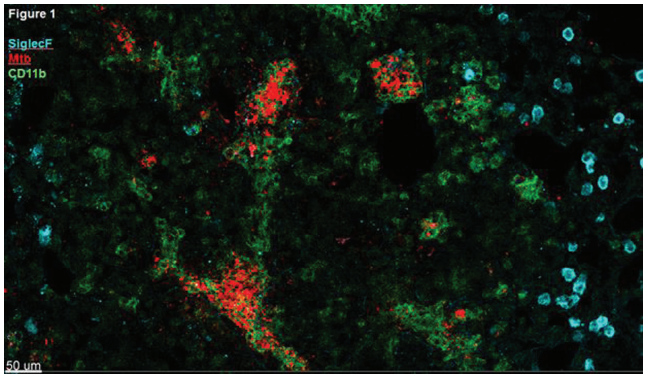
Session: 214. Host–pathogen Integration
Saturday, October 7, 2017: 8:30 AM

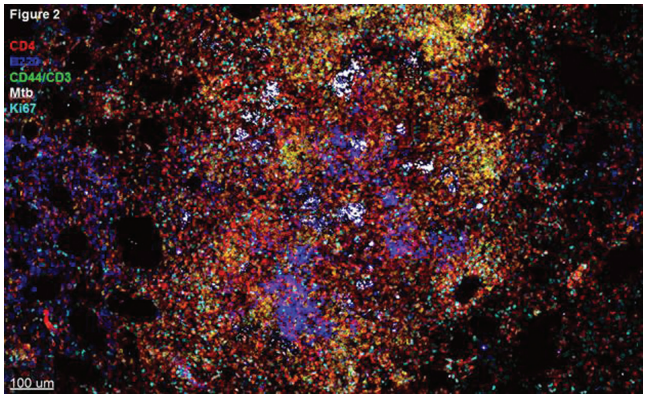
Background. Mycobacterium tuberculosis (*M.tb*) is the leading infectious cause of mortality; however, there is no vaccine that confers lasting protection. To investigate the immune response to *M.tb*, we have developed an ultra-low dose (ULD) infection model in mice that better reflects the heterogeneous outcomes of human infection. Additionally, we have identified a blood transcriptional signature, taken at day 24, that predicts future bacterial burden after day 70.

Methods. Mice were infected with an ULD (1–3 CFU) of H37Rv *M.tb*. Control mice were infected with 50–100 CFU. Blood was drawn at day 24 for RNA signature. At early (day 34–35), and late (day 82–83) time points, mice were injected with an intravascular label. Individual lungs were then assessed for bacterial burden, phenotypic and spatial analysis of immune cells by flow cytometry, and histocytometry, a type of immunohistochemistry that allows for imaging of >12 colors

Results. At day 35, the following cell populations were correlated with an RNA signature score predicting disease progression: ESAT-6 tetramer+ CD4+ T cells ($R^2 = 0.35$, $P < 0.01$), TB10.4 tetramer+ CD8+ T cells ($R^2 = 0.34$, $P < 0.01$), and B cells ($R^2 = 0.28$, $p = 0.01$) within the lung parenchyma, as well as CD11b+ cells, negative for CD64, Ly6c, Ly6g and MHCII ($R^2 = 0.38$, $p < 0.01$) within the lung vasculature. These same populations were correlated with elevated CFU at day 83, as well as dendritic cells ($R^2 = 0.53$, $p < 0.01$). No populations were correlated with a protective RNA score. We have observed the complex spatial organization of granulomas while optimizing our histocytometry panel. This includes infected macrophages (Fig 1) interdigitated with B cell aggregates, associated with naïve T cells, interspersed with CD44+ T cells, with diffuse staining for Ki67, suggestive of tertiary lymphoid structures (Figure 2).

Conclusion. This model replicates heterogeneity of TB seen in humans, while also providing a way to correlate differences in the immune response to future outcome. We have associated distinct immune cell subsets with the failure to control TB. With a larger sample size and data from histocytometry, we will have improved resolution to discern protective elements of the immune response to TB, which we can then test mechanistically in our model.





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

1765. Strain-level Determination of the Contribution of Gut Microbiota to the Development of Bacteremia in Patients Undergoing Stem Cell Transplantation
Tessa Andermann, MD, MPH[1]; Fiona B. Tamburini, BS[2]; Ekaterina Tkachenko, BS[3]; Fiona Senchyna, BS[4]; Niaz Banaei, MD[5] and Ami Bhatt, MD, PhD[2,3]; [1]Medicine/ID, Stanford, Stanford, California; [2]Genetics, Stanford, Stanford, California; [3]Hematology, Stanford, Stanford, California; [4]Pathology, Stanford, Stanford, California; [5]Departments of Pathology and Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University, Stanford, California

Session: 214. Host–pathogen Integration
Saturday, October 7, 2017: 8:30 AM

Background. Infection is a major preventable cause of transplant-related morbidity and mortality in patients undergoing hematopoietic stem cell transplantation (HCT). Bacteremia is the most common infectious complication in HCT, often occurring during periods of mucositis when the risk for microbial translocation from the intestine is increased. Prior research in HCT patients using 16S rRNA sequencing demonstrated that gut microbiota dominance by either *Enterococcus* spp. or Proteobacteria was associated with the development of bacteremia with *Enterococcus* spp. and Gram-negative organisms, respectively. No studies to date, however, have compared bacteremia isolates and gut microbiota samples at a strain-specific level using next-generation shotgun metagenomic sequencing (NGS).

Methods. In order to assess the degree of genetic similarity between bacteremia isolates and the gut microbiota, we identified patients who had undergone HCT at Stanford and developed a bacteremia between October 2015 and September 2016 for whom we had both saved blood culture isolates and stool samples within 30 days preceding bacteremia. We identified 15 patients from whom we had 17 bacteremia isolates, and performed NGS (Illumina HiSeq 4000) on stool and isolate DNA. We generated draft assemblies of isolate genomes using the SPAdes assembler, and aligned stool metagenomic reads to the draft isolate genomes using Bowtie2, filtering reads for perfect end-to-end alignment.

Results. Enteric gram-negative bacteremia isolates were identical to those in the gut microbiota, as has been demonstrated in prior studies using older strain-typing *Methods*. Surprisingly, we also identified gram-positive organisms that were identical in both the blood and stool prior to bacteremia, which challenges existing dogma regarding sources of gram-positive bacteremia-causing organisms.

Conclusion. Using a highly sensitive and accurate NGS-based strain typing method, we provide evidence of translocation of organisms from the gut microbiota and subsequent bacteremia. The gut was confirmed as a source for both classic enteric gram-negative and classically non-enteric Gram-positive bacteremia in HCT patients. These findings may have implications for the origins of bacteremia in HCT patients previously classified as CLABSIs.

Disclosures. **A. Bhatt**, Janssen Human Microbiome Institute / Johnson and Johnson: Consultant, Consulting fee

1766. The Gut Microbiota of Healthy Infants in the Community is a Reservoir for ESBL and Carbapenemase Producing Bacteria.
Ali Saleem, FCPS, MSc[1]; Ahreen Allana, MBBS[1]; Lauren Hale, BS[2]; Shahida M. Qureshi, MSc[1]; Aneeta Hotwani, MSc[1]; Najeeb Rahman, Massachusetts[1]; Asia Khan, BSc[1]; Patrick Seed, MD, PhD[3] and Mehreen Arshad, MD[4]; [1]Department of Paediatrics and Child Health, Aga Khan University Hospital, Karachi, Pakistan; [2]Biology, Duke University, Durham, North Carolina; [3]Ann & Robert H. Lurie Children's Hospital, Chicago, Illinois; [4]Pediatric, Duke University Medical Center, Durham, North Carolina

Session: 214. Host–pathogen Integration
Saturday, October 7, 2017: 8:30 AM

Background. The recent rapid rise of Extended-spectrum B Lactamase producing Gram-negative bacteria (ESBL-GNB) has seriously threatened the treatment of common infectious diseases. Neonates have an immature immune system and a delay in appropriate treatment due to ESBL-GNB sepsis can be fatal. This problem of delayed therapy is magnified in the developing world where 99% of the deaths from community acquired neonatal sepsis occur. Additionally ESBL *E. coli* such as the strain ST131 are known to be persistent gut and vaginal colonizers. In animal models, these strains out-compete colonization with drug-sensitive, commensal *E. coli*. Gut colonization with ESBL-GNB in infants may therefore have a profound impact on their microbiome and increase their risk of sepsis. Pakistan is a lower middle income country with high antibiotic use per capita and a sharp increase in ESBL-GNB infections. Recent data show that >50% of *E. coli* isolates from reproductive-aged women of Pakistan are resistant to more than one class of antibiotics. We aimed to determine the rates of gut colonization with ESBL-GNB among healthy infants in a community setting.

Methods. Stool samples were collected from 100 healthy infants living in a Pakistani suburban community between the ages of 5 and 7 months. Samples were plated on MacConkey agar to select for Gram-negative bacteria. Isolates were screened for resistance against several antimicrobial classes. Molecular testing of the stool samples was done using primers targeting conserved regions of ESBL and carbapenemase genes.

Results. Forty-eight percent of the infants were positive for ESBL producing Gram-negative bacteria, the majority of which were *E. coli*, and 7.5% were positive for carbapenemase producers, all of which belonged to *Klebsiella* spp. Molecular testing showed that 85% of the infant stools were positive for TEM β-lactamase gene, 68% for the CTX-M β-lactamase gene and 33% for the KPC carbapenemase gene.

Conclusion. The widespread colonization of infants in a developing country with ESBL-GNB is highly concerning. Further, our studies have revealed that the resistome of otherwise healthy infants may be a major reservoir of antibiotic genes in the community. Gut microbiome analysis of the potential impact of colonization with antibiotic-resistant bacteria is on-going.

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

1767. Longitudinal Comparison of the Microbiota During *Klebsiella pneumoniae* Carbapenemase-Producing *Klebsiella pneumoniae* (KPC-Kp) Acquisition in Long-Term Acute Care Hospital (LTACH) patients
Anna Seekatz, PhD[1]; Christine M. Bassis, PhD[1]; Karen Lolans, BS[2]; Rachel D. Yelin, MPH[2]; Nicholas M. Moore, MS[3]; Koh Okamoto, MD[4]; Yoona Rhee, MD, ScM[2];

Pamela Bell, BS[2]; Thelma Dangana, MBBS, MS[2]; Galina Sidimirova, BSN[5]; Robert A. Weinstein, MD, FIDSA, FSHEA[2]; Louis Fogg, PhD[2]; Michael Y. Lin, MD, MPH[2]; Vincent B. Young, MD, PhD[6]; Mary K. Hayden, MD[7] and The CDC Prevention Epicenter Program; [1]Internal Medicine/Infectious Diseases, University of Michigan, Ann Arbor, Michigan; [2]Rush University Medical Center, Chicago, Illinois; [3]Medical Laboratory Science, Rush University Medical Center, Chicago, Illinois; [4]Infectious Disease, University of Tokyo Hospital, Tokyo, Japan; [5]Infection Control, Rush Oak Park Hospital, Oak Park, Illinois; [6]Department of Internal Medicine, Division of Infectious Diseases, University of Michigan Medical School, Ann Arbor, Michigan; [7]Department of Internal Medicine, Division of Infectious Diseases, Rush University Medical Center, Chicago, Illinois

Session: 214. Host–pathogen Integration
Saturday, October 7, 2017: 8:30 AM

Background. Colonization with KPC-Kp precedes infection and represents a potential target for intervention. To identify microbial signatures associated with KPC-Kp acquisition, we conducted a prospective, longitudinal study of the fecal microbiota in LTACH patients at risk of acquiring KPC-Kp.

Methods. We collected admission and weekly rectal swab samples from patients admitted to one LTACH from May 2015 to May 2016. Patients were screened for KPC-Kp by PCR at each sampling time. KPC acquisition was confirmed by culture of KPC-Kp. To assess changes in the microbiota related to acquisition, we sequenced the 16S rRNA gene (V4 region) from collected rectal swabs. Diversity, intra-individual changes, and the relative abundance of the operational taxonomic unit (OTU) that contains KPC-Kp were compared in patients who were KPC-Kp negative upon admission and who had at least one additional swab sample collected.

Results. 318 patients (1247 samples) were eligible for analysis; 3.7 samples (mean) were collected per patient. Sixty-two patients (19.5%) acquired KPC-Kp (cases) and 256 patients remained negative for all carbapenem-resistant Enterobacteriaceae throughout their stay (controls). Median length of stay before KPC-Kp detection was 14.5 days. At time of KPC-Kp acquisition, levels of an Enterobacteriaceae OTU increased significantly compared with pre-acquisition samples and to samples from control patients (Wilcoxon test, $P < 0.0001$). Similarly, we observed a decrease in total diversity of the fecal microbiota at time of acquisition in cases ($P < 0.01$). Compared with controls, cases exhibited decreased intra-individual fecal microbiota similarity immediately prior to acquisition of KPC-Kp ($P < 0.01$). Comparison of microbial features at time of admission using random forest revealed a higher abundance of *Enterococcus* and *Escherichia* OTUs in controls vs cases.

Conclusion. We observed intra-individual changes in the fecal microbiota of case patients prior to acquisition of KPC-Kp. Compared with patients who did not acquire KPC-Kp, cases exhibited significant changes in microbiota diversity and increased abundance of potential KPC-Kp at acquisition. Our results suggest that shifts in the microbiota may precede colonization by KPC-Kp.

Disclosures. **N. M. Moore**, Cepheid: Research Contractor, Funded and provided reagents for associated research projects; **R. A. Weinstein**, OpGen: Receipt of donated laboratory services for project, Research support; CLorox: Receipt of contributed product, Conducting studies in healthcare facilities that are receiving contributed product; Molnlycke: Receipt of contributed product, Conducting studies in healthcare facilities that are receiving contributed product; Sage Products: Receipt of contributed product, Conducting studies in healthcare facilities that are receiving contributed product; **M. Y. Lin**, Sage, Inc.: receipt of contributed product, Conducting studies in healthcare facilities that are receiving contributed product; OpGen, Inc.: receipt of in-kind laboratory services, Conducting studies in healthcare facilities that are receiving contributed product; **M. K. Hayden**, OpGen, Inc.: Receipt of donated laboratory services for project, Research support; Clorox: Receipt of contributed product, Conducting studies in healthcare facilities that are receiving contributed product; Molnlycke: Receipt of contributed product, Conducting studies in healthcare facilities that are receiving contributed product; Sage Products: Receipt of contributed product, Conducting studies in healthcare facilities that are receiving contributed product.

1768. Reduction in the Prevalence of Healthcare-Associated Infections in U.S. Acute Care Hospitals, 2015 vs 2011

Shelley S. Magill, MD, PhD[1]; Lucy E. Wilson, MD, ScM[2]; Deborah L. Thompson, MD, MSPH[3,4]; Susan M. Ray, MD, FIDSA[5,6]; Joelle Nadle, MPH[7]; Ruth Lynfield, MD, FIDSA[8]; Sarah J. Janelle, MPH, CIC[9]; Marion A. Kainer, MBBS, MPH, FSHEA[10]; Samantha Greissman, MPH[11]; Ghinwa Dumyati, MD, FSHEA[12]; Zintars G. Beldavs, MS[13]; Jonathan R. Edwards, MStat[1] and Emerging Infections Program Hospital Prevalence Survey Team; [1]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; [2]Maryland Department of Health and Mental Hygiene, Baltimore, MD; [3]Presbyterian Healthcare Services, Albuquerque, New Mexico; [4]New Mexico Department of Health, Santa Fe, New Mexico; [5]Division of Infectious Diseases, Emory University School of Medicine, Atlanta, Georgia; [6]Georgia Emerging Infections Program, Decatur, Georgia; [7]California Emerging Infections Program, Oakland, California; [8]Minnesota Department of Health, St. Paul, Minnesota; [9]Colorado Department of Public Health and Environment, Denver, Colorado; [10]Tennessee Department of Public Health, Nashville, Tennessee; [11]Connecticut Emerging Infections Program, Hartford and New Haven, Connecticut; [12]New York Emerging Infections Program at the University of Rochester Medical Center, Rochester, New York; [13]Oregon Health Authority, Portland, Oregon

Session: 215. National Trends in HAIs
Saturday, October 7, 2017: 8:30 AM

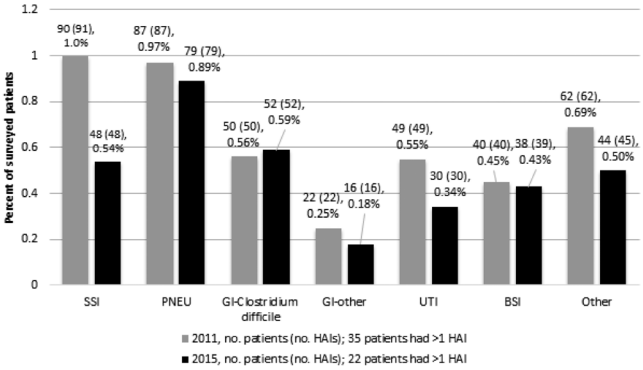
Background. A 2011 prevalence survey conducted by CDC and the Emerging Infections Program (EIP) showed that 1 in 25 hospital patients had ≥1 healthcare-associated infection (HAI). We repeated the survey in 2015 to assess changes in HAI prevalence.

Methods. In EIP sites (CA, CO, CT, GA, MD, MN, NM, NY, OR, TN) hospitals that participated in the 2011 survey were recruited for the 2015 survey. Hospitals selected 1 day from May–September 2015 on which a random patient sample was identified from the morning census. Trained EIP staff reviewed patient medical records using comparable methods and the same National Healthcare Safety Network HAI definitions used in 2011. Proportions of patients with HAIs were compared using chi-square tests; patient characteristics were compared using chi-square or median tests (OpenEpi 3.01, SAS 9.3).

Results. Data were available from 143 hospitals that participated in both surveys; data from 8954 patients in the 2011 survey were compared with preliminary data from 8833 patients in the 2015 survey. Patient characteristics such as median age, days from admission to survey, and critical care location were similar. Urinary catheter prevalence was lower in 2015 (1,589/8,833, 18.0%) compared with 2011 (2,052/8,954, 22.9%, $P < 0.0001$), as was central line prevalence (2015: 1,539/8,833, 17.4%, vs. 2011: 1,687/8,954, 18.8%, $P = 0.02$). The proportion of patients with HAIs was lower in 2015 (284/8,833, 3.2%, 95% confidence interval [CI] 2.9–3.6%) than in 2011 (362/8,954, 4.0%, 95% CI 3.7–4.5%, $P = 0.003$). Of 309 HAIs in 2015, pneumonia (PNEU) and *Clostridium difficile*infections (CDI) were most common (Figure); proportions of patients with PNEU and/or CDI were similar in 2015 (130/8833, 1.5%) and 2011 (133/8954, 1.5%, $P = 0.94$). A lower proportion of patients had surgical site (SSI) and/or urinary tract infections (UTI) in 2015 (77/8833, 0.9%) vs. 2011 (136/8954, 1.5%, $P < 0.001$).

Conclusion. HAI prevalence was significantly lower in 2015 compared with 2011. This is partially explained by fewer SSI and UTI, suggesting national efforts to prevent SSI, reduce catheter use and improve UTI diagnosis are succeeding. By contrast, there was no change in the prevalence of the most common HAIs in 2015, PNEU and CDI, indicating a need for increased prevention efforts in hospitals.

Figure: Prevalence and Distribution of HAIs, 2011 vs. 2015



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

1769. Assessing The Impact of The National Healthcare Safety Network's (NHSN's) New Baseline on Acute Care Hospital Standardized Infection Ratios (SIRs)

Minn Soe, MBBS, MPH; Allan Nkwata, MPH; Jonathan R. Edwards, MStat; Margaret Dudeck, MPH, CPH and Daniel Pollock, MD; Centers for Disease Control and Prevention, Atlanta, Georgia

Session: 215. National Trends in HAIs
Saturday, October 7, 2017: 8:30 AM

Background. To more accurately measure the progress of healthcare-associated infection (HAI) prevention efforts, the CDC's National Healthcare Safety Network (NHSN) surveillance system updated risk-adjustment models for computation of updated Standardized Infection Ratios (SIRs), the primary HAI summary measure by NHSN. This study sought to examine how the updated SIRs varied from the previous SIRs calculated using older baselines for acute care hospital HAIs.

Methods. We analyzed NHSN data for healthcare facility-onset laboratory-identified *Clostridium difficile* [CDI] and methicillin-resistant *Staphylococcus aureus* [MRSA] bacteremia reported in accordance with the CMS' inpatient quality reporting program requirement. The unit of analysis was CMS certification number (CCN) facility reporting in 2015. We compared overall distributions of CCN-level SIRs (CCN-SIRs) between new risk-adjustment models using a 2015 baseline (SIR_NEW) and old models using a 2011 baseline (SIR_OLD) and tested location shift (median away from null) of pairwise differences. We also examined the magnitude of shift in SIR from old to new baseline.

Results. For each HAI, the national pooled mean SIR of the new baseline was ~1.0. For CDI, the overall distributions of CCN SIR_NEW and CCN-SIR_OLD were different, and the median of pairwise difference was away from null with CCN-SIR_NEW slightly higher. For MRSA, the SIR differences were not significant. Most CCN-SIRs (83% for CDI, 93% for MRSA) remained in the same significance category across the old and new baselines ("worse," "better, 'not different from national benchmark'), and few CCN-SIRs were reclassified to a less favorable category. For 75% of