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News from the Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases

International Fellows Visit the Fisher Center

From time to time the Fisher Center provides office space for visiting researchers and physicians. Over the past year, the following international fellows have passed through the Fisher Center and we are grateful for the opportunity to have met them and wish them well as they return to their home countries.



Sharmila Sengupta, MD Head and Senior Consultant, Department of Clinical Microbiology & Infection Control, The Medicity Hospital, Gurgaon, (Delhi NCR),

India Dr. Sengupta had always dreamt of visiting Johns Hopkins University ever since she joined medical school, and the opportunity came in the form of a Fulbright Fellowship. She is extremely grateful to Trish Perl, MD who was her mentor and the US-India Education Foundation (USIEF) for awarding the fellowship. Dr. Sengupta came with a desire to learn the subject of healthcare epidemiology. Under the guidance of Dr. Perl, along with Drs. Aaron Milstone, Yukari Manabe and Amita Gupta, the team applied for a Bill and Melinda Gates Foundation grant to create an Antimicrobial Network

Surveillance in India. As resistant bacteria seen in Southeast Asia find their way within short order to North America and Europe, this work is directed at staunching the emergence of resistant bacteria.

The Fellowship also permitted Dr. Sengupta to attend a biostatistics class at the Bloomberg School of Public Health. She describes her time at Hopkins as an “enriching experience of great value” and likens the medical library to “visiting Alibaba’s cave of knowledge.” Hopkins staff benefited from Dr. Sengupta’s expertise when she presented “Burden of Antimicrobial resistance – Indian scenario” at our Clinical Conundrum meeting.

In her own words, Dr. Sengupta says, “I will be going back to my country, with the treasure of knowledge, skill and experiences I gained during this short duration in infectious disease and healthcare epidemiology. The memories of warmth, friendship and help received will be with me forever. I hope that this will be the beginning of a long relationship and future collaborative work.” Upon her return to India, Dr. Sengupta hopes to “improve on my work and add more value to my professional skills in patient service” and “build up an educational program

for healthcare epidemiologists in India.



Nouf Almaghlouth, MBBS, MPH, Postdoctoral Research Fellow, Saudi Arabia
Dr. Almaghlouth is a Postdoctoral Research Fellow from Saudi Arabia. In 2014, Dr.

Almaghlouth graduated from the Johns Hopkins University, Bloomberg School of Public Health with a concentration in infectious diseases, followed by 8 months of research on HIV and Hepatitis C infections under the mentorship of Mark Sulkowski, MD. At this time the research is awaiting publication.

In an oral presentation at the 2015 ID Week in San Diego, CA she reported statins are associated with decreased progression of liver disease in HIV/HCV co-infected patients. In addition, Dr. Almaghlouth won the 2015 ID Week trainee award (HIVMA) for a top abstract submission among other trainees. Dr. Almaghlouth has returned to Saudi Arabia to continue her work in infectious diseases, meanwhile awaiting the 2016 match result for US medical residency to continue her training.

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Mission Statement

The Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases is dedicated to the clinical research of environmental pathogens which improves the diagnosis and treatment of these infections.



A word from our Director Paul Auwaerter, M.D., M.B.A.

Clinical Director, Division of Infectious Diseases

News from Vienna ICLB 2015

Although the discovery of Lyme disease occurred following investigation of an epidemic of juvenile arthritis in Connecticut 40 years ago, descriptions of what has become known as Lyme disease trace back to the 1930s and potentially even earlier in European medical journals. While annual estimates of Lyme disease in the United States center around 300,000 cases, surveillance information in Europe suggests that more than 65,000 cases occur yearly mostly in temperate northern Europe. More recently, Lyme disease has been increasingly reported in northern China and neighboring states. Often Europeans refer to the infection as Lyme borreliosis rather than Lyme disease, as the agents of infection include additional strains other than *Borrelia burgdorferi* sensu stricto, such as *B. garinii* and *B. afzelii*.

Reflecting the global nature of Lyme disease, the premier scientific conference regarding *Borrelia* infection alternates every 2-3 years between North America and Europe. Now in its 14th iteration, the International Conference on Lyme Borreliosis and Other Tickborne Diseases was held recently in Vienna, Austria. Often referred to as the ICLB, the Fisher Center presented preliminary information on consultations for Lyme disease (2000-2013) at Johns Hopkins reflecting the significant work of Takaaki Kobayashi, MD who compiled the data

on 950 patients. The link to the full presentation can be found at the end of this article. Analysis suggested that patients being referred with more than six months of symptoms, female gender, history of unvalidated Lyme disease testing, use of three or more antibiotics and use of antibiotics for more than six months all correlated with Lyme disease as being less likely an explanation for their symptoms.

Among the many insightful talks and posters, there are two items of especial interest. One was the first report of a new *Borrelia* species closely related to *Borrelia burgdorferi*. This work, by Pritt et al, was a collaboration from the Mayo Clinic and the Centers for Disease Control. Using molecular technologies, these investigators described six patients who had a novel organism that caused an acute illness with rash, headache, joint swelling, neurologic and constitutional complaints. Provisionally called *Borrelia mayonii* in recognition of the discovering laboratory, all patients came from either Minnesota or Wisconsin. Deer ticks subsequently tested from these areas were found to be positive for *B. mayonii*. This now increases to a total of 3 different *Borrelia* species transmitted by deer ticks with the other *B. miyamotoi* besides the well-known agent of Lyme disease, *B. burgdorferi*. Though little is yet precisely known, and this report is unpublished, it is probably not the last

as we learn more of infections that ticks can transmit. It would be surprising if this new organism doesn't respond well to customary antibiotics such as doxycycline amoxicillin.

Anneleen Berende (Nijmegen, Netherlands) reported the results of a study funded by the Dutch Ministry of Health examining the effect of prolonged antibiotic treatment in patients believed to be suffering cognitive effects such as brain fog after infection by Lyme Borreliosis. The PLEASE (Persistent Lyme Empiric Antibiotic Study Europe) study was a blinded trial that examined whether 12 weeks of doxycycline or clarithromycin and hydroxychloroquine led to improvement compared to placebo. Each of the three arms in the study had 85 patients; however, after 52 weeks observation, there was no difference in those who received the antimicrobials versus those who got placebo. This is now the sixth study that has failed to show significant, durable benefit to prolonged antibiotic therapy. Although some have criticized that the treatment was not long enough or hadn't received the right types of antibiotics, it likely means that patients who suffer from prolonged symptoms after initial therapy likely have other mechanisms such as immunological or neurological rather than active infection.

<https://www.dropbox.com/s/u72vd6uduzpvaef/ICLB.pdf?dl=0>

Thank you to those who contributed so generously to Environmental Infectious Disease research this past year. Such gifts help facilitate innovative research, especially targeted to younger investigators.

In particular we would like to acknowledge:

- The Buck Foundation
- Leonard Hartwig
- The Scott Sherman and Julie Rothman Charitable Gift Fund

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William Wordria, MBChB, MMed, PhD Ministry of Health, Republic of Uganda and Senior

Consultant Physician, Mulago, Kampala, Uganda Dr. Worodria is a pulmonary specialist who is pursuing post-doctoral training through the Fogarty International Center D43 training grant entitled *HIV co-infections: tuberculosis, cryptococcus, and viral hepatitis* with Yuka

Manabe, MD. His research is in the area of TB-HIV co-infection and early complications of antiretroviral therapy including immune reconstitution inflammatory syndrome. At this time Dr. Worodria continues his work in Africa.

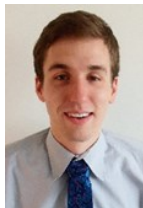
Fisher Center Discovery Program 2016

The Fisher Center Discovery Program (FCDP) was created in 2013 to provide research funds for environmental infectious disease projects that lack traditional funding mechanisms. In the first three years, \$710,812.12 has been distributed to 14 Johns Hopkins faculty members in the School of Medicine and Bloomberg School of Public Health. Data from these smaller, usually pilot, studies have been used by investigators for larger successful grant applications. In just this short time, FCDP supported investigators have received **\$4,126,017.00** in additional grants, which represents a robust **480.5%** return on investment (ROI). The ROI is indicative of the quality and clinical importance of proposals that have been awarded. The FCDP Board and supported investigators thank the Fishers and other generous donors for your support of innovative pilot studies not typically support by customary research grants.

Recently the Fisher Center Discovery Program Board reviewed 12 proposals for the 2016 grant cycle. After careful analysis the Board is pleased to have approved the following four projects headed by the following principal investigators.



Petros Karakousis, MD and William Matern, BS
Identifying molecular targets for preventing multidrug tolerance in *Mycobacterium avium* infection



Mycobacterium avium (*M. avium* intracellulare, MAI) is a major environmental pathogen in the United States and around the world, causing disease similar to tuberculosis, especially in older women, smokers, immunocompromised patients and those with structural lung disease. MAI is likely inhaled from household and environmental water sources. MAI is known to be particularly difficult to treat, requiring three or more drugs and requiring 12-24 months of therapy. Characterizing the genetic mechanisms behind observed multi-drug tolerance in *M. avium* could lead to novel treatments which boost the effectiveness of antibiotics. The team will identify and

investigate *M. avium* genes involved in the phenomenon of multi-drug tolerance using molecular and bioinformatics tools. This project will provide a foundation for future work to improve the success rate and simplify treatment of patients infected with *M. avium*.



Patricia Simner, PhD
Molecular Epidemiology of Carbapenem Resistant Gram-Negative Organisms (CROs) at Johns Hopkins Hospital: Do Patients Infected with CROs Contaminate the Hospital

Room Environment? In 2013, the U.S. Centers for Disease Control and Prevention assigned the highest threat level to carbapenem resistant Gram-negative organisms (CROs) and declared that they require urgent public health attention. Carbapenem-producing Gram-negative organisms (CPOs), are a subset of CROs and are increasing in prevalence and resistant to most available antibiotics. For hospitalized patients, they are a significant source of morbidity as well as mortality, reaching up to 80%. CPOs in hospitals may spread through multiple avenues to vulnerable patients causing devastating infections. The goals of this study are to use molecular technologies to quickly identify and then trace CPOs if they circulate in the hospital and determine if patients with CRO infections go on to contaminate the hospital environment such as their rooms. These data will further guide both infection control and treatment practices for CROs at Johns Hopkins Hospital, which should quickly benefit patient care.



Diane Griffin, MD, PhD
The role of nsP3 in neurovirulence of chikungunya virus
The chikungunya virus (CHIKV) is an important emerging mosquito-borne

infection that historically has caused infection in Africa and Southeast Asia. Increasingly CHIKV has in the last two years been introduced to the Caribbean causing an estimated million plus infections. Not just a risk for travelers, cases will likely be seen commonly in

the subtropical United States. Symptoms begin 3-7 days after a bite from an infected mosquito and include fever, headache, muscle pain, joint swelling, or rash. The joint pain can be severe and debilitating. Perhaps most devastating, some patients develop eye symptoms, heart inflammation and encephalitis. Symptoms usually resolve in 7-10 days, but the joint pain may persist for months. For those afflicted with encephalitis, some do not fully recover. At present there is no specific antiviral medication for CHIKV infection. There is very little funding for CHIKV research and this is thought to be the first CHIKV research at Johns Hopkins. This pilot study will explore the importance of CHIKV sequence variation in nonstructural protein (nsP3) which may be involved in neurotropism, using patient isolates from multiple independent outbreaks in India of chikungunya arthritis that varied in the incidence of neurologic complications.



Brian Schwartz, MD, MS and Melissa Poulsen, PhD
High-density poultry operations and associated infectious disease risks



Concern is mounting regarding community health impacts of industrial food animal production (IFAP). Pathogens from IFAP spread to the environment via ground, air, and water pollution and in animal waste used as fertilizer on crop fields. Indiscriminate

antibiotic use in IFAP also leads to antimicrobial-resistant bacteria, contributing to antibiotic-resistant diseases in humans. This study will investigate associations between residential proximity to high-density poultry operations and infectious disease risks in an area of Pennsylvania located near numerous poultry IFAP operations. By combining information in medical and non-health databases the team will assess patient illness while accounting for factors affecting pathogen transmission such as heavy rainfall, temperature, and land use surrounding poultry operations and crop fields. This study advances efforts in precision medicine and precision prevention.

Funding Our Future

Thanks to all of you that believe in the mission of environmental infectious disease research. As always, we are extremely grateful to those who have contributed. To donate, please consider the following options and designate the **Fisher Center for Environmental Infectious Diseases**

Online: To make a gift or pledge online, please complete our secure online giving form, <https://secure.jhu.edu/form/infdis>

Phone: To speak to someone directly about making a gift, please call 410-550-9893

Presentations

Six Drugs for Resistant pathogens: Good News from ID Week 2015. **Paul Auwaerter, MD, MBA.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/853456>. November 2, 2015

New Antimicrobials. **Paul Auwaerter, MD, MBA.** 10th Infectious Diseases Update for Primary Care and Hospital Medicine, at the Johns Hopkins University, School of Medicine, in Baltimore, MD. October 23, 2015

Lyme Disease. **Paul Auwaerter, MD, MBA.** 10th Infectious Diseases Update for Primary Care and Hospital Medicine, at the Johns Hopkins University, School of Medicine, in Baltimore, MD. October 22, 2015

Poster: Lyme Disease Consultations at Johns Hopkins 2000-2013. **Takaaki Kobayashi, MD, Yvonne Higgins, PA, MAS, MS/ITS,** Roger Samuels, MD, Aurasch Moaven, BS, Paul Lantos, MD, Michael Melia, MD, **Paul G. Auwaerter, MD, MBA.** ID Week, in San Diego, California. October 9, 2015

ID Week 2016: What to Expect. **Paul Auwaerter, MD, MBA.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/851853>. October 2, 2015

Poster: Lyme Disease Consultations at Johns Hopkins 2000-2013. **Takaaki Kobayashi, MD, Yvonne Higgins, PA, MAS, MS/ITS,** Roger Samuels, MD, Aurasch Moaven, BS, Paul Lantos, MD, Michael Melia, MD, **Paul G. Auwaerter, MD, MBA.** 14th International Conference on Lyme Borreliosis and other Tick-Borne Diseases, in Vienna, Austria. September 28, 2015

Fun, Friends, and Norovirus Down at the Good Old Swimming Hole. **Paul Auwaerter, MD, MBA.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/849390>. August 18, 2015

Time to Become Familiar With Babesiosis? **Paul Auwaerter, MD, MBA.** Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/846942>. July 1, 2015

Fisher Focus

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Recent Publications

Characteristics and Treatment Outcomes of Propionibacterium acnes Prosthetic Shoulder Infections in Adults. Damani A. Piggott; **Yvonne M. Higgins; Michael T. Melia;** Brandon Ellis; **Karen C. Carroll;** Edward G. McFarland; **Paul G. Auwaerter.** Open Forum Infectious Diseases 2015; doi: 10.1093/ofid/ofv191

Prescribing Ceftolozane/Tazobactam for Pediatric Patients: Current Status and Future Implications. Tamma, S.M., Hsu, A.J., & **Tamma, P.D.** *Pediatr Drugs* 2015 Dec 8. [Epub ahead of print] PMID: 26645401

Shigella Infection among Household Contacts of Pediatric Shigellosis Patients in Rural Bangladesh: Infection Characteristics and Environmental Risk Factors. **George CM,** Ahmed S, Talukder TA, Azmi IJ, Perin J, Sack BR, Sack D, Stine OC, Lauren Oldja L, Akter F, Ali S, Chakraborty S, Parvin T, Bhuyian SI, Bouwer E, Zhang Z, Faruque ASG. *Emerging Infectious Diseases.* 2015 Nov;21(11):2006-13. PMID: 26484778

Geographic Expansion of Lyme Disease in the Southeastern United States, 2000-2014. Lantos PM, Nigrovic LE, **Auwaerter PG,** Fowler VG Jr, Ruffin F, Brinkerhoff RJ, Reber J, Williams C, Broyhill J, Pan WK, Gaines DN. *Open Forum Infect Dis.* 2015 Sep 27;2(4):ofv143. doi: 10.1093/ofid/ofv143. eCollection 2015 Dec. PMID: 26550580

The use of a combination antibiograms to assist with the selection of appropriate antimicrobial therapy for carbapenem-resistant Enterobacteriaceae infections. Hsu, A.J., **Carroll, K.C., Milstone, A.M.,** Avdic, E., Cosgrove, S.E., Vilasoa, M., & **Tamma, P.D.** *Infect Contr Hosp Epidemiol* Aug 27:1-3. [Epub ahead of print].

Fecal Markers of Environmental Enteropathy are Associated with Animal Exposure and Caregiver Hygiene in Bangladesh. **George CM,** Oldja L, Biswas S, Perin J, Lee GO, Kosek M, Sack RB, Ahmed S, Haque R, Parvin T, Azmi IJ, Bhuyian SI, Talukder KA, Faruque AG. *Am J Trop Med Hyg.* 2015 Aug 5;93(2):269-75. PMID: 26055734

Impact of Toxigenic Clostridium difficile Colonization on the Risk of Subsequent C. difficile Infection in Intensive Care Unit Patients. **Tschudin-Sutter S, Carroll KC, Tamma PD,** Sudikum ML, Frei R, Widmer AF, Ellis BC, Bartlett J, **Perl TM.** *Infect Control Hosp Epidemiol.* 2015 Jul 30:1-6. [Epub ahead of print] PMID: 26223207

High prevalence of reduced chlorhexidine susceptibility in organisms causing central line-associated bloodstream infections. Suwantarat N, **Carroll KC,** Tekle T, Ross T, Maragakis LL, Cosgrove SE, **Milstone AM.** *Infect Control Hosp Epidemiol.* 2014 Sep;35(9):1183-6. doi: 10.1086/677628. Epub 2014 Jul 23. PMID: 25111928

Poor positive predictive value of Lyme disease serologic testing in an area of low disease incidence. Lantos PM, Branda JA, Boggan JC, Chudgar SM, Wilson EA, Ruffin F, Fowler V, **Auwaerter PG,** Nigrovic LE. *Clin Infect Dis.* 2015 Jul 20. pii: civ584. [Epub ahead of print]. PMID: 26195017