2618. Determination of the Chemical Structure of a Novel Pneumococcal Serotype, 39X

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Background: *Streptococcus pneumoniae* produces a diverse group of capsular polysaccharides (serotypes) that are important for the virulence of the organism and for the serotype-specific prevention of pneumococcal disease. As a consequence of widespread PCV usage and pneumococcal genome plasticity, the distribution of pneumococcal serotypes is changing with an increase in non-vaccine serotypes post-vaccine introduction, a phenomenon known as serotype replacement. Recently, a potentially novel serotype was described and was provisionally named as serotype 39X. Genetic studies suggest that this novel serotype may be a hybrid of serotypes 6C and 39/10A.

Methods: Three 39X strains with the distinct serological and genetic description of the *cps* biosynthetic loci were obtained from the Global Pneumococcal Sequencing project (www.pneumogen.net). Capsular polysaccharide from one (Camb.853/MNZ2334) of the 39X strains was purified by sequential ethanol precipitation followed by ion-exchange chromatography. To detect polysaccharide fractions during purification, an inhibition ELISA assay was developed using factor serum 10d. The chemical structure of the 39X repeating unit was determined using one-dimensional (1D) and 2D nuclear magnetic resonance (NMR).

Results: All three isolates were confirmed to have the 39X genotype by PCR amplification and sequencing of the 39X specific region ($wciN_{6c}$-*wcrO*-$wcrC_{39}$) of the *cps* locus. (Figure 1). The 39X capsule PS fractions were detected during purification and pooled for structural studies (Figure 2). 1D-NMR for 39X showed it to be chemically distinct (Figure 3). 2D-NMR studies revealed that five of the sugar residues in 39X PS are identical to those in 39 PS, except the acetylation (Figure 4). The remaining part of the structure is being investigated.

Conclusion: The 39X capsular PS has a distinct chemical structure in addition to its distinct serologic and genetic properties. Given that serotype 39X is a new serotype, it becomes the 100th pneumococcal serotype. The chemical structure supports the genetic depiction of serotype evolution as a result of recombination between well-characterized and unrelated serotypes. Structural elucidation of the 39X capsule PS will help facilitate our understanding of serotype replacement and vaccine development.

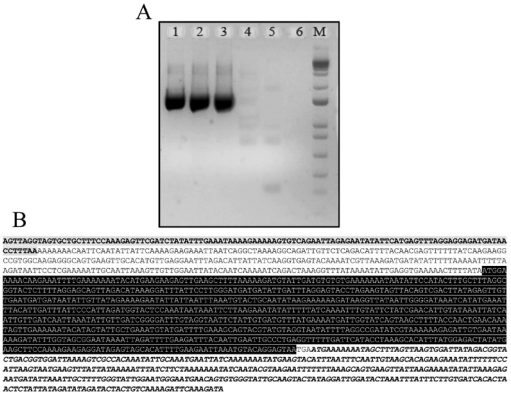

Figure 1. Confirmation of 39X genotype. (A). PCR amplification of $wciN_{6C}$-$wcrO$-$wcrC_{39}$ fragment of *cps* loci. Lane 1: PATH 4346/MNZ2332; Lane 2: Camb.657/MNZ2333; Lane 3: Camb.853/MNZ2334 (Lane 1-3: Serotype 39X); Lane 4: MJC705 (Serotype 6C); Lane 5: SSI/Serotype 39; Lane 6: No template control; M: 100bp marker. **(B).** Sequencing of the amplified PCR product. Gray shaded and bold region indicates $wciN_{6c}$ gene fragment, Black shaded region indicates *wcrO* gene. The sequence in bold and italics represents $wcrC_{39}$ gene fragment.

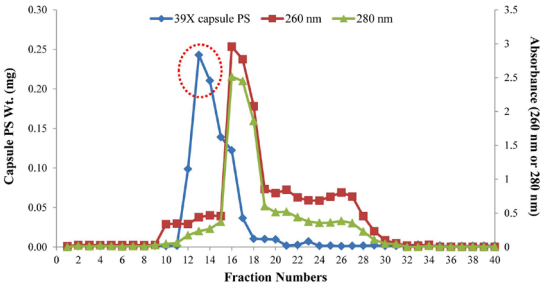

Figure 2. Purification of capsule PS from Camb.853/MNZ2334.
Capsule PS fractions were detected by inhibition ELISA assay after ion exchange chromatography. Absorbance at 260 nm (Red line), and absorbance at 280 nm (Green line) indicates the nucleic acid and protein impurities, respectively. The fractions 13 & 14 encircled were pooled and lyophilized for NMR studies

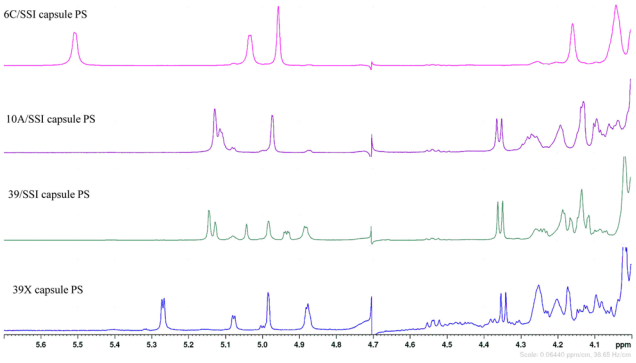

Figure 3. 1H NMR spectra of the anomeric region (4.8 to 5.6 ppm) of serotypes 6C, 10A, 39 and 39X capsular PS. 6C, 39 and 10A capsular PSs were obtained from (Staten's Serum Institute [SSI]). The NMR spectra indicates that 39X capsule PS is chemically distinct from 6C, 10A and 39 capsule PS.

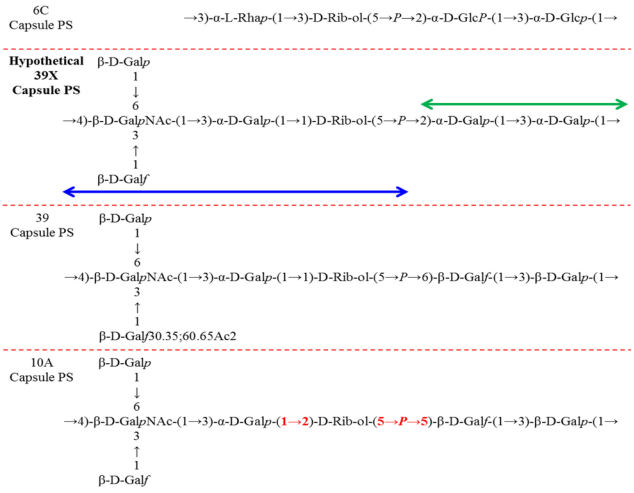

Figure 4. Hypothetical structure of 39X compared to 6C, 39 and 10A structures.
The blue arrow indicates the portion of 39X repeat unit which has been confirmed to be identical to 39 PS, except the acetylation. The green arrow indicates the part of 39X structure being studied. Red color in 10A PS indicates differences from 39 PS.

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2619. Clinical Characteristics and Etiology of Community-Acquired Pneumonia in Children: A Contemporary, Prospective, Multicenter Study in Ohio, 2015–2018

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Background: Worldwide, pneumonia is the leading cause of death in children <5 years of age and the second most common reason for hospitalization in children in the United States and Europe. This study was designed to describe the clinical characteristics and etiology of community-acquired pneumonia (CAP) in children.

Methods: We conducted a prospective, multicenter, observational study of CAP among previously healthy children aged 2 months through 18 years in six children's hospitals in Ohio. Blood, pleural fluid, and nasopharyngeal swabs were collected for pathogen detection by culture and/or molecular diagnostics. Patient clinical management including antibiotic therapy and respiratory support, followed the standard of care at each study site. Follow-up information regarding clinical outcomes was collected via a survey 6–8 weeks after enrollment.

Results: We enrolled 441 children (n = 380, 86% hospitalized) with CAP from 2015 to 2018. Median age was 5 years (IQR: 2.1–8.9y). Intensive care and respiratory support

were required for 15% and 49% of children, respectively. Consolidation and pleural effusion were identified in 26% and 21%, respectively. Among hospitalized children, 99% received antibiotics during hospitalization, and 91% continued antibiotic treatment at discharge. There were no children with any kind of sequelae or deaths from CAP, but 4.4% were readmitted within 30 days after discharge. Pathogens were identified in 64% patients; including pyogenic bacteria in 4%, atypical bacteria in 9%, and viruses in 56%. A total of 18 (4%) children had both bacterial (9 pyogenic and 9 mycoplasma) and viral pathogens. Among children with a virus detected ($n = 245$), 17% had more than one virus. The most commonly detected bacteria were *M. pneumoniae* ($n = 39$) and *S. pneumoniae* ($n = 10$). Rhinovirus was the most common virus detected (RV; $n = 81$, 28%), followed by respiratory syncytial virus (RSV; $n = 75$, 26%).

Conclusion: In this multicenter cohort, the most commonly detected viruses in children with CAP were RV and RSV, and *M. pneumoniae* and *S. pneumoniae* among bacteria. Clinical outcomes in children with CAP were overall good, but there was a high burden of hospitalization and antibiotic use.

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2620. Respiratory Syncytial Virus Rapid Antigen Detection Test, Can It Be Trusted?

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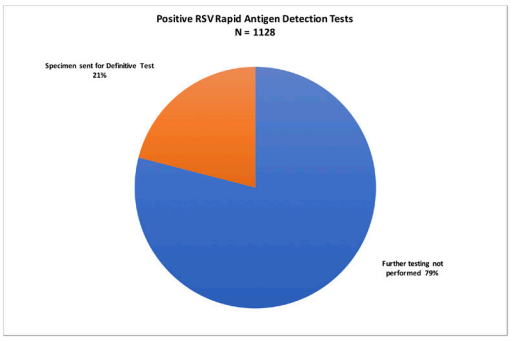
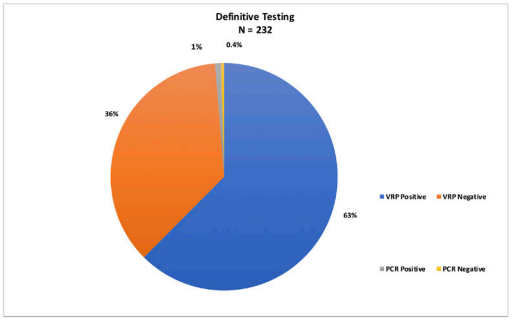
Background: Many emergency departments and urgent care settings use the commonly available Respiratory Syncytial Virus Rapid Antigen Detection Test (RSV RADT) to diagnose children with RSV. We noted discordant results between RADT and definitive testing. Our study looked at the positive predictive value (PPV) and the false discovery rate (FDR) of the RSV RADT at our facility.

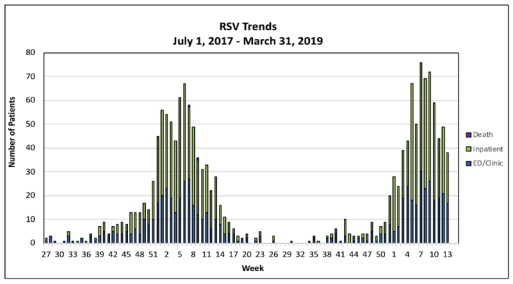
Methods: We pro- and retrospectively reviewed all patients with positive RSV RAPD tests from July 1, 2017 through March 31, 2019. The test utilized was the QuickVue® RSV Test Kit (QUIDEL Corp, CA, USA), which detects the viral fusion protein present in RSV. Of the tests performed, we chose patients who had definitive testing with either a direct fluorescent antibody (DFA) or a polymerase chain reaction (PCR). We then calculated the PPV as well as the FDR of the RSV RADT during the total interval period, as well as off-season periods (April 1 through October 31) and in-season periods (November 1 through March 31).

Results: During the study period there were 1128 RSV RADT tests performed, of which 232 had definitive testing with either DFA or PCR (Figures 1 and 2). We found the overall PPV during the study period was 63.3%. During the off-season 30 positive RSV RADT received definitive testing, of which 6 were positive, which yields a PPV of only 20%. In season, 202 RSV RADT received additional testing with 141 positive for RSV. The PPV was 69.8%. The FDR correlated with 36.7% throughout the entire studied period, 80% during the off-season and 30.2% during in-season. As expected, the PPV was higher during times of higher prevalence (Figure 3).

Conclusion: Based on our results, utilization of the RSV RADT during time of low prevalence yields a high false detection rate and should therefore be discouraged. The use during times of high prevalence yields only modest results and is unlikely to aid in clinical decision-making. Our results differ from those published by the manufacturer (PPV 84%), and may reflect differences in sample collection in the acute care setting.







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

2621. Influence of HIV Exposure Status on Carriage Rates and Density of *Streptococcus Pneumoniae* and *Pneumocystis Jirovecii* in Zambian Children

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Background: Low rates of mother to child HIV transmission in Zambia, translates into a high number of children who are HIV exposed but uninfected (HEU) who have increased mortality and morbidity when compared with children HIV unexposed and uninfected (HUU). We performed a secondary analysis on The Pneumonia Etiology Research in Child Health (PERCH), a case–control study focused on identifying the etiologies of pediatric pneumonia including two pathogens, *Streptococcus pneumoniae* and *Pneumocystis jirovecii* in Zambian children to evaluate if HIV exposure status influences carriage rates and density for these pathogens.

Methods: Children ages 1–59 months were enrolled as cases if they met the World Health Organization (WHO) definition of severe or very severe pneumonia. Controls did not have a diagnosis of pneumonia and were matched by age and HIV status to cases. Each case and control had a nasopharyngeal (NP) swab and an oropharyngeal (OP) swab specimen. A multiplex real-time polymerase chain reaction (PCR) assay was used to test the NP/OP specimens for *S. pneumoniae* and *P. jirovecii*. A density of $\log_{10}$ copies/mL in microbiology confirmed cases compared with controls was used to define positive infection with *S. pneumoniae* and *P. jirovecii*.

Results: The highest *S. pneumoniae* carrier rates were seen in HIV unexposed controls and the lowest carrier rates seen in HIV-infected controls. HIV-infected children who were *S. pneumoniae* carriers and were classified as controls had the highest *S. pneumoniae* density of all groups. Overall, the HIV-infected group had the highest *S. pneumoniae* density rates. There was minimal variation in the *S. pneumoniae* density of those in the HIV exposed and HIV unexposed. *P. jirovecii* was present only in 31% of HIV-infected cases and 7% of the same group controls. HIV exposed cases had half the carrier rates of their counterparts in the HIV-infected group, but the *P. jirovecii* carriage rates were the same as the carriage rates in HIV-infected controls. The *P. jirovecii* carriage density in HIV-infected and HIV-exposed cases was similar.

Conclusion: HIV exposure status in children can be a predictor factor in *S. pneumoniae* and *P. jirovecii* carriage and density. The results of our analysis could potentially explain the high rates of pneumonia in children exposed to HIV but uninfected. Our findings open the door to more in-depth studies about the immunological status in children exposed to HIV but uninfected.

Table 1. Demographics of study participants by (A) case-control and (B) HIV-status.

A.

	Total (N=1154)	Case (N=555)	Control (N=599)	p-value
Infant demographics				
Age in months, mean (SD)	9.6 (10.7)	8.4 (9.6)	10.8 (11.5)	< 0.01
Male	602 (52%)	295 (47%)	307 (49%)	0.56
HIV-Status				0.12
Unexposed	702 (62%)	332 (61%)	370 (63%)	
Exposed, uninfected	271 (24%)	123 (23%)	148 (25%)	
Infected	165 (14%)	91 (17%)	74 (13%)	
Infant birth outcomes & nutritional status				
Birthweight in grams, mean (SD)	2940 (571)	2944 (649)	2937 (490)	0.83
Low birthweight (<2500 g)	1104 (100%)	527 (100%)	579 (100%)	-
Preterm	69 (6%)	28 (5%)	41 (7%)	0.24
Stunted	435 (38%)	255 (47%)	180 (30%)	< 0.01
Wasted	161 (14%)	115 (22%)	46 (8%)	< 0.01
Protein Deficient	275 (24%)	183 (33%)	92 (15%)	< 0.01

B.

	Total (N=1154)	Unexposed (N=702)	Exposed, uninfected (N=271)	Infected (N=165)	p-value
Infant demographics					
Age in months, mean (SD)	9.6 (10.7)	9.6 (10.4)	7.3 (8.7)	13.2 (13.3)	< 0.01
Male	602 (52%)	329 (47%)	147 (54%)	83 (50%)	0.04
Cases	555 (48%)	332 (47%)	123 (45%)	91 (55%)	0.12
Infant birth outcomes & nutritional status					
Birthweight in grams, mean (SD)	2940 (571)	2985 (537)	2896 (630)	2854 (610)	0.01
Low birthweight (<2500 g)	1104 (100%)	674 (100%)	262 (100%)	154 (100%)	-
Preterm	69 (6%)	29 (4%)	24 (9%)	15 (9%)	< 0.01
Stunted	435 (38%)	231 (33%)	58 (37%)	101 (62%)	< 0.01
Wasted	161 (14%)	70 (10%)	41 (16%)	46 (29%)	< 0.01
Protein Deficient	275 (24%)	127 (18%)	59 (22%)	85 (52%)	< 0.01

Table 2. PCR-determined carriage rates and densities for S. pneumoniae and P. Jirovecii by case-control and HIV status

		HIV-Infected		HIV-Exposed		HIV-Unexposed	
		Case	Control	Case	Control	Case	Control
S. pneumoniae	% PCR-positive (N)	79% (72)	72% (53)	73% (90)	77% (114)	78% (260)	82% (304)
	Median density (IQR) (10^3 copies/mL)*	15.8 (0.6-66.4)	15.0 (2.36-48.2)	4.7 (0.2-26.9)	5.7 (0.4-26.8)	3.6 (0.3-25.0)	4.6 (0.6-20.5)
P. Jirovecii	% PCR-positive (N)*	31% (28)	7% (5)	15% (19)	7% (10)	10% (32)	12% (45)
	Median density (IQR) (10^3 copies/mL)†	63.9 (11.4-206.3)	0.6 (0.6-3.0)	20.9 (3.4-254.4)	0.7 (0.3-7.4)	4.8 (0.5-16.8)	2.6 (1.0-7.0)

*: $p < 0.05$ by Chi square test; †: $p < 0.05$ by Kruskal-Wallis test