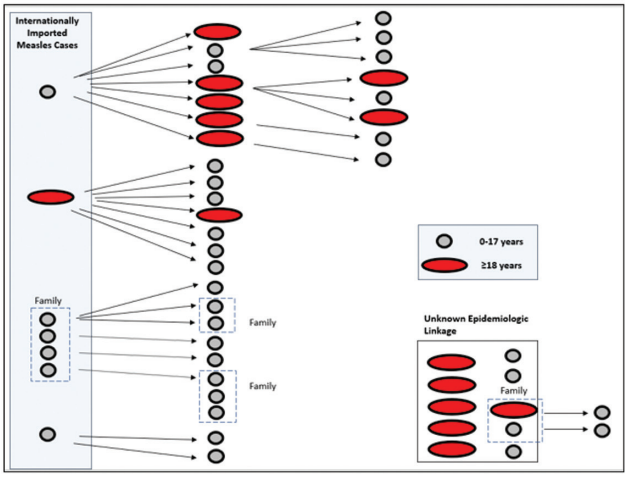


Figure 3. Measles Cases by Age and Epidemiologic Linkage, New York State (excluding New York City), October 2018



Disclosures. Kirsten St. George, MAppSc, PhD, Akonni Biosystems (Other Financial or Material Support), ThermoFisher (Grant/Research Support), Zeptometrix (Other Financial or Material Support, royalty generating collaborative agreement). .

LB17. Randomized Trial to Prevent Congenital Cytomegalovirus (CMV)

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Session: 294. Late Breaker Oral Abstract Session 2
Saturday, October 5, 2019: 2:05 PM

Background. Primary CMV infection during pregnancy carries a high risk of fetal transmission with the potential for severe sequelae. There is no universally accepted method of preventing congenital CMV. Our objective was to evaluate whether CMV hyperimmune globulin (HIG) administered to women with primary CMV during pregnancy reduces congenital infection.

Methods. Multicenter randomized double-masked trial of women with a singleton gestation <24 weeks with primary CMV infection defined by the presence of either CMV IgM and IgG with low avidity or IgG seroconversion, as assessed at a central reference laboratory. Those with presumptive or confirmed evidence of fetal CMV were not eligible. Monthly infusions of HIG (100 units/kilogram) or placebo were given until delivery. The primary outcome was fetal loss or neonatal CMV infection defined as CMV by PCR or culture in urine or saliva within 3 weeks of birth, in amniotic fluid prior to delivery or in postmortem tissue. A sample size of 800 was planned to detect at least 30% reduction in the primary outcome with 90% power and type I error 5%.

Results. From 2012 to 2018, 206,111 pregnant women were screened; 712 (0.35%) had primary CMV infection; of whom, 399 (56%) were enrolled at 17 centers. The trial was stopped for futility at the recommendation of the Data and Safety Monitoring Committee due to a planned interim analysis that revealed complete enrollment was unlikely to demonstrate a significant outcome. Mean gestational age at randomization was 16.2 and 15.6 weeks in the HIG and placebo groups, respectively. Primary outcome data were available for 394 participants (98.7%). The primary outcome rate was 22.7% in the HIG group and 19.4% in the placebo group (relative risk [RR], 1.17; 95% confidence interval [CI], 0.80 to 1.72; p=0.42). Overall, there was no significant difference in the proportion of women with a side effect; however, those receiving HIG had a higher rate of headache ($P = 0.05$) and shaking chills ($P = 0.03$). The rate of preterm birth was 12.2% in the HIG group and 8.3% in the placebo group (RR, 1.47; CI 0.81 to 2.67; $P = 0.2$) (table). No statistical interactions were found in pre-specified subgroup analyses.

Conclusion. CMV HIG was not effective at decreasing risk of congenital CMV infection or fetal death among women with primary CMV infection in early pregnancy.

Primary and Secondary Outcomes				
	HIG (N=206)	Placebo (N=193)	Relative Risk (95% CI)	P Value
	no. (%)			
Primary outcome	46 (22.7)	37 (19.4)	1.17 (0.80 - 1.72)	0.424
Neonatal CMV infection	37	32		
Neonatal death without evidence of CMV	0	0		
Fetal death with evidence of CMV infection	6	3		
Fetal death without evidence of CMV	3	2		
Fetal/neonatal outcomes				
Fetal death	9 (4.4)	5 (2.6)	1.69 (0.58 - 4.97)	0.330
Neonatal death	1	0	-	-
Fetal growth restriction < 5th percentile	21 (10.7)	10 (5.3)	2.01 (0.97 - 4.16)	0.052
Head circumference < 3rd percentile	6 (3.1)	6 (3.2)	0.97 (0.32 - 2.95)	0.956
Maternal outcomes				
Any side effects	81 (39.3)	62 (32.1)	1.22 (0.94 - 1.60)	0.134
Preterm birth < 37 weeks	25 (12.2)	16 (8.3)	1.47 (0.81 - 2.67)	0.200

Disclosures. **Brenna Hughes, MD**, **Merck** (Consultant).