

for American Indian Health, Baltimore, Maryland; ⁴Pfizer, Inc., Bowie, Maryland; ⁵Pfizer, Pearl River, New York; ⁶Pfizer Vaccines, Collegeville, Pennsylvania

Session: 244. Bacterial Respiratory Infections
Saturday, October 5, 2019: 12:15 PM

Background. Native Americans experience a high burden of community-acquired pneumonia (CAP). Thirteen-valent pneumococcal conjugate vaccine (PCV13) was introduced for adults ≥65yrs in 2014. Data on CAP etiology can guide prevention and treatment.

Methods. We enrolled adults hospitalized with CAP and age-group-matched non-hospitalized controls on Navajo and White Mountain Apache tribal lands. Nasopharyngeal/oropharyngeal (NP/OP) swabs from cases and controls were tested by multiplex PCR for respiratory pathogens. Urine from cases and controls was tested for pneumococcus (Sp) by conventional (BinaxNOW) and serotype-specific urine antigen detection (UAD) for 24 serotypes (PCV13 types plus 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F). Blood culture and chest radiographs (CXRs) were obtained from cases at the provider's discretion. Radiographic pneumonia was determined by clinical interpretation of CXRs.

Results. From March 2016 to March 2018, we enrolled 580 CAP cases with CXR confirmation and 411 controls. Positive blood culture was identified in 42/483 (9%), of which 29 (69%) were Sp. Sp was detected in 164/572 (29%) cases (table). Of 125 cases with serotype information available, serotypes 3 (n = 35; 28%) 8 (n = 19; 15%) and 20 (n = 15; 12%) were the most common. Among 53 Sp cases aged ≥65 years, 26 (49%) were PCV13-type. Compared with blood culture, UAD was 100% sensitive and 100% concordant (n = 24). Viruses were detected by NP/OP PCR in 43% of CAP cases and 18% of controls. Influenza A, parainfluenza type 3, rhinovirus, and RSV were statistically significantly associated with case status. Among 263 cases in whom all diagnostic tests were collected, 63% had a pathogen detected: bacteria alone in 19%, viruses alone in 23%, and both bacterial and viral infection in 22%. Bacterial causes outnumbered viral causes when adjusting for virus detection in the control population.

Conclusion. Pneumococci were the most common etiology identified among Native American adults with CAP. UAD improved detection of pneumococcal CAP. Respiratory viruses also contributed substantially to CAP burden. Broader prevention strategies, including new vaccines, are required to prevent viral pneumonia and pneumococcal pneumonia caused by serotypes not contained in currently-available vaccines.

Table. Pneumococcal test results in cases hospitalized with CAP and controls

		Cases with ≥1 pneumococcal test		
		≥18 years N=572	18-64 years N=274	≥65 years N=298
		n(%)	n(%)	n(%)
Total Culture+		29 (5.1)	19 (6.0)	10 (3.4)
Total UAD+		120 (21.0)	71 (25.9)	49 (16.4)
Total BinaxNOW+		102 (17.8)	52 (19.0)	50 (16.8)
Positive by any		164 (29.4)	87 (31.8)	77 (25.8)
Serotype available ¹		125 (76.2)	72 (82.8)	53 (68.8)
PCV13-type ²		49 (8.6)	23 (8.4)	26 (8.7)
Non-PCV13 UAD type ³		72 (12.6)	48 (17.5)	24 (8.1)
Non-PCV13 type		79 (13.8)	50 (14.6)	29 (9.7)
		Controls ⁴		
		≥18 years N=393	18-64 years N=185	≥65 years N=208
		n(%)	n(%)	n(%)
Not done	+	15 (3.8)	6 (3.2)	9 (4.3)
Not done	-	0 (0.0)	0 (0.0)	0 (0.0)
Not done	+	10 (2.5)	2 (1.1)	8 (3.8)

CAP: community-acquired pneumonia; UAD: urine antigen detection assay

¹Among those positive for *S. pneumoniae* by any test

²Three cases were counted as both PCV13-type and non-PCV13 UAD type / non-PCV13 type because they had both a PCV13-type and a non-PCV13-type serotype detected by UAD.

³Serotypes 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F

⁴Excludes 18 controls missing BinaxNOW and UAD results.

Disclosures. All authors: No reported disclosures.

2214. Comparison of Cefepime-Zidebactam (WCK 5222), Ceftazidime-Avibactam, and Ceftolozane-Tazobactam Tested Against Gram-Negative Organisms Causing Pneumonia in United States Hospitals in 2018

Helio S. Sader, MD, PhD¹; Cecilia G. Carvalhaes, MD, PhD¹; Rodrigo E. Mendes, PhD¹; Mariana Castanheira, PhD¹; Robert K. Flamm, PhD²; ¹JMI Laboratories, North Liberty, Iowa; ²United States Committee on Antimicrobial Susceptibility Testing (USCAST), North Liberty, Iowa

Session: 244. Bacterial Respiratory Infections
Saturday, October 5, 2019: 12:15 PM

Background. Zidebactam (ZID) is a bicyclo-acyl hydrazide antibiotic with a dual mechanism of action: selective Gram-negative PBP2 binding and β-lactamase inhibition. We evaluated the frequency and antimicrobial susceptibility (S) of Gram-negative bacilli (GNB) isolated from patients with pneumonia in US hospitals.

Methods. All 3,086 clinical isolates were consecutively collected from patients hospitalized with pneumonia (1/patient) in 29 US medical centers in 2018, and the GNB (n = 2,171) were S tested against cefepime (FEP)-ZID (1:1 ratio) and comparators by reference broth microdilution methods. The FEP S breakpoint of ≤8 mg/L (CLSI, high dose) was applied to FEP-ZID for comparison purposes. An FEP-ZID S breakpoint of ≤64 mg/L has been proposed for non-fermentative GNB based on pharmacokinetic/pharmacodynamic target attainment and was applied. *Enterobacteriales* (ENT) isolates were screened for β-lactamase genes by whole-genome sequencing.

Results. GNB represented 70.3% of the collection, and the most common GNB were *P. aeruginosa* (PSA; 34.9% of GNB), *K. pneumoniae* (10.9%), *E. coli* (9.7%), *S. marcescens*

(7.7%), and *S. maltophilia* (XM; 6.4%). FEP-ZID was highly active against PSA (MIC_{50/90} 2/8 mg/L; 98.8% and 99.9% inhibited at ≤8 and ≤16 mg/L, respectively; highest MIC, 32 mg/L), including resistant subsets (table). Among comparators, colistin (99.6% S), ceftazidime-avibactam (CAZ-AVI; 95.2% S), and ceftolozane-tazobactam (C-T; 94.5% S) were the most active compounds against PSA. FEP-ZID inhibited all ENT at ≤4 mg/L, including ESBL-producers (MIC₉₀ 0.25 mg/L) and carbapenem-resistant ENT (MIC₉₀ 4 mg/L). The most active comparators against ENT were CAZ-AVI (99.9% S), amikacin (98.5% S), and meropenem (MEM; 98.3% S). FEP-ZID inhibited 75.0% and 97.9% of XM isolates at ≤8 and ≤16 mg/L, respectively (highest MIC, 64 mg/L). The only other compounds active against XM were co-trimoxazole (MIC_{50/90} ≤0.12/2 mg/L; 95.7% S) and levofloxacin (MIC_{50/90} 1/2 mg/L; 70.7% S). FEP-ZID inhibited 71.0% and 98.9% of *A. baumannii* isolates at ≤8 and ≤64 mg/L, respectively.

Conclusion. FEP-ZID showed potent *in vitro* activity against GNB causing pneumonia in US hospitals and may represent a valuable therapeutic option for these difficult-to-treat infections

Organism (no. tested)	MIC ₅₀ (mg/L) / % Susceptible (CLSI)				
	FEP-ZID ^a	CAZ-AVI	C-T	PIP-TAZ	MEM
<i>P. aeruginosa</i> (757)	2 / [98.8/100.0]b	2 / [95.8]	1 / 94.5	8 / 75.2	0.5 / 74.4
MEM-NIS (194)	4 / [95.4/100.0]b	4 / 84.5	2 / 82.9	32 / 41.2	8 / 10.0
MDR (186)	4 / [95.2/100.0]b	4 / 81.20	2 / 79.7	64 / 23.1	8 / 25.8
XDR (119)	8 / [92.4/100.0]b	8 / 74.8	2 / 70.1	128 / 8.4	16 / 10.9
<i>Enterobacteriales</i> (1,012)	0.06 / [100.0]b	0.12 / 99.9	0.5 / 90.9	2 / 87.9	0.03 / 98.3
<i>K. pneumoniae</i> (236)	0.03 / [100.0]b	0.12 / 100.0	0.5 / 93.3	4 / 89.8	0.03 / 95.8
<i>E. coli</i> (210)	0.03 / [100.0]b	0.12 / 100.0	0.25 / 97.2	2 / 94.3	≈0.015 / 99.5
<i>S. marcescens</i> (166)	0.06 / [100.0]b	0.25 / 100.0	0.5 / 94.0	2 / 91.6	0.06 / 98.2
<i>S. maltophilia</i> (140)	4 / [75.0/100.0]b	32 / [31.4]c	>16 / [12.9]c	>128 / [0.0]c	>32 / [2.1]c
<i>A. baumannii</i> (53)	4 / [71.0/98.9]b	8 / [60.2]c	2 / [63.0]c	4 / 57.0	0.5 / 63.4

a. % inhibited at the ≤32/64 mg/L; b. % inhibited at ≤8 mg/L; c. % inhibited at the *P. aeruginosa* susceptible breakpoint (CLSI) for comparison purpose. MDR, multidrug-resistant; XDR, extensively drug resistant.

Disclosures. All authors: No reported disclosures.

2215. Diarrheal Illness as a Risk Factor for Subsequent Respiratory Infection Among Women and Infants in Nepal

Kira L. Newman, MD, PhD¹; Kathryn Gustafson¹; Janet A. Englund, MD²; Subarna Khatri, MBBS³; Stephen LeClerq, MPH, BA³; James Tielsch, PhD, MA⁴; Joanne Katz, ScD⁵; Helen Y. Chu, MD, MPH¹; ¹University of Washington, Seattle, Washington; ²Seattle Children's Hospital/University of Washington, Seattle, Washington; ³Johns Hopkins, Kathmandu, Bagmati, Nepal; ⁴The George Washington University, Washington, DC

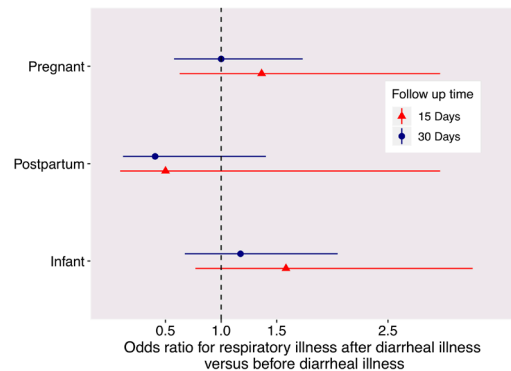
Session: 244. Bacterial Respiratory Infections
Saturday, October 5, 2019: 12:15 PM

Background. Globally, diarrheal and respiratory infections are responsible for nearly one-quarter of deaths in children under 5 years old. Historically these diseases have been studied separately; recent evidence suggests that preceding diarrheal disease may be a risk factor for subsequent respiratory illness. We sought to identify whether diarrhea was associated with subsequent respiratory illness in adult women and infants in Nepal.

Methods. We used data from a community-based, prospective randomized trial of maternal influenza immunization of pregnant women and their infants conducted in rural Nepal from 2011 to 2014. Diarrhea episodes were defined as at least three self-reported watery bowel movements per day for one or more days. Respiratory illness episodes were defined as the presence of fever with an additional respiratory symptom. Diarrhea and respiratory illness episodes were identified through longitudinal household-based weekly symptom surveillance. A case-crossover design was used to determine whether risk of respiratory infection was increased in the 30 days following a diarrhea episode compared with the 30 days prior.

Results. Of 3,693 women in the study and their 3,646 infants, 525 (14.2%) women experienced one or more episodes of diarrhea during pregnancy, 226 (9.4%) women experienced one or more episodes of diarrhea after pregnancy, and 342 (9.4%) infants had one or more episodes of diarrhea. The incidence of respiratory episodes during the exposure and control periods was approximately 2-5% in adults and 8-10% in infants. Preceding diarrhea was not significantly associated with respiratory infection in adult women or infants. There was a slight trend toward greater incidence of diarrhea during the exposure period among infants (Figure 1), but it was not statistically significant. These results held after a sensitivity analysis limiting follow-up time to 15 days before and after diarrhea episode.

Conclusion. In this study of pregnant and postpartum women and their infants in Nepal, diarrheal illness was not a significant risk factor for subsequent respiratory illness.



Disclosures. All authors: No reported disclosures.