Disclosures. All Authors: No reported Disclosures.

970. Antibiotic Use Variability Among US Nursing Homes—2016 Sarah Kabbani, MD, MSc1; Stanley Wang, MA, MS2; Laura Dietz, RN2; Danielle Palma, MPH3; Theresa Rowe, DO, MS1; David Y. Hyun, MD; Nancy Chi, MHA1; Nimalie D. Stone, MD, MS1; and Laura Hicks, DO1; 1Centers for Disease Control and Prevention, Atlanta, Georgia; 2PointClickCare, Mississauga, ON, Canada; 3Pointclickcare, Mississauga, ON, Canada; 4The Pew Charitable Trusts, Washington, DC.

Session: 124. Out of the Box and Out of the Hospital: Stewardship Outpatient Services
Friday, October 4, 2019: 11:30 AM

Background. Antibiotics are frequently prescribed in nursing homes (NH). National data describing facility-level antibiotic use (AU) in NH are lacking. The objectives of this analysis were to use NH electronic health records (EHR) to describe AU in NH and variability in AU rates across NH.

Methods. We analyzed antibiotic orders for 309,884 residents in 1,664 US NHs using one EHR company in 2016. We calculated AU rates as antibiotic days-of-therapy (DOT) per 1,000 resident-days and compared by the type of stay (short-stay (SS) ≤ 100 days vs. long-stay (LS) > 100 days). We also examined prescribing indications and the duration of nursing home-initiated antibiotic orders. We assessed facility-level correlates of AU using resident health and NH facility characteristics publicly available through NH Compare and LTCFocuss using a univariate linear regression.

Results. In 2016, 57% of NH residents received at least one systemic antibiotic; overall rate of AU was 90 DOT/1,000 resident-days. The median facility-level AU at a facility was 74% (IQR 60–84%). The SS and LS AU rates were 241 DOT/1,000 resident-days (IQR 136–322) and 24 DOT/1,000 resident-days (IQR 14–37), respectively. Overall, the three most common antibiotic classes prescribed were fluoroquinolones (18%), cephalosporins (18%), and extended-spectrum β-lactams (10%). Antibiotics were most frequently prescribed for urinary tract infections, and the mean duration of an antibiotic order was 9 days (range 1–365). Higher facility AU rate correlated positively with the following facility characteristics: proportion of SS residents, urban location, proportion of residents with mild cognitive impairment and lower activities of daily living scores, presence of ventilator beds, proportion of SS residents with urinary catheters or pressure ulcers, facility case-mix index, and for-profit ownership and multiorganization facilities.

Conclusion. Significant variability in NH AU rates exist, and SS residents have higher AU rates. Identifying NH with high rates of AU after adjusting for facility-level predictors of AU may identify opportunities for targeting efforts to improve prescribing practices.

Disclosures. All Authors: No reported Disclosures.

971. The Role of Inflammation and Innate Effectors in Passive Immunization for Acinetobacter baumannii Infections Travis B. Nielsen, PhD1; Jun Yan, MS2; Brian M. Luna, PhD3; Yuli Talyansky1; Robert A. Benomor, MD4 and Brad Spellberg, MD5; 1Loyola University Chicago, Forest Park, Illinois; 2University of Southern California, Los Angeles, California; 3Loma Linda Stokes Cleveland VA Medical Center, Cleveland, Ohio; 4Los Angeles County + University of Southern California, Los Angeles, California

Session: 125. Pathogenesis and Inflammatory Response
Friday, October 4, 2019: 10:30 AM

Background. We have previously demonstrated that A. baumannii virulence is driven by avoidance of innate effector clearance, resulting in LPS-TLR4 triggering of excess inflammation in the host. We also raised a monoclonal antibody (MAb) that improved survival of mice lethally infected with A. baumannii.

Methods. Mice were selectively depleted of innate effectors (macrophages with liposomal clodronate, neutrophils with cyclophosphamide, and/or complement with coxib venom factor), infected with an XDR clinical blood isolate of A. baumannii, and treated with placebo, anti-macrophage, anti-neutrophil, or anti-A. baumannii MAb.

Results. Single disruption of macrophages or neutrophils did not enhance lethality but complement deficiency did. In contrast, singly disrupting complement or neutrophils did not impact bacterial density but macrophage disruption markedly increased it. Thus, a dissociation of bacterial density and survival was observed. MAb therapy was completely protective in mice depleted of a single effector. While dual depletion resulted in diminished MAb efficacy in terms of survival, mice retaining neutrophils had marked improvements in survival with MAb therapy compared with other dual-depletion groups. The dissociation of bacterial density and survival suggested that inflammation was a primary driver of host outcome. Levels of IL-10 and TNFα and a reciprocal relationship in mice across effector depletion groups and were lower in mouse groups with higher survival when adjusted for bacterial density. IL-10 disruption completely abrogated the survival benefit of MAb therapy without altering bacterial clearance mediated by MAb. In contrast, TNFα disruption enhanced MAb efficacy for survival, and the presence of TNFα was antagonistic to MAb treatment. Conclusion. These results confirm that host outcomes from A. baumannii infection are driven by host inflammatory response rather than bacterial density alone. Furthermore, novel therapeutic approaches seeking to improve outcomes from such infections must seek to shift the balance of pro-anti-inflammatory cytokines to favor a down-modulated inflammatory response.

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972. A Mycobacterium tuberculosis Secreted Lipid Triggers Cough Through a Neuronal Cough Receptor Paxton Cruz, BS1; Cody Buhl, BS2; and Michael Shiloah, MD, PhD2; 1University of Texas Southwestern Medical Center, Dallas, Texas; 2University of Texas Southwestern, Dallas, Texas

Session: 125. Pathogenesis and Inflammatory Response
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Background. A hallmark symptom of active pulmonary tuberculosis vital for disease transmission is cough. The current paradigm for tuberculosis-related cough is that it results from airway damage or irritation. However, there is limited experimental data to support this theory, and whether Mycobacterium tuberculosis (Mt) induces cough to facilitate its own transmission has not been explored. The cough reflex is a complex and coordinated event involving both the nervous and musculoskeletal systems initiated by particulate or chemical molecules activating nociceptive neurons, which sense pain or irritation. This activation induces a signaling cascade ultimately resulting in a cough.

Respiratory nociceptive neurons innervate the airways of humans and most mammals and thus are poised to respond to noxious molecules to help protect the lung from damage. Because Mtb is a lung pathogen, cough is a primary mechanism of Mtb transmission, and respiratory nociceptive neurons activate cough, we hypothesized that Mtb produces molecules that stimulate cough thereby facilitating its spread from infected to uninfected individuals. We previously identified a cough molecule produced by Mtb, and in this work characterize its neuronal receptor using genetics, biochemistry, and pharmacology.

Methods. We used an in vitro neuronal activation bioassay to study Mtb cough-inducing molecules. We also used a biochemical assay to identify the cough receptor. Finally, we used gene silencing, biochemistry, and pharmacologic inhibition to validate and characterize the activity of the newly discovered cough receptor.

Results. We isolated a complex lipid produced by Mtb that activates nociceptive neurons. Both an organic Mtb extract and the purified molecule alone were sufficient to induce cough in a conscious guinea pig cough model and guinea pigs infected with wild-type Mtb cough much more frequently than guinea pigs infected with Mtb strains unable to produce nociceptive molecules. Using genetics, biochemistry, and pharmacologic techniques, we identified and validated a cough receptor for the Mt lipid expressed on nociceptive neurons.

Conclusion. We conclude that Mt produces a molecule that activates nociceptive neurons and induces cough through a specific neuronal receptor. These findings have significant implications for our understanding of Mt transmission.

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973. Single-cell RNA Sequencing Analysis of Zika Virus Infection in Human Stem Cell-Derived Cerebral Organoids Karen Ocwoiea, MD, PhD; Alexandria Stanton2; Alexis Richards, PhD3; Jenna Antonucci, PhD4; Travis Hughes1; Alex Shalek, PhD5; Rudolph Jaenisch, PhD3 and Lee Gehrkze; 1Boston Children’s Hospital, Somerville, Massachusetts; 2Graduate Program in Virology, Harvard University, Cambridge, Massachusetts; 3Whitehead Institute, Cambridge, Massachusetts; 4Institute for Medical Engineering and Science, Massachusetts Institute of Technology, Cambridge, Massachusetts; 5Virology Graduate Program, Harvard Medical School, Cambridge, Massachusetts; 6Massachusetts Institute of Technology, Cambridge, Massachusetts; 7Massachusetts Institute of Technology, Harvard Medical School, Cambridge, Massachusetts

Session: 125. Pathogenesis and Inflammatory Response
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Background. The molecular mechanisms underpinning the neurologic and congenital pathologies caused by Zika virus (ZIKV) infection remain poorly understood. One barrier has been the lack of relevant model systems for the developing human brain; however, thanks to advances in the stem cell field, we can now evaluate ZIKV central nervous system infections in human stem cell-derived cerebral organoids which recapitulate complex 3-dimensional neural architecture.

Methods. We apply Seq Way—a simple, portable platform for massively parallel single-cell RNA sequencing—to characterize cerebral organoids infected with ZIKV.

Using this sequencing method, and published transcriptional profiles, we identify