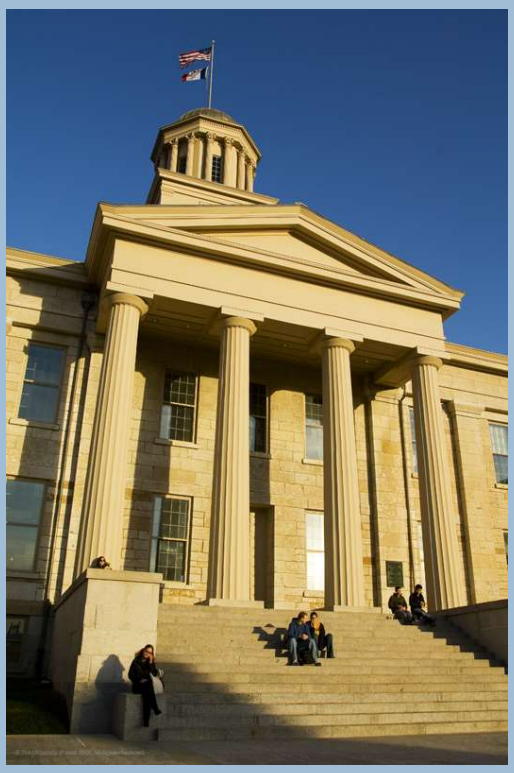
Great Plains Emerging Infectious Diseases Conference

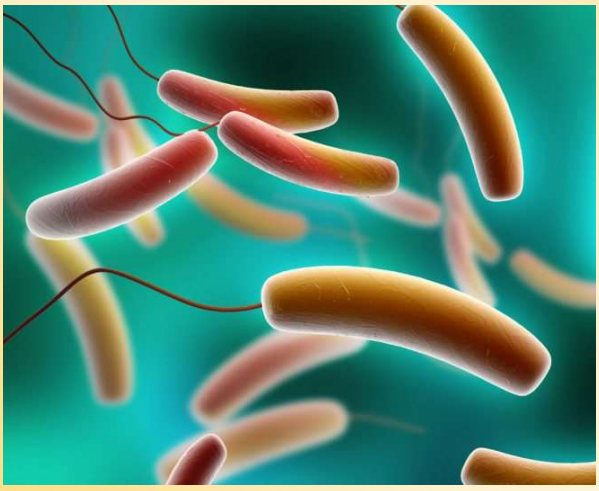


April 4-5, 2019

The University of Iowa

College of Public Health

Iowa City, Iowa



GREAT PLAINS EMERGING INFECTIOUS DISEASES CONFERENCE

April 4th and 5th, 2019
University of Iowa College of Public Health
Iowa City, Iowa

WELCOME to the eighth-annual Great Plains Emerging Infectious Diseases Conference sponsored by the University of Iowa College of Public Health, Department of Epidemiology, the Iowa State Hygienic Laboratory, the University of Iowa Center for Emerging Infectious Diseases (CEID), the National Institute for Antibiotic Resistance Research and Excellence, the Iowa State University College of Veterinary Medicine and One Health program.

This conference will serve to bring together public health professionals, researchers, faculty, and students in microbiology, infectious diseases, and related fields working in the Great Plains and Midwestern states. The GPEID Conference highlights basic, applied, epidemiological, and translational research in biomedical and veterinary disciplines. Major topics may include but are not limited to antimicrobial resistance, zoonotic and vector-borne diseases including global health, healthcare-associated infections, molecular diagnostics and epidemiology, public health preparedness, and science communication.

We thank you for your participation and look forward to the many opportunities for intellectual exchange over the next two days and into the future.

CEID UI Center for Emerging Infectious Diseases
The University of Iowa College of Public Health
AMR Consortium
Iowa One Health
The University of Iowa State Hygienic Laboratory

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4:00-4:50p Keynote address, N110 CPHB

Dr. Megin Nichols, DVM, MPH, Diplomate ACVPM
Antimicrobial Resistant Zoonotic Disease Outbreaks: A Case for One Health Data Sharing

5:00-6:00p Poster presentations and Reception, CPHB Atrium

6:00-7:00p Networking, CPHB Atrium

FRIDAY, APRIL 5TH, 2019

7:30-8:00a Registration and breakfast (doors open at 7:00 a.m.), Atrium / C217 CPHB

8:00-8:15a Introduction and Welcome, Christine Petersen CEID Director

8:15-9:15a Research session I, S030 CPHB

Geneva Wilson
Debora Goulart
Annette O'Connor
Kelly Baker

9:15-9:30a Break, C217 CPHB

9:30-10:30a Breakout session/Roundtable

Choose between the two breakout sessions:

Cross-talk across the AMR data streams and beyond
Moderators: Drs. Paul Plummer and Kelly Baker (S030 CPHB)

Chronic Wasting Disease (CWD): What is it and why is it a big deal in Iowa?
Moderators: Dr. Christine Petersen and Jim Kacer (C217 CPHB)

10:30-10:45a Break with Coffee Available, C217 CPHB

10:45-11:45a Research session II, S030 CPHB

Erin Cox
Wesley Hottel
Marie Ozanne
Eric Kontowicz

11:30a-1:30p Lunch, C217 CPHB

SCHEDULE

1:30-2:30p Discussion session, S106AB CPHB

The complexity of AMR data sharing: a discussion on the confidentiality and ethical issues surrounding one-health data sharing and liability.
Moderators: Drs. Paul Plummer and Kristen Obbink

2:30-3:30p Q & A with keynote speakers, S106AB CPHB

3:30-4:00p Networking, Atrium / C217 CPHB

4:00-5:00p Keynote address, N110 CPHB

Patrick McDermott, MS, PhD
The National Antimicrobial Resistance Monitoring System: Measuring and Monitoring Resistance Using Genomics

KEYNOTE ADDRESS

This year's keynote speakers are **Dr. Megin Nichols, DVM, and Dr. Patrick McDermott, PhD.**

Dr. Megin Nichols, DVM, MPH, DACVPM
Lead, Enteric Zoonoses Activity
Division of Foodborne, Waterborne, and Environmental Diseases
Centers for Disease Control and Prevention

Keynote Address
"Antimicrobial Resistant Zoonotic Disease Outbreaks: A Case for One Health Data Sharing"
Thursday, April 4th, 4:00-5:00 p.m.
Room N110 CPHB

Megin Nichols, DVM, MPH, DACVPM serves as the Enteric Zoonoses Activity Lead at the Centers for Disease Control and Prevention. In this role, she works on multistate outbreaks of Salmonella and E. coli resulting from exposure to animals and pet products. Dr. Nichols has focused her work on investigating multistate outbreaks of human illness linked to petting zoos, small turtles, livestock with strains of multidrug-resistant Salmonella, and pet food products. In 2016, Dr. Nichols led the investigation of nine multistate outbreaks linked to live poultry in backyard flocks. Almost 900 people became ill in these outbreaks, the largest number of illnesses CDC has recorded linked to live poultry. Prior to joining CDC, Dr. Nichols worked as the Principal Investigator of the Active Bacterial Core Surveillance Program at the New Mexico Department of Health for 5 years. She received a Bachelor of Science degree in Animal Science from New Mexico State University, a Doctor of Veterinary Medicine from Colorado State University and a Master of Public Health in Food Safety and Biosecurity from the University of Minnesota. She was an Epidemiologic Intelligence Service (EIS) Officer from 2008–2010 with the New Mexico Department of Health. Prior to obtaining a D.V.M., she spent several years as a clinical veterinary assistant. Her areas of interest include zoonotic disease, food safety, and pediatric health.

KEYNOTE ADDRESS

Dr. Patrick McDermott, MS, PhD
Director, National Antimicrobial Resistance Monitoring System
Food and Drug Administration

Keynote Address
"The National Antimicrobial Resistance Monitoring System: Measuring and Monitoring Resistance Using Genomics"
Friday, April 5th, 4:00-5:00 p.m.
Room N110 CPHB

Dr. Patrick McDermott, M.S., Ph.D., is Director of the National Antimicrobial Resistance Monitoring System (NARMS) at the Food & Drug Administration. NARMS was established in 1996 and is an interagency collaborative effort between the FDA, USDA and CDC that tracks antibiotic resistance in bacteria from retail meats, food producing animals and human clinical cases of infection. He led studies to develop the first standardized antimicrobial susceptibility testing methods for *Campylobacter*, conducted work to show the impact of antimicrobials in animals, and coordinated the implementation of whole genome sequencing into NARMS national surveillance. His collaborative work aims to understand the mechanisms of antimicrobial resistance in foodborne microorganisms, how they emerge and spread, and the impact of interventions designed to limit resistance in food animal production. He is a fellow of the American Academy of Microbiology, and recipient of the FDA's Francis Kelsey award for excellence and courage in protecting the public health.

Breakout Sessions:

Cross-talk across the AMR data streams and beyond

Moderators: Drs. Paul Plummer and Kelly Baker

Chronic Wasting Disease (CWD): What is it and why is it a big deal in Iowa?

Moderators: Dr. Christine Petersen and Jim Kacer

Discussion Session:

The complexity of AMR data sharing: A discussion on the confidentiality and ethical issues surrounding one-health data sharing and liability.

Moderators: Drs. Paul Plummer and Kristen Obbink

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University of Iowa, Department of Epidemiology
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Erin Cox, DVM
University of Iowa, Department of Epidemiology
Splenic Architecture alterations and Cell Phenotypes between Symptomatic and Asymptomatic US Dogs with Visceral *Leishmania*sis

Debora Goulart
Iowa State University, College of Veterinary Medicine
Effect of enrofloxacin treatment on the prevalence of fluoroquinolone resistant *Campylobacter* in cattle

Wesley Hottel, MS
University of Iowa, Department of Epidemiology
Identification of Antibiotic Resistance Genes in *Legionella* found in Hospital Water Using Whole Genome Sequencing

Eric Kontowicz, MPH
University of Iowa, Department of Epidemiology
Quantifying the influence of a flooded environment on influenza rates in Iowans

Annette O'Connor, BVSc, MVSc, DVSc
Iowa State University, College of Veterinary Medicine
Using a Bayesian latent class model to changes in antibiotic resistance in *Salmonella enterica* serovar Typhimurium and *S. enterica* serovar 4,[5],12:i:- from swine submissions at a veterinary diagnostic laboratory: A multi-year prevalence survey

Marie Ozanne
University of Iowa, Department of Biostatistics
Whose Fault Is It Anyway? Calculating Reproductive Numbers for Multiple Infectious Sources

Geneva Wilson, PhD
University of Iowa, Department of Epidemiology
Measuring the Bioaerosol Concentration of *C. difficile* spores in Infected Patient's Rooms during Select Activities

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in alphabetical order by last name

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Iowa State University, College of Veterinary Medicine
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Megan Keller
University of Iowa, Department of Microbiology and Immunology
The Composition and Function of Extracellular Vesicles in *Leishmania*sis

Kurayi Mahachi, MPH
University of Iowa, Department of Epidemiology
Regional and exposure risk factors that driving hunting dog seropositivity to tick-borne pathogens

Kai Rogers
University of Iowa, Department of Microbiology and Immunology
Acute Plasmodium infection promotes resistance to Ebola virus via type 1 immunity

Brandon Ruddell
Iowa State University
RNAseq reveals a complex survival response by *Campylobacter* jejuni in close association with the ovine gallbladder mucosa in an experimental model of infection

Breanna M. Scorza, PhD
University of Iowa, Department of Epidemiology
Altered circulating NK cell response during *Ehrlichia*/*Leishmania* co-infection and potential role in progressive disease

ABSTRACTS

Kelly K. Baker, Reid Senesac, Daniel Sewell, Ananya Sen Gupta, Oliver Cumming, and Jane Mumma
University of Iowa

The role of markets versus households in enteric pathogen transmission via infant food in low-income countries

Young children are infected by a diverse range of enteric pathogens in high disease burden settings, suggesting pathogen contamination of the environment is equally diverse. This study aimed to characterize across- and within-neighborhood diversity in enteric pathogen contamination of public domains in urban informal settlements of Kisumu, Kenya, and to assess the relationship between pathogen detection patterns and human and domestic animal sanitation conditions. Microbial contamination of soil and surface water from 166 public sites in three Kisumu neighborhoods was measured by enterococcal assays and quantitative reverse transcription polymerase chain reaction (qRT-PCR) for 19 enteric pathogens. Regression was used to assess the association between observed sanitary indicators of contamination with enterococci and pathogen presence and concentration, and pathogen diversity. Seventeen types of pathogens were detected in Kisumu public domains. Enteric pathogens were codetected in 33% of soil and 65% of surface water samples. Greater pathogen diversity was associated with the presence of domestic animal feces but not with human open defecation, deteriorating latrines, flies, or disposal of human feces. Sanitary conditions were not associated with enterococcal bacteria, specific pathogen concentrations, or "any pathogen". Young children played at 40% of observed sites. Managing domestic animal feces may be required to reduce enteric pathogen environmental contamination in high-burden settings.

Ashenafi Beyi, Alan Hassall, Gregory J. Phillips, Paul Plummer
Iowa State University

Use of Hi-C metagenomic sequencing for tracking antimicrobial resistance genes: tetracycline resistance genes in a sample of bovine digital dermatitis case

Bovine digital dermatitis (DD) is a leading cause of lameness in cattle and is characterized by a complex polymicrobial process for which most of the organisms are not cultivable. Topical tetracycline is the treatment of choice, but anecdotal reports of clinical resistance exist. Given that DD is caused by the consortium of bacteria, identifying antimicrobial resistance genes (ARGs) and their bacterial reservoirs is critical to improve treatment outcomes and approaches. Objective was to evaluate sensitivity of Hi-C metagenomics in detecting bacterial taxa that harbor ARGs in clinical samples from DD lesions. Shotgun metagenomic sequencing has been used to discover ARGs in complex environments, however, it is incapable definitively identifying the taxonomic source of ARGs. To overcome this limitation, we used Hi-C DNA sequencing, which preserves linkage relationships by crosslinking DNA within bacterial cells prior to whole shotgun sequencing. The list of bacterial taxa with >80% complete genome that have been detected in our sample include Bacteriodetes (5.27%), Spirochaetaceae (5.12%), Clostridiales (2.43%), Lactobacillales (1.15%), and Mycoplasma (0.84%). In addition, specific bacterial species such *Porphyromonas levii* (1.04%), *Treponema phagedenis* (1.00%), *T. medium* (0.51%), and *Mycoplasma fermentans* (0.63%) were observed in the sample. Based on the genome annotation, Spirochaetaceae have been predicted to harbor ARGs against tetracycline such as tet32, tetM, tetO, tetQ, and tetT. To our knowledge this study presents the first report of genetic evidence of tetracycline resistant gene markers harbored in bacteria involved in the DD disease process. Hi-C sequencing holds promise as a sensitive and robust DNA sequencing method to identify and track specific bacterial taxa that participate in spread of ARGs.

Erin Cox, Breanna Scorza, Kurayi Mahachi, Angela Toepp, Diogo Valadarez, Katherine Gibson-Corley, Christine A Petersen
University of Iowa

Splenic Architecture alterations and Cell Phenotypes between Symptomatic and Asymptomatic US Dogs with Visceral Leishmaniasis

Dogs are the reservoir species for visceral Leishmaniasis and canine visceral Leishmaniasis closely models the course of disease in human patients. Secondary lymphoid organs particularly spleen undergo alterations in immune function and microscopic structure as VL progresses from asymptomatic to clinically symptomatic stages. How and why these changes occur are not well understood. We hypothesized that dogs with symptomatic canine visceral leishmanaisis will have fewer splenic follicles poorly organized follicles and germinal centers and lower splenic white pulp area when compared to asymptomatic *Leishmania*-infected dogs. These alterations in follicular organization will be associated with changes in population size and distribution of splenic CD4+CXCR5+TfH cells and CD19+PDL1+ Breg cells. Dogs were selected from an outbred cohort previously shown to have *L. infantum* infection and determined to be asymptomatic or symptomatic through physical examination. These dogs were humanely euthanized for tissue collection. Light microscopy was used to evaluate splenic structure from H&E stained slides. Staining on slides was secondarily analyzed with digital imaging software to measure follicle area total white pulp area and total red pulp area. From these initial results we conclude that when measured by digital imaging software adult symptomatic dogs exhibited a greater total follicle area than adult asymptomatic dogs. Adult asymptomatic dogs also had a higher ratio of primary (immunologically dormant) to secondary (immunologically active) follicles. Juvenile asymptomatic dogs exhibited a higher manual follicle count/mm2 of splenic area than adult symptomatic or adult asymptomatic dogs. These results suggest greater immunologic activity in adult symptomatic dogs and age-related differences in follicle size and activation within the cohort.

Debora Goulart, Anastasia Schroeder, Ashenafi Beyi, Melda Ocal, Zuowei Wu, Kritika Singh, Orhan Sahin, Paul Plummer, Grant Dewell, Renee Dewell, Qijing Zhang
Iowa State University

Effect of enrofloxacin treatment on the prevalence of fluoroquinolone resistant *Campylobacter* in cattle

Cattle are significant reservoirs for *Campylobacter* a major foodborne pathogen. Recent studies have shown a rise in fluoroquinolone-resistant (FQ-R) *Campylobacter* in cattle but it is unclear if this is directly related to FQ use in cattle. The aim of this study is to assess the effect of Enrofloxacin treatment on FQ resistance in cattle. Calves derived from commercial farms were inoculated with FQ-susceptible (FQ-S) strains of C. jejuni followed by treatment with a single dose of Enrofloxacin (12.5 mg/kg by injection). Fecal samples were collected during the course of study for isolation and identification of *Campylobacter*. Interestingly the calves were naturally infected with FQ-R C. jejuni prior to inoculation with the laboratory strains. After the inoculation FQ-R *Campylobacter* decreased which was accompanied by increase of FQ-S *Campylobacter*. However after Enrofloxacin treatment was given the calves were recolonized by FQ-R *Campylobacter*. Pulsed field gel electrophoresis and multilocus sequence typing revealed genetic diversity of the isolates but certain genotypes dominated during different stages of the study. Prior to inoculation the calves were predominantly colonized by FQ-R cluster A (ST982). After inoculation the predominant genotypes changed to FQ-S clusters C (ST929) and D (ST61). Following the treatment with Enrofloxacin the primary genotypes shifted to FQ-R clusters A (ST982) and B (ST922). These results indicate that commercial cattle harbor genetically diverse FQ-R *Campylobacter* and a single treatment with Enrofloxacin enriched pre-existing FQ-R populations but had little effect on de novo selection of FQ-R *Campylobacter* from the inoculated strains.

ABSTRACTS

Wesley Hottel, Valerie Reeb, Alankar Kampoopwale, Nancy Hall, and Lucy DesJardin
University of Iowa

Identification of Antibiotic Resistance Genes in *Legionella* found in Hospital Water Using Whole Genome Sequencing

Legionellosis caused by *Legionella* bacteria is an important public health concern in the United States. One species *Legionella* pneumophila is considered to be responsible for over 90% of severe cases of clinical disease classified as Legionnaires' disease. A clinical indication of Legionnaires' disease is a lack of response to beta-lactam antibiotics and most strains of L. pneumophila are considered to be resistant to Ampicillin. Legionnaires' disease can be treated with antibiotics typically macrolides and fluoroquinolones however resistance to antibiotics and subsequent treatment failure has been reported. *Legionella* bacteria have the potential to share genomic elements via horizontal gene transfer and mobile elements and it is not known whether *Legionella* share other genes such as those related to antibiotic resistance. This study included 46 *L. pneumophila* and 44 *L. anisa* isolates to compare the presence of antibiotic resistance genes between *Legionella* species and strains. There were differences in identified antibiotic resistance genes among *L. pneumophila* strains and following subsequent in vitro testing two genes associated with macrolide resistance (LpeA and LpeB) were found to be functional.

ABSTRACTS

Megan M. Keller, Patrick H. Kelly, R. Marshal Pope, Fabien Thery, Mary E. Wilson
University of Iowa

The Composition and Function of Extracellular Vesicles in Leishmaniasis

Leishmaniasis is a group of diseases caused by obligate intracellular *Leishmania spp.* protozoa residing in macrophages. Despite remaining intracellular *Leishmania spp.* have dramatic effects on systemic immune responses most evident during visceral Leishmaniasis caused by *Leishmania* donovani or *L. infantum*. Most eukaryotic cells including human macrophages release small protein- and RNA-laden extracellular vesicles called exosomes that deliver protein and RNA between cells facilitating communication. We hypothesized that the exosome proteomes (exoproteomes) of uninfected versus infected human macrophages will differ and differences may reflect the functional state of the macrophage. Monocyte derived macrophages (MDMs) from 4 healthy human donors were infected with *L. infantum* and extracellular parasites removed. After 4 days MDMs were transferred to serum free medium and exosomes in medium were collected 24h later. Exoproteomes were isotope labeled and identified by LC-MS/MS. Data were exported in MaxQuant 1.6.3.3 [false discovery rate (FDR) 0.05; 1-peptide minimum; peptide length minimum 7] and analyzed with Perseus 1.6.2.3. After filtering for quality and proteins found in all 5 technical replicates of at least one group 246 proteins were quantified. Pairwise comparison of donors revealed proteins significantly different (0.05 S0=1) between infection status included histone proteins depleted in the infected samples of multiple donors. 2-way ANOVA ($p<0.05$) revealed 52 proteins differed significantly by infection status including HSP-70 leukocyte surface markers including tetraspanins and histocompatibility antigens. These findings highlight a need to investigate Heat Shock proteins tetraspanins histocompatibility antigens and histones in released vesicles as potential contributors to the immune dysregulation observed during Leishmaniasis.

ABSTRACTS

Eric Kontowicz and Christine Petersen
University of Iowa

Quantifying the influence of a flooded environment on influenza rates in Iowans

Flooding is a common event in Iowa. It is suspected that states in the Midwest are at risk for an increase in flooding events due to shifting and more extreme weather patterns. Flooding has a myriad of effects on human health via an increased exposure to molds infectious agents allergens and increased humidity. These health effects can have acute and chronic consequences for human respiratory health. Compromises in respiratory health can make individuals more susceptible to influenza in the following flu season. The WHO has stated that another influenza pandemic is inevitable but unpredictable. It is likely that extreme weather patterns will increase in frequency therefore greater understanding of how extreme weather patterns might influence influenza rates among the human population is needed. The specific aim of this proposed research is to quantify the association between exposure to flooding defined by the number of days an Iowa zip code experiences a flooding event and influenza rates in that area. We hypothesize that there will be a positive association between an increased number of days a zip code is above flood stage and subsequent influenza rates in that zip code. We additionally hypothesize that humidity will mediate this relationship. To investigate the hypothesis set forth in this aim we will conduct a retrospective longitudinal study We have a multidisciplinary team that brings together environmental science experts medical geographers with experience in influenza outbreak research and geocoded data and infectious disease epidemiologists with expertise in laboratory diagnostics and large data studies.

ABSTRACTS

Kurayi Mahachi
University of Iowa

The hunting dogs plight: Risk factors for hunting dog exposure to tick-borne pathogens

Background: Ticks and tick-borne diseases have increased in range and incidence across the United States. Given people and dogs share their environment, dogs can act as sentinel animals for tick-borne disease distributions. Measures taken to understand tick-borne diseases among dogs can improve control and prevention of human disease. Our study sought to identify demographic and biological risk factors for canine seropositivity to *Anaplasma* spp., *Babesia* spp., *Ehrlichia spp.*, and *B. burgdorferi* in a cohort of highly exposed hunting dogs across the United States

Results: Controlling for age and *Anaplasma* spp. seroprevalence, dogs from regions compared to the west were 2.3x more likely (90% CI: 1.1274 – 4.5438, p=0.0216) to test seropositive for *B. burgdorferi*. Dogs seropositive for *Anaplasma* spp. were 1.4x more likely (90% CI: 1.0412 – 1.7846, p=0.0242) to test seropositive for *Babesia* spp. Dogs seropositive for *Babesia* spp. were 1.6x more likely (90% CI: 1.2043 – 2.1826, p=0.0014) to test seropositive for *Anaplasma* spp.. Dogs living in the west had a 5% decrease in risk (90% CI: 0.0118 – 0.2226, p=0.0001) for test seropositive for *Ehrlichia* spp compared to other regions. Dogs seropositive for *B. burgdorferi* were 1.6x more likely to test seropositive for *Anaplasma* spp. (0.981 – 2.1225, p = 0.0569.

Conclusions: Region significantly influenced the likelihood of hunting dog's exposure to tick-borne pathogens. Further, hunting dogs were exposed to greater levels of tick-borne co-infections than anticipated. *Babesia* spp. exposure among hunting dogs was greater than previously reported. Through our study, we have provided insight regarding protection of human and animal.

Min Zhang, Chong Wang, Chaohui Yuan Amanda Kreuder, Adam Krull, **Annette O'Connor**
Iowa State University

Using a Bayesian latent class model to changes in antibiotic resistance in *Salmonella enterica* serovar Typhimurium and *S. enterica* serovar 4,[5],12:i:- from swine submissions at a veterinary diagnostic laboratory: A multi-year prevalence survey

Surveillance programs for *Salmonella enterica*, an important pathogen for food animals, have existed for many years in the United States. One of the purposes of the surveillance is to monitor the emergence of antibiotic resistance. In this study, our objective was evaluate the changes over time in antibiotic resistance of two food borne pathogens with high relevance to food safety: *Salmonella enterica* serovar Typhimurium and *S. enterica* serovar 4,[5],12:i:-. The evaluation was based on a longitudinal survey for 16 years of swine submissions to the Veterinary Diagnostic Laboratory. Unlike the existing approaches of analyzing the minimum inhibitory concentration (MIC) that rely solely upon dichotomization of bacterial population, in our study, we additionally utilized a latent class mixture model with hierarchical structure using Bayesian analysis, to estimate mean MIC data. Two metrics were obtained from the statistical model, one is the proportion of the isolates above an MIC cut-off threshold (resistant population), the other is the mean MIC for the population below the threshold (non-resistant group), each estimated annually. This approach enabled us to describe the proportion of resistant isolates to multiple critical antibiotics changes over time and evaluate MIC creep in the non-resistant population. The inferences drawn from our model can serve as signals of the emergence of antibiotic resistance and the need for interventions or modifications.

Marie Ozanne
University of Iowa

Whose Fault Is It Anyway? Calculating Reproductive Numbers for Multiple Infectious Sources

Reproductive numbers are important quantities in epidemiology because they allow researchers to determine whether an infectious disease is likely to spread in a population. Usually reproductive numbers are calculated assuming that there is a single infectious source. For some pathogens however multiple hosts contribute to maintaining an infection in a population. For example both humans and dogs can become infected with *Leishmania infantum* the protozoan parasite that causes Leishmaniasis in the Americas after being bitten by an infected sand fly. These infected individuals can remain asymptomatic or manifest clinical disease. This yields four potential infectious sources: asymptomatic humans symptomatic humans asymptomatic dogs and symptomatic dogs which transmit infection to the sand fly vector with different probabilities. To quantify the contributions of each of multiple infectious sources to maintaining infection in a population we propose the Infection Source-specific Empirically Adjusted Reproductive Number (ISEARN). This quantity may provide insight into which infectious sources need to be targeted via control measures and into the effectiveness of these measures.

ABSTRACTS

Kai Rogers, Rahul Vijay, Laura Malinger, Olena Shtanko, Chester Joyner, Mary Galinski, Noah Butler, Wendy Maury
University of Iowa

Acute Plasmodium infection promotes resistance to Ebola virus via type 1 immunity

Ebola virus (EBOV) outbreaks occur sporadically in Central and West Africa with case fatality rates as high as 90%. Individuals are often infected with other pathogens endemic to these regions but consequences of such co-infections are understudied. Epidemiological studies from the 2014-2016 epidemic indicate that a significant number of EBOV patients were co-infected with P. falciparum when admitted to Ebola treatment units. Currently there is no consensus regarding how or whether malaria impacts EBOV infection with different epidemiological studies suggesting better or worse outcomes associated with co-infection. Here we investigated the effect of pre-existing malaria on EBOV challenge. C57BL/6 interferon alpha/beta receptor knock out mice were infected with *Plasmodium yoelii* and subsequently challenged intraperitoneally with a BSL-2 model of Ebola virus recombinant VSV encoding Ebola GP (EBOV/rVSV). Acute infection with *P. yoelii* protected mice from a lethal challenge with EBOV/rVSV and facilitated long-lived immunity against EBOV. Mice remained protected against EBOV challenge weeks after resolution of malarial disease suggesting the host response to *P. yoelii* rendered mice resistant to EBOV. Mechanistically we identified that protection against EBOV was linked to IFN?-mediated M1 polarization of peritoneal macrophages (pmacs) in P. yoelii-infected mice. Serum from mice acutely infected with *P. yoelii* induced M1 polarization of pmacs and reduced EBOV/rVSV infection ex vivo. Similarly human macrophages treated with serum from rhesus macaques acutely infected with P. cynomolgi were protected against EBOV/rVSV challenge. Protection in these assays was abolished by neutralizing anti-IFN?. Finally P. yoelii-infected mice lacking the IFN? receptor (IFNgR-/-) were not protected from EBOV/rVSV yet their serum containing IFN? induced an M1 phenotype and protected wild-type pmacs. Furthermore (IFNgR-/-) mice were not protected from EBOV/rVSV when co-infected

ABSTRACTS

Brandon Ruddell, Paul Plummer, Jennifer Schleining, Michael Yaeger, Amanda Kreuder
Iowa State University

RNAseq reveals a complex survival response by *Campylobacter jejuni* in close association with the ovine gallbladder mucosa in an experimental model of infection

Certain enteric bacterial pathogens are known to possess the ability to colonize the gallbladder and survive within this unique environment. However little is known about the bacterial mechanisms that allow survival in this otherwise inhospitable location. Over the past decade *C. jejuni* sheep abortion (SA) clone has emerged as the predominant cause of sheep *Campylobacter*iosis in the United States. Previous studies have indicated that *C. jejuni* clone SA can frequently be isolated from the gallbladders of healthy sheep suggesting that the gallbladder may serve as an important locus for *C. jejuni* persistence and transmission. The objective of this study was to gain insight into the molecular mechanisms of survival of *C. jejuni* found in direct association with the mucosal surface of the ovine gallbladder. A clinical isolate of SA clone *C. jejuni* IA3902 was exposed for up to 24 h to the natural ovine host gallbladder environment. Next total RNA was isolated from bacteria directly associated with the gallbladder mucosa. Subsequently high throughput sequencing of strand specific rRNA-depleted total RNA was used to characterize the transcriptome of IA3902. Comparison of the transcriptome of *C. jejuni* in direct association with the gallbladder mucosa as compared to when free within bile demonstrated significant differences in gene expression including both protein coding and non-coding RNA genes. An additional subset of genes were also found to be differentially expressed in both locations when compared to pre-inoculation. This study enables further insight into the molecular mechanisms required for survival of *C. jejuni* within ovine gallbladder.

ABSTRACTS

Breanna M Scorza, Kurayi Mahachi, Erin C Cox, Jennifer Foltz, Dean Lee, Jill Saucier, Phyllis Tyrrell, Christine A Petersen
University of Iowa

Altered circulating NK cell response during *Ehrlichia*/*Leishmania* co-infection and potential role in progressive disease

Zoonotic Visceral Leishmaniasis (CanL) is driven by transmission of protozoan *Leishmania* parasites from canine reservoirs to humans. We recently identified a causal association between tick-borne infection and progression to CanL. *Ehrlichia spp. rickettsia* transmitted by ticks were among the most common tick-borne pathogens in dogs with clinical CanL (Toepp 2019). How *Ehrlichia* co-infection alters *Leishmania* immunity is unknown. For this study circulating Natural Killer (NK) cell subsets were compared between endemic controls (ECs) and dogs with CanL +/- *Ehrlichia* co-exposure (L+ and L+E+) by flow cytometry. We hypothesized *Ehrlichia* co-infection would be associated with increased activated NK cells. Compared to EC circulating NK cell frequency significantly increased in L+ dogs further increased in dogs co-infected with asymptomatic *Ehrlichia* and symptomatic *Ehrlichia*. NKT cell frequency was not modulated. The proportion of NKp46+ NK cells decreased significantly in L+ and L+E+ dogs which may signal recruitment of this subset to sites of infection. Similarly the proportion of NKp46+ NKT cells decreased in L+E+ dogs. Both NK and NKT cells trended to have less Granzyme B gMFI in L+E+ dogs indicating granule release. In agreement both circulating NK and NKT cell frequencies correlate with PBMC cytotoxic activity. Based on this we hypothesize NK cells from L+E+ dogs will have increased effector functions with important implications for anti-*Leishmania* immunity compared with EC or L+ dogs Finally doxycycline treatment of L+E+ dogs with symptomatic *Ehrlichia* returned NK cell frequencies to near EC levels indicating treating comorbid tick infections may indirectly benefit CanL.

Geneva Wilson
University of Iowa

Measuring the Bioaerosol Concentration from *Clostridium difficile* Infected Patients' Hospital Toilets

Background: *Clostridium difficile* is the number one reported hospital acquired infection in the United States. Toilet flushing has been suggested as a possible mechanism for the spread of pathogens in clinical settings.

Design: Using a cross-sectional study design bioaerosols were collected 0.15 0.5 and 1.0 meters from the rim of the toilet in hospital rooms of *C. difficile* infected patients. Room air was collected continuously for twenty minutes with a bioaerosol impactor before and after flushing the toilet and particle concentration was measured both pre- and post-flush. Patient and healthcare workers activity levels in the rooms were also measured. Wilcoxon rank sum tests were used to assess the difference in bioaerosol production before and after toilet flushing.

Results: A total of 24 patient rooms were sampled. Bacteria cultured from 8/24 (33%) rooms. Clostridium difficile was found in two (25%) of the eight positive rooms. There was a total of 72 pre-flush and 72 post-flush samples taken; 9/72 (13%) of the pre-flush and 19/72 (26%) of the post-flush samples cultured positive. The predominant bacterial species found were *Enterococcus faecalis* and *Enterococcus faecium*. There was a significant increase in concentration within the two largest particle sizes post flush 5.0?m (p-value=0.0095) and 10.0?m (p-value=0.0082) compared to pre-flush.

Conclusions: Bioaerosols produced by toilet flushing in clinical settings could be an important source of bacterial environmental contamination specifically *Clostridium difficile, Enterococcus faecalis* and *Enterococcus faecium*. Prevention measures including providing toilet lids should be evaluated as potential interventions to prevent toilet-associated environmental contamination in hospital settings.

LIST OF CONFERENCE ATTENDEES

Jennifer Auchtung
University of Nebraska-Lincoln
jauchtung2@unl.edu

Tyler Baccam
University of Iowa
tyler-baccam@uiowa.edu

Kelly Baker
University of Iowa
kelly-k-baker@uiowa.edu

Bryan Bellaire
Iowa State University
bbella@iastate.edu

Ashenafi Beyi
Iowa State University
afbeyi@iastate.edu

David Clarke
Streck Inc.
dclarke@streck.com

Erin Cox
University of Iowa
eccx@uiowa.edu

Debora Goulart
Iowa State University
dgoulart@iastate.edu

Michelle Grevengoed
Augustana College
michellegrevengoed17@augustana.edu

Sarah Hanson
Augustana College
sarahhanson15@augustana.edu

Wesley Hottle
University of Iowa
wesley-hottel@uiowa.edu

Ryan Jepson
University of Iowa
ryan-jepson@uiowa.edu

Craig Just
University of Iowa
craig-just@uiowa.edu

Megan Keller
University of Iowa
megan-keller@uiowa.edu

Eric Kontowicz
University of Iowa
eric-kontowicz@uiowa.edu

Haley Kornfiend
Augustana College
haleykornfiend15@augustana.edu

Emma Leof
Minnesota Dept. of Health
emma.leof@state.mn.us

Kurayi Mahachi
University of Iowa
kurayi-mahachi@uiowa.edu

Wendy Maury
University of Iowa
wendy-maury@uiowa.edu

Kristen Obbink
NIAMRRE
kobbink@nationalamrinstitute.org

Annette O'Connor
Iowa State University
oconnor@iastate.edu

Jacob Oleson
University of Iowa
jacob-oleson@uiowa.edu

Marie Ozanne
University of Iowa
marie-ozanne@uiowa.edu

Michael Pentella
University of Iowa
michael-pentella@uiowa.edu

LIST OF CONFERENCE ATTENDEES

Christine Petersen
University of Iowa
christine-petersen@uiowa.edu

Paul Plummer
Iowa State University
pplummer@nationalAMRinstitute.org

Jake Riley
Johnson County Public Health
jriley@co.johnson.ia.us

Kai Rogers
University of Iowa
kai-rogers@uiowa.edu

Sierra Rood
Augustana College
sierrarood15@augustana.edu

Brandon Ruddell
Iowa State University
bruddell@iastate.edu

Orhan Sahin
Iowa State University
osahin@iastate.edu

Emma Sandstrom
Augustana College
emmasandstrom15@augustana.edu

Marin Schweizer
University of Iowa
marin-schweizer@uiowa.edu

Breanna Scorza
University of Iowa
breanna-scorza@uiowa.edu

Pallavi Singh
Northern Illinois University
psingh1@niu.edu

Laurie Spencer
Northern Illinois University
lspencer@niu.edu

Kenni Sterns
University of Iowa
kenni-sterns@uiowa.edu

Dara Wegman-Geedey
Augustana College
darawegman-geedey@augustana.edu

Kevin Tsai
University of Iowa
meng-hsien-tsai@uiowa.edu

Geneva Wilson
University of Iowa
geneva-wilson@uiowa.edu

Qijing Zhang
Iowa State University
zhang123@iastate.edu

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