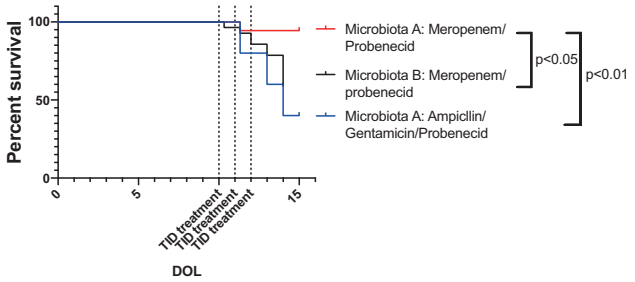
Background. Premature infants receive antibiotics frequently for culture-negative sepsis, which diminishes gut microbial diversity and increases susceptibility to infections by antibiotic-resistant pathogens. Neonates with decreased gut microbiota diversity, termed dysbiotic, have dysregulated immune systems marked by increased concentrations of circulating activated T cells and decreased concentrations of circulating neutrophils and dendritic cells. We hypothesize that antibiotics (1) enrich for pathobionts within the gut, (2) promote a systemic, proinflammatory host response, and (3) cause death in an antibiotic specific manner in a gnotobiotic model of preterm gut microbiota development.

Methods. We colonized germ-free (GF) dams and sires with stools from preterm infants. Mouse pups acquire this neonatal microbiota, and at 10 days of life (DOL), we treat them with clinically relevant doses of antibiotics subcutaneously for 3 days. We use metagenomic shotgun sequencing of individual pup fecal samples longitudinally to ascertain phylogenetic composition, and use flow cytometry and multiplex cytokine arrays to determine the local and peripheral immune response.

Results. Using two representative microbiota from human neonates (hereafter referred to as microbiota A or B), we show that 94% of pups given microbiota A survive vs. 64% given microbiota B after meropenem/probenecid treatment (Figure 1; $P < 0.05$; $n = 18–28$ mice in > independent experiments). 40% of pups given microbiota A treated with ampicillin/gentamicin/probenecid survived (Figure 1; $P < 0.01$ relative to meropenem/probenecid or probenecid). *Klebsiella* species dominated the gut microbiota of microbiota A-humanized pups who succumbed and were found in the lung, liver, and spleen of one animal at necropsy. *Enterococci* dominated the gut microbiota of microbiota B-humanized pups who died during treatment. Pups colonized with microbiota B had increased peripheral CD4+ T cells at sacrifice after treatment compared with microbiota A-humanized pups (61% vs. 44% of circulating T cells, $P < 0.0005$).

Conclusions. Our model of preterm microbiota development and perturbation by antibiotics demonstrates potential bacterial translocation, proinflammatory immune response, and death dependent on the microbiota–antibiotic combination. Our transgenerational humanized-microbiota mouse model can be utilized to determine antibiotic by microbiota perturbation and examine risks of late-onset sepsis from antimicrobials.



#39: *Streptococcus anginosus* Group Infections in Children: A Retrospective Cohort Study, 2015–2019

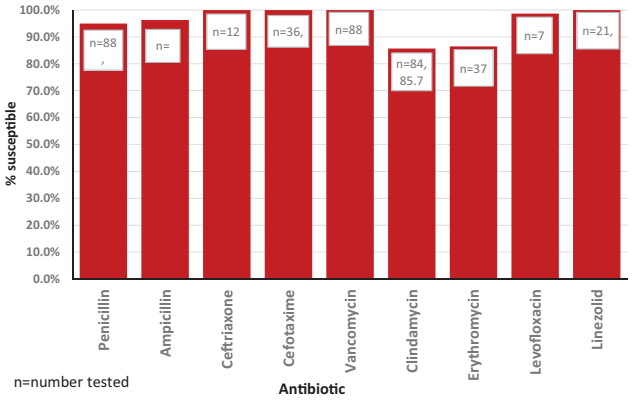
O. Amin[1]; O. Smith[1]; F. Berkowitz[1]; T. Lyon[2]; C. Kao[1]; A. Shane[1]; Ia. Yildirim[3]; M. Gonzalez[4]; [1]Emory University, School of Medicine, Division of Pediatric Infectious Diseases, Atlanta, Georgia; [2]Emory University, School of Medicine, Department of Pediatrics; Atlanta, Georgia; [3]Rollins School of Public Health, Emory University School of Medicine, Department of Epidemiology, Atlanta, Georgia; and [4]Children's Healthcare of Atlanta, Department of Pathology and Laboratory Services, Atlanta, Georgia

Background. Infections attributed to the *Streptococcus anginosus* group (SAG), which includes *Streptococcus anginosus*, *Streptococcus constellatus,* and *Streptococcus intermedius*, have varying clinical presentations. SAG infections are difficult to identify initially, and members of the group may require different management strategies.

Methods. A retrospective review of SAG-positive cultures from January 2015, to September 2019, was conducted to describe the demographic, clinical, and laboratory features including the site of infection, antibiotic susceptibility, management, and clinical outcome.

Results. We identified 561 patients [median age 11.3, interquartile range (IQR) 7.1–14.9 years, male:female ratio 3:2, non-Hispanic–non-Latino 454 (81%), White 279 (49%)]. Thirty-nine (7%) had at least one underlying condition. Of these, inflammatory bowel disease 15 (39%), diabetes 7 (18%), immunodeficiency 5 (13%). SAG was found in exudate, fluid, or aspirate (537/561, 96%), blood (11/561, 2%), and tissue (11/561, 2%) samples; 388 (69%) were polymicrobial infections. The most common site of infection was intra-abdominal (175, 31%), followed by neck/odontogenic (114. 20%) and genitourinary tract (66, 12%). The median length of stay was 6 days (IQR 3–10 days) and was statistically significantly longer for patients with blood, central nervous system, and pulmonary infections compared with soft tissue and upper respiratory tract infections ($P < 0.001$). Beta-lactams were the most commonly used antibiotics (38%), followed by clindamycin (30 %) (see Figure for antibiotic susceptibility results) and 33 (56%) patients received combination therapy. We did not observe any SAG attributed to mortality.

Conclusions. In our retrospective cohort, SAG infections were more commonly identified in males, were associated with abscess formation, and presented as polymicrobial infections. Children with underlying comorbidities are more likely to present with systemic SAG infections. SAG-associated infections can be variable in presentation site and severity and should be considered as pathogens when managing patients.



#53: High Burden of Serious Bacterial Infections in African Children Treated for Cancer

G. Naidu[1,2]; A. Izu[1,3]; R. Wainwright[1]; S. Poyiadjis[1]; D. MacKinnon[1]; B. Rowe[1]; S. A. Madhi[1,3]; [1]Medical Research Council: Respiratory and Meningeal Pathogens Research Unit, Faculty of Health Science, University of the Witwatersrand, South Africa; [2]Division of Paediatric Oncology, Department of Paediatrics, Chris Hani Baragwanath Academic Hospital; Faculty of Health Science, University of the Witwatersrand, South Africa; and [3]Departments of Science/ National Research Foundation: Vaccine Preventable Diseases, Faculty of Health Science, University of the Witwatersrand, South Africa

Background. Infectious complications in children treated for cancer contribute to their morbidity and mortality. There is a paucity of studies on the incidence, microbiological etiology, risk factors, and outcome of serious bacterial infections in African children treated for cancer.

Aim. The aim of the study was to delineate the epidemiology of infectious morbidity and mortality in South African children with cancer.

Methods. This prospective, single-center, longitudinal-cohort study enrolled children one-19 years old hospitalized for cancer treatment at the Paediatric Oncology Unit, Chris Hani Baragwanath Academic Hospital, Soweto, South Africa. Children were investigated for infection as part of the standard of care.

Results. In total, 169 children were enrolled, 82 with hematological malignancy (HM), 87 with a solid tumor (ST), median age was 68.5 months and 10.7% were living with HIV. The incidence (per 100 child-years) of septic episodes (SE) and microbiologically confirmed SE (MSCE) was 101 (138 vs. 70, $P < 0.001$) and 70.9 (99.1 vs. 47.3; $P < 0.001$), respectively; higher in children with HM than ST. The incidence of MCSE in children with high-risk HM (137.7) was 4.32-fold greater compared with those with medium-risk HM (30.3; $P < 0.001$). Children with metastatic ST had a higher incidence (84.4) of MSCE than those with localized ST (33.6; aOR: 2.52; $P < 0.001$). The presence of an indwelling catheter was 3-fold ($P < 0.001$) more likely to be associated with MCSE compared with those without. There was no association for age group, nutritional status or HIV-status, and incidence of MCSE. The incidence of gram-positive (GPB) and gram-negative (GNB) SEs was 48.5 and 37.6, respectively, and higher in children with an HM. The most commonly identified GPB were Coagulase-negative *Staphylococci, Streptococcus viridans* and *Enterococcus faecium*; while the most common GNB were *Escherichia coli, Acinetobacter baumannii,* and *Pseudomonas* species. The median CRP was higher in children with MSCE compared with those with culture-negative SE (CNSE) (116.5 vs. 92; $P < 0.001$) in both HM (132.5 vs. 117; $P < 0.001$) and ST (87.5 vs. 46; $P < 0.001$). The procalcitonin was higher in those with MSCE compared with those with CNSE (2.30 vs. 1.40; $P < 0.001$) in both HM (2.95 vs. 1.60; $P = 0.002$) and ST (2.10 vs. 1.20; $P < 0.001$). The case fatality risk was 40.4%; 80% was attributed to sepsis. Of these, 35 (72.92%) had HM and 34 of the 35 (97.14%) had HR-HM. Children with HM had an overall sepsis CFR of 42.68%. Four (30.77%) of the 13 sepsis-related deaths in STs had metastatic disease and 8 (16.67%) of the total number of sepsis-related deaths were in children living with HIV. There was no association between malnutrition or HIV-positivity and death. The odds of dying from sepsis were higher in children with profound (aOR 3.96; $P = 0.004$) and prolonged (aOR 3.71; $P = 0.011$) neutropenia. Pneumonia (58.85% vs. 29.23%; aOR 2.38; $P = 0.025$) and tuberculosis (70.83% vs. 34.91%; aOR 4.3; $P = 0.005$) were independently associated with a higher CFR.

Conclusion. The current study emphasizes the high burden of sepsis in African children treated for cancer, and especially HM, and highlights the association of tuberculosis and pneumonia as independent predictors of death in children with cancer.

#57: The Clinical Significance of Changes in the Microbial Communities of the Nasal Cavity in Patients with Solid Tumors of Parameningeal Localization During Radiation Therapy

Tatyana Gorbunova; Anastasia Rodina; Oleg Merculov; Vladimir Polyakov; Research Institute of Pediatric Oncology and Hematology of N.N. Blokhin National Medical Research Center of Oncology