Conclusion. Vector control methods focusing on prevention must be implemented to avoid epidemics of WNV if high temperature is leading to an unusual drought especially at the risk areas, such as Texas and California. However, high temperature with moist spell anomalies in the south central region showed a negative influence on WNV outbreak.

Figure 1. The CCA ordination is shown the relationships between WNV human cases and climatic variables for the 32 States of the United States in 2010. The circles represent south central (left) and northern Great Plains (right) regions.

Disclosures. All authors: No reported disclosures.

693. Congenital Zika Syndrome: Assessing the Fatality Rate Since the 2015 Zika Outbreak. Nilson N. Mendes Neto, MD1; Jessika Maia, MD2; Igor Thiago Queiroz, MD, PhD1; Marcelo Rodrigues Zacarim, MD, MS1; Maria Goretti Lins, MD3; A. Desiree Labeaud, MD, MS4 and David Aronoff, MD, FIDSA5; 1Extension Center, University of California-Davis, Davis, California; 2Medical School, Hospital e Heliocentro de Minas, Belo Horizonte – RN, Brazil; 3HUOL, Natal – RN, Brazil; 4Universidade Potiguar, Natal, Brazil; 5Harvard Medical School, Boston, MA; 6Hospital Infantil Varela Santiago, Natal, Brazil; 7Pediatric Infectious Diseases, Stanford University, Stanford, California; 8Medical, Vanderbilt University School of Medicine, Division of Infectious Diseases, Nashville, Tennessee

Session: 66. Public Health: Epidemiology and Outbreaks

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Background. Many studies have demonstrated a causal link between Zika virus (ZIKV) infection, microcephaly (MCP) and other congenital abnormalities (CA). This study aimed to determine the perinatal case fatality rate in cases of Congenital Zika Syndrome (CZS) in the Rio Grande do Norte State (RN), a Brazilian Northeast State highly impacted by the Zikavirus outbreak.

Methods. A cross-sectional study was conducted using data obtained through the State Health Department (SHD) for cases of MCP and CA in Rio Grande do Norte from April 2015 to December 31, 2017. Definition of perinatal period: commences at 22 completed weeks (154 days) of gestation and ends seven completed days after birth. Perinatal case fatality rate is defined as the number of deaths as a fraction of the number of sick persons with a specific disease (>100).

Results. During the study period, there were 519 cases of MCP and others CA notified in RN, of which 150 were confirmed and 126 remain under investigation. The remaining 243 cases have been ruled out by presenting normal exams or due to presenting microcephaly by non-infectious causes. Of the total confirmed cases, 30.0% (45/150) died after birth or during pregnancy: 64.4% (29/45) of confirmed deaths had ZIKV by serological tests (Laboratory and imaging). Due to the high rate of lethality, findings predict an increase in the infant mortality rate in areas endemic for arboviruses. Because the severe neurological complications caused by CZS, it is likely to pose a substantial burden on public spending on healthcare. This study may be used to better describe the congenital Zika syndrome, its prognosis and natural history.

Disclosures. All authors: No reported disclosures.

694. The CAGE Study: Prevalence of Acute Gastroenteritis and Enteric Virus Infection in the Community. Mark A Schmidt, PhD, MPH1; S. Bianca Salas, MPH1; Vladimir Yamshchikov, PhD2; Holly Groom, MPH1; Gabriela Rosales, MS1; Judy Donald, MS2; Zach Marsh, MPH1; Rachel Burke, PhD, MPH1; Claire Mattison, MPH1; Allison Naleway, PhD1 and Aron J. Hall, DVM, MS(Phy),3; 1Kaiser Permanente Center for Health Research, Portland, Oregon; 2Oregon State Public Health Laboratory, Hillsboro, Oregon; 3Centers for Disease Control and Prevention, Atlanta, Georgia

Session: 66. Public Health: Epidemiology and Outbreaks

Thursday, October 4, 2018: 12:30 PM

Background. There are currently limited data about the occurrence and characteristics of sporadic acute gastroenteritis (AGE). In this study, we sought to (1) estimate the average point prevalence of AGE over a 1-year period; (2) describe health-seeking behaviors among those with AGE; and (3) calculate the proportion of stool samples testing positive for enteric viral pathogens.

Methods. Starting in October 2016, we recruited 52 weekly, age-stratified, random samples of Kaiser Permanente Northwest members to complete an online survey and, for a subset of participants, to submit a stool specimen. The survey included questions about the occurrence of vomiting and/or diarrhea within the previous 30 days and, for those reporting AGE, related health-seeking behaviors. Collected stool samples were tested for norovirus, astrovirus, sapovirus, and rotavirus by RT-qPCR.

Results. We received a total of 3,483 surveys from eligible participants, 417 (12%) of whom reported having had AGE symptoms (Figure 1). Of these, 70 (17%) sought related medical care across a spectrum of clinical encounter types (Figure 2). We also received a total of 531 stool samples, 74 from symptomatic and 457 from asymptomatic individuals. Among them, we detected norovirus in 12% and 3% of samples (P = 0.0005), respectively; astrovirus and sapovirus in 1% of samples in each group; and rotavirus in 8% and 7% of samples, respectively.

Conclusion. Our findings of AGE within the community are consistent with previous estimates using models of medically attended AGE occurrence and reported rates of health-seeking behavior. The prevalence of enteric viral infection among people in the community without AGE was generally low. These data can be used to generate age-stratified incidence estimates of community AGE and specifically that associated with enteric viral pathogens. Such disease burden data are needed to guide the development, targeting, and anticipated impacts of interventions, such as vaccines.

Disclosures. M. A. Schmidt, Takeda Vaccines, Inc.: Investigator, Research grant. S. B. Salas, Takeda Vaccines, Inc.: Investigator, Research grant. H. Groom, Takeda Vaccines, Inc.: Investigator, Research grant. G. Rosales, Takeda Vaccines, Inc.: Investigator, Research grant. J. Donald, Takeda Vaccines, Inc.: Investigator, Research grant. A. Naleway, Takeda Vaccines, Inc.: Investigator, Research grant.

695. Regional and Longitudinal Mapping of Escherichia coli Antibiotic Susceptibility. Laurel Legenzna, PharmD, MS1; Susanne Barnett, PharmD2; Jim Lacy, MS3; Natalee Desotell, MS1; Andrea Eibergen, BS Candidate1 and Warren Rose, PharmD, MPH1; 1Pharmacy Practice Division, University of Wisconsin School of Pharmacy, Madison, Wisconsin; 2State Cartographer’s Office, University of Wisconsin-Madison Department of Geography, Madison, Wisconsin; 3Yale School of Public Health, New Haven, Connecticut; 4School of Pharmacy, University of Wisconsin-Madison, Madison, Wisconsin

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Background. Antimicrobial resistance (AMR) is a serious threat to global health with local implications. AMR varies regionally; however, limited tools are available to aid practitioners in appropriate antibiotic selection based on statewide antimicrobial susceptibilities. The objective of this study was to map E. coli antibiotic susceptibility regionally and longitudinally in Wisconsin.

Methods. Antibiograms from 2009, 2013, and 2015 were collected from health systems, hospitals, and clinics in Wisconsin, resulting in 218 antibiograms representing 201,091 Gram-negative isolates. E. coli antibiotic susceptibility percentages were weighted by number of isolates and aggregated by county per year.

Results. Spatial interpolation methods (inverse distance weighted, Kriging) were tested by both county center points and facility geocode where available. Susceptibility data for clinically relevant urinary tract infection antibiotics were interpolated to create geographic visualizations of AMR in Wisconsin. Antibiotics included amoxicillin, trimethoprim/sulfamethoxazole, ciprofloxacin, nitrofurantoin, ampicillin, ampicillin/sulbactam, levofloxacin. The interpolation extends to the furthest health system point
in each direction and is presented within state boundaries. Facility geocodes were masked from public display for confidentiality. City names were added for orientation. The mapping depicts regional differences, such as 2015 ampicillin susceptibilities ranging 55–64% (Figure 1). The maps provide a preliminary susceptibility prediction in areas where no AMR data were available. Average susceptibilities were compared across 2009, 2013, and 2015 to map areas with the highest rates of AMR change.

**Conclusion.** The described mapping provides a novel visualization of AMR across Wisconsin. The maps created will be utilized in continued efforts to improve the functionality of AMR data in clinical practice to optimize antimicrobial choice.

![Interpolated Wisconsin Escherichia coli susceptibility to ampicillin](image)

**Figure 1: Interpolated Wisconsin Escherichia coli susceptibility to ampicillin**

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

696. **Mechanism of Cefiderocol high MIC mutants obtained in non-clinical FoR studies**

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**Session: 67. Resistance Mechanisms: Gram-Negative**

**Background.** Cefiderocol (S-649266, CFDC) is a novel siderophore cephalosporin with activity against a wide variety of Gram-negative bacteria including carbapenem-resistant strains. We previously reported that CFDC is efficiently transported into *Pseudomonas aeruginosa* via iron transporter FiuA. In this study, we examined frequency of resistance of *P. aeruginosa* to CFDC, and investigated the resistance mechanisms of appeared colonies.

**Methods.** Frequency of resistance (FoR) was determined by plating an overnight culture of *P. aeruginosa PAO1* on Mueller–Hinton Agar containing 4× or 10×MIC of CFDC or ceftazidime (CAZ). Appeared colonies were analyzed by whole-genome sequencing (WGS) to identify genomic mutations. The mRNA expression was determined on periplasmic extracts with varying concentrations of nacubactam and expression of outer membrane protein was analyzed by SDS–PAGE and TOF/MS and expression of pvdS and fecA were determined via iron transporter FiuA. In this study, we examined frequency of resistance of *P. aeruginosa* to CFDC, and investigated the resistance mechanisms of appeared colonies.

**Results.** Frequency of resistance (FoR) was determined by plating an overnight culture of *P. aeruginosa PAO1* on Mueller–Hinton Agar containing 4× or 10×MIC of CFDC or ceftazidime (CAZ). Appeared colonies were analyzed by whole-genome sequencing (WGS) to identify genomic mutations. The mRNA expression was determined on periplasmic extracts with varying concentrations of nacubactam and expression of outer membrane protein was analyzed by SDS–PAGE and TOF/MS and expression of *pvdS* and *fecA* were determined via iron transporter FiuA. In this study, we examined frequency of resistance of *P. aeruginosa* to CFDC, and investigated the resistance mechanisms of appeared colonies.

**Conclusion.** The MIC increase of CFDC against *P. aeruginosa* occurred due to the mutation of iron transporter-related genes. The resistance acquisition risks should be low as the frequency of resistance to CFDC was lower and the MIC increase of CFDC against the mutants was smaller than that of CAZ. In addition, no cross-resistance between CFDC and CAZ was observed.

**Disclosures.** A. Ino, Shionogi & Co., Ltd.; Employee, Salary. T. Nishikawa, Shionogi & Co., Ltd.; Employee, Salary. R. Ishii, Shionogi & Co., Ltd.; Employee, Salary. M. Kuroiwa, Shionogi & Co., Ltd.; Employee, Salary. Y. Ishioka, Shionogi & Co., Ltd.; Employee, Salary. N. Kuiraha, Shionogi & Co., Ltd.; Employee, Salary. I. Sakikawa, Shionogi & Co., Ltd.; Employee, Salary. T. Ota, Shionogi & Co., Ltd.; Employee, Salary. M. Rokushima, Shionogi & Co., Ltd.; Employee, Salary. M. Tsuji, SHIONOGI & CO., LTD.; Employee, Salary. T. Sato, SHIONOGI & CO., LTD.; Employee, Salary. Y. Yamano, SHIONOGI & CO., LTD.; Employee, Salary.

697. **Pseudomonas aeruginosa PcrV and Psl, the Molecular Targets of Bispecific Monoclonal Antibody MED13902, Are Conserved Among Diverse Hospital Isolates Collected From an International Surveillance Study**

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**Session: 67. Resistance Mechanisms: Gram-Negative**

**Thursday, October 4, 2018: 12:30 PM**

**Background.** *Pseudomonas aeruginosa* is a frequent cause of life-threatening infections in mechanically ventilated patients and is associated with high mortality rates. Bispecific monoclonal antibody MED13902 targeting Pa type-3-secretion system (PcrV) and the Ps lipo polysaccharide is currently under phase 2b development for the prevention of pneumonia in mechanically ventilated subjects with *P. aeruginosa* colonization in the lower respiratory tract. In this study, we sought to survey a vast collection of global *P. aeruginosa* clinical isolates for presence of pcrV and psl loci and MED13902 epitope conservation to evaluate the magnitude of Pa strain coverage by MED13902.

**Methods.** Pa clinical isolates were collected from diverse patients and geographical locations in 2004–2014. Whole genome sequencing of the full collection was performed via MiSeq 2 × 250 runs (Illumina.), PcrV and Psl expression was detected by in situ hybridizing and ELISA, respectively. The crystal structure of anti-P. aeruginosa PcrV and Psl fragment complex-crystals was solved at 2.8 A resolution. MED13902 activity against representative isolates was tested in cytotoxicity and opsonophagocytosis assays and in a murine pneumonia model.

**Results.** Whole-genome sequencing revealed intact pcrV and psl genetic elements in 99% and 94% of isolates, respectively. We identified 46 variants of PaV that were all bound by the anti-PcrV moiety of MED13902 and confirmed through crystal structure analysis that antibody-antigen contact residues were preserved in all variants. Similarly, anti-Psl binding was confirmed for selected isolates containing the complete Psl operon and strains lacking non-essential *psl* genes. Importantly, 99.9% of isolates contained the full complement of either genetic element. Consistent with these results, we observed potent MED13902 activity against diverse strain types, including strains that expressed only a single target.

**Conclusion.** The results indicate PcrV and Psl are highly prevalent in recent clinical isolates from around the world, suggesting that MED13902 can mediate broad coverage against Pa.

**Disclosures.** D. E. Tabor, Astra Zeneca: employee, Salary.

698. **Nacubactam Inhibits Class A β-lactamases**

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**Session: 67. Resistance Mechanisms: Gram-Negative**

**Thursday, October 4, 2018: 12:30 PM**

**Background.** Nacubactam, formerly RG6089 and OP0595 (Figure 1A), is a bridged diazabicyclooctanote (DBO) that inactivates class A and class C β-lactamases. Unlike avibactam, the DBO that is approved for use in combination with ceftazidime, nacubactam also inhibits penicillin binding proteins (i.e., PBZβ) in Enterobacteriaceae. We set out to determine the effectiveness of nacubactam and bacabactam against Klebsiella pneumoniae clinical strains and to elucidate the structure–function relationships.

**Methods.** Minimal inhibitory concentration (MIC) measurements using broth microdilution according to Clinical and Laboratory Standards Institute for meropenem (MERO) alone or nacubactam±bacabactam against Klebsiella pneumoniae clinical strains and to elucidate the structure–function relationships.

**Results.** Minimal inhibitory concentration (MIC) measurements using broth microdilution according to Clinical and Laboratory Standards Institute for meropenem (MERO) ± nacubactam (fixed concentration of 4 mg/L or fixed 1:1 ratio) was performed on 50 clinical *K. pneumoniae* strains (6 having OXA-48-like β-lactamases and 44 harboring KPC-2 or KPC-3) and 47 isogenic *Escherichia coli* strains harboring bla genes encoding *K. pneumoniae* carbapenemase (KPC) variants with single amino acid substitutions in residues that are conserved in catalysis. IC50 for selected KPC-2 variants were determined on periplasmic extracts with varying concentrations of nacubactam using nitrocellin as a reporter substrate.

**Results.** The MERO combinations with either 4 mg/L or a 1:1 ratio of nacubactam effectively lowered the MERO MICs of *K. pneumoniae* strain (Figure 1B). Similarly, all E. coli strains expressing blatoc were susceptible to the MERO-nacubactam