



◀ *P. falciparum* sporozoite in a mosquito midgut



Infectious Diseases

Washington University in St. Louis
SCHOOL OF MEDICINE

DIVISION NEWSLETTER

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IN THIS ISSUE

- Feature Article.....page 1**
Aging with HIV William G. Powderly, M.D.
- Featured Colleague.....Page 2**
Raymond Johnson, M.D.
- Awards & Announcements.....page 3**
- Welcome New Facultypage 4**
- Hepatitis C Does Not Affect the Brain..page 5**
David B. Clifford, M.D.
- Supporting the ID Division.....page 6**
- HIV and HCV Symposiumpage 7**

Calendar Highlights

HIV and HCV: Optimal Management in the Era of New Regimens

Guest Faculty

Kenneth E. Sherman, M.D., PhD

Gould Professor of Medicine

Director, Division of Digestive Diseases

University of Cincinnati College of Medicine

Cincinnati OH

Tuesday, May 12, 2015

Engineers' Club of St. Louis

5:30 p.m. Hors d'oeuvres Reception

(Meet & Greet)

6:30 p.m. Dinner/Program Commences

Click below for more details:

<http://actu.im.wustl.edu/ResourcesProfessionals.htm?Link=4>

We are interested in your achievements, clinical and/or research activities, and other personal news since leaving Washington University School of Medicine. Please contact Dr. Gerald Medoff at gmedoff@dom.wustl.edu with any information you would like to share. All division newsletters can be found at: ID Division Newsletters

Aging with HIV

William G. Powderly, M.D.



William G. Powderly, M.D.

One of the most positive features of the current era of HIV, particularly in the Western world, is the fact that patients are aging successfully.

In the 1980s, when the disease was first recognized, the average survival after someone was given a diagnosis of AIDS was approximately two years; indeed, on average, the interval between acquisition of HIV infection and the development of AIDS was about ten years.

In contrast, we are now looking at a situation where survival is significantly better. It is now possible for physicians to say to a young person in whom HIV has been recently diagnosed that if they start therapy and take it as prescribed, they can

expect a normal lifespan. What this reflects is the fact that effective treatment for HIV (antiretroviral therapy, ART) has become easier and less toxic since it first became available in the mid-1990s.

As a result of these medical advances, the population of patients living with HIV is graying. In the western world (including the US) nearly one third of all HIV-infected patients are over 50 years of age. So, whereas previously the challenge for HIV-infected patients was to survive initial AIDS illnesses and prevent AIDS-related infections and cancers, they now face the same challenges as the rest of the population as it gets older. Increasingly the major causes of sickness and death in older HIV-positive patients are the same as other patient groups – heart disease, cancer, kidney disease and age-associated neurological decline.

The first thing is to realize that we still need more research – especially to determine if there is a need for a different approach to diagnose and prevent these chronic illnesses in HIV-infected patients.

Interestingly, there are quite a number of epidemiologic studies that suggest that these illnesses may be more common among HIV-infected patients and, they may occur earlier in life than one might see in uninfected patients. This has given rise in some circles to the concept that in some way HIV may accelerate aging. Personally, I do not subscribe to the view that the biologic process of aging is in any way accelerated by HIV infection. For one, it is difficult to generate a unifying hypothesis that explains all the clinical data. Moreover, many of the studies cited to justify something very different for HIV are poorly controlled, especially for factors that might also predispose

continued

Above image (*P. Falciparum*): CDC/Dr. Mae Melvin (PHIL #2704), 1973. == Licensin). Masthead image: Ute Frevert; false color by Margaret Shear; Copyright: © 2005 Frevert et al.

Aging with HIV continued



Raymond M. Johnson, M.D.

I left Washington University for an Assistant Professor position at Indiana University in July of 2001. During my time as a fellow, my research co-mentor Eric Brown moved to UCSF, and my second mentor, Fred Lindberg, left academia for Cheetah Mail. Fortunately, Dr. Brown recruited me to co-write a Chapter in Mandel and helped me land a Howard Hughes Fellowship before he departed. In retrospect, I cherish my ID clinical training with some great physicians: Gerald Medoff, Russ Little, Bill Powderly, among others. I get together regularly with my ID fellow compatriots, Rich Groger and Kaili Fan. At Wash U I learned how to practice ID proactively rather than reactively. I believe this distinction and art are being lost in the “evidence-based medicine” world that permeates academia. While the turbulence I experienced as an ID fellow was not helpful in the short term, it probably helped me subsequently navigate difficult situations.

I am currently an Associate Professor, Department of Medicine, Infectious Diseases at Indiana University School of Medicine. I am an active Chlamydia basic and translational researcher doing patient care and animal model research in approximately equal portions. I’m of an age where one considers changes before making changes is no longer an option. Along those lines I am packing up and moving to Yale University to join the Section of Infectious

continued next column

to chronic illness. Nevertheless, from a public health perspective, understanding the factors that might lead to increased rates of chronic illness are important, in order to develop strategies that might prevent them.

So why might HIV-infected patients get more chronic diseases of aging? First of all, we know that many of these diseases – cardiovascular disease and cancer in particular – are diseases of lifestyle. Lifestyle factors that influence chronic disease are more common in HIV infected patients. In most studies, they have twice the rate of cigarette smoking, have more mental illness, and are more likely to have used drugs at some point in their life. Certain viral infections, notably human papilloma virus (HPV), are more common in HIV-infected patients, and are increasingly implicated in a number of cancers. Drugs used to treat HIV may contribute to high blood lipids, diabetes, osteoporosis, and kidney diseases.

There may, too, be a contribution from HIV infection itself. One of the hallmarks of chronic HIV infection is persistent chronic inflammation. Indeed there is some evidence that even with effective control of the virus by ART (where there is no evidence of virus in the blood) there may be persistent inflammation. Increasingly we are realizing that inflammation may be an important contributor to chronic diseases – implicated especially in the development of atherosclerosis (which can lead to heart disease and stroke) and kidney disease.

What does this mean for the person living with HIV infection? The first thing is to realize that we still need more research – especially to determine if there is a need for a different approach to diagnose and prevent these chronic illnesses in HIV-infected patients. Equally, we need to ensure that we pay the same (if not greater) attention to the risk of chronic illness in these older HIV-positive patients as we do in the general population. Patients need regular assessment of their cardiovascular risk, with testing for cholesterol and diabetes. They should have cancer screening as is recommended for the general population – colonoscopy, mammography, etc. – as well as regular screening for HPV-related cancers of the cervix and anus. Above all, they should be encouraged, counseled, and supported in their efforts to stop smoking, as this is singly the most important preventive effort we can offer.

Dr. Powderly is the Director of the Institute for Public Health and the J. William Campbell Professor of Medicine. He is also the Co-director of the Division of Infectious Diseases.



Raymond Johnson, MD *continued from left column*

Diseases. The change in venue offers enhanced opportunities to collaborate and surf the technological wave. Hopefully my lab will be at or near ground zero when the Chlamydia vaccines start to rollout.

The year before I became an ID fellow I married Sarah Davidson, a Wash U medical resident. We have 3 children who cannot legitimately be called children any longer. Our oldest, Arielle, will finish college next year. Aaron is going off to college this fall, and Talon is pondering the turbulence that he will experience moving to Connecticut as a junior in high school. Rarely have there been dull moments in the past 14 years.

My research:
Indiana University Hospital is a teaching hospital in Indianapolis, Indiana, USA, affiliated with the Indiana University School of Medicine and Indiana University Health.

awards & announcements

| RECENT AWARDS | | |
|-----------------------------|---|---|
| PRINCIPAL INVESTIGATOR(S) | AWARD | PROJECT TITLE |
| Michael S. Diamond, MD, PhD | NIH RO1 grant with James E. Crowe, Jr., M.D. | Structural and functional basis of ultra-potent Chikungunya (CHKV) virus neutralization by human monoclonal antibodies (mAbs) |
| Michael S. Diamond, MD, PhD | Defense Threat Reduction Agency/ Department of Defense (DTRA/DOD) | A novel inactivated trivalent vaccine to prevent infection by Venezuelan, Eastern, and Western equine encephalitis viruses |
| Robyn S. Klein, MD, PhD | Direct Threat Reduction Agency | Targeting the blood-brain barrier to limit infection with encephalitic alphaviruses \$4.2M |

special recognition

James M. Fleckenstein, Ph.D., Associate Professor of Medicine, Division of Infectious Diseases, has been appointed a member of the Vaccines Against Microbial Diseases Study Section, Center for Scientific Review of the National Institutes of Health. Study sections review NIH grant applications, make recommendations to the appropriate national advisory councils and survey the status of research in their respective fields. Members are selected on the basis of their demonstrated competence and achievement in their scientific discipline as evidenced by the quality of research accomplishments, scientific publications and other achievements and honors.

congratulations...



Nigar Kirmani, M.D., was selected by the Class of 2016 as Lecturer of the Year.

(From left) Steven C. Cheng, MD, Erika C. Crouch, PhD, MD, and Nigar Kirmani, MD, listen as teaching award winners are announced. Each of the three was honored at the ceremony.

Steven Lawrence, M.D., received the Class of 2016 Distinguished Service Teaching Award.

Andy Mohapatra, president of the third-year class at the School of Medicine, (far left) prepares to present a teaching award. Among those honored were (from left of Mohapatra) Richard D. Brasington Jr., MD, Alan I. Glass, MD, Scot G. Hickman, MD, Steven J. Lawrence, MD, and Deborah C. Rubin, MD.



David B. Clifford, M.D., was selected by medical students of Washington University as the school's 2015 nominee for the Association of American Medical Colleges (AAMC) annual Humanism in Medicine Award (HIM). Humanism nominations recognize the important qualities of community service, positive mentoring skills, compassion and sensitivity, ethics, and collaboration, which are vital and diverse qualities in a physician.

David Clifford, M.D., accepts an award for humanism in medicine from third-year medical student Agnes Dardas.



Makhawadee (Joy) Pongruangporn, M.D., Instructor of Medicine/Bone Marrow Transplantation Unit, and her husband, Jonathan, celebrate the birth of their son, Josiah Sagum, on April 15, 2015. Josiah weighed in at 7 lbs 8 oz and joins his big brother Joshua Sagum. Joy completed her infectious diseases fellowship here in 2012.



welcome new faculty



Jessica Grubb, MD
Assistant Professor of Medicine

Jessica R. Grubb, M.D., Assistant Professor of Medicine

I am very pleased to rejoin the Infectious Diseases faculty here at Washington University School of Medicine. I grew up in Maryland and then stayed in Baltimore for college at The Johns Hopkins University. I attended medical school at the University of Maryland, then moved to St. Louis for internship and residency at Barnes- Jewish Hospital. I returned to Maryland when my husband started his fellowship at the NIH.

I started working at the NIH in the HIV Research Clinic and enjoyed it so much that I stayed on to complete my Infectious Diseases fellowship at NIAID/NIH. While in fellowship I worked with Henry Masur, MD to investigate metabolic effects of antiretrovirals and statins.

I started my career at Washington University School of Medicine Infectious Diseases Division working in the clinic and with the AIDS Clinical Trials Unit from 2005-2012. While away from Washington University, I worked as an attending for the Internal Medicine Residency Clinic at Mercy Hospital, medical consultant for Places for People as well as medical director for Anthem.

I am very excited to return to Washington University as the HIV clinic medical director. I look forward to working to continue the excellent care of our patients and education of fellows and residents.

Haina Shin, PhD, Assistant Professor of Medicine

I am excited to be a new faculty member in the Infectious Diseases Division within the Department of Medicine. My laboratory will be working on immunity against sexually transmitted infections with a focus on herpes simplex virus (HSV). As my research interests include understanding the antiviral defense mechanisms of the peripheral nervous system, I am pleased to also be a part of the Center of Neuroimmunology and Neuroinfectious Diseases.

I received my BA in chemistry at Northwestern University in Evanston, IL and then obtained my PhD in immunology at the University of Pennsylvania in Philadelphia, PA. Under the mentorship of Dr. E. John Wherry, I examined how chronic viral infections could alter memory differentiation of CD8 T cells using a model of LCMV infection. I continued my studies on CD8 T cells during my postdoctoral training at Yale University with Dr. Akiko Iwasaki. Here, I took advantage of the unique properties of tissue-resident memory CD8 T cells to design a prophylactic vaccine strategy against genital herpes. This strategy, called "prime and pull" was shown to provide neuroprotection against HSV infection.

Having joined Washington University in February of 2015, I intend to continue my studies in understanding the features of a protective immune response against genital herpes, which is a sexually transmitted infection with global prevalence. Currently, there is no cure or vaccine available for this disease.

Using both an in vivo mouse model and an in vitro neuron culture system, the laboratory will examine how tissue-resident memory CD8 T cells function in the context of a local viral infection, and how they support antiviral defense of the peripheral nervous system against neuroinvasive viruses such as HSV. Greater understanding of the factors that constitute a protective immune response against HSV will aid in the design of efficacious vaccines against genital herpes and other viral sexually transmitted infections.



Haina Shin, PhD
Assistant Professor of Medicine

hepatitis c does not cause mental impairment

Advances in treatment for human immunodeficiency virus (HIV) have made it possible for people with HIV to survive much longer. As they age, however, many experience impaired thinking, memory loss, mood swings and other evidence of impaired mental function.

To stop these changes, scientists have to learn what is causing them. One possibility researchers are considering is that long-term infections with other pathogens, common in HIV-positive patients, are affecting the brain. But a new study has eliminated one of their prime suspects: the hepatitis C virus, which infects about one in every three HIV-positive patients in the United States.

The research, conducted by a team that includes scientists at Washington University School of Medicine in St. Louis, appeared December 10, 2015 in *Neurology*.

“Hepatitis C infection has serious long-term side effects, such as damage to the liver, but our research indicates that it does not affect the brain,” said lead author David Clifford, MD, of Washington University.

The research was conducted as part of the CNS HIV Anti-retroviral Therapy Effects (CHARTER) study, a multicenter collaborative that is examining the long-term neurological effects of HIV infection.

Hepatitis C most commonly infects illicit-drug users who share needles used to inject the drugs. Drug abuse can harm the brain, making it difficult to determine whether hepatitis C or problems caused by drug use contribute to brain impairment in patients with both HIV and hepatitis C.

To answer this question, Clifford and his colleagues studied 1,582 HIV patients, 408 of whom were also infected with hepatitis C. Each patient received a detailed neuropsychological exam devised by Clifford and other CHARTER researchers to detect signs of HIV-associated mental deficits.

The exam takes two to 2 1/2 hours, and includes written examinations taken by the patient and physical exams given by medical professionals. Patients are tested for their ability to express themselves, to make decisions, to learn and retain new information using multiple types of memory, and to move the body and control muscles.

“In all, we looked at seven domains of mental function,” said Clifford, who is the Melba and Forest Seay Professor of Clinical Neuropharmacology in Neurology. “We studied their overall performance and looked at each domain individually and found no evidence that the group with hepatitis C performed worse.”

According to Clifford, this was particularly impressive because the participants in the group with hepatitis C were older, had less education and had lower scores on tests of reading, comprehension, spelling and math.

With hepatitis C eliminated, Clifford and his colleagues are turning their attention to the immune responses triggered by HIV in the brain and the bowel during the initial stages of infection. He and others believe these early responses, which include bursts of inflammation, lead to chronic inflammation that adversely affects the brain.

“If a hepatitis C infection gets to the point where it damages liver function, the resulting inflammation might well contribute to mental impairment,” Clifford said. “Beyond that, though, it doesn’t seem to be an active collaborator in the harm HIV does to the brain.”



*David B. Clifford, MD
Melba and Forest Seay Professor of Clinical
Neuropharmacology in Neurology*

*Modified from the original publication in the Washington University Record, December 11, 2014
author: Michael C. Purdy*

Thank You to Our Supporters

Gerald Medoff, M.D. Lectureship Infectious Diseases

Dr. Hilary M. Babcock
Dr. Gregory Storch & Dr. Lisa Ring

Dr. Gerald Medoff Lectureship Infectious Diseases Fund

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.

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. Please consider an unrestricted gift to the Division that will be used to honor Dr. Medoff with an annual lectureship.

*Gerald Medoff, M.D.
Emeritus Professor of Medicine*



The Infectious Diseases Division has established a prize in Tom Steinberg's honor that will be awarded annually. Contributions can be made to this Memorial Award by donating to the

Thomas H. Steinberg Memorial Trainee Award

Thomas H. Steinberg, M.D.

In Memoriam

Your Donations Are Greatly Appreciated!

To make a gift to the Infectious Diseases Division, please contact Dan Korte, Division Administrator, Infectious Diseases Division, or mail your contribution to Dan, designating where you would like us to direct your gift.

Make checks payable to :

Washington University School of Medicine

Infectious Diseases Division,

Campus Box 8051, 660 S. Euclid Ave., St. Louis, MO 63110

phone: 314-454-8354

email: dkorte@dom.wustl.edu

Online gifts can be made through <http://id.wustl.edu/giving.html>. Please be sure to designate Infectious Diseases Division.

HIV and HCV: Optimal Management in the Era of New Regimens

Engineer's Club of St. Louis
4359 Lindell Blvd.
St. Louis, Missouri

TUESDAY
MAY 12, 2015

5:30 pm Registration Reception (meet & greet)
6:30 pm Dinner Meeting Commences



sponsored by

The AIDS Clinical Trials Unit
Infectious Diseases Division
Department of Internal
Medicine

St. Louis STD/HIV
Prevention Training Center

We are grateful for
the support of



This activity is partially
supported by grants from
**AbbVie, Inc. and
Gilead Sciences, Inc.**

COURSE DESCRIPTION

This course is designed to provide frontline providers in two distinct but overlapping fields—HIV and hepatitis C—with an interactive, engaging, and practical learning experience to enhance their knowledge, competence, and ability to better manage HIV and HCV-monoinfected and/or coinfecting patients upon return to their practice setting.

ACCREDITATION

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Missouri State Medical Association (MSMA) through the joint providership of the Infectious Disease Division of Washington University School of Medicine and the St. Louis STD/HIV Prevention Training Center. The St. Louis STD/HIV Prevention Training Center is accredited by the MSMA to provide continuing medical education for physicians.

DESIGNATION

The St. Louis STD/HIV Prevention Training Center is accredited by the MSMA to provide continuing medical education for physicians. The St. Louis STD/HIV Prevention Training Center designates this educational activity for 3 Category 1 credits toward the AMA Physician's Recognition Award.

\$65.00 Registration (The registration fee includes a meal.)

ONLINE Secure online registration available at www.wustl.edu/etransact, scroll down to and click on:

HIV and HCV: Optimal Management in the ERA of New Regimens

6:30 pm Welcome and Opening Remarks

CHAIR: Rachel Presti, M.D., PhD
Assistant Professor of Medicine
Washington University School of Medicine

6:40 pm
*Therapeutic Advances for the Management of
Hepatitis C and Hepatitis C/HIV Co-infection*

Kenneth E. Sherman, M.D., PhD
Gould Professor of Medicine
Director, Division of Digestive Diseases
University of Cincinnati College of Medicine
Cincinnati OH

7:40
Hepatitis C: In the Trenches

Jeffrey S. Crippin, M.D.
Professor of Medicine,
Division of Gastroenterology
Medical Director, Liver Transplantation
Co-Director, GI Center, Clinical Operations
Washington University School of Medicine

8:30 pm
Break

8:45
*Strategies in HIV Management: Treating a chronic
condition in an aging population*

Rachel Presti, M.D., PhD
Assistant Professor of Medicine
Division of Infectious Diseases
Washington University School of Medicine

9:15
Pre-exposure Prophylaxis for HIV (PrEP)

Rupa Patel, M.D., MPH, DTM&H
Instructor of Medicine
Director, PrEP Program WUSTL Clinic
Division of Infectious Diseases
Washington University School of Medicine

9:45 Closing/Adjourn

EDUCATIONAL OBJECTIVES

At the conclusion of this symposium, attendees should be able to:

- integrate the results of recent clinical studies of approved HCV therapies into patient management strategies for patients with HCV
- incorporate recommended treatment strategies in the management of HCV/HIV co-infected patients
- effectively prevent or manage complex drug interactions that can occur between DAAs and antiretroviral medications and co-morbidities
- identify targeted HCV-infected populations and potential obstacles to starting antiviral therapy
- effectively manage regimen simplification and co-morbidities in aging population
- to review the evidence and the current guidelines for pre-exposure prophylaxis for HIV (PrEP)