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

Understanding *Shigella* Infection in Rural Bangladesh



Principal Investigator, **Christine Marie George, PhD**, is a 2014 Fisher Center Discovery Program (FCDP) award recipient.

Background *Shigella* is a bacteria that causes diarrhea, bloody stools, and stomach cramps, occurring worldwide, including the US. *Shigella* historically was termed dysentery or “the bloody flux,” causing sporadic infection and food or water-borne illness outbreaks. An estimated 165 million cases occur annually with the greatest number in children under the age of five. Two recent studies have found Bangladesh to have the highest rates of *Shigella* infections making this locale an opportune area for study of this infection.

FCDP Supported Study “Identifying Transmission Routes for *Shigella*” is an essential foundation for developing appropriate intervention strategies. Because there has been little work done to identify environmental and clinical transmission factors for *Shigella* infection among family members and household contacts of shigellosis patients, Dr. George and her colleagues at the International Center for Diarrheal Diseases, Bangladesh,

conducted a study to identify such risk factors for acquiring infection. For this study, a group of household contacts of shigellosis patients were matched with families in the community without infection and both followed prospectively. Stool and drinking water samples were tested for *Shigella*. Dr. George found that household contacts of shigellosis patients were 44 times more likely to develop a *Shigella* infection than were control contacts. The majority of household contacts of shigellosis patients were infected with the same or closely related strain as the patient. In addition, latrine area fly counts were significantly higher in patient households compared with control households.

Research Impact Through this work Dr. George demonstrated that family members of Shigellosis patients were at a high risk of a *Shigella* infection and that high fly counts were an important association for transmission. These findings highlight the essential need for improved household hygiene practices to reduce *Shigella* transmission in rural Bangladesh.

Recently, there have been major outbreaks of *Shigella* across the US, including in California and New York. High shigellosis rates have also been observed in both rural and Native

American communities residing on reservations. Both settings typically have limited access to treated municipal water supplies and sanitation infrastructure. Understanding *Shigella* infection in Bangladesh should translate into improved disease prevention practices also applicable in the US. **Additional Research** Dr. George has found her Fisher Center supported funding invaluable for next steps in advancing research into diarrhea as well as her professional development. The research has led to six publications, with other articles under preparation, in addition to numerous poster and oral presentations. Data gathered in this Fisher Center supported study led to Dr. George receiving a prestigious NIH Career Development Award and two USAID (United States Agency for International Development) grants. Recently she received the Johns Hopkins University Catalyst Award for early career faculty. Per Dr. George, “The FCDP has allowed me to build training that has been extremely valuable during my current transition to an independent investigator. This is a wonderful program. I am truly grateful for this support.” Dr. George will continue her efforts in implementing interventions to reduce exposure to intestinal pathogens such as *Shigella*.

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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

Legionella Infections: Increasing Cases Suggest Need for Better Prevention

Just over forty years ago, a group of convention attendees in Philadelphia developed severe and often lethal pneumonia. I remember reading about this still mysterious illness as a teen during the family vacation that summer when Time magazine had on its cover story: “Tracing the Philly Killer.” Originally called “Broad Street Pneumonia” for the location of the hotel used for the meeting, it quickly became known as Legionnaires’ disease as most of the afflicted were older American Legion members who had significant smoking histories or other major health problems. In December 1976, a Centers for Disease Control (CDC) scientist, Dr. Joseph McDade, isolated the cause by inoculation of guinea pigs, the bacteria that was later named *Legionella pneumophila*.

In the years since, we now know that there are over 60 species of *Legionella* that can cause human disease. It is fairly common in the environment including streams and ponds but is thought to be most threatening when in warmer water sources. The infection is usually acquired by people inhaling aerosols of contaminated water. Examples include the droplets that might come from mists of industrial air

conditioning chillers, large hot water systems such as in hotels or hospitals, and even municipal water supplies.

There has been a steady increase in the number of *Legionella* cases in the past decade for unclear reasons. Some higher profile outbreaks include Flint, Michigan when the municipal water supply changed sources resulting in 78 infections over two years with 14 deaths as well as the recent outbreak this summer on the Upper East Side of Manhattan that remains without a clear source.

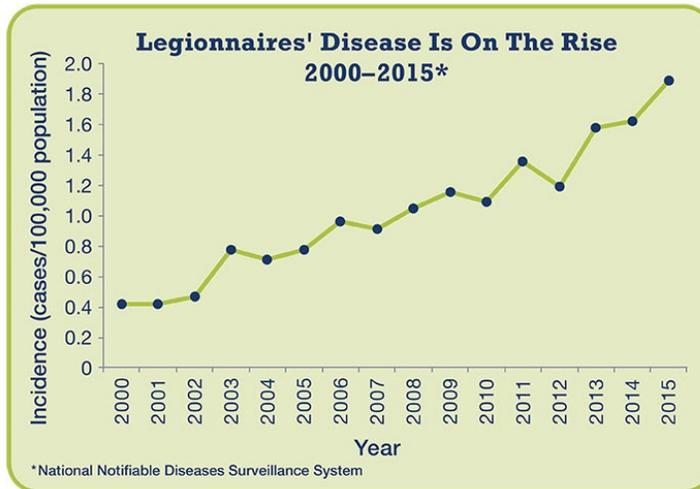
most important, is that many buildings do not have a water maintenance routine for buildings. *Legionella* is famously resistant to typical sterilization strategies, and therefore remains difficult to eradicate without costly interventions.

In hospitals where ill patients are particularly vulnerable, oddly the emphasis to use hand sanitizers means that water spigots are less commonly opened in rooms and hallways leading to stagnation and to an increased risk of not only *Legionella* contamination but also other organisms such as *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia* and *Aspergillus* species.

More attention to well-maintained water and cooling systems as well as clean water is now a major focus that falls to the relatively unsexy pending more money on regular and proper maintenance. Environmental pathogens such as *Legionella* find their niches, and only by good surveillance and sound routines can the trend be reversed given our increasingly large-scale buildings and infrastructure systems that make up modern life for so many. For dwellers

and workers in large buildings, you may wish to ask the superintendent if there is a water management practice in place.

Image source: CDC



In the United States, reported cases of Legionnaires’ disease have increased by nearly four and a half times since 2000. More illness occurs in the summer and early fall but can happen any time of year.

Recent research by the CDC and others suggest that improper maintenance of water and commercial air conditionings systems account for many of the noted outbreaks. Probably

Thank you to those who contributed so generously to support environmental Infectious disease research and education in the past six months. Such gifts help facilitate innovative research, especially targeted to early career investigators.

In particular we would like to acknowledge:

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Why Fisher Center Supported International Research Helps in the U.S. and Abroad

Global Health Program

The federally funded **Fogarty International Center**, a part of the National Institutes of Health (NIH) supports and facilitates global health research conducted by US and international investigators by facilitating exchange visits, providing training, and supporting research in low-resource settings. Established in 1968, 6000 scientists worldwide have received research training through Fogarty programs. Fogarty awards \$54 million through 500 grants each year.

The Fisher Center is pleased to offer space to visiting Fogarty Fellows during their stay at Johns Hopkins. While at Johns Hopkins, the majority of Fellows take classes in the Bloomberg School of Public Health, along with personalized mentoring by a Hopkins faculty member, that continues when Fellows return to their home countries. For more information about Fogarty's mission, please go to their webpage: <https://www.fic.nih.gov/Pages/Default.aspx>

The Fogarty Global Health Fellows Program here at Johns Hopkins offers competitive fellowships to trainees to spend 11 months in low and middle – income countries to conduct research.



The Principal Director, **Yukari Manabe, MD**, is the Associate Director of Global Health Research and Innovation at the Hopkins Center for Global Health in the Bloomberg School of

Public Health and is the Clinical Director of the John G. Bartlett Specialty Practice (infectious diseases) in the School of Medicine. Her research interests include global health, epidemiology, tuberculosis, and HIV/AIDS, as well as cost-efficient diagnostic innovations for acute febrile illness in low resource settings. She also runs two other Fogarty training programs based in Uganda to train researchers to build research capacity

Visiting Fogarty Fellow

Dr. Stella Zawedde-Muyanja, MBChB, MPH is a post-doctoral



research fellow from Uganda where she works to improve tuberculosis care in public health facilities around the country. In Uganda, despite widespread TB diagnostics, half of all people with TB are not enrolled in the National TB Program. Her research work is focused on strengthening healthcare systems to increase the number of patients entering and completing the TB Cascade of Care. She is supported by the Fogarty International Center D43 (HIV Co-infections) training grant and is attached to the Infectious Diseases Institute (IDI) in Mulago, Uganda.

While visiting Johns Hopkins, Dr. Zawedde-Muyanja found her mentorship with **Dr. Richard Chaisson**, Director of the Johns Hopkins Center for Tuberculosis Research, to be immensely helpful. Per Dr. Zawedde-Muyanja, "Coming to Johns Hopkins University gave me a unique opportunity to meet and interact with thought leaders in the field of TB clinical care and research. Attending the weekly TB Clinical and Research meetings led by Dr. Chaisson and meeting with him in person greatly enriched my understanding of TB research around the world and helped me refine my research questions and to align them closer to the international TB research agenda."

Dr. Chaisson received funding last year from the Fisher Center for his Zika virus research in Brazil.

Funding International Research

Why fund international research? It is a good question in these times of budgetary constraints. As a reminder from the Fogarty International Center, infectious diseases know no borders.

Local Experts Programs that develop and mentor scientific expertise in developing countries will help ensure that future pandemics may be detected and managed earlier, hopefully at the point of origin, thereby containing and minimizing their impact. Strengthening the local response can protect other countries by preventing the spread of disease across international borders. As the dynamics of human and animal health change with increased

globalization, more new infections and outbreaks are now occurring. Training local healthcare workers and policy makers and linking them to a global network of experts can reduce costs as compared to an external response managed solely by the United States.

Accelerating Discovery For diseases more prevalent in a foreign country than in the US, there may be better conditions for research such as a greater number of available cases and providers sensitive to local culture. This may result in accelerating discoveries and providing more conclusive research outcomes, the results of which may be applicable to public health measures in the US.

Drug Development Trials Academic institutions and pharmaceutical companies often conduct research in low and middle-income countries. Clinical trials provide medical care, local jobs and training, reduced operational costs, and local infrastructure improvements. However, there is the risk of exploiting those in financial need and possibly exposing them to unknown safety issues and side effects. To ensure research is conducted in a safe and ethical manner, local and US academic review boards evaluate research proposals for safety, efficacy, and ethical protection of human subjects.

Protecting Americans As expressed by Dr. Richard Chaisson, "Global infectious diseases have an outsized impact on our welfare here in the US. For example, two-thirds of all tuberculosis cases in the US occur in people born elsewhere. If we don't learn how to control TB globally, we can never control it at home. Major public health threats like Zika and Ebola cost the nation millions of dollars for surveillance and control, even when few cases land on our shores.

Understanding how to manage these types of outbreaks is essential for our national health and security." Adds Dr. Zawedde-Muyanja, "The world is increasingly a 'smaller' place. Epidemic prone diseases and the emergence of antimicrobial resistance, prove that health research funding in the developing world is beneficial to us all. By funding research into the development of vaccines or effective cures for diseases the US decreases the likelihood of facing these threats."

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.

Mail: The Fisher Center, 725 N. Wolfe St., Suite 211, Baltimore, MD 21205

Recent Publications

Antibiotics for the neurological complications of Lyme disease.

Cadavid D, **Auwaerter PG**, Rumbaugh J, Gelderblom H. *Cochrane Database Syst Rev.* 2016 Dec 8;12:CD006978. doi: 10.1002/14651858.CD006978.pub2. Review. PMID: 27931077

Geographic Expansion of Lyme Disease in Michigan, 2000-2014.

Lantos PM, Tsao J, Nigrovic LE, **Auwaerter PG**, Fowler VG, Ruffin F, Foster E, Hickling G. *Open Forum Infect Dis.* 2017 Jan 9;4(1):ofw269. doi: 10.1093/ofid/ofw269. eCollection 2017 Winter. PMID: 28480261

Older Adults and Management of Medical Devices in the Home: Five Requirements for Appropriate Use.

Keller SC, Gurses AP, Werner N, Hohl D, Hughes A, Leff B, Arbaje AI. *Popul Health Manag.* 2017 Jan 11. doi: 10.1089/pop.2016.0070. [Epub ahead of print] PMID: 28075698

Comparison of 11 Phenotypic Assays for Accurate Detection of Carbapenemase-Producing Enterobacteriaceae.

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ADP-ribosylhydrolase activity of Chikungunya virus macrodomain is critical for virus replication and virulence.

McPherson RL, Abraham R, Sreekumar E, Ong SE, Cheng SJ, Baxter VK, Kistemaker HA, Filippov DV, **Griffin DE**, Leung AK. *Proc Natl Acad Sci U S A.* 2017 Feb 14;114(7):1666-1671. doi: 10.1073/pnas.1621485114. Epub 2017 Jan 31. PMID: 28143925

Mouthing of Soil Contaminated Objects is Associated with Environmental Enteropathy in Young Children.

Morita T, Perin J, Oldja L, Biswas S, Sack RB, Ahmed S, Haque R, Bhuiyan NA, Parvin T, Bhuyian SI, Akter M, Talukder KA, Shahnaiz M, Faruque AG, **George CM**. *Trop Med Int Health.* 2017 Jun;22(6):670-678. doi: 10.1111/tmi.12869. Epub 2017 Apr 20. PMID: 28319300

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Recent Presentations

Characterization of Borrelia burgdorferi-Specific T-Cell

Subpopulations Recruited During Acute Lyme Disease. Maria G. Gutierrez, Alycia Curlee, Aarti Vadalia, John Aucott and **Mark Soloski**. Poster Session: Lyme Disease in the Era of Precision Medicine Conference, Mount Sinai School of Medicine, NY, October 4, 2016

Cost-Effectiveness of an Outpatient Parenteral Antimicrobial

Therapy (OPAT) Care Coordination Service. Aleksandra Mihailovic, ScM; Zhenchun Jiang, BS; Shanshan Wang, BS; Komal Kumar, BS; Daniel Timko, PharmD; William Padula, PhD; **Sara Keller, MD, MPH, MSHP**. Poster Session: ID Week, New Orleans, Louisiana, October 28, 2016

Lyme Disease, a complicated tick borne disease. Mark Soloski, PhD. Seminar: College of Mount Saint Vincent, Bronx, N.Y., November 8, 2016.

Candida auris: Time to Prick Up Your Ears? **Paul G.**

Auwaerter, MD, MBA. Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/872986>. December 15, 2016

Lyme Disease: Treat Mice to Treat Ourselves? **Paul G.**

Auwaerter, MD, MBA. Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/874169>. January 17, 2017.

More of Everything: Characteristics of Those Seeking Opinions Regarding Lyme Disease. Takaaki Kobayashi, **Yvonne Higgins**, Sarah Salter, Gayane Yenokyan, Paul Lantos, **Michael Melia**, **Paul Auwaerter**. Poster Session: Mid-Atlantic Tick Summit VI, Maryland Department of Health and Mental Hygiene, Laurel, MD, February 22, 2017 and JHU Department of Medicine Research Retreat, Johns Hopkins University School of Medicine, Baltimore, MD, March 7, 2017

C difficile: Why Good ID Advice Still Matters. **Paul G.**

Auwaerter, MD, MBA. Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/877084>. March 20, 2017

Sepsis Guidelines and Antibiotics: Empiric Recommendations

Going a Bit Too Far? **Paul G. Auwaerter, MD, MBA**. Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/879819>. May 16, 2017.

No New Antibiotics? Go to the Attic, Build Better Mousetraps.

Paul G. Auwaerter, MD, MBA. Medscape Infectious Diseases. <http://www.medscape.com/viewarticle/881910>. June 27, 2017.