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Focus

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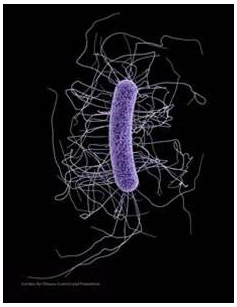
News from the Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases

Clostridium difficile: Impact of colonization vs. transmission

Included in inaugural class (2013) of Fisher Center Discovery Program awarded grants, **Sarah Tschudin-Sutter, MD, MSc** and **Trish Perl, MD, MSc** conducted research on *Clostridium difficile*.

Background Clostridium *difficile* (*C diff*) is a bacteria widely found in soil, water, human and animal waste and processed meats. If hands are not adequately washed, people can spread *C diff* to food and surfaces, on which the spores can live for weeks. People then eat the contaminated food or touch the surfaces and put their hands in their mouth, accidently ingesting *C diff*.

Per the CDC, approximately 3% of the general population are asymptomatic colonized carriers. The use of antibiotics can alter the balance of bacteria that live in our intestines, allowing those colonized with *C diff* to develop an infection. Symptoms of *Clostridium difficile* infection (CDI) include watery diarrhea, abdominal pain and tenderness, fever, nausea, loss of appetite, and blood or pus in bowel movements. Treatment includes antibiotics, fecal transplant, and surgery in severe cases. Left untreated, *C diff* can cause dehydration, colon inflammation, colon perforation, sepsis, kidney failure, and death.



Older adults develop the majority of *C diff* infections. Those with cancer, inflammatory bowel disease, or weakened immune systems are also at higher risk of infection. The CDC estimates almost 500,000 Americans had CDI in 2011, with 29,000 dying within 30 days of the diagnosis. Healthcare costs for CDI in the US are estimated at $2.4-4.8 billion per year. Infections are often associated with health care facilities, although rates of community-acquired *C diff* are increasing. In addition, new strains of *C diff* have developed, which produce toxins (toxigenic) and may be resistant to antibiotics.

FCDP Supported Study The purpose of this study was to determine if patients were admitted to the hospital colonized with *C diff* or were infected with *C diff* during the hospital stay and what are the risks of developing a symptomatic CDI. Sample collection took place in 2013 at the Johns Hopkins Hospital. Among 542 patients, 17 (3.1%) were colonized with *C diff* on admission. Three additional patients were colonized during hospitalization. CDI developed in only 8 patients (1.5%). Colonization on admission and colonization during hospitalization were predictors of CDI. The low rate of colonization questions the utility of screening all patients for *C diff*. Further studies to identify risk factors for patients at higher risk for developing CDI may allow for targeted surveillance, rather than wide-spread screening. This may reduce costs associated with *C diff* screening and treatment, lead to development of improved infection control measures, and improve the health and well-being of individuals with CID.

The research was presented at the 24th European Congress of Clinical Microbiology and Infectious Diseases in Barcelona, Spain in 2014 and was published in July 2015 in Infection Control & Hospital Epidemiology.

Dr. Sarah Tschudin-Sutter completed her fellowship at JHU in 2013. In 2014 she was appointed Assistant Professor of Medicine at the University of Basel in Switzerland. She continues to conduct research in hospital acquired infections.

Image source: CDC.gov

Inside

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

Mosquito-borne Infections: Hot Topics in a Hot Summer

Among vectors that transmit environmental pathogens, the mosquito has perhaps the most notorious record in spreading human disease efficiently and quickly. The rapid emergence of a heretofore unknown viral infection in the Western Hemisphere caused significant anxiety because of its potential effect on brain function. This resulted in widespread efforts to limit spread through spraying programs, investigating infected birds and checking blood banked for human transfusion to avoid infections.

Though this sounds like the current problem we face in the Zika virus, rather this infection emerging was West Nile virus first seen in Queens, New York in 1999 and subsequently spreading across North America. After the first few years of rampant infection among birds, horses and humans, the virus is now a part of our landscape causing as of this writing 146 reported neuroinvasive infections this year in the United States.

Zika and West Nile viruses are flaviviruses related to Yellow Fever, Dengue and Chikungunya viruses. Each has the capability of causing serious and lethal infection. Like many successfully spread pathogens, on average most people who acquire infection don't know they are infected. This is especially true of Zika virus where approximately 80% of people infected have no symptoms. With the first detection of infection acquired in southern Florida, it is easy to predict that this infection will also become more widespread in the United States as people who aren't ill with this virus are outdoors and have mosquito bites that then will transmit to others.

One difference is the preferred mosquito vectors that appear to transmit these viral infections. Aedes mosquitoes transmit Zika virus along with chikungunya, dengue and yellow fever while Culex mosquitoes transmit West Nile virus. The Aedes mosquitoes mostly bites during the daytime hours and generally prefers urban environments, breeding in shallow water which includes common areas about homes including flower pot saucers, outdoor containers and puddles. While Aedes mosquitos are thought to be mostly in the southern United States, current range shows that that only the more northerly and usually drier states may avoid spread of Zika virus.

Efforts to halt the spread will go on as it is now clear that Zika virus definitely harms some fetuses during early pregnancy as well as causing occasional Guillian-Barré syndrome in adults. It is unlikely health officials will completely stymie infection which is now so widespread in South and Central America. Rather, the virus will probably spread throughout the United States over the next couple of summer seasons and then considerably lessen when enough people become infected to develop immunity.

Efforts to understand why these flaviviruses cause disease in brain cells is a focus of two efforts funded by the Fisher Center. **Diane Griffin** and colleagues are examining the neurovirulence factors of the viral protein nsP3 in chikungunya virus, while **Richard Chaisson** and colleagues are using a well-characterized cohort of people in Brazil infected with Zika virus to describe immunological consequences of this infection. Such efforts may lead to prevention strategies as the mosquito has long been part of human history spreading diseases such as these viruses as well as malaria.

Until such efforts materialize, the noted tropical medicine specialist William Gorgas offered advice to empty standing water during the construction of the Panama Canal in the early 20th century that is still relevant today: "The *Aedes aegypti,* which transmits yellow fever (and Zika virus), is one of the feeblest species in its ability for flight and it is at once blown away and destroyed when it gets into a breeze. It therefore seldom wanders from the house in which it was bred."

Estimated range of Aedes albopictus and Aedes aegypti in the United States, 2016*

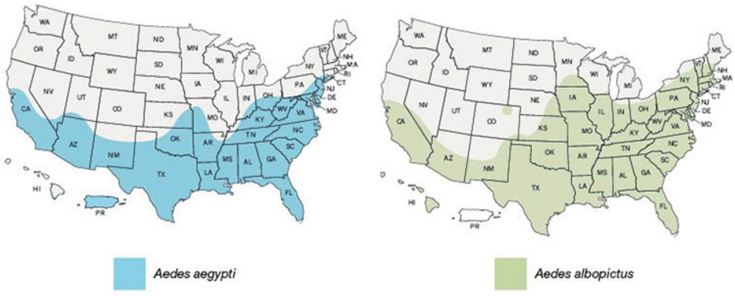


Image source: CDC.gov

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:

- Helen R. Buck Foundation
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- Ms. Ramona L. Lampell
- Barbara and Leslie Isaacs
- Michael Melia and Paul Auwaerter

FCDP Supported Research Update

Diagnostics for latent histoplasmosis

Principal Investigator, Kieren Marr, MD, is a 2015 Fisher Center Discovery Program (FCDP) award recipient

Background *Histoplasmosis capsulatum* is a fungus that is found in the soil, especially where there is high nitrogen content. Previously thought localized in the US to Ohio's Mississippi River valley, the fungus is now causing illness in other states such as Montana and the infection has become a common cause of death.

When the soil is disturbed, microscopic spores are released, which are in turn inhaled by people, cats, or dogs. Most people do not get sick from inhaled spores, but can develop latent (asymptomatic) infections, which can be reactivated at a later date. Persons with weakened immune systems, such as those with HIV, organ transplant patients, patients on biologic immunosuppressive therapies, and the elderly can develop disease. The infection can cause pneumonia, or dissemination to other parts of the body. It can also cause inflammatory conditions like arthritis, pericarditis, and persistent fever; these manifestations are more difficult to diagnose. Currently, diagnosis is by testing for antigen or antibody but neither point out latent infections. Cultures of tissue and body fluids may be helpful, but results may take up to six weeks and sensitivity is very poor. There is clear need for better diagnostics to aid in detection of established disease, and to identify latent infection in people with immunosuppression.

FCDP Supported Study Recognizing that faster and more accurate methods to determine latent and early infection are needed, Dr. Marr proposed to leverage technologic advances of other latent infections (example TB) towards developing a diagnostic test that detects infection by probing memory T cell responses. Early proof of concept for a diagnostic interferon gamma release assay (IGRA) was demonstrated using ELISPOT technology to accurately identify both disease and latent infection caused by *H. capsulatum*. The prototype "HistoSPOT" assay has been tested for both latent infection and active histo disease by the Johns Hopkins University (JHU) research team, partnered with Richard LaRue, MD at Vanderbilt University in Nashville, Tennessee, where the infection is particularly prevalent in the environment.

So far, using the prototype IGRA, 48 samples from JHH and 63 samples from Vanderbilt have been tested; the analysis is ongoing. Based on 39 JHH samples completely evaluated, the IGRA has detected 11 true positives, with 2 false negatives; 2 proven histoplasmosis cases from Vanderbilt were also detected. Dr. Marr's team is currently evaluating optimizations of software-based discrimination criteria to arrive at a reasonable Assay Response Definition for the HistoSPOT based on a complex, un-optimized antigen. Simultaneously, efforts are underway to identify other Histoplasma antigens, which can aid in optimization of the diagnostic test.

Earlier diagnosis of latent histo infection can enable development of preventative methods in people with impending immunosuppression. Earlier diagnosis of active histoplasmosis disease could reduce delays in treatment, leading to cost reduction and improved patient outcomes.

Kausik Datta and Ashley Irving performing the HistoSPOT assay in the Marr lab

Farewell to FCDP Principal Investigator, Dr. Trish Perl

Congratulations to **Dr. Trish Perl** who recently became the Jay P Sanford Professor of Medicine and the Director of Infectious Diseases at the University of Texas Southwestern (UTSW). Dr. Perl will lead expansion efforts in patient care, clinical research, the fellowship program, and healthcare epidemiology.

While at Johns Hopkins University, Dr. Perl served with distinction in the School of Medicine as a Professor of Medicine (Infectious Diseases) and Pathology and at the Bloomberg School of Public Health in Epidemiology. She was also the Senior Epidemiologist for the Johns Hopkins Health System.

Dr. Perl is an internationally recognized expert in the field of healthcare associated infections, antimicrobial resistance, and antibiotic stewardship. She has served on advisory panels for the Institute of Medicine, Centers for Disease Control and Prevention and the World Health Organization and has been a consultant to the National Institutes of Health and Agency for Healthcare Research and Quality.

Dr. Perl received a BA and MD from the University of North Carolina at Chapel Hill and an MSc from McGill University in Montreal, Canada, followed by an internal medicine residency at McGill University and fellowships in Infectious Diseases and Clinical Epidemiology at the University of Iowa in Iowa City, Iowa.

In addition, Dr. Perl has been a mentor to young clinicians and researchers. In her role as mentor, Dr. Perl served as Principal Investigator on two **Fisher Center Discovery Program** grants: *Clostridium difficile: Impact of Colonization Versus Transmission on Development of Infection* with **Sarah Tschudin Sutter, M.D.** in 2013 and *The Home Environment: Infections among Patients Discharged Home with Venous Catheters* with **Sara Keller** in 2015.

Although we are sad to see her go, the Fisher Center joins her Hopkins colleagues in congratulating Dr. Perl on her new position as we look forward to future research collaboration.

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
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Recent Presentations

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