ID Today

Winter 2017

Newsletter of the Duke Division of Infectious Disease

Advancing our missions

Perfect

As we assess the ending of 2016, the Division of Infectious Diseases has been blessed with successes. Our primary missions have remained the same: first-rate medical care; committed teaching and mentoring of students, housestaff and fellows; and a "state of the art" research portfolio to help push the knowledge base further.

In all respects, the Division has pushed our missions forward in an exceptional manner. We are now 46 faculty and 14 fellows with a support staff of 58. In a recent survey of research support, we rank second in research dollars among all divisions in the Department of Medicine. Our research platform is supported by 38 grants, including 8 R01 grants, 1 R21 grants, 2 P01 grants, CDC Epic Center Grants and a multitude of industry and investigator-initiated grants. Furthermore, our clinical consult volume ranks substantially higher than any other division in the Department of Medicine.

On a national/international scale, at the recent Infectious Disease Society meeting for 2016 in New Orleans, the Division presented 45 abstracts and had two plenary presentations. We published more than 275 manuscripts in 2016.

We have strengthened all areas of our expertise, including:

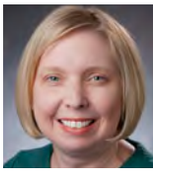
- The DICON/DASON network;
- The Transplant ID initiative;
- Global Health and One Health Focus;
- Basic studies in bacterial and fungal pathogenesis;
- Drug resistance and drug development;
- Our interactions with Duke Clinical Research Unit (DCRI);
- HIV Care and Research; and
- Expanding our outpatient clinical services including hiring a physician assistant for OPAT.

As a team, we have accomplished much, but as the saying goes, "There is much more to accomplish." In all aspects – including design of the clinical services, the structure of our clinical research unit, the growth and support of our research platform and the challenges of supporting and sustaining the fellowship program – we must continue to evolve and find internal/external support. There are many changes ahead, but our missions are sound; our worth is great; our commitment is unwavering and our team is well positioned to lead our patients, our colleagues, our university and our health care system, and the larger world of infectious diseases health care nationally and internationally.

John R. Perfect, MD
James B. Duke Professor of Medicine
Chief, Division of Infectious Divisions

Welcome new faculty

Arthur W. Baker, MD, MPH Art comes into our program from a fellowship at Duke, in which he was trained both in transplant ID and infection control. As an assistant professor, he will lead the work on the epidemiology and control of infections in transplant recipients and other immunocompromised patients. His first project was telling the story around the outbreak of Mycobacterium abscessus in our cardiopulmonary units.

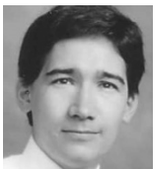


Elizabeth Dodds-Ashley, PharmD, MHS, FCCP, BCPS Libby has joined our Antibiotic Stewardship team, and will be an associate professor. She came to us from the University of Rochester.

Feng Gao, PhD A professor of medicine, Feng has transferred from the Duke Human Vaccine Institute. His work is based on the humoral response to HIV and the development of viral vaccines.

See more new faculty continued on page 2

Message from the Fellowship Program Director



Gary M. Cox, MD, Fellowship Program Director

The fellowship program is a major mission for the Division, with the focus on training the next generation of academic Infectious Diseases physicians. We have been fortunate to place more than ninety percent of fellows into an academic position after leaving the program.

- In 2016, 6 of the 8 senior fellows were supported by NIH T32 grants.
- The program continues to evolve in the teaching of the fellows, and we are committed to sustaining our 3-year fellowship training program.
- **Eileen Maziarz**, a former trainee, will become associate program director to help our 14 current fellows.

In June 2017 we will bring in this next group of outstanding fellows:

- **Julie Steinbrink** from the University of Michigan with interest in transplant ID
- **Alberto Carena** from Buenos Aires with interest in gram-negative infection
- **John Bonnewell** from Brown University with interest in global infectious diseases
- **Michael Yarrington** from Northwestern with interest in antibiotic stewardship.

The viability of the Division rests with the fellowship training program and our commitment to excellence is unwavering.

New faculty *continued from page 1*

Rachel Ann Miller, MD Rachel came to us from the University of Iowa Medical Center, where she had been director of the Infectious Diseases Transplant Service for over 20 years. As a professor of medicine, she will provide senior leadership and scholarship to the Transplant team.

Lance Okeke, MD Lance also came out of our fellowship program. He is an assistant professor focusing on the complication of chronic HIV infection and access to medicine for HIV individuals.

Megan Reller, MD, MPH Megan comes to us from John Hopkins Medical Center, where she was involved in microbiology and laboratory medicine and international studies of infectious diseases. As an associate professor, she will help in leading our focus on global health and developing a travel clinic.

Matthew Palmer Rubach, MD Matt was a fellow in our program and then completed a Medical Microbiology Fellowship in Utah. He recently came onto faculty as assistant professor, and he received a K23 award to study febrile illness in children and various zoonosis in Moshi, Tanzania.

Becky Smith, MD A former Duke fellow, Becky has returned from NorthShore University Health System, where she headed the Infection Control group. As an associate professor, she will now lead the Infection Control Team in the Duke University Health System.

Gayani Tillekeratne, MD Gayani, an assistant professor, completed a Global Health Fellowship at Duke, and established a global health care platform. She was recently awarded a K23 award to study diagnostic algorithms and antibiotic stewardship in Sri Lanka.

Antimicrobial center established at Duke

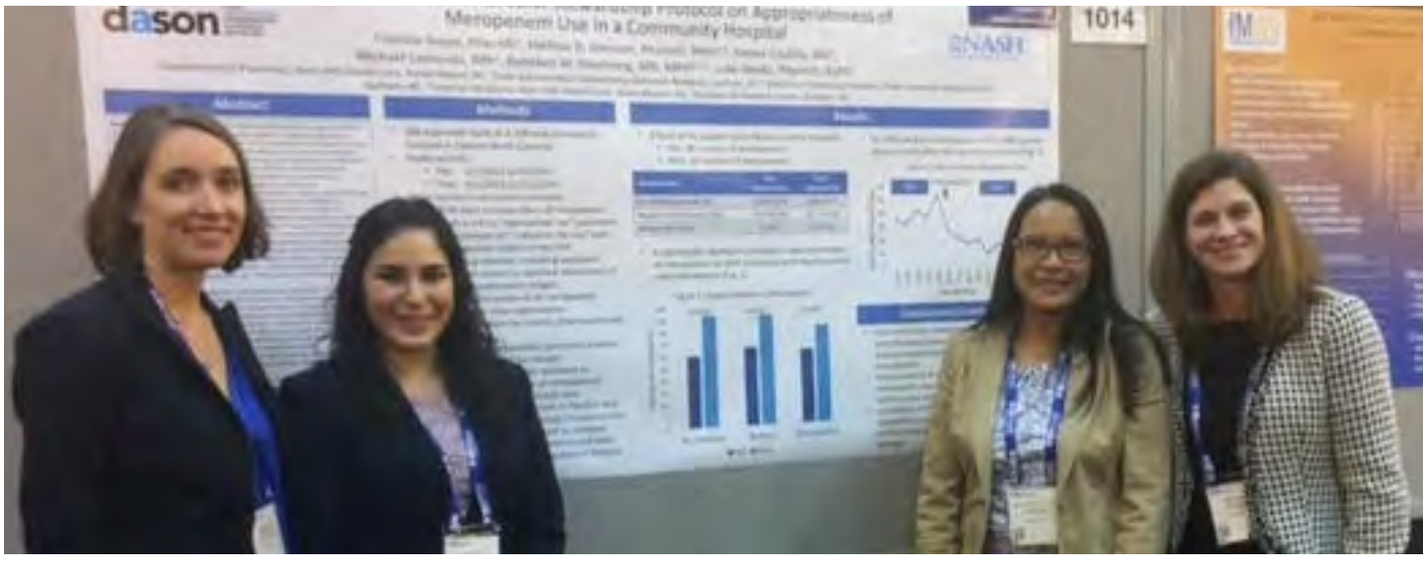

Anderson

In 2016, Duke University created the Duke Center for Antimicrobial Stewardship and Infection Prevention. Directed by **Deverick Anderson, MD, MPH**, associate professor of Medicine, this new center is now the home for all stewardship and infection prevention activities at Duke University, including the Duke Infection Control Outreach Network (DICON), the Duke Antimicrobial Stewardship Outreach Network (DASON), and Duke University Hospital programs. DICON and DASON represent unique partnerships with community hospital partners throughout the Southeastern US. Community hospital members of these networks have access to and regular interaction with experts at Duke University to improve patient safety, prevent infections, and better use antibiotics.

The Center also houses the Program for Antimicrobial Stewardship and Healthcare Epidemiology Sciences. In 2016, this research program received funding from the CDC, NIH/NIAID, and AHRQ. For example, The Centers for Disease Control and Prevention (CDC) awarded $26 million to Duke University (PI: Anderson), the University of North Carolina, and four other academic medical centers to create epicenters where researchers will develop and test innovative approaches to prevent healthcare-associated infections and the spread of dangerous bacteria infections, and to improve patient safety in healthcare settings. In September 2016, Duke (PI: Anderson) was one of the 35 organizations across the United States awarded a CDC contract to participate in the CDC Safety and Healthcare Epidemiology Prevention Research Development (SHEPheRD) Program to develop and conduct research and innovative prevention projects related to safety, healthcare-associated infections, and antibiotic resistance across the healthcare spectrum. The maximum amount of all orders issued and awarded under all contracts over the 5-year period of performance is estimated to be $200 million. Duke is the only institution that was approved to submit proposals in four of the seven research domains included in the SHEPheRD program. In fact, Duke was awarded the first contract from this program in October 2016, a $3 million contract for a three-year project in the area of antibiotic stewardship (PI: Dodds-Ashley). Under the 3-year contract, Duke stewardship experts have recruited 10 additional community hospitals to join DASON and will work with local personnel at these hospitals to implement the CDC's Core Elements of Hospital Antibiotic Stewardship.

Important Links

DICON: https://dicon.medicine.duke.edu/
DASON: https://dason.medicine.duke.edu/
CDC Epicenters: https://www.cdc.gov/hai/epicenters/
CDC SHEPheRD: https://www.cdc.gov/hai/research/safe-healthcare.html
CDC's Core Elements of Hospital Antibiotic Stewardship: https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html



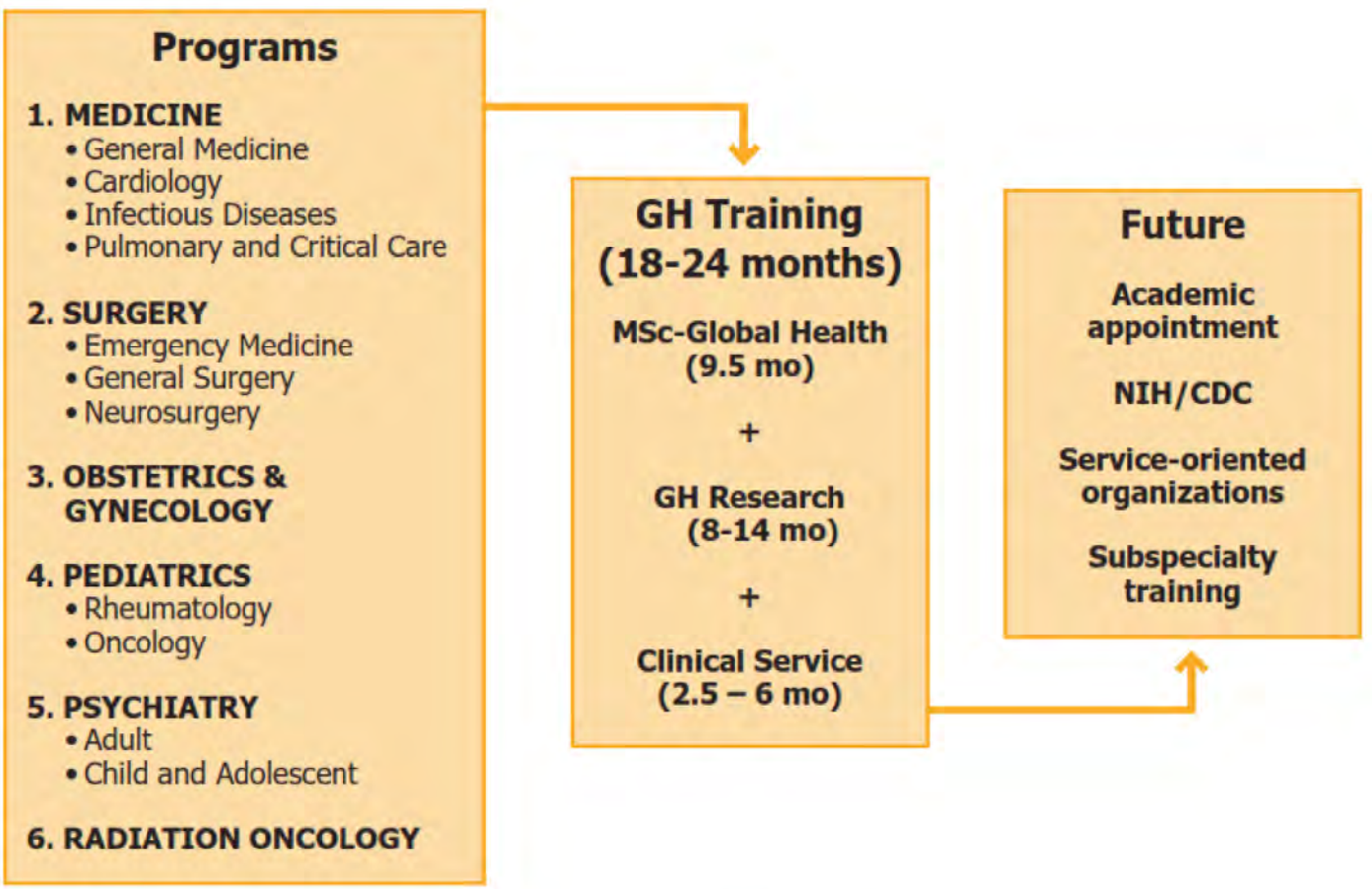
(L to R) Rebekah Moehring, Christina Reyes, Emma Castillo, and Melissa Johnson present their DASON research

The Global Health Pathway: An "On-ramp" for Academic Careers in Global Health

Established as a post-graduate medical training program in 2008, the Global Health Pathway (GH Pathway) offers a unique opportunity for Duke residents and fellows, including Infectious Diseases fellows, to develop academic careers in Global Health. The GHP, which is led by Infectious Diseases faculty member **Nathan Thielman**, has established academic relationships suitable for robust research at sites in Tanzania, Kenya, Nicaragua, South Africa, Rwanda, Sri Lanka, Peru, and Brazil. Trainees spend a minimum of 9 months at one of these locations and 9 months engaged in coursework towards a Master of Science in Global Health (MSc-GH) degree. To date, 23 residents and fellows have completed the GH Pathway, currently 10 are enrolled, and 5 more will join the program in July 2017. Fifteen trainees have successfully competed for Fogarty Global Health Fellowships and five have received early career development awards.

Residents and fellows from the GH Pathway have been academically productive. Since entering the program, trainees have published more than 70 Global Health manuscripts in diverse journals such as Lancet Global Health, JAMA, Clinical Infectious Diseases, Circulation, Injury, PLoS Neglected Tropical Diseases, Diabetes Care, and the International Journal of Gynecology & Obstetrics. Two former Duke Infectious Diseases fellows, Holly Biggs and Tom Holland, are graduates of the GH Pathway. Holly Biggs, who participated as an Internal Medicine resident, is now Medical Epidemiologist with the Centers for Disease Control and Prevention, and Tom Holland, who completed the GHP as an ID fellow in 2011, is Assistant Professor of Medicine and ID faculty member at Duke. Deng Madut, a second year ID fellow is currently in the GH Pathway, and Preeti Manavalan, a first year ID fellow will join the program in July 2017.

Global Health Pathway

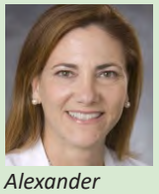


Duke | Hubert-Yeargan Center FOR GLOBAL HEALTH

Duke | GLOBAL HEALTH INSTITUTE

Awards and Honors

- Dr. Barbara Alexander received the prestigious CLSI Excellence in Consensus Management Award
- Dr. Dan Sexton gave the SHEA Lecture at IDSA
- Dr. John Perfect gave the KASS Lecture at IDSA
- Dr. Matt Rubach was awarded a K23.
- Dr. Gayani Tillekeratne was awarded a K23
- Dr. Steve Taylor was selected as a Duke Heath Scholar, a new research honor (with funding) in the School of Medicine


Alexander


Chu


Maziarz


Perfect


Rubach


Sexton


Taylor


Tillekeratne

New Awards - December 2016

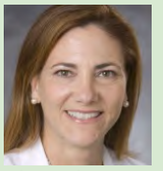
Dr. Vivian H. Chu of Infectious Diseases has received an award (1R25-HL135304-01) from the National Institutes of Health for a project entitled "Bridging the Gap to Enhance Clinical Research Program (BIGGER)." Total funding will be $487,229.

Dr. Eileen K. Maziarz of Infectious Diseases has received an award through the University of Nebraska Medical Center for a project entitled "Global Survey of Bloodstream Infections in High Risk Neutropenic Cancer Patients." Total funding will be $16,170.

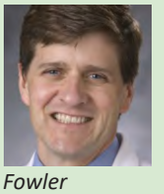
Dr. Steve Taylor of Infectious Diseases has received an award through the Fundacao Manhica for a project entitled "New approaches for malaria surveillance in an era of changing malaria transmission: the potential of pregnant women."

Grants and Funding

Industry Sponsored Clinical Trials


Alexander

Dr. Barbara D. Alexander of Infectious Diseases has received an award from Scynexis Inc for a project entitled "Open-Label Study to Evaluate the Efficacy and Safety of SCY-078 in Patients with Invasive Fungal Infections that are Refractory to or Intolerant of Standard Antifungal Treatment (FURII)." Total funding will be $3,042,194.


Fowler

Dr. Vance G. Fowler of Infectious Diseases has received an award from the ContraFect Corporation for a project entitled "CF-301-102 Study." Total funding will be $496,529.

Dr. Vance G. Fowler of Infectious Diseases has received an award from Genetech for a project entitled "Study of Prognostic Biomarkers of Severe Systemic Bacterial Infection." Total funding will be $215,000.

Large grants and funding

Two major program projects from NIH:

1. Transdiscplinary Program to Identify Novel Antifungal Targets and Inhibitors

2. Integrase Defective Lentiviral Vector (IDLV)-ENV Immunogen Strategy for an HIV Vaccine

Two Large NIH Multicenter Trials/Consortiums:

1. A Randomized, Double Blind, Placebo-Controlled Trial in Adults with community Acquired Pneumonia to Assess the Effect of Early Empiric Antifungal Treatment of Coccidioidomycosis (VTU/DCRI)

2. Antibiotic Resistance Leadership Group (DCRI)

High-Impact Publications

1. Clement ME, Park LP, Navar AM, Okeke NL, Pencina MJ, Douglas PS, Naggie S. "Statin Utilization and Recommendations Among HIV and HCV-Infected Veterans: A Cohort Study." *Clin Infect Dis*. 2016; 63:407-13. PMID: 27143663.

2. Patel JC, Mwapasa V, Kalilani L, ter Kuile FO, Khairallah C, Thwai KL, Meshnick SR, Taylor SM. "Absence of association between sickle trait hemoglobin and placental malaria outcomes." *Am J Trop Med Hyg* 2016; 94: 1002, 2016.

3. Lantos PM, Hoffman K, Anderson BD, Gray GC. "Early Peaking of Human Influenza-like Illnesses Near Swine Production Facilities, 2009-2011." *Clin Infect Dis* 83:1158-1563, 2016.

4. Esher SE, KS Ost, L Kozubowski, D-H Yang, MS Kim, Y-S Bahn, JA Alspaugh, and CB Nichols 2016. "Relative contributions of prenylation and post-prenylation processing in Cryptococcus neoformans pathogenesis." *mSphere* 1(2):e00084-15. doi:10.1128/mSphere.00084-15, 2016. PMCID 4894686.

5. Tsalik EL*, Henao R*, Nichols M, Burke T, Ko ER, McClain MT, Hudson LL, Mazur A, Freeman DH, Veldman T, Langley RJ, Quackenbush EB, Glickman SW, Cairns CB, Jaehne AK, Rivers EP, Otero RM, Zaas AK, Kingsmore SF, Lucas J, Fowler VG, Carin L, Ginsburg GS, Woods CW. "Host gene expression classifiers diagnose acute respiratory illness etiology." *Sci Transl Med*. 20 January 2016 8:322ra11. (*equally contributing first authors)

6. Thielman NM, Cunningham CK, Woods C, Petzold E, Sprenz M, Russell J (2016). "Ebola clinical trials: Five lessons learned and a way forward." *Clin Trials* 13(1):83-6. doi: 10.1177/1740774515619897. PubMed PMID: 26768559.

7. McClain MT, Nicholson BP, Park LP, Liu TY, Hero AO 3rd, Tsalik EL, Zaas AK, Veldman T, Hudson LL, Lambkin-Williams R, Gilbert A, Burke T, Nichols M, Ginsburg GS, Woods CW. "A Genomic Signature of Influenza Infection Shows Potential for Presymptomatic Detection, Guiding Early Therapy, and Monitoring Clinical Responses." *Open Forum Infect Dis*. 2016 Jan 19;3(1):ofw007. doi: 10.1093/ofid/ofw007.

8. Dicks KV, Lofgren E, Lewis SS, Moehring RW, Sexton DJ, Anderson DJ. "A Multicenter Pragmatic Interrupted Time Series Analysis of Chlorhexidine Gluconate Bathing in Community Hospital Intensive Care Units." *Infect Control Hosp Epidemiol.* 2016 Feb 10:1-7. PMID: 26861417

9. Cronan MR, Beerman RW, Rosenberg AF, Saelens JW, Johnson MG, Oehlers SH, Sisk DM, Jurcic Smith KL, Medvitz NA, Miller SE, Trinh LA, Fraser SE, Madden JF, Turner J, Stout JE, Lee S, Tobin DM. "Macrophage epithelial reprogramming underlies mycobacterial granuloma formation and promotes infection." *Immunity* 2016; 45(4): 861-876.

10. Baker AW, Dicks KV, Durkin MJ, Weber DJ, Lewis SS, Moehring RW, Chen LF, Sexton DJ,Anderson DJ. "Epidemiology of Surgical Site Infection in a Community Hospital Network." *Infect Control Hosp Epidemiol*. 2016 May;37(5):519-26.

11. Baker AW, Lewis SS, Alexander BD, et al. "Two-Phase Hospital-Associated Outbreak of Mycobacterium abscessus: Investigation and Mitigation." *Clinical Infectious Diseases*. [Accepted for publication November 22, 2016]

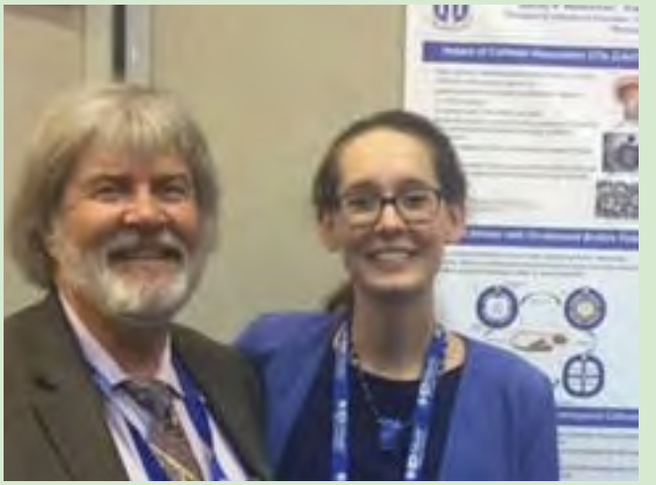
12. Evans, SR, Rubin, D, Follmann, D, Pennello, G, Huskins, WC, Powers, JH, Schoenfeld, D, Chuang-Stein, C, Cosgrove, SE, Fowler, VG, Jr, Lautenbach, E, Chambers, HF. "Desirability of Outcome Ranking (DOOR) and Response Adjusted for Duration of Antibiotic Risk (RADAR)." *Clinical Infectious Diseases* 2015; 61: 800-6. PMID: 26113652

13. Anderson DJ, Chen LF, Weber DJ, Moehring RW, Lewis SS, Triplett PF, Blocker M, Becherer P, Schwab JC, Knelson LP, Lokhnygina Y, Rutala WA, Kanamori H, Gergen MF, Sexton DJ; CDC Prevention Epicenters Program. "Enhanced terminalroom disinfection and acquisition and infection caused by multidrug-resistant organisms and Clostridium difficile (the Benefits ofEnhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study." *Lancet*. 2017 Jan 16. pii:S0140-6736(16)31588-4. doi: 10.1016/S0140-6736(16)31588-4

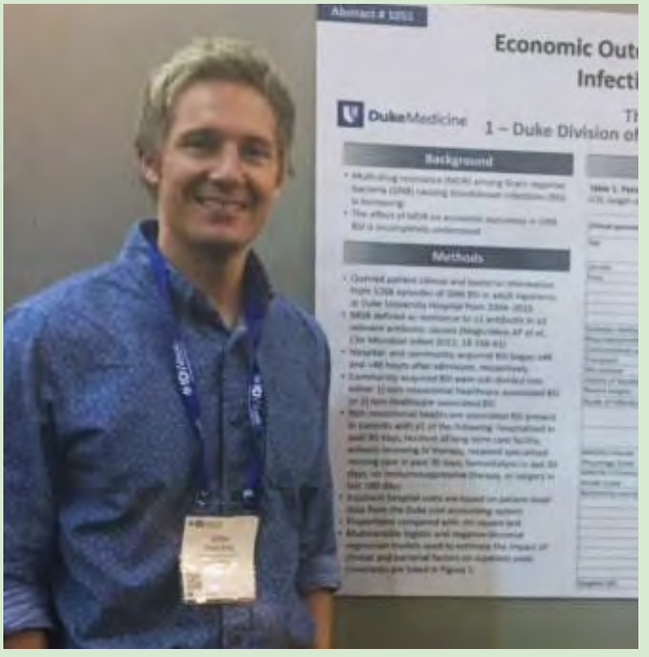
Other

ID 'on the scene'

Marion Hemmersbach-Miller, Jasime Chung, Andrew Strand, and Julia Messina



John Perfect and Stacey Maskarinec



Josh Thaden

Becky Smith, Elieen Maziarz, Tom Holland, and Anna Person

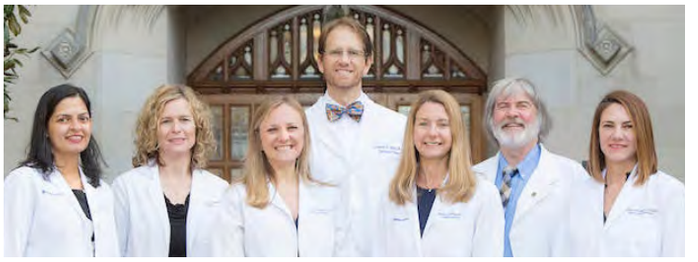
Art Baker

Duke Transplant/Immunocompromised Host Infectious Diseases Service; Providing Concierge Level Care for Populations at High Infectious Risk

Organ transplantation and cancer chemotherapy are life-saving interventions for an increasing number of patients who survive rather than succumb to their underlying illness. Despite important advances in surgical technique, immunosuppressive regimens, and the development of novel antimicrobial agents, these immunocompromised hosts remain at substantial risk for developing infections. Not only are these vulnerable hosts direct targets for emerging pathogens, they may serve as 'super-spreaders' of infectious diseases within the community and hospital by shedding large amounts of pathogens for prolonged durations, thereby increasing the potential for transmission to others. In fact, infectious diseases are among the leading causes of death in immunocompromised hosts, especially those patients receiving organ and stem cell transplantations and cancer chemotherapy. Care of this complex patient population requires unique knowledge that differs from that of the general Infectious Diseases clinician. Accordingly, Transplant Infectious Diseases has emerged as a subspecialty within the field of Infectious Diseases (ID) and the American Society of Transplantation has developed a core curriculum for training specialists in Transplant ID. Hospitals across the country are increasingly providing support for this expertise in an effort to improve patient care and contain costs.

Duke Hospital is a major transplant and cancer care center. In 2016, 433 solid organ transplants including 96 lung/heart-lung, 70 heart, 98 liver, 164 kidney/kidney-pancreas/pancreas, 3 intestinal and one hand transplant were performed at Duke. The lung transplant program is one of the largest in the world, performing over 1700 lung transplants since 1994 and boasting excellent outcomes compared with national averages. The heart transplant program is one of the top five in the U.S., with an active population of patients living with durable ventricular assist devices (VADs) as a bridge to transplant. While life sustaining, these devices are prone to infection. Approximately 140 durable long term VADs were placed in 2015 (largest implanting center in the US) and ~ 250 patients are on-going VAD support.

In addition, ~ 280 adult HSCT transplants are performed at Duke each year, of which a substantial number are unrelated umbilical cord blood transplants. The hematologic malignancy inpatient service (9100) treats approximately 200 AML patients each year including 100 requiring induction, 50 aggressive first re-induction, and 50 have had multiply relapses but trying other aggressive chemotherapy. Another 125 receive treatment for ALL and MDS. The Duke Transplant/Immunocompromised Host ID (TxID) Service has provided essential and comprehensive care for these patient populations since its creation in 1999, by Dr. Barbara Alexander, Director of the program. Dr. Alexander and a team of nine additional ID faculty including Drs. Cam Wolfe, Eileen Maziarz, Sana Arif, Rachel Miller, Jennifer Saullo, Art Baker, John Perfect, Andy Alspaugh and Aimee Zaas, and one Physician Assistant, dedicate their clinical time to the TxID service . These clinicians cover the inpatient service which averages a daily census of ~ 50 patients, staff 12 outpatient clinics per week to ensure these immunocompromised and transplant patients have timely access for acute infectious issues, and ensure infection related protocols are continuously updated based on national and center specific data. They also serve as first line responders for infection outbreaks and are available 24/7 to assist the primary medical and surgical teams with acute issues, for example, determining infectious risk and suitability of organs under consideration for use in recipients at Duke.



(L to R) Drs. Arif, Horan, Maziarz, Wolfe, Miller, Perfect and Alexander

The TxID Faculty are also heavily involved in education, routinely precepting ID Fellows, PharmD Residents and PA students rotating on the service. The Duke University Transplant ID Physician Scientist Training Program is the only NIH funded (T32 AI100851) Transplant ID training program in the country. Current trainees include Dr. Julia Messina, whose research is focused on the evolution of the gut microbiome over the course of chemotherapy/stem cell transplantation and predictors of enterococcal bloodstream infection, and Dr. Marion Hemmersbach-Miller, who is working to identify the types of infections that occur and their impact on morbidity and mortality in older (age >65 years) kidney transplant recipients. These research platforms are targeted to provide critical information which will translate into improved patient care and outcomes.

HOPE IN ACTION

Another recent and exciting initiative by the TxID team includes helping to implement the HOPE Act at Duke. In 2013, President Obama, signed into law the HIV Organ Policy Equity (HOPE) Act, a bipartisan piece of legislation that allows scientists to carry out research into organ donations from one person with HIV to another. Drs. Wolfe and Hemmersbach-Miller have worked with the transplant teams to operationalize a protocol for using HIV infected organs for HIV infected recipients at Duke, including obtaining approval from the State Health Director and the Duke Regulatory Authorities. These efforts will aid in expanding the donor pool for HIV infected patients and will accelerate our understanding of transplant immunology. The multi-faceted efforts of the Transplant/Immunocompromised Host Service at Duke are far reaching, ultimately helping to ensure excellence in patient care and facilitating a deeper understanding of preventing and managing the infections that compromise our patients' health.