Consultation with ID specialists is associated with lower patient mortality for some infections. When infectious diseases (ID) specialists were involved in the care of patients with certain kinds of drug-resistant infections, the patients' 30-day mortality rates were about 50 percent lower, according to a new study published in Open Forum Infectious Diseases. The findings provide additional evidence for the beneficial impact ID physicians have on patient care and outcomes, particularly when individuals have difficult to treat infections that are resistant to multiple antibiotics.

“These are serious infections that anybody can get and end up in the hospital,” said study author Jason P. Burnham, MD, of Washington University School of Medicine in St. Louis. “Understanding how we can help improve outcomes in patients like these is really important.”

For the single-center, retrospective study, researchers reviewed records from 2006 to 2015 for approximately 4,200 patients with infections resistant to multiple antibiotics who were treated at Barnes-Jewish Hospital, an academic medical center affiliated with Washington University School of Medicine. Patients with positive cultures for a multi-drug resistant pathogen from one of several different types of bacteria were included in the analysis: Enterobacteriaceae, Staphylococcus aureus, Enterococcus, Pseudomonas, and Acinetobacter.

Among patients with multi-drug resistant Enterobacteriaceae infections, ID consultation was associated with a 59 percent reduction in 30-day mortality. In line with previous research, ID consultation was also associated with a 52 percent reduction in 30-day mortality for patients with resistant S. aureus infections. For individuals suffering from several infections simultaneously, each one resistant to multiple antibiotics, an ID consult was associated with a 49 percent drop in 30-day mortality.
Since leaving Washington University in 2005, my wife Kaili Fan (ID fellowship 1996-1999) and I have worked at South Dayton Acute Care Consultants, a private multispecialty practice group with 5 infectious diseases physicians, including James Galbraith, who also trained with us at Wash U. We are an independent group, working in two competing hospital systems. The practice is quite busy, and we see some fairly interesting cases along with a lot that are more routine.

In addition to the practice, I also serve as medical director for the Dayton office of Equitas Health. This began as an HIV clinic which was an outgrowth of the AIDS Resource Center Ohio and is now going through a major, and occasionally awkward transition to becoming a federally qualified health center look alike. While that clinic accounts for only a small part of my effort, it provides a unique mix of rewards and challenges that differentiate this not for profit organization from the private practice setting that occupies the majority of my time.

Outside of work, we are very busy with our sons John John (grade 11) and William (grade 10) who are avid and nationally ranked Quizbowl and History Bee and Bowl players as well as violinists in the Dayton Philharmonic Youth Orchestra and the Dayton Philharmonic Youth Strings respectively. We come back to St. Louis every year for the Washington University Fall Academic Tournament.

ID consults

Even one year later, the involvement of an ID physician in treating a patient’s initial S. aureus infection was associated with a 27 percent reduction in all-cause mortality. For resistant Enterobacteriaceae infections, researchers found a similar 26 percent reduction in one-year all-cause mortality when a patient’s initial care included an ID physician. Among those with resistant Enterobacteriaceae infections, ID consultation was also associated with a 26 percent reduction in hospital readmissions in the 30 days following their initial hospital stay for infection.

Is ID consultation associated with reductions in readmissions and mortality for multidrug resistant organisms?

For the other types of bacteria (Enterococcus, Pseudomonas, and Acinetobacter), small sample sizes limited the authors’ ability to associate ID consults with clinical outcomes. According to Dr. Burnham, larger studies are needed to better understand the role of ID consultants for these infections, though he said he suspects it would be positive. In addition, future research will clarify what specific aspects of care provided by ID specialists help patients the most, such as expertise in appropriate antibiotic use or application of relevant clinical practice guidelines.

As antibiotic resistance continues to increase, the specialized care provided by ID physicians will become even more integral to the daily operations of hospitals and for the promotion of patient and public health, Dr. Burnham said. “I think we’re moving in a direction where having ID experts on board for these increasingly hard to treat drug-resistant infections will be necessary to ensure that our patients have the best possible outcomes.”

Fast Facts

- Researchers analyzed records for approximately 4,200 patients with infections resistant to multiple antibiotics from 2006 to 2015 at one academic medical center.
- Thirty-day mortality rates were about 50 percent lower among patients with certain multidrug-resistant infections who had infectious diseases (ID) specialists involved in their care.
- Among patients with Enterobacteriaceae infections resistant to several antibiotics, an ID consultation was associated with a 59 percent reduction in 30-day mortality.

### RECENT AWARDS

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<td>Jennie H. Kwon DO, MSCI</td>
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Recruitment video reaches out to ID Fellow candidates
Jennie H. Kwon, DO, MSCI receives Outstanding Citizenship Award

Jennie H. Kwon, DO, MSCI, assistant professor of medicine, was selected to receive the 2018 CRTC Scholar Outstanding Citizen Award. The CRTC is the educational core of the Institute of Clinical and Translational Sciences that provides clinical and translational research training for predoctoral students, house-staff, postdoctoral fellows, staff, and junior faculty.

Citizenship awards are nominated by the Program Directors based on strength and participation of the scholar in the classroom. KL2 Career Development Program director, Victoria J. Fraser, MD, chair of department of medicine and co-director, Jane Garbutt, MBChB, research professor, departments of medicine and pediatrics and co-director of the Center for Community Health Partnership and Research, nominated Jennie Kwon and Jonathan Mitchem, assistant professor, University of Missouri School of Medicine for this award.

Steve Lawrence appointed Assistant Dean for Curriculum and Clinical Sciences

Steve Lawrence, MD, MSc, associate professor of medicine, Infectious Diseases Division, has been appointed to the position of Assistant Dean for Curriculum and Clinical Sciences. In this capacity he will be working in the Office of Medical Student Education focusing on the clinical aspects of the medical program curriculum. Dr. Lawrence currently co-directs the Infectious Diseases course and was a 2016 – 2018 Loeb Fellowship recipient. "The pool of candidates was truly outstanding", indicated Thomas M. De Fer, MD, FACP, Professor of Medicine and Associate Dean for Medical Student Education. We congratulate Steve Lawrence.

Escota receives 2017-2018 teaching award

Gerome Escota, MD, assistant professor of medicine, was selected by the Department of Medicine House Staff to receive the House Staff Teaching Award for "Distinguished Faculty - Infectious Diseases" 2017-2018.

The Distinguished Faculty awards recognize outstanding achievements in clinical care, community service, research and teaching. They are cosponsored by the dean's office, the Office of Faculty Affairs, Central Administration and the Executive Committee of the Faculty Council.

Additionally, Dr. Escota was selected by the current infectious diseases fellows to receive the 2018 J. Russell Little Clinical Education Award. The award is given to a faculty member for their outstanding clinical teaching and honors emeritus professor, Dr. Little, for his years of practice and teaching at the Washington University School of Medicine.
Baldridge named a 2018 Pew Biomedical Scholar

Megan T. Baldridge, MD, PhD, assistant professor of Infectious Diseases at Washington University School of Medicine, was named a Pew Biomedical Scholar on June 14. The award supports early career faculty members who have demonstrated “outstanding promise as contributors in science relevant to human health”. Each awardee will receive $300,000 over four years to help support their growing labs and advance their explorations of biological mechanisms underpinning human health and disease.

“These scientists have shown the boldness and creativity that drives great discoveries, and Pew’s unrestricted support will help them follow the facts wherever they lead,” said Rebecca W. Rimel, president and CEO of The Pew Charitable Trusts. “We’re proud to invest in this gifted group at a pivotal stage in their careers when funds to pursue new concepts and methods can be scarce.”

The selected scholars enter a vibrant community of researchers who have received awards from Pew since 1985. Current scholars meet annually to discuss their research, and exchange ideas with peers in fields outside of their own. The Baldridge Lab will explore the conditions that influence the evolution of severe strains of norovirus, a culprit of gastrointestinal illness. “Some individuals are able to rapidly clear norovirus infection, while others experience prolonged episodes of vomiting and diarrhea,” said Baldridge, “Limiting the duration of infection is not only beneficial for the individual, but can potentially curb the outbreak of epidemics. Sustained infection may allow the virus time to evolve into strains that can avoid immune detection.”

As a postdoctoral fellow, Dr. Baldridge discovered that the immune molecule, interferon-lambda, curtails norovirus infection in mice, while normal gut bacteria sustain it. “Now, using methods in virology, immunology, molecular biology, and genomics, our lab will manipulate the interferon-lambda signaling pathway and the composition of the microbiota in norovirus-infected mice and determine how these modifications affect the elimination of the virus, the evolution of viral variants, and the infectiousness of newly evolved viral strains. These findings could lead to novel probiotic treatments for eliminating viral infections and to interventions that can prevent the emergence of more dangerous viral variants, a problem not only for norovirus but for other epidemic viruses such as influenza.”

“The 2018 scholars bring fresh curiosity and insight to aspects of health and biology in critical need of investigation,” said Craig C. Mello, Ph.D., a 1995 Pew scholar, 2006 Nobel laureate in physiology or medicine, and chair of the national advisory committee for the scholars program. “I’m excited to see their work invigorated by new resources and opportunities to collaborate with Pew’s community of nearly a thousand biomedical researchers.”

The Infectious Diseases Division congratulates Dr. Megan Baldridge as a 2018 Pew Biomedical Scholar.

New treatment combination (IDA) will accelerate elimination of lymphatic filariasis

Gary Weil, MD, professor of medicine and molecular microbiology, was interviewed at a recent international meeting on filariasis in India in May 2018. Interview questions relate to a triple drug treatment pioneered by the Death to Onchocerciasis and Lymphatic Filariasis (DOLF) Project at Washington University. See interview http://youtu.be/R6hW5BZeljc
Philips and Henderson selected to receive LEAP Inventor Challenge Awards

Leadership in Entrepreneurial Acceleration Program, better known as the LEAP Inventor Challenge (LEAP) exists to propel Washington University intellectual property towards commercialization. The competition supports all Washington University faculty, postdoc, staff and graduate student teams. Finalists are selected based on feedback from domain experts. They receive funding to help progress their early stage research from concepts and ideas to viable products and services.

Several university departments work together on LEAP to maximize industry engagement and funding opportunities. Such facilitators include the Skandalaris Center for Interdisciplinary Innovation and Entrepreneurship (Skandalaris), the Office of Technology Management (OTM), the Institute of Clinical and Translational Sciences (ICTS), and the Center for Drug Discovery (CDD).

Jennifer A. Philips, MD, PhD, associate professor of medicine and molecular microbiology, Infectious Diseases Division, received the award for host directed metabolic therapy for TB, re-purposing an existing drug to treat Mycobacterium tuberculosis (Mtbb), the world’s leading infectious disease killer.

Jeffrey P. Henderson, MD, PhD, associate professor of medicine and molecular microbiology, Infectious Diseases Division, and director of the Center for Women’s Infectious Diseases, also received a LEAP Award for his work on the “Virulence system of gram-negative enterobacteria as a therapeutic target”. The project focuses upon a new therapeutic candidate that selectively prevents pathogenic bacteria from causing disease while sparing beneficial microbes.

In 2016-2017, the Skandalaris Center and its partner organizations awarded over $718,000 in funding to Washington University-affiliated ventures. The center aims to inspire and develop creativity, innovation, and entrepreneurship at Washington University.

Storch Named Research Integrity Officer

Gregory Storch, MD, the Ruth L. Siteman Professor of Pediatrics, with joint appointments in the Departments of Medicine and Molecular Microbiology, has recently accepted the role of Research Integrity Officer for Washington University.

Greg will have responsibility for fostering a research environment that promotes the responsible conduct of research. He also will be responsible for administering Washington University’s policy and procedures on research integrity, including authorship on scientific and scholarly publications. In this capacity, he will serve as the Chair of the Research Integrity Committee for both campuses.
IDSA names Barnes-Jewish Hospital
Antimicrobial Stewardship Center of Excellence

The Infectious Diseases Society of America (IDSA) recently designated Barnes-Jewish Hospital in St. Louis as an Antimicrobial Stewardship Center of Excellence (CoE). The program, launched in the fall of 2017, recognizes institutions that achieve standards established by the Centers for Disease Control and Prevention (CDC) for antimicrobial stewardship programs led by Infectious Disease physicians and ID-trained pharmacists.

“IDSA is committed to infectious diseases-led antimicrobial stewardship programs as an essential component in the fight against antimicrobial resistance that leads to more than 23,000 deaths per year and over $20 billion in unnecessary health care costs,” said IDSA President Paul Auwaerter, M.D. “The IDSA Antimicrobial Stewardship Centers of Excellence program recognizes institutions that lead in establishing highly effective antimicrobial stewardship programs that help clinicians give their patients optimal anti-infective therapies.”

Kevin Hsueh, MD, medical director of the antimicrobial stewardship program at Barnes-Jewish Hospital, is an assistant professor of medicine in the Infectious Diseases Division. He joined Washington University in 2014 to lead the hospital stewardship program. The core criteria for the IDSA Antimicrobial Stewardship Centers of Excellence were developed by a workgroup of infectious diseases physicians and ID-trained pharmacists and built upon the criteria detailed in the CDC’s Core Elements of Hospital Antibiotic Stewardship Programs. The CoE program places particular emphasis on an institution’s ability to implement stewardship protocols, using their electronic health records system, as well as to provide ongoing education to its medical staff. The goals of the program are to recognize those that have achieved high standards in their stewardship programs and highlight the value of stewardship over the valuable – but vulnerable – drug supply. Additional information is available at www.idsociety.org/ascoe.

faculty promotions . . .

We congratulate the following faculty on their promotions:

Merilda Blanco-Guzman, MD, Yasir Hamad, MD, F. Matthew Kuhlmann, MD, Caline Mattar, MD, Lem Non, MD, and Anupam Pande, MD, MPH, to Assistant Professors of Medicine,

Jennifer A. Philips, MD, PhD and Rachel M. Presti, MD, PhD to Associate Professors of Medicine,

James M. Fleckenstein, MD, Erik Dubberke, MD, MSPH, and Peter U. Fischer, PhD to Professors of Medicine.
Inaugural George S. Kobayashi Lecture 2018

The Infectious Diseases Division hosted the first George S. Kobayashi Lecture on May 16, 2018 in Clopton Auditorium. Our guest speaker was David R. Andes, MD, visiting professor of medicine, University of Wisconsin. The topic addressed was “Medical Mycology”.

George Kobayashi was a professor emeritus of medicine at Washington University School of Medicine and a world-class mycologist. From 1973-1999, Kobayashi served as the associate director of the Clinical Microbiology Laboratory. He spent many years researching the control of cellular differentiation of the pathogenic fungus Histoplasma capsulatum and served in various capacities in the American Society for Microbiology and the Medical Mycology Society of America. He was a member of peer-review committees for the National Institutes of Health, the Food and Drug Administration and the American Type Culture Collection.

Dr. Andes’ clinical interests include general infectious diseases, transplant infectious diseases, mycology, antimicrobial pharmacokinetics and pharmacodynamics.

ONE STREPT AT A TIME.....

Members of the ID Division participated in the GO! Missouri KT82 Trail Relay on June 2, 2018. This was an exciting one day, 82-Mile trail relay that started in St. Louis County and finished in beautiful Hermann, MO.

ID division team members ran as the team “Washington University Infectious Diseases ONE STREPT AT A TIME. The team came in at #34 of 104 teams among the non-competitive division. The majority of the KT82 utilized the scenic Katy Trail.

Team members in photo are (left to right) Carlos Mejia, MD (2nd year fellow), Maureen M. Mercier, AGPCNP-BC, Debra Gase, RN, MSN, FNP-BC, Jason Newland, MD, MEd, Mike Durkin, MD, MPH (assistant professor of medicine), and Katie Faletti, MS, PA (physician assistant - Infectious Diseases Hospitalist Service).

congratulations . . .

Best wishes to Medrilda Cordero Blanco, instructor in medicine and her husband,

Jed Cordero, respiratory therapist at Barnes Jewish Hospital, on the birth of their daughter,

Natalie Cordero Blanco. Natalie was born April 24, 2018 and weighed in at 6 lbs, 9 oz.

Anupam Pande, MD, instructor in medicine, and his wife Juee welcomed a baby boy at 4:39 pm on June 13, 2018. They named him Kartik Pande. Kartik weighed 6 lbs, 5 oz at delivery.
recent activities

World TB Day Symposium

The Third Annual World TB Day Symposium was hosted at Saint Louis University on April 10, 2018. The event was co-organized by St. Louis University’s Daniel Hoft, MD, PhD, professor of medicine, infectious diseases division, and Washington University’s Shabaana Khader, PhD, associate professor, molecular microbiology. This event is organized to commemorate World TB Day, the date Robert Koch first reported his findings identifying Mycobacterium tuberculosis as the cause for tuberculosis.

This meeting brought together researchers from SLU and Wash U and focused on various aspects of Tuberculosis Research. The Keynote address was given by Dr. Willem Hanekom, Deputy Director, TB, and Initiative Lead for TB Vaccines from the Bill & Melinda Gates Foundation. There were 6 additional talks led by Saint Louis University and Washington University researchers, and 16 posters presented at the symposium. The topics discussed ranged from basic research on host immunity to TB, vaccine development for TB, drug development for TB as well as discussions on clinical TB.

PrideFest 2018

The John T. Milliken Department of Medicine is proud to be an equality corporate sponsor of PrideFest 2018. Members of the Infectious Diseases Division joined members of OutMed for the Pride parade on Sunday, June 24th, downtown St. Louis. OUTmed is an organization for LGBTQIA-identified faculty, residents, fellows and staff at Washington University School of Medicine. OUTmed is supported by the Department of Medicine, and is open to members of the entire School of Medicine, regardless of departmental affiliation.

2018 WORLD & EUROPEAN CONGRESS
JUNE 27 - 30, DUBLIN IRELAND

Brad Stoner, MD, associate professor of medicine and anthropology, organized and chaired a symposium on syphilis during the IUSTI 2018 (International Union Against Sexually Transmitted Infections) Congress in Dublin. Brad is the membership secretary for the IUSTI.

Drs. Stoner and Hilary Reno, MD, PhD, assistant professor of medicine, presented posters at the congress.

Brad Stoner, MD, Dodie Rother, MPH and Hilary Reno, MD, PhD at the IUSTI 2018 World & European Congress in Dublin Ireland.
**fellows’ corner**

**next steps for 2018 graduates**

**Darrell McBride, DO**

**Next Steps:** I am going to work for Geisinger Medical Center in Danville, PA as an Infectious Disease Physician and will specialize in HIV/AIDS as well as Hepatitis C care and treatment.

**Highlights of fellowship:** The highlight of my fellowship was interacting, learning, laughing, and growing with well-established, internationally known, and well-respected faculty and fellows. I have learned a lot from these great people and grown to consider many of them my friends.

**Krunal Raval, MD**

**Next Steps:** I will be doing a Critical Care fellowship at Mercy Hospital in St. Louis. My future long-term plan is to combine ID and critical care in my practice to provide care to critically ill and complex patients. I plan to stay and practice in St. Louis.

**Highlights of fellowship:** I had a very wonderful experience during my training at Barnes-Jewish Hospital. The training gave me exposure to seeing a wide array of patients with varied ID issues. The friendliness and camaraderie within the department make it the best place to learn from a fellow standpoint. I thoroughly enjoyed my work in the department and saw myself grow as a budding ID physician.

**Abdullah Aljorayid, MD**

**Next Steps:** I will be staying at Washington University to further my training in clinical epidemiology and continue clinical research related to fungal infections. I will be working with Adrej Spec, MD as my mentor.

**Juan Calix, MD, PhD**

**Next Steps:** I will be staying at Washington University to complete the research component of my Physician Scientist Training Program. I will be performing research to further understand the pathogenesis of Acinetobacter infections, both with epidemiological studies and basic science. One thing that I took away from the program was the ability to navigate the ever-more-complex healthcare delivery system in order to optimize the care received by our patients. As Infectious Disease doctors we typically have a bird's eye view of the system, and it is important to know how to go to with questions and how to improve healthcare delivery.

**Carlos Mejia, MD**

**Next Steps:** I will continue my training as a third year ID fellow focusing on clinical research related to HIV.

**Jane O’Halloran, MD**

**Next Steps:** I plan to stay at Washington University as a third year fellow to continue research on co-morbidities in people living with HIV.

**Brett Jagger, MD, PhD**

**Next Steps:** I am entering my fourth and final year of training in the division as an Oliver Langenberg Physician Scientist Training Program trainee. I will continue to work with Division faculty, Michael Diamond, on Zika virus vaccines.


**third year fellows**

**fourth year fellow**
First and second year fellows receive travel grants to IDWeek 2018

First year fellows, Matthew Hevey, MD and Kap Sum Foon, MD, along with second year fellows, Abdullah Aljorayid, MD, Juan Calix, MD, PhD, Carlos Mejia, MD, and Jane O’Halloran, MD, PhD, and will be attending IDWeek 2018 October 3-7 in San Francisco, CA. Each have submitted abstracts which have been accepted for poster presentations and awarded IDWeek Trainee Travel Grants.

Congratulations, ID fellows!

2018 ID Division Annual Spring Picnic – hosted by second-year fellows

A great time was had by all in attendance at the second year fellows’ picnic. This is an annual occasion when 2nd year fellows plan, organize, bar-b-que and serve up a delicious meal for ID Division faculty and staff. This year’s picnic was located in Tower Grove Park which affords plenty of room to play soccer with adults and the little ones, and to gather in the shade beneath the Turkish Pavilion.
The faculty of the ID Division at Washington University School of Medicine are working on a variety of research endeavors from basic science to clinical practice. This section of the newsletter showcases recent publications/reviews and the author’s spin on why the publication is relevant and the significance in medicine today.

Below is a list of several publications, followed by the author’s comment.


Michael Diamond, MD, PhD: A team led by Washington University School of Medicine researchers reports using a genome-wide CRISPR-Cas9 screen to identify a cell surface receptor used by the chikungunya virus to infect cells. The researchers performed the screen to find host cell factors potentially required for chikungunya infection — which is transmitted to humans via mosquitos and can result in long-term joint pain — and uncover the cell adhesion molecule Mxra8 as a key player in viral attachment and internalization into cells. In a mouse model, blocking Mxra8 was found to inhibit chikungunya infection and associated foot swelling. Pharmacological targeting of Mxra8 could form a strategy for mitigating infection and disease by multiple arthritogenic alphaviruses (see story on page 15).


Erik Dubberke, MD, MSPH: This was a double blinded randomized controlled trial of RBX2660, a microbiota containing product, for the prevention of recurrent Clostridium difficile infection (CDI), the first such FDA-registration trial for a microbiome based product. Although it has been recognized that fecal transplantation is effective at preventing recurrent CDI, a limitation has been ready access to a microbiome based product. An FDA-approved microbiome based product would significantly increase access to this treatment.

There were several important learning points in this study. One is, the baseline CDI recurrence rate is lower than what has previously be reported in the literature for patients with multiple prior recurrences of CDI. This finding has since been confirmed in several other recurrent CDI studies. In addition, the efficacy of a single dose of a microbiome based product is not has high as indicated in reports of fecal transplantation. This is likely because most of those reports allowed repeat dosing after additional recurrences developed, but still considered that patient a treatment success if eventually the recurrences stopped. Both of these points are important when determining sample size calculations for future studies. Another key point was a single dose of RBX2660 was significantly better than placebo at preventing additional CDI recurrences. With this success, the product is now in phase 3 trial, and we are one of the study sites. The sooner the phase 3 trial is completed, the sooner an FDA-approved microbiome based product will be available by prescription.

Margie A. Olsen, PhD: In this study we compared the incidence of surgical site infection (SSI) after immediate, delayed, and secondary breast reconstruction using private insurer claims data. We wanted to determine if infection rates were lower after delayed reconstruction, typically done months to years after mastectomy, in comparison to immediate reconstruction, which is done at the time of mastectomy. Reconstruction is an elective procedure and can be performed at a later time, which may be of benefit to high risk women. We found that the incidence of SSI was significantly higher after immediate implant (8.9%) compared to delayed implant reconstruction (5.7%), despite the fact that women undergoing delayed reconstruction had more underlying risk factors for infection. In addition, we also found that women who had an SSI after immediate implant reconstruction were at greatly increased risk of SSI (over 4-fold higher) after a subsequent reconstructive procedure, compared to women who did not have an SSI after immediate implant reconstruction. This shows that women who develop an infection after immediate reconstruction may suffer from morbidity, not only from the initial infection, but are also at increased risk of morbidity in future after additional procedures.


Rachel M. Presti, MD, PhD: In this study we looked at the communities of bacteria in the mouth in HIV-infected people before and after taking 6 months of the antiretroviral combination, Atripla. We did not see any significant changes after treatment, but we did see significant differences in the baseline bacterial communities in patients who started with lower CD4 counts or higher HIV viral loads, i.e. people with more advanced disease. These changes in the bacteria in the mouth seemed to correlate with markers of inflammation and immune recovery and may be important in the recovery of CD4 counts after starting therapy.


Rachel M. Presti, MD, PhD: Currently the HPV vaccine is recommended for ages 9-26 to prevent cervical and anal cancer and genital warts. In this study we looked at whether the HPV vaccine would decrease HPV presence and precancerous lesions in the anal canal in HIV-infected participants over age 27. The study was stopped early for futility. These results do not support HPV vaccination of HIV-infected adults age 27 or older to prevent new anal HPV infections or to improve anal outcomes. However, our data suggest a role for prevention of oral HPV infections, but this finding should be confirmed in future studies.
Blood type affects severity of diarrhea caused by E. coli

A new study shows that a kind of E. coli most associated with “travelers' diarrhea” and children in underdeveloped areas of the world causes more severe disease in people with blood type A.

The bacteria release a protein that latches onto intestinal cells in people with blood type A, but not blood type O or B, according to a study led by researchers at Washington University School of Medicine in St. Louis. A vaccine targeting that protein could potentially protect people with type A blood against the deadliest effects of enterotoxigenic E. coli (Escherichia coli) infection.

“We think this protein is responsible for this blood-group difference in disease severity,” said senior author James Fleckenstein, MD, a professor of medicine at Washington University. “A vaccine targeting this protein would potentially protect the individuals at highest risk for severe disease.”

The study is published May 17 in The Journal of Clinical Investigation. The work was conducted in collaboration with investigators at Johns Hopkins University, the National Institutes of Health (NIH), and the Naval Medical Research Center.

Enterotoxigenic E. coli are responsible for millions of cases of diarrhea and hundreds of thousands of deaths every year, mainly of young children. It primarily infects people living in or visiting developing countries. Some people infected with the bacterium develop severe, cholera-like, watery diarrhea that can be lethal. Others experience unpleasant symptoms but recover easily, while some don’t get sick at all.

Enterotoxigenic E. coli are not the cause of the recent romaine lettuce-related outbreak. That outbreak involves a different kind of E. coli known as Shiga toxin-producing E. coli O157:H7.

Years ago, doctors noted that children naturally infected with enterotoxigenic E. coli in Bangladesh seemed to get sicker if they had blood type A, but the reason for this was never tested. Fleckenstein, instructor in medicine Matthew Kuhlmann, MD, post-doctoral researcher Pardeep Kumar and colleagues investigated whether blood type influences disease severity by looking at what happened to people of different blood types who drank a cup of water laced with E. coli.

In controlled human infection clinical trials, researchers at Johns Hopkins University gave healthy volunteers a dose of an E. coli strain originally isolated from a person in Bangladesh with severe, cholera-like diarrhea. Then, they observed the volunteers for five days. Those who developed moderate to severe diarrhea were treated with antibiotics. The disease comes on quickly, so anyone who was still healthy at the end of five days was unlikely to get sick later. Nonetheless, any remaining healthy participants also were given antibiotics to clear the bacteria before going home.

Kuhlmann and colleagues obtained data and blood samples from 106 people, each of whom participated in one of four such studies. They found that people with blood type A got sick sooner and more seriously than those of other blood types. More than eight out of 10 (81 percent) of blood group A people developed diarrhea that required treatment, as compared with about half of
Blood type and E. coli

people with blood group B or O.

Blood groups are based on the sugars that decorate the surface of red blood cells and other cells. People with group A blood have sugars that are distinct from those present in either B or O blood groups. People with blood group AB carry both A- and B-type sugars on their cells.

The researchers found that the bacteria produce a specific protein that sticks to A-type sugars – but not B- or O-type sugars – on intestinal cells. Since the protein also sticks to E. coli, it effectively fastens the bacteria to the intestinal wall, making it easy for them to deliver diarrhea-causing toxins to intestinal cells.

The effect of blood group in people infected with this strain of E. coli was striking and significant, but it doesn't mean people should change their behavior based on blood type, the researchers said.

“I don't want anyone to cancel their travel plans to Mexico because they have type A blood,” Kuhlmann said. “Or the converse: I don't want anyone to think they're safe because their blood group is not A. There are a lot of different species of bacteria and viruses that can cause diarrhea, so even though this blood-group association is strong, it doesn't change your overall risk. You should continue taking the same precautions whatever your blood type.”

There are many strains of enterotoxigenic E. coli, and developing a vaccine that protects against all of them has been a challenge because no single protein is found in all strains. To defend against as many strains as possible, scientists are studying dozens of proteins – but they still haven't found a way to cover all strains. The protein identified in this study is found in many strains, so adding it to the mix could provide broader protection, especially for people at the highest risk for severe disease.

Senior author, Mike Diamond, MD, PhD, on Why chikungunya, other arthritis-causing viruses target joints

Chikungunya virus is a growing threat to the United States and other regions of the world as the mosquito that carries the virus expands its reach. Telltale symptoms of chikungunya infection are fever and joint pain that last about a week. But in up to half of patients, the virus can cause a debilitating form of arthritis that persists for months or even years.

Scientists have understood little about how chikungunya and related viruses cause arthritis. Now, researchers at Washington University School of Medicine in St. Louis have identified the molecular handle that chikungunya grabs to get inside cells. The findings, published May 16 in the journal Nature, could lead to ways to prevent or treat disease caused by chikungunya and related viruses.

The handle, or receptor, is located on cells that build cartilage, muscle and bone. Joints are filled with such cells, which helps explain patients’ painful symptoms. Further, by creating decoy handles, the researchers showed that they could reduce chikungunya infection...
and signs of arthritis.

“The name chikungunya comes from the Makonde language of Tanzania, and it means ‘to walk bent over.’ That’s how painful the arthritis can be,” said senior author Michael S. Diamond, MD, PhD, the Herbert S. Gasser Professor of Medicine at the School of Medicine. “We now know how chikungunya gets into cells, and we may have found a way to block the infection. If the virus cannot get into the cell, it is unable to replicate and cause infection and disease.

There are no specific treatments or vaccines for chikungunya and related viruses, known as arthritogenic alphaviruses. Doctors simply recommend rest, fluids and over-the-counter pain relievers such as acetaminophen or ibuprofen. With the aid of a warming planet and modern means of transportation, mosquitoes that carry chikungunya and related viruses are spreading. Once limited to Asia and Africa, chikungunya virus has infected more than a million people in the Caribbean and South America in an outbreak that began in 2013 and continues to this day.

Figuring out how the virus gets inside cells is considered a step toward slowing its spread. Diamond, first author and postdoctoral researcher Rong Zhang and colleagues identified the protein on cells that chikungunya virus latches onto. The protein is called Mxra8, and it is needed for chikungunya to invade both human and mouse cells, the researchers found. Additional experiments showed that not just chikungunya but its arthritis-causing relatives – Mayaro, Ross River, O’nyongnyong and Barmah Forest viruses – require the protein to get into cells.

Since chikungunya uses Mxra8 protein as a handle to open a door into cells, the researchers tested whether preventing the virus from grabbing that handle could reduce infection. They deluged the virus with decoy handles, reasoning that chikungunya would grab the decoy and be locked out of cells. Only the few individual viruses that lucked onto a true handle could infect cells, so the overall infection rate – and signs of arthritis – would fall.

And that’s just what they found. A day after infection, the level of virus in the mice’s ankles and calf muscles was between tenfold and a hundredfold lower in the animals that had been treated with Mxra8 proteins or blocking antibodies than those that received placebo, and the numbers remained lower over the next two days. In addition, three days after treatment, the mice that had received the protein exhibited much less swelling in their ankles than those that received the placebo.

The results suggest that a compound that blocks the virus from attaching to Mxra8 on the surface of cells could prevent or reduce arthritis.

“Not much is known about what Mxra8 does in the human body, so we need more information before developing a drug that targets Mxra8,” said Diamond, who also is a professor of molecular microbiology, and of pathology and immunology. “But we could more immediately develop a drug that targets the virus and prevent it from attaching to this protein.”

The researchers are working on mapping the structure of the protein and locating the exact spot to which the virus attaches. Such information could help researchers design a compound to interfere with the virus’s ability to hold onto the protein, or to design vaccines to prevent infection.

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Dr. Gerald Medoff has been among the most influential leaders in the School of Medicine in the past half century, and the contributions of Dr. Medoff to the field of medicine are clearly reflected in the quality of the School and in the extraordinary individuals he has mentored. It is therefore only appropriate that we honor him by creating a fund that will provide support for young trainees and junior faculty in the Division, helping them transition their independent careers. Additionally, we rely heavily on outside donations to continue to recruit, train, and retain high quality staff to support the research, education, and clinical mission of the division.

We believe that you share our sense of pride in what we have been able to build, much of which is due to the leadership of Dr. Medoff. To make a gift online please visit the Washington University “LEADING Together” page and designate your gift to honor Dr. Medoff to the Division of Infectious Disease Fund (90991).

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