ARLG
Antibacterial Resistance Leadership Group

29 March 2018
Q1 Newsletter

Welcome to the ARLG Quarterly Newsletter!

Here, you will receive important updates from the ARLG regarding recent events, grants, publications, and the committees that help us work toward our mission: to prioritize, design and execute clinical research that will reduce the public health threat of antibacterial resistance.

Get Involved with ARLG

The ARLG continuously accepts proposals for clinical studies designed to prevent, diagnose, treat, or eradicate antibiotic-resistant bacterial pathogens. We also award grants and fellowships to qualified investigators. If you are interested in getting involved with ARLG, apply now or contact us for more information.

Apply for Grant

Contact Us

Recapping Our Retreat

The ARLG 2018 Operations Retreat took place from January 9-11, 2018.

This was our fourth ARLG face to face meeting where we continue to grow and prioritize our research efforts. During this meeting our goal was to present, discuss, make decisions and establish action items so that we can continue on a productive path in reducing the public health threat of antibacterial resistance.

We were able to gather a group photo of the attendees. This was a memorable event and we were excited to see all of our colleagues at this Retreat.

Upcoming Events

- The Statistics and Data Management Center (SDMC), directed by Dr. Scott Evans, will be moving from Harvard University to George Washington University in April 2018.
- ECCMID 2018 will take place April 21-24 in Madrid, Spain.

Meet Our Committees

Special Populations Special Emphasis Panel: Bringing Expertise to a New Focus Area

Chair: Melinda Pettigrew, PhD

We sat down with Melinda Pettigrew, head of ARLG's Special Populations Committee and Special Populations Special Emphasis Panel, and she let us in on some big news: Special Populations will be refining its focus to reflect a greater interest in immunocompromised hosts (specifically neutropenic patients and transplant recipients, which are populations uniquely affected by multi-drug resistant organisms (MDROs)). The committee previously focused on a wider range of issues, ranging from sexually transmitted infections to racial and health disparities.

"Rates of infection with MDROs are prevalent and increasing among immunocompromised individuals," said Pettigrew. "These patients rely on immediate active antibiotic therapy when infected with bacteria because of defects in innate immunity. Thus, they are uniquely threatened by MDR bacteria that may be resistant to the empirical therapies that they receive."

Even though immunocompromised individuals are highly impacted by MDROs, they are often excluded from and not helped by clinical trials. That's because when a sponsor writes eligibility criteria for a trial, some of their good intentions (e.g., to protect study participants from unnecessary harm), result in outcomes that cannot be generalized to immunocompromised patients.

"Moving forward the Special Populations Group would like to work to see more studies on the clinical effectiveness of newer antibiotics, combinations of antibiotics, and diagnostics in immunocompromised populations," said Pettigrew. "We are also very interested in studies that seek to identify novel means to

Pediatrics Committee: Four Things to Know

Chair: Theoklis Zaoutis, MD, MSCE

ARLG's Pediatrics Subcommittee has a mission to represent pediatric-specific issues and questions as they relate to ARLG's broader mission. Here are four interesting things you should know about this team:

1. They're a party of eight, expertly aligned. The Pediatrics Subcommittee has eight members, and each possesses expertise that corresponds to one or more of the ARLG's main areas of focus. These include Gram-negative infections, Gram-positive infections, antimicrobial stewardship, and diagnostics.

2. The numbers are in: kids aren't tiny adults. The group is passionate about tailoring trials to the unique needs of children and quick to share credible facts to support their claim. For example, a JAMA 2006 publication showed that medicines that are proven to be effective in adults fail approximately 40 percent of the time when used in children.

3. Pediatrics research is a balancing act. The team says that one of the biggest challenges in pediatric research is balancing the risk of the intervention with the potential benefits to the specific child. Pediatric investigators also have to balance assent in young children. How does one assess the willingness of a toddler who is crying due to the possibility of a blood draw? For these reasons, pediatric investigators must be trained in understanding the behavioral indications of assent in order to protect pediatric clinical trial participants.

4. When it comes to research, they know that informed kids are engaged kids. Committee member Charlie Huskins has been working with an innovative group called InsciedOut that is using hypothesis-

prevent acquisition of MDROs in these groups of patients."

based research as a means of improving science education in elementary and secondary schools. When kids realize their contribution matters to science, they are more likely to engage.

Mentoring Committee Corner

Meet Ritu Banerjee, MD, PhD

Ritu Banerjee, MD, PhD, wears a lot of hats in her professional capacity. She is an associate professor of Pediatrics and director of the pediatric antimicrobial stewardship program at the Children's Hospital at Vanderbilt University Medical Center; a practicing physician for children with complex infections; and a clinical researcher. Each of these roles is unique, and yet they all support a single common mission: helping providers and patients better understand antimicrobials and the pressing need to use them judiciously.

Through the mentorship of Dr. Robin Patel, ARLG's Diagnostic Committee chair at the time, Dr. Banerjee was awarded ARLG's Early Stage Investigator Seed Grant in 2014. She used it to launch her first trial, which showed that a rapid blood culture diagnostic was helpful for treatment of Gram-positive bacteremia, but less helpful for treatment of Gram-negative bacteremia, for which rapid phenotypic resistance detection was needed.

Today, Dr. Banerjee is building off of that initial study's results with the RAPIDS-GN study, which she launched with other ARLG investigators in 2017. This study, which stands for **Rapid** Identification and **S**usceptibility Testing for **G**ram-**N**egative Bacteremia, is evaluating antimicrobial utilization, clinical outcomes, and healthcare costs among patients with Gram negative blood system infections using a diagnostic platform that rapidly detects organisms and phenotypic drug resistance. The study is currently enrolling, and Dr. Banerjee credits the ARLG as essential to its successful progress.

"I've been fortunate to have connected with the ARLG early on in my career and benefit from incredible mentorship from senior investigators," said Dr. Banerjee. "The collaborative nature of this group is inspirational, and the infrastructure ARLG and the Duke Clinical Research Institute provide are absolutely essential to keep the study up and running."

Find out more about the **RAPIDS-GN study here**.

Recent Awards

Barbara E. Murray, MD
Alexander Fleming Lifetime Achievement Award from the Infectious Diseases Society of America (IDSA)

Arjun Srinivasan, MD
Distinguished Alumni Award - Davidson June 10, 2017

Pranita Tamma, MD and Sara Cosgrove, MD
Pranita Tamma, MD, MHS, has received the 2017 Pediatric Scholarship Award from the Society of Healthcare Epidemiology of America (SHEA), under the mentorship of Sara Cosgrove, MD.

Recent Achievements

Vance G. Fowler, MD
MIDG (Melbourne Infectious Diseases Group) - Visiting International Fellow at Forbes Week

2017

Danielle M. Zerr, MD, MPH
Seattle's Top Doctor- 2017; Seattle Magazine

Recent Publications

ARLG investigators have published 27 papers since January 2017. We have listed the most recent ones, beginning from June 2017, below:

Rojas LJ, Hujer AM, Rudin SD, Wright MS, Domitrovic TN, Marshall SH, Hujer KM, Richter SS, Cober E, Perez F, Adams MD, van Duin D, Bonomo RA **NDM-5 and OXA-181 Beta-Lactamases, a Significant Threat Continues To Spread in the Americas.**Antimicrob Agents Chemother. 2017 Jun 27;61(7). pii: e00454-17. doi: 10.1128/AAC.00454-17. Print 2017 Jul.

Martirosov DM, Bidell MR, Pai MP, Scheetz MH, Rosenkranz SL, Lodise TP **Relationship Between Vancomycin Exposure and Outcomes Among Patients with MRSA Bloodstream Infections With Vancomycin Etest® MIC Values of 1.5-2 mg/L.** Diagn Microbiol Infect Dis. 2017 Jul;88(3):259-263.

Thom KA, Rock C, Jackson SS, Johnson JK, Srinivasan A, Magder LS, Roghmann MC, Bonomo RA, Harris AD **Factors Leading to Transmission Risk of Acinetobacter baumannii.** Crit Care Med. 2017 Jul;45(7):e633-e639. doi: 10.1097/CCM.0000000000002318.

Henig O, Cober E, Richter SS, Perez F, Salata RA, Kalayjian RC, Watkins RR, Marshall S, Rudin SD, Domitrovic TN, Hujer AM, Hujer KM, Doi Y, Evans S, Fowler VG, Bonomo RA, van Duin D, Kaye KS, for the Antibacterial Resistance Leadership Group **A Prospective Observational Study of the Epidemiology, Management and Outcomes of Skin and Soft Tissue Infections due to Carbapenem-Resistant Enterobacteriaceae.** Open Forum Infect Dis 2017;4(3):ofx157. https://doi.org/10.1093/ofid/ofx157.

Nielsen TB, Pantapalangkoor P, Yan J, Luna BM, Dekitani K, Bruhn K, Tan B, Junus J, Bonomo RA, Schmidt AM, Everson M, Duncanson F, Doherty TM, Lin L, Spellberg B **Diabetes Exacerbates Infection via Hyperinflammation by Signaling through TLR4 and RAGE.** MBio. 2017 Aug 22;8(4). pii: e00818-17.

Chotiprasitsakul D, Han JH, Cosgrove SE, Harris AD, Lautenbach E, Conley AT, Tolomeo P, Wise J, & Tamma PD for the Antibacterial Resistance Leadership Group **Comparing the Outcomes of Adults with Enterobacteriaceae Bacteremia Receiving Short-Course versus Prolonged-Course Antibiotic Therapy in a Propensity-Score Matched Multicenter Cohort.** Clin Infect Dis. 2018 Jan 6;66(2):172-177. doi: 10.1093/cid/cix767.

Van Duin D, Lok J, Earley M, Cober E, Richter S, Perez F, Salata R, Kalayjian R, Watkins R, Doi Y, Kaye K, Fowler V Jr, Paterson D, Bonomo R, Evans S **Colistin Versus Ceftazidime-Avibactam in the Treatment of Infections due to Carbapenem-Resistant Enterobacteriaceae.** Clin Infect Dis. 2018 Jan 6;66(2):163-171. doi: 10.1093/cid/cix783.